2019 Spring Current Concepts in Dermatology

JW Marriott Orlando Grande Lakes
Orlando, FL
April 10 - 13, 2019

John Minni, D.O., FAOCD
Activity Chair

Acknowledgement of Commercial Support

2019 American Osteopathic College of Dermatology Corporate Members

Diamond Level
Pfizer

Gold Level
AbbVie • Ortho Dermatologics

Bronze Level
Almirall • Galderma Laboratories

Pearl Level
Dermpath Diagnostics • Novartis • Verrica Pharmaceuticals

Product Theater

Almirall • Celgene • Novartis • Regeneron Sanofi Genzyme

2019 American Osteopathic College of Dermatology Spring Meeting Exhibitors

Abbvie
Aclaris Therapeutics
Acuderm
Advanced Dermatology and Cosmetic Surgery
Almirall
Aurora
Biofrontera
Castle Biosciences
Celgene
Dermpath Diagnostics
Dermtech
Galderma
Genentech
Heartland Payment Systems
Janssen Biotech
Kroger Specialty Pharmacy
Leo Pharma
Lilly
Novartis
Ortho-Dermatologics
Pfizer
ProPath
PruGen
Ra Medical
Regeneron & Sanofi Genzyme
Sagis Dermatology
The Shade Project
SkinPathSolutions
StrataDx
Strata Skin Solutions
Sun Pharma
Syneron-Candela
Tiemann Surgical
Verrica Pharmaceuticals
Xstrahl Limited
Zero Skin Gravity

Continuing Medical Education Statements

This activity will change your practice and improve patient outcomes!

Content included in AOCD's Educational conferences will not include individually identifiable health information, in accordance with the Health Insurance Portability and Accountability Act (HIPAA), as amended.

The American Osteopathic College of Dermatology (AOCD) is accredited by the Accreditation Council for Continuing Medical Education (ACCME) to provide continuing medical education for physicians.

The American Osteopathic College of Dermatology AOCD designates this live activity for a maximum of 22 *AMA PRA Category 1 Credit(s)*™. Physicians should claim only the credit commensurate with the extent of their participation in the activity.

The American Osteopathic College of Dermatology is accredited by the American Osteopathic Association to provide osteopathic continuing medical education for physicians.

The American Osteopathic College of Dermatology designates this program for a maximum of 22 AOA Category 1-A credits and will report CME and specialty credits commensurate with the extent of the physician's participation in this activity.

This meeting will provide a diversified CME presentation focusing on the art and science of dermatology. Information will be presented through lectures and scientific paper presentations. The activity actively encourages members to develop enduring materials as an evolving tool for continuing education. The College is committed to exploring the development of its capacity to expand resources in other educational techniques, including Web-based activities and point-of-care technologies.

American Osteopathic College of Dermatology
Mission Statement &
Continuing Medical Education Needs Assessment

The Continuing Medical Education Program of the American Osteopathic College of Dermatology will support, enhance and advance new models of academic excellence and community health care.

The mission of the American Osteopathic College of Dermatology is to create innovative education, support, and opportunities in dermatology that promote excellence in patient care and community health through advocacy, consciousness, inclusivity, and osteopathy.

Purpose
The purpose of the CME program is to provide AOA-accredited continuing medical education activities to inform the dermatologist physician. The program will provide a mechanism by which its constituents can improve competency, maintain board certification and cultivate lifelong learning. CME will provide physicians with the opportunity to further develop their knowledge through individual and group learning activities. The Continuing Medical Education Committee will monitor the quality of all programs conducted by the AOCD.

Accreditation:
Content included in AOCD's Educational conferences will not include individually identifiable health information, in accordance with the Health Insurance Portability and Accountability Act (HIPAA), as amended.

The American Osteopathic College of Dermatology (AOCD) is accredited by the Accreditation Council for Continuing Medical Education (ACCME) to provide continuing medical education for physicians.

The American Osteopathic College of Dermatology AOCD designates this live activity for a maximum of 22 *AMA PRA Category 1 Credit(s)™*. Physicians should claim only the credit commensurate with the extent of their participation in the activity.

The American Osteopathic College of Dermatology is accredited by the American Osteopathic Association to provide osteopathic continuing medical education for physicians.

The American Osteopathic College of Dermatology designates this program for a maximum of 22 AOA Category 1-A credits and will report CME and specialty credits commensurate with the extent of the physician's participation in this activity.

This meeting will provide a diversified CME presentation focusing on the art and science of dermatology. Information will be presented through lectures and scientific paper presentations. The activity actively encourages members to develop enduring materials as an evolving tool for continuing education. The College is committed to exploring the development of its capacity to expand resources in other educational techniques, including Web-based activities and point-of-care technologies.

Commercial Support Disclosure
AOCD CME will identify relevant financial relationships prior to awarding AOA Category 1A and/or *AMA PRA Category 1 Credit™* for CME activities. All persons in a position to influence or control CME content (course directors, program planning committee members, speakers, authors and staff) will complete a standardized disclosure form. Information about funding will be requested to identify CME activities at higher risk for commercial bias.

All AOCD CME activities will be evaluated by learners and possibly peer reviewers to determine if the content was free of commercial bias. All those identified as having influence and/or control of CME content perceived as either manifesting conflicts of interest or being biased may be disqualified from consideration as resources (planning group member, authors, faculty, etc) in subsequent CME activities.

Learners will be provided with information on identified COI from any of the above categories of persons that affect the content of CME, and that information will be positioned in course materials such that it is read by learners prior to the execution of the CME activity. Speakers for the AOCD will be required to provide disclosure information to

meeting attendees during their introduction of their topic. Additionally, disclosure statements are provided in the program schedule given to each meeting attendee and is available online at www.aocd.org.

In accordance with the ACCME's Standards for Commercial Support of Continuing Medical Education, the Policy on Collection of Financial Relationships and Resolution of Conflicts of Interest (COI) exists to provide guidance for staff, instructors, planners, reviewers and managers of CME activities sponsored by **The American Osteopathic College of Dermatology, (AOCD**). This policy addresses the underlying philosophy of disclosure to learners, mechanisms to collect disclosure information and the parties from whom financial disclosure shall be collected, the mechanisms to resolve COI, and requirements to make disclosure to learners prior to the start of an activity.

Professional Practice Gap Statement:
Physicians need to understand, update and manage changes in dermatology in order to provide optimal patient care. Dermatologists in private practice may not have immediate access to new updates in therapies and treatments. This activity will help to close gaps in physician's areas of Mohs micrographic surgery, skin cancer, psoriasis updates, cosmetic dermatology updates, allergies, practice management and pediatric dermatology.

Expected Outcomes:
As a result of participation in the AOCD/CME activity, practicing clinicians will improve competency; maintain specialty board certification; and cultivate lifelong learning. It is expected that attendees of this meeting will improve their diagnostic competence regarding a wide range of dermatologic conditions. In addition to increased diagnostic competence, enhanced concepts of therapy and treatment in dermatologic care will be gained for implementation in everyday practice.

- Attendees will learn about tailor-made psoriasis treatment in the era of biologics and dermal fillers histopathology reactions.
- Attendees will be able to identify comorbidities, understand the immunological relationships, consideration to objectify these associated issues in clinical practice to buffer our outcomes.
- Attendees will understand the gender differences, modes of spread, and anatomic distribution of metastatic carcinoma; understand the clinical and microscopic features of various types; and understand prognosis and palliative treatment options.
- Attendees will understand the manifestations of cutaneous venous hypertension, recognize the patterns of venous pathology, and become familiar with primary/secondary venous ulcers and treatment.
- Attendees will be able to recognize the clinical features that allow diagnosis of neutrophilic dermatoses, determine the best strategies for evaluating patients, understand the therapeutic ladder of treatment.
- Attendees will learn about new treatment options for common pediatric dermatology conditions, diagnosis of various pediatric dermatology conditions, and management of several common pediatric dermatology conditions.
- Attendees will review several examples of VIP customer service and learn several practical ways to improve customer service and patient satisfaction.
- Attendees will review the core principles of osteopathic dermatology, dermatologic conditions, common treatments, and an osteopathic approach to dermatologic conditions.
- Attendees will be able to identify ideal patients for anti-IL-23 therapy, understand the mechanism of action of anti-IL-23 drugs, and recognize the risks and benefits of anti-IL-23 therapy.
- Attendees will review Mohs Micrographic Surgery, the evolution of Mohs techniques, and the indications of Mohs surgery.
- Attendees will review dermatopathology features of cutaneous malignant tumors, early detection, prognostic issues and treatment options of cutaneous malignant tumors.
- Attendees will review newer therapies that are available or in development for common dermatologic disorders, MOAs of individual therapies and how correlation of MOAs with specific disease manifestations can optimize therapeutic response, and potential adverse effects of specific therapies and devise monitoring approaches including both clinical and laboratory assessments and testing.
- Attendees will better understand when free tissue transfer is appropriate for a cancer defect, better understand the technical aspects, considerations and philosophy behind microvascular surgery, and better understand the use of technology in facilitating and optimizing complex reconstructions.
- Attendees will review the most advanced surgical techniques in cosmetic facial surgery, complicated Mohs reconstruction, and charity work in impoverished countries.
- Attendees will review the safety of biologics for psoriasis, relative efficacy of different biologics for psoriasis, and patient adherence to self-administered biological treatment.
- Attendees will be able to differentiate among types of allergy testing for food and drug allergies, understand limitations of tests to assess drug-induced skin rash, and recognize various patterns of skin reactions caused by drug allergies.
- Attendees will review the historic precedent for radiation therapy in skin cancer treatment, understand how to select patients for radiation therapy, and review several different radiation technologies available for delivery of treatments in a dermatology office setting.

The overall result being improved physician/provider performance and increased positive patient outcomes.

These objectives will be achieved in a setting which is evidence-based, culturally sensitive and free of commercial bias. The AOCD is committed to the practice of continuing program improvement. The AOCD will actively explore new educational technologies, develop collaborative relationships with other CME providers and seek to build the capacity to evaluate competency-based outcomes among the clinicians we serve. CME will provide physicians with the opportunity to further develop their knowledge through individual and group learning activities.

Needs Assessments:
The activity was developed based upon the needs of physicians within the association identified through:

- An evaluation/survey provided to meeting participants at both our annual and midyear meeting
- Consensus of faculty members within a department or service area
- New advances in dermatologic treatment identified in major publications or research studies
- New methods of diagnosis or treatment
- Availability of new medication(s) or indication(s)
- Development of new technology
- Acquisition of new facilities or equipment
- Input from experts regarding advances in medical knowledge
- Legislative, regulatory, or organizational changes effecting patient care
- Epidemiological data
- Quality assurance/audit data
- Statistics infection control data
- Surgical procedures statistics
- Journal articles/literature citations

The AOCD Continuing Medical Education Committee works to assure the inclusion of appropriate Osteopathic content in the Continuing Medical Education activities presented by AOCD, and to assure that the Continuing Medical Education Programs of the AOCD will achieve the stated objectives of each meeting in a setting which is evidence-based, culturally sensitive and free of commercial bias.

The Continuing Medical Education Committee of the AOCD will monitor the quality of all activities conducted.

Content Areas:
The AOCD approves the CME activities based upon needs assessment data to ensure that all offerings present current, up to date and cutting edge information. Specific areas of emphasis include, new advances in dermatologic treatment, new methods of diagnosis or treatment, availability of new medication(s) or indication(s), development of new technology, advances in medical knowledge and legislative, regulatory, or organizational changes effecting patient care. The Osteopathic Core Competencies of Osteopathic Philosophy, Principles, Practice and Manipulative Medicine, Medical Knowledge, Patient Care, Interpersonal and Communication Skills, Professionalism, Practice-Based Learning and Improvement and System-Based Practice will also be incorporated into all CME activities.

Target Audience:
The primary target audience of the CME activities conducted by the AOCD are the dermatologist physician members. The College also serves community physicians, volunteer clinical faculty, academic clinicians and students affiliated with the AOCD. The activity will also actively seek to broaden its audience through developing affiliations with CME providers on the national level.

Faculty Disclosure:
As a sponsor accredited by the AOA, it is the policy of the AOCD to require the disclosure of anyone who is in a position to control the content of an educational activity. All relevant financial relationships with any commercial interests and/or manufacturers must be disclosed.

AOCD Anti-Trust Statement
Members participating in meetings, events or activities conducted or sponsored by the American Osteopathic College of Dermatology or the Foundation for Osteopathic Dermatology, have an obligation to review and follow the AOCD's Antitrust Compliance Policy. They should particularly refrain from making statements or distributing materials at AOCD, Foundation meetings or events that would violate the policy, such as suggesting minimum fees for particular services, urging AOCD members to boycott third party payers based on reimbursement levels or other terms of contracting with such entities, or recommending that AOCD members avoid competing with each other in certain geographic areas or markets or across specialties.

Disclosure of Commercial Support of CME:
As you undoubtedly know from the national media, there has been much discussion concerning the relationships between CME sponsors, faculty and commercial companies providing support of CME.

Both the American Osteopathic Association and the Committee on Continuing Medical Education have adopted regulations for ethical actions in this area which the American Osteopathic College of Dermatology endorse and have adopted for all our educational activities.

Please be assured that having an affiliation with a company does not imply in any way that something is wrong or improper; however, we want to inform attendees that such a relationship exists.

Should you have any questions regarding the facilities, handouts, activity content, or concerns about CME compliance with the AOA "Uniform Guidelines," feel free to contact the AOCD representative:

Marsha A. Wise, BS
Executive Director
P.O. Box 7525
Kirksville, MO 63501
660-665-2184
800-449-2623

Unresolved issues regarding compliance with the AOA "Uniform Guidelines" can be brought to the attention of the AOA Division of CME by calling: 800-621-1773, or by writing:

AOA CME Office
142 East Ontario Street
Chicago, IL 60611

AOCD Board of Trustees Disclosures

Daniel Ladd, DO, FAOCD
President
Board Certified in Dermatology by American Osteopathic Board of Dermatology
Disclosures: Physician Training: Sensus Healthcare; Medical Officer/Minority Shareholder: SkinCure Oncology; Director, Officer or Employee of: Shade Project; Spouse is Director, Officer or Employee of: Shade Project

John Minni, DO, FAOCD
President-Elect
Board Certified in Dermatology by American Osteopathic Board of Dermatology
Disclosures: Speaker: Abbvie, Janssen, Promius, Leo, Novartis, Galderma

Reagan Anderson, DO, FAOCD
First Vice-President
Board Certified in Dermatology by American Osteopathic Board of Dermatology
Disclosures: Director, Officer or Employee of: RVUCOM; Principal Investigator: Novartis, Abbvie

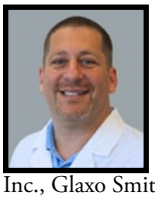
David Cleaver, DO, FAOCD
Second Vice-President
Board Certified in Dermatology by American Osteopathic Board of Dermatology
Disclosures: Director, Officer or Employee of: KCOM (Assistant Professor); Speaker: Abbvie; Sibling is speaker for: Abbvie

Amy Spizuoco, DO, FAOCD
Third Vice-President
Board Certified in Dermatology by American Osteopathic Board of Dermatology
Disclosures: Speaker: Pfizer, Celgene

Steven Grekin, DO, FAOCD
Secretary-Treasurer
Board Certified in Dermatology by American Osteopathic Board of Dermatology
Disclosures: Research Sponsors: Allergan, Valeant, Coherus, Mimetica, Galderma, Promise, J&J Psolar, HedgePath; Director, Officer or Employee of: Advanced Dermatology

Danica Alexander, DO, FAOCD
Trustee
Board Certified in Dermatology by American Osteopathic Board of Dermatology
Disclosures: No relevant financial relationships to disclose

Steven Brooks, DO, FAOCD
Trustee
Board Certified in Dermatology by American Osteopathic Board of Dermatology
Disclosures: Speaker: Pfizer



Jonathan Crane, DO, FAOCD
Trustee
Board Certified in Dermatology by American Osteopathic Board of Dermatology
Disclosures: Research, Consultant, or Speaker's Bureau for: 3M, Allergan, Candella Laser Company, Fujisawa, Genetech Inc., Glaxo Smith Klein, Novartis

Jerome Obed, DO, FAOCD
Trustee
Board Certified in Dermatology by American Osteopathic Board of Dermatology
Disclosures: No relevant financial relationships to disclose

Peter Saitta, DO, FAOCD
Trustee
Board Certified in Dermatology by American Osteopathic Board of Dermatology
Disclosures: No relevant financial relationships to disclose

Michael Whitworth, DO, FAOCD
Trustee
Board Certified in Dermatology by American Osteopathic Board of Dermatology
Disclosures: Director, Officer or Employee of: Wayne County Osteopathic Medical Association (Board Member 2012-2013)

Karthik Krishnamurthy, DO, FAOCD
Immediate Past President
Board Certified in Dermatology by American Osteopathic Board of Dermatology
Disclosures: Advisory Board: Aclaris; Speaker Bureau: Abbvie

AOCD CME Committee Disclosures

Nathan Cleaver, DO, FAOCD
CME Committee
Board Certified in Dermatology by American Osteopathic Board of Dermatology
Disclosures: Speaker: Castle Biosciences

Laura DeStefano, DO, FAOCD
CME Committee
Board Certified in Dermatology by American Osteopathic Board of Dermatology
Disclosures: No relevant financial relationships to disclose

Dwayne Montie, DO, FAOCD
CME Committee
Board Certified in Dermatology by American Osteopathic Board of Dermatology
Disclosures: No relevant financial relationships to disclose

Stephen Verral, DO, FAOCD
CME Committee
Board Certified in Dermatology by American Osteopathic Board of Dermatology
Disclosures: No relevant financial relationships to disclose

Sadaf Waqar, DO, FAOCD
CME Committee
Board Certified in Dermatology by American Osteopathic Board of Dermatology
Disclosures: No relevant financial relationships to disclose

AOCD Staff Disclosures

Marsha Wise
Executive Director
Disclosures: No relevant financial relationships to disclose

Kristin Ayer
Administrative Assistant
Disclosures: No relevant financial relationships to disclose

John Grogan
Resident Coordinator
Disclosures: No relevant financial relationships to disclose

Shelley Wood
Grants Coordinator
Disclosures: No relevant financial relationships to disclose

Meeting Faculty & Needs Assessments

John Minni, DO, FAOCD
Program Chair
Dr. John Minni is board-certified in dermatology. He graduated, with honors, from Nova Southeastern College of Osteopathic Medicine in Fort Lauderdale, FL. He completed his internship at Union Hospital/St. Barnabas Healthcare System in New Jersey. He then returned to Florida and completed both family medicine and dermatology residencies at Columbia Hospital and the VA Medical Center in West Palm Beach, FL. Dr. Minni also served as chief resident in dermatology. Between residencies, Dr. Minni practiced family medicine at the Palm Beach County Health Department, while training residents, interns and medical students. Prior to medical school, Dr. Minni attended the University of Notre Dame as a Notre Dame Scholar and graduated with honors with a B.S. in biology.

Disclosures: ***Speaker for:*** Abbvie, Janssen, Promius, Leo, Novartis, Galderma

James Azzi, MD
James Azzi, MD, is a board-certified head & neck and micro-vascular surgeon with advanced fellowship training. His scope of practice is broad and includes head and neck cancer surgery, free tissue transfer, facial paralysis and reanimation, facial trauma, and sinus and skull base surgery. He holds an M.D. from Brown University. He completed his residency training at The New York Eye and Ear Infirmary of Mount Sinai in Manhattan and his fellowship training at Oregon Health and Sciences University in Portland. He is a native Floridian.

Dr. Azzi is an accomplished writer and researcher having published numerous chapters in textbooks and articles in medical and surgical journals ranging from *Oral Oncology* to *Aesthetic Plastic Surgery*.

Dr. Azzi follows the core philosophy of the Palm Beach Center for Facial Plastic & Laser Surgery. He approaches each patient individually, takes time to listen and understand their goals, and together formulate a comprehensive treatment plan. These problems can be complex and require a multidisciplinary approach where the expertise of many physicians from different perspectives can be heard and considered during a conference.

Introduction to Microvascular Head and Neck Reconstruction

Objectives:
1. Better understand when free tissue transfer is appropriate for a cancer defect
2. Better understand the technical aspects, considerations and philosophy behind microvascular surgery
3. Better appreciate the use of technology in facilitating and optimizing complex reconstructions

Needs:
1. Development of new technology

References:

1. Eugene K. Kim, MD, Maristella Evangelista MD, Gregory R.D. Evans, MD. "Use of Free Tissue Transfers in Head and Neck Reconstruction". *The Journal of Craniofacial Surgery*, Nov 2008;Vol. 19(6):1577-1582.
2. Keith A. Hurvitz, MD, Mark Kobayashi, MD, Gregory R.D. Evans, MD. "Current Options in Head and Neck Reconstruction". *Plastic and Reconstruction Surgery*, October 2006;Vol, 118(5):127-130.

Core Competencies: 2, 3, 6, 7

Disclosures: None

Jean-Paul Azzi, MD
Jean-Paul Azzi, MD, is a Palm Beach facial plastic and reconstructive surgeon specializing exclusively in cosmetic and reconstructive procedures of the face, nose and neck.

Dr. Azzi completed his residency in head and neck surgery/facial plastic surgery at the world-renowned New York Eye and Ear Infirmary in Manhattan and received his board certification. He then completed

a fellowship in exclusively facial plastic & reconstructive surgery with the past president of the American Academy of Facial Plastic & Reconstructive Surgery, where he learned cutting edge techniques in facelifting, endoscopic, minimally invasive facelifting, endoscopic brow lifting, endoscopic midface lifting, blepharoplasty (eyelid lifting), otoplasty (ear pinning), neck lifting, fat grafting, skin resurfacing, facial reconstruction, hair transplantation and facial injectable treatments.

In addition to his cosmetic private practice, Dr. Azzi also performs charitable reconstructive procedures in underdeveloped countries such as Vietnam, Guatemala, Ecuador and Colombia. These procedures include repairing cleft lips and palates and reconstructing children with microtia (missing ears) using their rib cartilage.

Dr. Azzi is a Hobe Sound, FL native who enjoys spending time with his family and friends. His interests include tennis, golf and boating. His patients love his sense of humor and warm, caring demeanor.

Facial Plastic Surgery

Objectives:
1. Overview of the most advanced surgical techniques in cosmetic facial surgery
2. Complicated Mohs reconstruction
3. Charity work in impoverished countries

Needs:
1. New advances in dermatologic treatment
2. New methods of diagnosis and treatment
3. Development of new technology

References:

1. Rousso, DE, Brys, AK. "Extended Lower Eyelid Skin Muscle Blepharoplasty". *Facial Plastic Surgery* 2011;27(1):067-076.
2. Jacono, AA, Parikh, SS. "The Minimal Access Deep Plane Extended Vertical Facelift". *Aesthetic Surgery Journal* Nov 2011;31(8):874-890.

Core Competencies: 1, 2, 3, 4, 5, 6, 7

Disclosures: None

Edwin Bayo, JD

Ed was born in San Juan, Puerto Rico. After graduating in 1978 with a bachelor's degree in economics (cum laude) from the University of Puerto Rico, he moved to the United States to pursue his legal education. He received his Juris Doctorate from Stetson Law School in 1981.

Ed worked in various capacities for the Florida Office of the Attorney General, including tax litigation, administrative law, cabinet affairs and inspector general. His primary area of practice while in government involved providing advice and representation to regulatory boards under the umbrella of the Department of Health and the Department of Business and Professional Regulation. As Senior Assistant Attorney General in the Administrative Law Section, Ed served as counsel to various professional regulatory boards, including pharmacy, dentistry, osteopathic medicine, chiropractic medicine, veterinary medicine, professional engineers, landscape architecture, clinical social work and harbor pilots. In addition, he handled temporary duties or litigation for several other boards including medicine, psychology, nursing, architecture and accountancy. In 2002, Ed served as the Attorney General Representative to the Pedigree Paper Task Force, created by the Legislature to review and reform Florida's regulation of the prescription drug wholesale industry.

Ed's current practice at Grossman, Furlow and Bayo includes the representation of professional licensees, regulated entities and interested parties before regulatory agencies, Florida Courts and the Division of Administrative Hearings. He concentrates his practice in the areas of administrative and regulatory law with emphasis on the laws and regulations affecting pharmacies, drug manufacturers and drug wholesalers. He is a frequent speaker before local, state and national professional organizations on licensure and regulatory issues. He has published several articles on these topics.

Prescribing Laws and Rules Controlled Substances
This course addresses the mandatory content for Physicians in Florida registered to prescribe controlled substances as allowed by Florida law, effective January 1, 2017.

Objectives:
Upon completing this course and reviewing the resources, participants should be able to:
1. Explain why the issue of prescribing issue is so important and illustrate best practices
2. Identify the extent of problems that may be encountered in prescribing controlled substances
3. Identify substance abuse screening tools that you can use in your practice
4. Illuminate where to find substance abuse treatment resources in your area
5. Identify the criteria for substance use disorders
6. Highlight the legal requirements for prescribing controlled substances in your practice
7. Describe different prescribing practices that will help keep you out of trouble while prescribing controlled substances

References:

1. https://www.niddk.nih.gov/health-information/healthy-moments/episodes/prescription-drug-misuse
2. https://www.drugabuse.gov/publications/research-reports/misuse-prescription-drugs/what-scope-prescription-drug-misuse
3. https://www.drugabuse.gov/publications/research-reports/misuse-prescription-drugs/how-can-prescription-drug-misuse-be-prevented

Disclosures: None

Howard Busch, DO
Dr. Howard M. Busch founded the Family Arthritis Center in 1987 and has built a tremendous following through his diagnostic skills and compassionate treatment of his patients. He obtained his Bachelor of Science degree from Hobart and William Smith Colleges in New York, followed by his medical studies at the New York College of Osteopathic Medicine at the New York Institute of Technology. He performed his internship at Metropolitan Hospital in Philadelphia, followed by a Medical Residency at Norwalk Hospital, an affiliate of Yale University. He was chosen to be Chief Medical Resident and an instructor at Yale. His Rheumatology Fellowship was completed at the University of Medicine and Dentistry in Newark, New Jersey, where he was awarded the Northeast Regional Fellow Award for Research. He is the author of several articles and was selected to be the Chief Fellow. Dr. Busch is a noted national speaker and is a member of the Speaker's Bureau for numerous pharmaceutical companies. He has been an investigator for numerous clinical trials. His wife Stacey is an active participant in the practice. They have three beautiful daughters and is a proud grandfather.

PSO/PSA Comorbidities: A New Prospective?

Objectives:
1. Identify comorbidities
2. Understanding of the immunological relationships
3. Consideration to objectify these associated issues in clinical practice to buffer our outcomes

Needs:
1. New methods of diagnosis or treatment
2. Advances in medical knowledge
3. Changing perspective on patient evaluation

References:

1. Junko Takeshita, MD, Phd, MSCE et al. "Psoriasis and Comorbid Diseases." *JAAD* March 2017;76(3):377-390.
2. H Yeung, BS, J. Takeshita, MD, PhD, N. Mehta, MD, MSCE, et al. "Psoriasis Severity and the Prevalence of Major Medical Comorbidity: A Population-Based Study". *JAMA Dermatol* 2013;149(10):1173-1179.

Core Competencies: 2, 3, 6

Disclosures: Consultant and speaker for numerous companies – none that impact this talk.

Ronald Bush, MD
Ronald Bush, MD, FACS, is one of the nation's foremost specialists in venous disease. Dr. Bush co-founded and is the Medical Director for Vein Experts, a national group of professionals specializing in the care and treatment of venous disease. He has published numerous peer-reviewed journal articles and is an innovator of many techniques utilized in the treatment of venous disease. He is board-certified in vascular surgery and was certified in cardio thoracic surgery.

Dr. Bush trained at Indiana University School of Medicine and Walter Reed Army Medical Center in cardio thoracic surgery. His knowledge and skill as a surgeon qualify him as a Fellow in the American College of Surgeons. For the past 20 years, Dr. Bush has devoted his practice solely to the treatment of venous disease. Physicians throughout the world have visited and have been trained by Dr. Bush.

Cutaneous Venous Hypertension: From Spider Veins to Ulcers

Objectives:
1. Understand the manifestations of cutaneous venous hypertension
2. Recognize the patterns of venous pathology
3. Become familiar with primary and secondary venous ulcers and treatment

Needs:
1. New methods of diagnosis or treatment
2. Development of new technology

References:

1. Bihari I, Magyar E. "Microshunt histology in telangiectasias." *Int J Angiol* 1999;8(2):98-101.
2. Bush, R. (2015). Image retrieved 2015 from http://www.veinexperts.org/.
3. Mariani F, Bianchi V, Mancine S, Mancini S. "Telangiectases in venous insufficiency: Point of reflux and treatment strategy". *Phlebol* 2000;15(1):38-42.
4. Sommer A, Van Mierlo P, Neumann H, Kessels A. "Red and blue telangiectasias". *Phlebol* 1997;23:5-59.

Core Competencies: 2, 6

Disclosures: ***Spouse has stock options for:*** Dermalex Cream

James Del Rosso, DO, FAOCD
Dr. James Q. Del Rosso, DO, FAOCD, FAAD, was born in Brooklyn, New York, and attended pharmacy school at St. John's University in Jamaica, New York. He completed a hospital pharmacy residency at Temple University in Philadelphia, PA. Dr. Del Rosso graduated from medical school at Ohio University with honors and then completed his approved dermatology residency at the Atlantic Skin Disease Association in Fort Lauderdale, Florida.

He additionally completed a fellowship approved by the American College of Mohs Surgery in Mohs Micrographic Surgery and Cutaneous Oncology at Ohio State. Dr. Del Rosso is board certified in Dermatology and Mohs Micrographic Surgery and is fully licensed in the State of Nevada.

Dr. Del Rosso is an internationally renowned educator and speaker with several publications in recognized dermatology journals. He is a frequently invited presenter at major dermatology meetings in both the United States and globally, often talking about what is new in therapeutics and drug development. Additionally, he has written and published several articles on a variety of skin diseases including proper care of the skin barrier, acne, rosacea, psoriasis, atopic dermatitis, and eczemas, actinic keratosis, and skin cancers. He is also the co-editor of the textbook, *Acne Vulgaris*.

He is a past president of the American Acne & Rosacea Society, the American Society for Mohs Surgery, and the American Osteopathic College of Dermatology. He is editor-in-chief of the *Journal of Clinical Aesthetic Dermatology* since its inception in 2005. He has also authored several recognized publications on guidelines for management of acne, rosacea, atopic dermatitis, psoriasis, and skin cancer.

He founded the Scientific Panel for Antibiotic Use in Dermatology in 2005, with three meetings and scientific publications authored by the group under his direction to guide clinicians on optimal antibiotic use.

Dr. Del Rosso is research director and principal investigator of JDR Dermatology Research, in addition to having his dermatology clinic that is fully dedicated to the care of people with skin disorders or have concerns about their skin. The research center conducts studies for a wide variety of skin conditions, such as acne, rosacea, psoriasis, eczemas, urticaria, actinic keratosis, and skin cancer. Dr. Del Rosso has over 25 years of experience in dermatology research and related publications, and he employs a highly experienced and skilled staff. Dr. Del Rosso is in dermatology practice at Thomas Dermatology in Las Vegas, Nevada. He has been practicing dermatology in the Las Vegas area for 20 years.

Dr. Del Rosso was the recipient of a lifetime achievement award by the American Academy of Dermatology (AAD) in March 2016 for his lifelong commitment to dermatology and his contributions to the field. He now has the distinguished title of Honorary Member with the Academy.

Outside of his professional activities, Dr. Del Rosso is an avid lover of music and sports. He is the proud owner of what can be considered to be a "museum" of sports memorabilia and rock and roll music memorabilia, including a collection of limited edition guitars and vintage guitars. He also attends many concerts, usually sitting in the first row middle section. His motto about attending concerts is admittedly a selfish one: "The concert is being put on specifically for me…I am just nice enough to let everyone else in". In 2015, Dr. Del Rosso recorded a CD entitled "My Royal Dream by Dr. D and the LL-7", at the legendary Royal Studios in Memphis Tennessee. The producer and recording engineer of this CD was Lawrence "Boo" Mitchell, who has recorded several major artists, and won a Grammy Award for being the recording engineer for "Uptown Funk" by Bruno Mars, which was also recorded at Royal Studios. Dr. Del Rosso is proud to say he is a good father and a "very cool" grandfather. The loves of his life are his wife Karyn, his daughter Jaclyn, his sister Marilyn and brother-in-law Pat, his stepchildren Chrystyna and Ron, his son-in-law David, and his grandchildren Allyson, Blake, Emily, and Asher. He is also thankful for having had great parents and loves his inner circle of great loyal friends. Dr. Del Rosso is proud and happy to say, "I have no bucket list. I have done everything I have wanted to do and I believe it has always been done well. It is time for the icing on the cake at this point in my life. I do what I enjoy and get great pleasure in giving back through personal generosity and the professional work that I do. My hope is to record another CD with Boo Mitchell. That was the greatest week of my life".

So Many Drugs, So Little Time: A Therapeutic Update

Objectives:

1. Summarize newer therapies that are available or in development for common dermatologic disorders, such as atopic dermatitis, psoriasis, acne, rosacea, actinic keratosis, alopecia, cutaneous infections, skin barrier management, and others
2. Explain modes of action (MOAs) of individual therapies and how correlation of MOAs with specific disease manifestations can optimize therapeutic response
3. List potential adverse effects of specific therapies and devise monitoring approaches including both clinical and laboratory assessments and testing

Needs:

1. New advances in dermatologic treatment
2. New methods of diagnosis or treatment
3. Availability of new medication(s) or indication(s)
4. Development of new technology
5. Advances in medical knowledge

References:

1. Del Rosso JQ, et al. "Consensus Recommendations on Adjunctive Topical Management of Atopic Dermatitis". *J Drugs Dermatol*. 2018;17(10):1065-1071.
2. Del Rosso JQ, Thiboutot D, Gallo R, et al. "Consensus recommendations from the American Acne & rosacea Society on the management of rosacea, part 1: a status report on the disease state, general measures, and adjunctive skin care". *Cutis*, 2013;92(5):234-40.
3. Del Rosso JQ, Webster GJ, Rosen T, et al. "Status report from the scientific panel on antibiotic use in dermatology of the American Acne and Rosacea Society: part 1: antibiotic prescribing patterns, sources of antibiotic exposure, antibiotic consumption and emergence of antibiotic resistance, impact of alterations in antibiotic prescribing, and clinical sequelae of antibiotic use". *J Clin Aesthet Dermatol*, 2016;9(4):18-24.

Core Competencies: 2, 3

Disclosures: ***Research investigator for:*** Aqua/Almirall, Athenex, BioPharma, Botanix, Celgene, Dermira, Epi Health, Foamix, Galderma, Genentech, Leo Pharma, Novan, Ortho, Regeneron, Sun Phamra, Taro;

Consultant/Advisor for: Aqua/Almirall, Biopharmx, Celgene, Dermira, Epi Health, Ferndale, Fomix, Galderma, Leo Pharma, La Roche Posay, Novan, Ortho, Pfizer, Regeneron, Sanofi-Genzyme, Sonoma (Intraderm), Sun Phamra, Taro. ***Speaker for:*** Aqua/Almirall, Celgene, Encore, Epi Health, Ferndale, Galderma, Genentech, Leo Pharma, Ortho, Pfizer, Regeneron, Sanofi-Genzyme, Sun Pharma, Taro

Theresa Durchhalter, DO
Dr. Theresa Durchhalter is a second-year dermatology resident at St. John's Episcopal Hospital in Far Rockaway, NY. She completed her undergraduate degree in biochemistry at Adelphi University and attended medical school at Edward Via College of Osteopathic Medicine. She completed an intern year at St. John's Episcopal Hospital in 2017. She currently lives in Long Island, NY with her fiancé. Her dermatological interest include medical and cosmetic dermatology.

Onychomycosis

Objectives:
1. Understand different diagnostic techniques to aid in the diagnosis of onychomycosis
2. Understand which therapeutic options to use for patients with onychomycosis
3. Review currently used treatments and explore new treatments being investigated

Needs:
1. New advances in dermatologic treatment
2. New methods of diagnosis or treatment

References:

1. Lipner, S.R., Scher, R.K. "Onychomycosis: Treatment and prevention of recurrence." *J Am Acad Dermatol* 2019 Apr;80(4):853-867.
2. Watanabe D, Kawamura C, Masuda Y, Akita Y, Tamada Y, Matsumoto Y. "Successful treatment of toenail onychomycosis with photodynamic therapy." *Arch Dermatol*. 2008 Jan;144(1):19-21.
3. Piraccini, Bianca & Alessandrini, Aurora. "Onychomycosis: A Review". *J Fungi* (Basel). 2015 Jun;1(1):30-43.

Core Competencies: 1, 2, 3, 4, 5, 6, 7

Disclosures: None

Steven Feldman, MD
Chronic skin diseases have a huge impact on patients' lives. We can help make great improvements in our patients' lives, if they will use the medicine we prescribe. That's a big if. Dr. Steven Feldman has opened our understanding of adherence issues in the treatment of psoriasis, atopic dermatitis and acne. He is author of over 700 MEDLINE-referenced publications and serves as editor of the *Journal of Dermatological Treatment*.

Dr. Feldman is a board-certified dermatologist and dermatopathologist. He is Professor of Dermatology, Pathology and Public Health Sciences at the Wake Forest University School of Medicine in North Carolina. He earned his M.D. and PhD degrees from Duke University in Durham, NC, and then completed a dermatology residency at the University of North Carolina at Chapel Hill and his dermatopathology residency at the Medical University of South Carolina, in Charleston.

Practical Issues Using Biologics for Psoriasis

Objectives:
1. To describe the safety of biologics for psoriasis
2. To list relative efficacy of different biologics for psoriasis
3. To describe how well patients adhere to self-administered biologic treatment

Needs:
1. New methods of diagnosis and treatment
2. Availability of new medication(s) or indication(s)
3. Advances in medical knowledge

References:

1. Kamata M, Tada Y. "Safety of biologics in psoriasis". *J Dermatol*. 2018 Mar;45(3):279-286.
2. Campanati A, Molinelli E, Brisigotti V, Offidani A. "Biologic Therapy in Psoriasis (Part I): Efficacy and Safety of Tumor Necrosis Factor – a Inhibitors". *Curr Pharm Biotechnol*. 2017;18(12):945-963.
3. Molinelli E, Campanati A, Brisigotti V, Offidani A. "Biologic Therapy in Psoriasis (Part II): Efficacy and Safety of New Treatment Targeting IL23/IL-17 Pathways". *Curr Pharm Biotechnol*. 2017;18(12):964-978

Core Competencies: 2, 3, 4

Disclosures: ***Speaker for:*** Abbvie, Celgene, Janssen, Leo Pharma Inc., Lilly, Novartis Pharmaceuticals Corporation, Pfizer Inc., Regeneron, Sanofi, Sun Pharma, Taro, Ortho Dermatology; ***Grant Support from:*** Abbvie, Celgene, Galderma Laboratories, L.P., Janssen, Lilly, Novartis Pharmaceuticals Corporation, Pfizer Inc., Regeneron, Sanofi, Taro; ***Consultant for:*** Abbvie, Alvotech, Advance Medical, Caremark, Celgene, Galderma Laboratories, L.P., Gerson Lehrman Group, Guidepoint Global, Janssen, Kikaku, Leo Pharma Inc., Lilly, Merck & Co., Inc., Mylan, Novartis Pharmaceuticals Corporation, Pfizer Inc., Regeneron, Sanofi, Sienna, Sun Pharma, Suncare Research, Ortho Dermatology, Xenoport; ***Royalties from:*** Informa, UpToDate, Xlibris; ***Stockholder of:*** Causa Technologies, Medical Quality Enhancement Corporation (majority owner); ***Founder of:*** Causa Technologies; ***Chief Technology Officer of:*** Causa Technologies

David Herold, MD

Dr. David Herold is one of the few board-certified radiation oncologists in the country to have specialized in the treatment of skin cancer using therapeutic radiation. He has practiced both in general and specialty radiation oncology in Palm Beach County since 1999 and has served for over a decade as the Medical Director of Jupiter Medical Center Department of Radiation Oncology and the Palm Beach Cancer Institute - Center for Radiation Oncology.

Dr. Herold attained his undergraduate degree from Cornell University in Ithaca, NY. Prior to medical school, he spent a year studying psychology and neurophysiology at Oxford University in England. He attended the University College of Medicine in Gainesville, FL and completed his internship in internal medicine at Northwestern University – Evanston Hospital in Evanston, IL. Dr. Herold completed his radiation oncology residency training at the prestigious Fox Chase Cancer Center in Philadelphia, PA. He spent time during residency training to learn specialized radiation techniques with experts at MD Anderson Cancer Center in Houston, TX and Thomas Jefferson University Hospital and Children's Hospital of Pennsylvania in Philadelphia. After serving as chief resident at Fox Chase Cancer Center, he began working in private practice at Jupiter Medical Center. Over the next fifteen years he established countless radiation oncology programs, protocols and treatment plans and diligently cared for hundreds of cancer patients. Dr. Herold pioneered the skin cancer program at Jupiter Medical Center and was responsible for all aspects of the radiation oncology program. He has refined the management of skin cancer treatment using advanced radiation techniques.

The Art of Radiotherapy for Skin Cancer Management

Objectives:
1. To review the historic precedent for radiation therapy in skin cancer treatment
2. To understand how to select patients for radiation therapy
3. To discuss several different radiation technologies available for delivery of treatments in a dermatology office setting

Needs:
1. New advances in dermatologic treatment
2. Development of new technology
3. Advances in medical knowledge

References:

1. S. McGregor, J. Minni, D. Herold. "Superficial Radiation Therapy for the Treatment of Nonmelanoma Skin Cancers". *J Clin Aesthet Dermatol*. 2015 Dec; 8(12):12-14.
2. Armand B. Cognetta, MD, Brett M. Howard, BA, Henry P. Heaton, BA, Earl R. Stoddard, MD, Hyokyoung Grace Hong, PhD, W. Harris Green, MD. "Superficial x-ray in the treatment of basal and squamous cell carcinomas: A viable option in select patients". *JAAD*, Dec. 2012; 67(6):1235-1241.

3. National Comprehensive Cancer Network: *Squamous Cell Skin Cancer*, version 2.2019. Oct. 23, 2018 – Accessed Nov 12, 2018. www.nccn.org/professionals/physician_gls/recently_updated.aspx.

Core Competencies: 2, 3

Disclosures: None

Camille Howard-Verovic, D.O.
Camille Howard-Verovic, D.O., is a second year Dermatology resident at St. John's Episcopal Hospital. She completed her undergraduate studies at the University of Central Florida and attended medical school at New York College of Osteopathic Medicine in Long Island, NY. Dr. Howard-Verovic also completed a Family Medicine residency in 2017 at St. John's Episcopal Hospital. Her dermatological interests include medical and cosmetic dermatology. She resides in New York City with her husband and young daughter.

Reddit: An Uncommon Source for Common Derm Conditions

Objectives:
1. Review common dermatological conditions
2. Explore insightful information and emerging therapies in the current literature
3. Identify unconventional self-prescribed therapies for a few common dermatological conditions

Needs:
1. New advances in dermatologic treatment
2. Availability of new medication(s) or indication(s)

References:
1. JAAD. 72(5) 754-758.
2. Exp Ther Med. 2019 Apr. 17(4) 2725-2733.

Core Competencies: 2, 3, 4, 5

Disclosures: None

Joseph Jorizzo, MD
Dr. Joseph Jorizzo is a Professor and former and founding Chair of the Department of Dermatology. He is also a Professor of Clinical Dermatology at the Weill Cornell School of Medicine. He has served on multiple councils, committees and advisory boards and has participated on the editorial boards of major dermatology journals, including the *Archives of Dermatology, Journal of the American Academy of Dermatology, Journal of the European Academy of Dermatology and Venereology*, among others.

Dr. Jorizzo is a member of many professional dermatologic groups, including the American Dermatologic Association Society of Investigative Dermatology, Dermatology Foundation, Women's Dermatology Association and the American Academy of Dermatology, where he served as Vice President. He has co-edited several books, including *Dermatological Signs of Internal Disease* and *Dermatology* for Elsevier. Additionally, he has authored and co-authored more than 200 articles and abstracts.

Dr. Jorizzo has been the recipient of a number of national and international honors, including multiple "Best Doctors in America" listings. He has spoken at hundreds of dermatology meetings in the U.S. and around the world.

Neutrophilic Dermatoses: Practical Aspects

Objectives:
1. What are the clinical features that allow diagnosis of neutrophilic dermatoses
2. Determine the best strategies for evaluating patients with neutrophilic dermatoses
3. Understand the therapeutic ladder for the treatment of neutrophilic dermatoses

Needs:
1. New advances in dermatologic treatment
2. New methods of diagnosis or treatment
3. Advances in medical knowledge

References:

1. Alavi A, Sajic d, Cerci FB, Ghazarian D, Rosenbach M, Jorizzo J. "Neutrophilic dermatoses: an update". *Am J Clin Dermatol*. 2014 Oct;15(5):413-23.
2. Neutrophilic Dermatoses. Chapter Bolognia et al. *Dermatology*.

Core Competencies: 2, 3, 4, 5, 6

Disclosures: ***Speaker for:*** Amgen

Leon Kircik, MD
Dr. Kircik is a Board Certified Dermatologist who graduated with AOA Honors from State University of New York at the Health Sciences Center at Brooklyn after completing his undergraduate work with Phi Beta Kappa at New York University. He completed a Mohs Micrographic Surgery and Cutaneous Oncology Fellowship under the auspices of Dr. Frederick Mohs at the University of Wisconsin after completing his dermatology residency at State University of New York in Buffalo.

He currently teaches as Associate Clinical Professor of Dermatology at Indiana University Medical Center in Indianapolis, IN, as well as at Icahn School of Medicine at Mount Sinai Medical Center in New York City. Dr. Kircik is also the Medical Director of DermResearch, PLLC and Physicians Skin Care, PLLC in Louisville, Kentucky. He has been the principal investigator of numerous clinical trials for psoriasis, acne, rosacea, atopic dermatitis, skin cancers, and actinic keratosis, just to name a few.

Dr. Kircik is an author of many scientific articles, abstracts and posters. He has lectured extensively nationally and internationally on all aspects of dermatologic conditions. In addition, he also serves on the advisory boards of several pharmaceutical companies as a consultant. He is on the editorial board of *Journal of Drugs in Dermatology*, *Practical Dermatology*, *The Journal of Clinical & Aesthetic Dermatology*, and *Case Report in Clinical Pathology*. He volunteers for multiple local and national medical society committees.

History of Mohs Surgery

Objectives:
1. Understand Mohs Micrographic Surgery
2. Understand the evolution of Mohs techniques
3. Understand the indications of Mohs surgery

Needs:
1. New advances in dermatologic treatment

References:

1. "Surgery in Dermatology". *Fitzpatrick's Dermatology in General Medicine. 4th ed*. p. 2917.
2. "Non-Melanoma Skin Cancers". *Fundamentals of Cutaneous Surgery*. Richard Bennett p. 619.

Core Competencies: 2, 3, 6

Disclosures: ***Speaker for:*** Abbott Laboratories, Allergan, Inc., Amgen, Inc., Assos Pharma, Astellas Pharma US, Inc., Cipher, CollaGenex, Connetics Corporation, Dermik Laboratories, Embil Pharmaceuticals, Exeltis, Foamix, Genentech, Inc., Innocutis, Innovail, Johnson & Johnson, Leo, L'Oreal, 3M, Onset, OrthoNeutrogena, PediaPharma, PharmaDerm, Serono (Merck Serono International SA), SkinMedica, Inc., Stiefel Laboratories, Inc., Sun Pharma, Taro, Triax, UCB, Valeant Pharmaceuticals Intl, Warner-Chilcott; ***Advisory Board for:*** Aclaris, Allergan, Inc., Almirall, Anacor Pharmaceuticals, Biogen-Idec, Colbar, Celgene, Cipher, Connetics Corporation, EOS, Exeltis, Ferndale Laboratories, Inc., Foamix, Genentech, Inc., Intendis, Innocutis, Isdin, Johnson & Johnson, Nano Bio, OrthoNeutrogena, Promius, Quinnova, SkinMedica, Inc., Stiefel Laboratories, Inc., Sun Pharma, Valeant Pharmaceuticals Intl, Warner-Chilcott; ***Investigator for:*** Acambis, Allergan, Inc., Amgen, Inc., Anacor Pharmaceuticals, Astellas Pharma US, Inc., Asubio, Berlex Laboratories (Bayer HealthCare Pharmaceuticals), Biolife,

Biopelle, Boehringer-Ingleheim, Breckinridge Pharma, Celgene, Centocor, Inc., Cellceutix, Coherus, CollaGenex, Combinatrix, Connetics Corporation, Coria, Dermavant, Dermira, Dow Pharmaceutical Sciences, Inc., Dusa, Eli Lilly, Exeltis, Ferndale Laboratories, Inc., Foamix, Genentech, Inc., GlaxoSmithKline, PLC, Health Point, LTD, Idera, Intendis, Johnson & Johnson, Leo, L'Oreal, 3M, Maruho, Merck, Medicis Pharmaceutical Corp., Nano Bio, Novartis AG, Noven Pharmaceuticals, Nucryst Pharmaceuticals Corp, Obagi, Onset, OrthoNeutrogena, Promius, QLT, Inc., PharmaDerm, Pfizer, Quinnova, Quatrix, SkinMedica, Inc., Stiefel Laboratories, Inc., Sun Pharma, TolerRx, UCB, Valeant Pharmaceuticals Intl, Warner-Chilcott, XenoPort; ***Consultant for:*** Allergan, Inc., Almirall, Amgen, Inc., Anacor Pharmaceuticals, Colbar, Cipher, CollaGenex, Connetics Corporation, Exeltis, Foamix, Genentech, Inc., Intendis, Isdin, Johnson & Johnson, Laboratory Skin Care Inc., Leo, Medical International Technologies, Merck, Merz, Novartis AG, OrthoNeutrogena, Promius, PuraCap, SkinMedica, Inc., Stiefel Laboratories, Inc., Sun Pharma, Taro, UCB, Valeant Pharmaceuticals Intl, ZAGE; ***Stockholder of:*** Johnson & Johnson

Lawrence Kraska
Larry Kraska is currently the CEO of Water's Edge Dermatology, a leading provider of dermatology, vein care, and plastic surgery with 35 locations across Florida. He has over 30 years of executive level healthcare services experience, including hospital administration, physician group practice management, outpatient services, consulting, and healthcare staffing. During his career, he has served as a hospital administrator, CEO of a national healthcare staffing company, and held CEO and COO roles with a number of regional and national physician medical practices.

Larry obtained his B.S and M.B.A degrees from Kennesaw State University and he is currently on the Board of Trustees for the University. He has presented at numerous regional and national healthcare conferences on topics which include practice management, best practices, M&A, recruiting, and staffing. In 1996, he was named an "Up and Comer" by *Modern Healthcare*, a national designation given each year to 12 healthcare executives under the age of 40 who are viewed as future leaders in healthcare.

A VIP Approach to Customer Service

Objectives:
1. Learn several examples of VIP customer service in other industries
2. Learn several practical ways to improve customer service and patient satisfaction within their office

Needs:
1. Organizational changes effecting patient care

Core Competencies: 3, 4, 5

Disclosures: ***CEO of:*** Water's Edge Dermatology

Mark Lebwohl, MD
Dr. Mark Lebwohl graduated summa cum laude from Columbia College in 1974 and graduated from Harvard Medical School in 1978. He completed residencies in internal medicine and dermatology, both at Mount Sinai. Dr. Lebwohl has been practicing dermatology since 1983. He is professor and chairman of the Kimberly and Eric J. Waldman Department of Dermatology of the Icahn School of Medicine at Mount Sinai. Dr. Lebwohl is the President of the American Academy of Dermatology. He is chairman emeritus of the Medical Board of the National Psoriasis Foundation. He is the founding editor of *Psoriasis Forum* as well as a medical editor of the bulletin of the National Psoriasis Foundation, *Psoriasis Advance*. He is editor of the Dermatology Section of *Scientific American Medicine*. Dr. Lebwohl has chaired numerous symposia and has written, edited or co-edited several books including *Psoriasis, Mild-to-Moderate Psoriasis and Moderate-to-Severe Psoriasis*. He has authored or co-authored over 500 publications including peer-reviewed articles, invited articles and book chapters. Dr. Lebwohl is actively involved in clinical trials of many new dermatologic treatments.

New Anti-IL-23 Drugs

Objectives:
1. Identify ideal patients for anti-IC-23 therapy

2. Understand the mechanism of action of anti-IC-23 drugs
3. Recognize the risks and benefits of anti-IL-23 therapy

Needs:
1. New advances in dermatologic treatment
2. New methods of diagnosis or treatment
3. Availability of new medication(s) or indication(s)
4. Advances in medical knowledge
5. Legislative, regulatory, or organizational changes effecting patient care

References:

1. "Four effective anti-IL 23 drugs for psoriasis" Fall Clinical, Plaque Psoriasis By Bob Kronemyer. *Dermatology Times*, Oct. 2018;Vol 39(12).
2. "First IL-23 blocker, guselkumab, earns FDA approval for psoriasis" By Elizabeth Mechcatie. *Dermatology News*, July 13, 2017.
3. C. Fotiadou, E. Lazaridou, E. Sotiriou, D. Ioannides. "Targetting IL-23 in psoriasis: current perspectives". *Psoriasis: Targets and Therapy*, Dovepress 2018:81-5.

Core Competencies: 2, 3, 7

Disclosures: ***Research funds from:*** Abbvie, Amgen, Arcutis, Bausch Health (Valeant), Boehringer Ingelheim, Celgene, Eli Lilly, Incyte, Johnson & Johnson (Centocor, Janssen), Leo Pharmaceuticals, Medimmune/Astra Zeneca, Novartis, Pfizer (anacor), Regeneron, Sciderm, UCB, Inc., and ViDac; ***Consultant for:*** Allergan, Aqua, Arcutis, Inc., Boehringer-Ingelheim, Bristol-Myers Squibb, LEO Pharma, Menlo, Mitsubishi, Neuroderm, Promius, Theravance, and Verrica

Arnold Mackles, MD
Arnold Mackles, MD, MBA, LHRM is a nationally-recognized expert on patient safety. The mission of Dr. Mackles' 35-year healthcare career has been to provide access to the highest quality care; first, during his 23 years of practice as a neonatal physician and then, for the past 12 years as a National Patient Safety Expert in all areas of medical practice. Dr. Mackles' specific areas of expertise include: proactive prevention of medical errors, risk management, healthcare performance improvement strategies, creating/maintaining a culture of patient safety excellence, benchmarking industry leading communication protocols, safe and accurate medication delivery, root cause analysis, healthcare technology, medical documentation and emerging leadership strategies in patient safety.

Dr. Mackles is an industry thought leader who brings a refreshing, no-nonsense, and solutions-based approach to all areas of patient safety. He plays many roles within the healthcare space that include expert witness, continuing medical and nursing education program developer and facilitator, keynote speaker, and industry consultant. As an expert witness and consultant, Dr. Mackles' fundamental philosophy is based on identifying root causation in the event of adverse patient safety circumstances and medical errors. He leads the field in his commitment to improving patient safety, reducing medical errors and enhancing the overall reputation of the healthcare industry. Program evaluations from physicians, nurses, CME directors, senior management and attorneys are outstanding and verifiable. Dr. Mackles is an industry change agent, a problem solver and a creator of a positive organizational culture.

His background as a neonatologist, patient safety expert witness, physician reviewer, author and presenter position Dr. Mackles as one of the nation's top experts on the subjects of patient safety and risk management. He teaches and promotes new, cutting-edge subject matter, while researching emerging trends to ensure full compliance with healthcare protocols and policies to meet stringent client mandates and objectives.

Dr. Mackles is a former hospital-based physician with more than 23 years of experience, specializing in neonatology. He was a neonatologist/pediatrician for Pediatrix Medical Group, Florida Regional Neonatal Associates, and St. Mary's Hospital (all located in South Florida), between 1983 and 2005. His experience and background as a physician clearly exposed him to the challenges the medical profession faced and the need to significantly improve patient care to reduce medical errors. In 2006, Dr. Mackles made the decision to become a full time advocate for patient safety.

He now travels the country as a speaker, trainer, expert witness, and consultant to improve patient safety and reduce or eliminate avoidable medical errors. Dr. Mackles' credentials include a neonatology fellowship from Cornell

University Medical Center, a pediatric residency from Lenox Hill Hospital in New York, a medical degree (MD) from the University of Bologna in Italy, an MBA Degree from Nova Southeastern University, and he received his bachelor's degree (pre-med) from Syracuse University. Dr. Mackles attained his healthcare risk management licensure through studies at the University of South Florida. He is a Certified Professional Compliance Officer (CPCO) awarded by Healthcare Compliance Resources (currently certified by the AAPC, Salt Lake City, UT). He has served as an Instructor and Program Developer for the Risk Management and Patient Safety Program at the University of Florida, and participated as an instructor and faculty member of the University of South Florida Distance Education Risk Management Licensure Program. Dr. Mackles is currently a physician reviewer for the monthly newsletter "Healthcare Risk Management," published by Relias Learning (formerly AHC Media). He is also a member of the Publication's Editorial Board. In addition, Dr. Mackles is the author of 10 accredited online continuing medical and nursing education courses on patient safety topics offered by the Sullivan Group. Dr. Mackles is an active member of the Florida Society of Healthcare Risk Management and Patient Safety (FSHRMPS) and was elected to the Board of Directors from 2006 to 2008, and again between 2014 and 2015. He is a member of the American Society of Healthcare Risk Management (ASHRM) and has presented at their national meetings. In addition, Dr. Mackles is affiliated with the American Society of Professionals in Patient Safety.

Prevention of Medical Errors

Objectives:
This course addresses the mandatory content for Physicians in Florida. The purpose of this educational activity is to provide physicians with the most current information regarding the prevention of common performance and diagnostic errors. This monograph is specific to Florida statutes. After completing this activity, learners will be able to:

1. Identify the two most common qualities of care violations
2. Name four of the most prevalent diagnostic and performance errors
3. Cite two necessary elements of a root cause analysis
4. Create two risk management measures designed to prevent medical errors and increase patient safety

References:

1. http://cme.med.miami.edu/documents/Medical_Errors_Brochure.pdf
2. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2723204/
3. https://www.fda.gov/Drugs/DrugSafety/MedicationErrors/default.htm

Disclosures: ***Author of CME Courses:*** The Sullivan Group, Innovative Healthcare Comp. Group, Inc.; ***Speaker for:*** Innovative Healthcare Comp. Group, Inc.

Raymond Mosely, PhD
Dr. Moseley received his Master's Degree in Philosophy and Medical Ethics at the University of Tennessee and completed his Doctorate in Bioethics at the Kennedy Institute of Ethics at Georgetown University in Washington, D.C.

Dr. Moseley teaches Bioethics in the Program in Bioethics, Law and Medical Professionalism in the UF College of Medicine where he is the Grace H. Osborn Professor in Bioethics. He is also an active clinical bioethics consultant at the UF/Shands Medical Center as well as at several other Florida Hospitals.

He is the founder and Board Member of the Florida Bioethics Network (FBN), and has played a key role in the development of the FBN as a significant statewide resource. Dr. Moseley is an expert on hospital ethics committees and research ethics, and he serves as vice chair of the UF IRB and is the author of CITI Hospital Ethics Committees training program. He regularly consults with national and international governments/institutions on the development of health care ethics committees and human subject's protections programs.

Currently, he is the Principal Investigator on a major NIH research grant developing and evaluating an innovative web-based informed consent process with "information on demand" features. He was recently the PI on a grant which created an iPad App which assists with developing and documenting advance directives, including video advance directives. His publications include articles on "Withdrawal of Life-Sustaining Medical Treatment", "Advance Medical Directives", "Genetic Testing", and "Ethics Committees".

Professional Medical Ethics

Objectives:
This course addresses the mandatory content for Physicians in Florida. Upon completing this course and reviewing the resources, participants should be able to:
1. Fulfill the requirements of the Florida Mandatory CME course on professional medical ethics
2. Address current ethical issues regarding medical ethics in Florida
3. Describe the meaning and importance of medical professionalism
4. Discuss how conflict of interest may compromise professionalism
5. Identify three significant boundary issues and proper limits in relation to each
6. Describe two important ethical issues with respect to operating a practice

References:

1. A. Jonsen, M. Sigler, W. Winslade. *"Clinical Ethics: A Practical Approach to Ethical Decisions in Clinical Medicine". 7th ed*. McGraw Hill pp 51-64 and 174-180.
2. T. Beachamp, J. Childress. "*Principles of Biomedical Ethics". 7th*. Oxford Press, Chapter 3, pp. 56-81.

Disclosures: None

Michael Nowak, MD
Dr. Michael Nowak is board-certified in anatomic and clinical pathology and dermatopathology. Dr. Nowak earned a Bachelor of Science degree from Xavier University, followed by a medical degree from Wright State University. After completion of an internship in internal medicine, he served as chief resident and cancer fellow at Western Reserve Care System where he completed a residency in anatomic and clinical pathology. Dr. Nowak finished his training in Providence, RI at Brown University, where he completed fellowship training in dermatology and dermatopathology.

After his training, Dr. Nowak joined Palm Beach Dermatology in 1999. He organized the development and staffing of Palm Beach Dermatology's CLIA-certified diagnostic dermatopathology laboratory, where he serves as Medical Director. The laboratory is equipped with the latest technology and staffed with five ASCP-certified and state-licensed technologists who specialize in dermatology samples.

Dr. Nowak has authored over 15 articles in major medical journals on a variety of subjects including malignant melanoma, extramammary Paget's disease, generalized pruritis and infectious diseases of the skin. He is also a member of the medical staff at Columbia Hospital in West Palm Beach, FL, where he conducts weekly teaching sessions with dermatology residents and has been awarded "Dermatology Attending of the Year" by his peers at the hospital. He is also a reviewer for the journal titled the *Physician and Sports Medicine*, and is on the editorial board for the journal *Postgraduate Medicine*. Resident lectures and review of journal articles ensures that Dr. Nowak stays current with the latest advances in the science of dermatopathology. Dr. Nowak's practice is dedicated to the evaluation and diagnosis of skin pathology samples.

Metastatic Carcinoma to the Skin

Objectives:
1. Attendees will gain a better understanding of the gender differences, modes of spread, and anatomic distribution of metastatic carcinoma involving the skin
2. Attendees will gain a better understanding of the clinical and microscopic features of various types of metastatic carcinoma involving the skin
3. Attendees will gain a better understanding of prognosis and palliative treatment options for metastatic carcinoma involving the skin

Needs:
1. New methods of diagnosis and treatment
2. Advances in medical knowledge

References:

1. Hussein MR. "Skin metastasis: a pathologist's perspective." *J Cutan Pathol* 2010 Sep;37(9):1-20.
2. Wong JK, Minni JP, Nowak MA. "A novel case of NKX3.1-positive metastatic cutaneous prostate cancer." *Dermatol Online J*. 2018 Oct 15;24(10).

Core Competencies: 1, 2, 3, 4, 5, 6, 7

Disclosures: ***Stockholder of:*** Modernizing Medicine

Paolo Romanelli, MD
Paolo Romanelli, MD, Professor at the Dr. Phillip Frost Department of Dermatology and Cutaneous Surgery, is Board Certified in both Dermatology and Dermatopathology. He is the Director of the ACGME-certified UM Dermatopathology fellowship. He has an extensive background in anatomical pathology and dermatology with special expertise in the histopathology of wound healing, deposition disorders and immunohistochemistry. His work on wound histology has been presented nationally and internationally and appears in numerous peer-reviewed journals. His clinical interests are in psoriasis, mycosis fungoides and collagen vascular diseases.

A native of Italy, Dr. Paolo Romanelli earned his undergraduate degree at Collegio Alla Querce and his M.D. from the University of Pisa School of Medicine. He has won several Best Teacher awards, published in peer-reviewed journals, presented lectures at national and international dermatology meetings including the AAD, EADV, and Masters of Pediatrics and co-authored a *Dermatology Therapeutics* book. Dr. Romanelli also sees general dermatology patients and is Director of the Psoriasis Biologics Clinic at Jackson Memorial Hospital.

Dermatopathology and Immunohistochemistry, the Future of Targeted Therapy in Skin Disease

Objectives:
1. Learn about the UM rapid pathology service, a skin biopsy service to better assess non-healing skin wounds
2. Psoriasis tailor-made treatment in the era of biologics
3. Dermal fillers histopathology reactions

Needs:
1. New advances in dermatologic treatment
2. New methods of diagnosis or treatment
3. Development of new technology
4. Advances in medical knowledge

References:

1. E. Lee et al. "Psoriasis Targeted Therapy" *J. Drugs Dermatol* 2015 Oct;14(10):1133-6.
2. Yin NC et al. "The Importance of Wound Biopsy in the Accurate Diagnosis of Acral Malignant Melanoma Presenting as a Foot Ulcer" *Inj. J Low Extrem Wounds*, 2013 Dec;12(4):289-92.

Core Competencies: 2, 3, 5, 6

Disclosures: None

Shoni Rozenberg, DO
Dr. Rozenberg is a third year Dermatology Resident at St. John's Episcopal Hospital in Queens, NY. Her interests include surgical, cosmetic and general dermatology. Shoni enjoys traveling, art history and spending time with family and friends.

Pediatric Dermatology: Bumps and Lumps

Objectives:
1. Identify common skin lesions on pediatric patients
2. Treatment approach for pediatric skin lesions
3. Discuss availability of new medications and treatment options

Needs:
1. New advances in dermatologic treatment
2. New methods of diagnosis or treatment
3. Availability of new medication(s) or indication(s)
4. Advances in medical knowledge

References:

1. Paller Amy, Sidney Hurwitz, and Anthony J. Macini. *Hurwitz Clinical Pediatric Dermatology*.
2. Bernard Cohen. *Pediatric Dermatology*.

Core Competencies: 2, 3, 4, 5, 6, 7

Disclosures: None

Suzanne Sirota Rozenberg, DO, FAOCD
Dr. Suzanne Sirota Rozenberg is a board-certified dermatologist practicing in Woodmere, NY. She earned her Doctor of Osteopathic Medicine degree at New York College of Osteopathic Medicine in 1988. After medical school, she completed both an internship and residency in family practice at Peninsula Hospital Center in Far Rockaway, NY, in 1992. She has been board-certified in family medicine since 1992. She then practiced for the next ten years with her brother and father. From 2002-2005, she trained in the dermatology residency program at St. John's Episcopal Hospital in Far Rockaway, where she now serves as Program Director. She served as Associate Director of Medical Education from 2005-2012. She is a Clinical Adjunct Professor at TouroCOM and LECOM. She has a full-time dermatology practice as well.

Dr. Sirota Rozenberg's memberships include the AOA, ACOFP, AOCD and AAD. She is a Past President of the AOCD and the ACOFP-NYS Chapter. She served on the AOCD Board of Trustees from 2008-2015, holding the positions of Trustee, Vice President and President. She represents the AOCD on the Program and Trainee Review Council of the AOA. She has served on the AOCD Education Evaluating Committee since 2009. For her years of service to the AOCD, Dr. Sirota Rozenberg has earned the title of Fellow of Distinction. She is a member of the AAD Ad Hoc Task Force for Osteopathic Dermatology Recognition and NBOME POCKET member. Dr. Sirota Rozenberg lectures locally and nationally, speaking at meetings of the AOCD, EROC, ROC-NY and the New York State Chapter of ACOFP. In addition to dermatology, she is board-certified in family practice and sclerotherapy.

Osteopathic Approach in Dermatologic Disease

Objectives:
1. Review of the core principles of osteopathic dermatology
2. Review dermatologic conditions and common treatments
3. Osteopathic approach to dermatologic conditions

Needs:
1. New advances in dermatologic treatment
2. New methods of diagnosis or treatment
3. Availability of new medication(s) or indication(s)
4. Advances in medical knowledge

References:

1. *JAOCD*
2. *JAOA*
3. "Defining the DO" *Dermatology World*, 2015 June.
4. "Dermatology Incorporated" *Dermatology World*, 2012 August.
5. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3486778/.

Core Competencies: 1, 2, 3, 4, 5, 6, 7

Disclosures: ***Master Injector for:*** Galderma; ***Speaker for:*** Aerolase

Michael Wein, MD
Michael Wein, MD, is Chief of Allergy at Indian River Medical Center and serves on the faculty at Florida State University College of Medicine. He completed his undergraduate work at Brown University, an internal medicine residency at Vanderbilt University, and his post-doctoral fellowship at Johns Hopkins Hospital in the division of Allergy & Immunology. He is board-certified by the American Board of Allergy and Immunology and also by the American Board of Internal Medicine.

Dr. Wein is Past President of the Florida Allergy, Asthma, and Immunology Society and is a Fellow of the American Academy of Allergy, Asthma and Immunology. He has authored several publication including the chapter on allergic rhinitis in *Conn's Current Therapy, 2006 edition*, and has served editorial roles for *DynaMed Online* and *Prescribers Letter* and is currently an Advisory Board Member of Boston-based *Wellness Workdays*. He co-authored a study on Epi-pen which was published in *Annals of Allergy* in 2015 and subsequent featured on CNN. His previous publications relate mostly to allergic inflammation, eosinophils, and adhesion molecules.

His offices are located in Vero Beach and Port Saint Lucie and he enjoys learning about dermatology from his friends practicing dermatology in his community.

Allergy for the Dermatologist

Objectives:
1. Differentiate among types of allergy testing for food and drug allergy
2. Understand limitations of tests to assess drug-induced skin rash
3. Recognize various patterns of skin reactions caused by drug allergy

Needs:
1. New advances in dermatologic treatment
2. New methods of diagnosis or treatment
3. Availability of new medication(s) or indication(s)
4. Advances in medical knowledge

References:

1. Kwatra Shawn G, et al. "PD-1 Blockade-Induced Pruritus Treated with a Mu-Opioid Receptor Antagonist". *N Engl J Med* 2018;379:1578-1579.
2. Joshua A. Boyce, Amal Assa'ad, A. Wesley Burks, Stacie M. Jones, Hugh A. Sampson, Robert A. Wood, Marshall Plaut, Susan F. Cooper, and others. "Guidelines for the Diagnosis and Management of Food Allergy in the United States: Summary of the NIAID-Sponsored Expert Panel Report". *JAAD*, January 2011,Vol. 64(1):175-192.

Core Competencies: 2

Disclosures: None

Jason D. Winn, Esq.
Jason D. Winn, Esquire, is a 1996 graduate of the University of Maryland and received his Juris Doctorate from Nova Southeastern University - Shepard Broad Law in Ft. Lauderdale, FL. Mr. Winn was admitted to the Florida Bar in September 2001.

From 2001 until 2004, Mr. Winn worked for the Assistant Public Defender in the Fifth Judicial Circuit where he conducted over 15 jury trials, numerous non-jury trials, and many hearings including, violations of probation, restitution and early termination motions for defendants in juvenile, misdemeanor and felony court. Mr. Winn was also an adjunct professor at Lake Sumter Community College teaching business law during this time. In 2003, Mr. Winn was appointed by Governor Bush to serve a one-year term on the Judicial Nominating Commission for Judicial Compensation Judges. From 2004-2006, Mr. Winn worked for the law office of Clyde M. Taylor, Jr. focusing on both state and federal criminal defense and parole violation hearings. In 2006, he opened his own practice, where he is managing partner and continues to focus on criminal, administrative, governmental, civil, wills and trusts.

Mr. Winn currently serves as general counsel for the Florida Osteopathic Medical Association (FOMA), the Florida Podiatric Medical Association (FPMA) and the Florida Society of Hearing Healthcare Professionals (FSHHP). Mr. Winn lectures throughout Florida on the laws and rules that affect health care practitioners, including osteopathic, allopathic, podiatric, and various other licensed health care providers.

He is a member of the Florida Bar, Tallahassee Bar, Legal Services of North Florida, a lifetime member of the state Florida Association of Criminal Defense Lawyers (FACDL), and the local FACDL chapter. As a member of the Tallahassee Bar, Mr. Winn volunteers his legal services to the Wakulla County Senior Citizens Center and Legal Services of North Florida. Mr. Winn is a devoted husband and father to three boys. During his downtime, he enjoys hunting, fishing, golfing and the great outdoors.

Florida Laws and Rules Osteopathic Medicine

Objectives:
This course addresses the mandatory content for Physicians in Florida. Upon completing this course and reviewing the resources, participants should be able to:

1. Understand the CME requirements for continued Florida licensure
2. Be aware of any necessary office signage that must be posted
3. Understanding of applicable laws & rules for licensed osteopathic physicians
4. Knowledge of the disciplinary process
5. Learning of rights afforded to physicians in licensure disciplinary cases
6. Ability to locate applicable statutes and rules through online resources
7. How to protect their right to practice

References:

1. http://www.leg.state.fl.us/statutes/index.cfm?App_mode=Display_Statute&URL=0400-0499/0458/Sections/0458.347.html

Disclosures: None

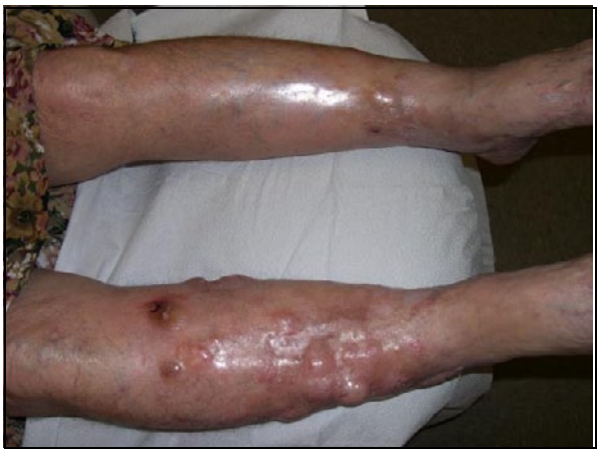
Wednesday, April 10, 2019

9:00 a.m. - 12:00 p.m.	Exhibitor Set Up Palazzo D
10:00 a.m. - 11:00 a.m.	*Dermatopathology and Immunohistochemistry, the Future of Targeted Therapy in Skin Disease* **Paolo Romanelli, MD**
11:00 a.m. - 12:00 p.m.	*PSO/PSA Comorbidities: A New Prospective?* **Howard Busch, DO**
12:00 p.m. - 1:00 p.m.	Novartis Product Theater *COSENTYX Aproach – An Educational Series: Moderate to Severe Plaque Psoriasis* **Nishit Sharadchandra Patel, MD, MS** Palazzo A-C *(No CME Awarded)*
1:00 p.m. - 2:00 p.m.	*General Dermatology - Topic(s) TBA* **Camille Howard-Verovic, DO & Theresa Durchhalter, DO**
2:00 p.m. - 3:00 p.m.	*Cutaneous Venous Hypertension: From Spider Veins to Ulcers* **Ronald Bush, MD**
3:00 p.m. - 3:30 p.m.	Break with Exhibitors Palazzo D
3:30 p.m. - 4:30 p.m.	*Neutrophilic Dermatoses: Practical Aspects* **Joseph Jorizzo, MD**
4:30 p.m. - 5:30 p.m.	*Pediatric Dermatology* **Shoni Rozenberg, DO**
5:30 p.m. - 6:30 p.m.	Celgene Product Theater Palazzo A-C *(No CME Awarded)*

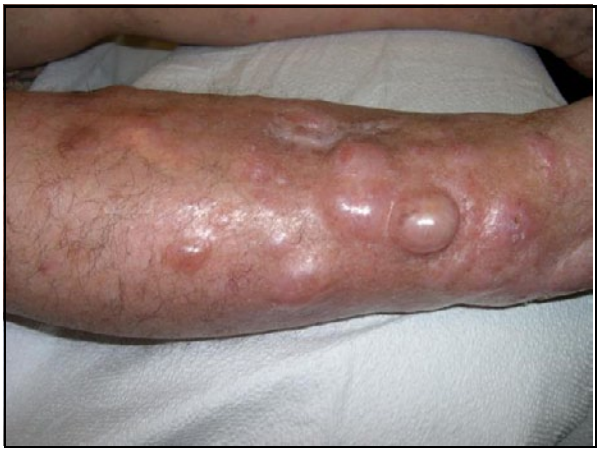
Dermatopathology and Immunohistochemistry, the Future of Targeted Therapy in Skin Disease

Paolo Romanelli, M.D.
Professor Dermatology and Cutaneous Surgery
Dermatopathology
Director JMH Psoriasis Biologics Clinic
Dr. Phillip Frost Department of Dermatology
L. Miller School of Medicine, University of Miami

I do not have any relevant relationships with industry.

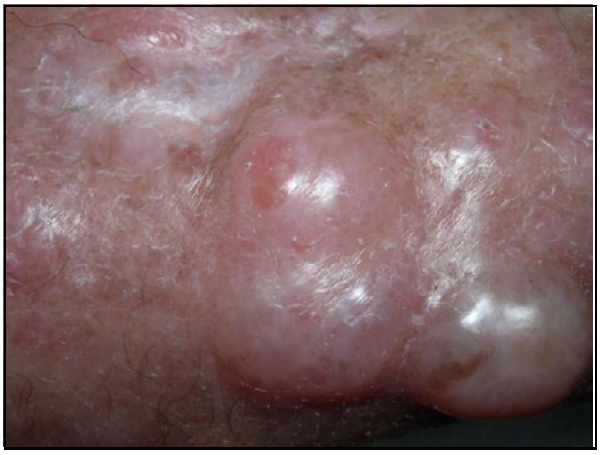


- 83 year old woman
- Location lower extremities
- Giant skin colored tumors
- Duration 9 years



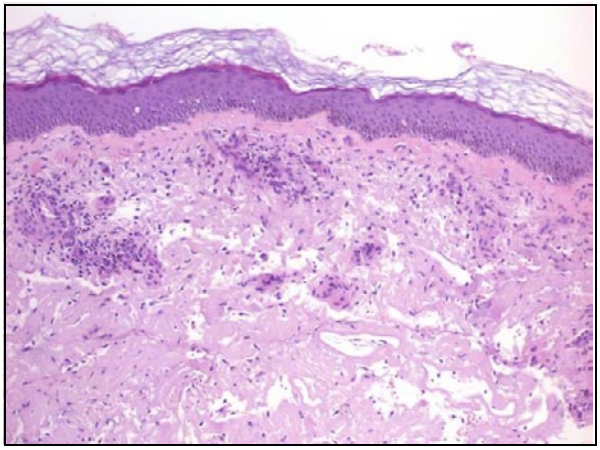
Clinical course

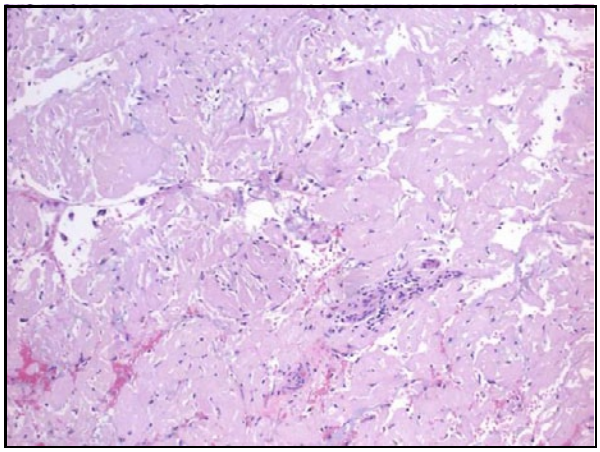
- Lower extremities surgery approximately 12 years ago
- Non tender, gradually enlarging, skin colored nodules
- Punch biopsy 2006 read as “Scar tissue”
- Punch biopsy for bacterial, fungal and mycobacteria cultures: Heavy growth of Gram– bacteria, negative for fungi and atypical mycobacteria

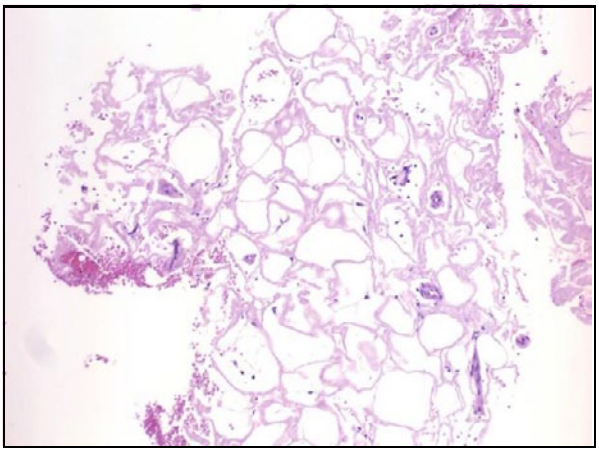


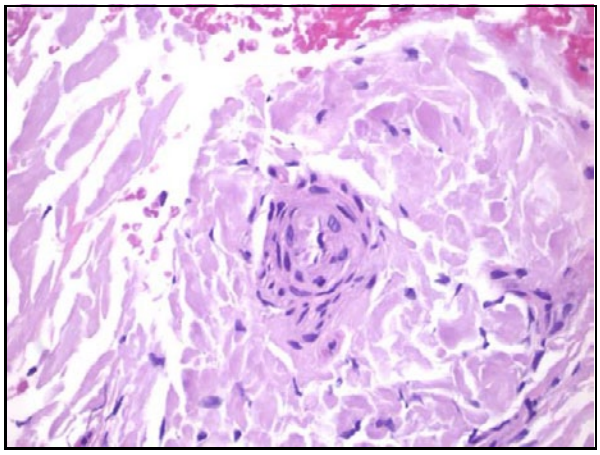
Clinical course

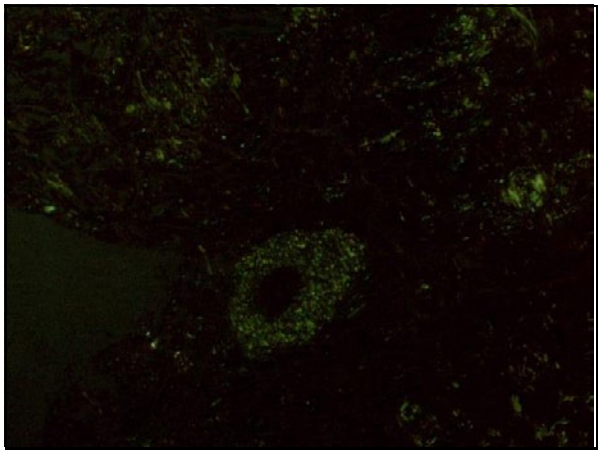
- Patient treated with Clarythromycin 500 mg bid and Doxycyclin 100 mg qd for 6 months with no improvement
- Patient comes back for follow up appointment
- Re-biopsy

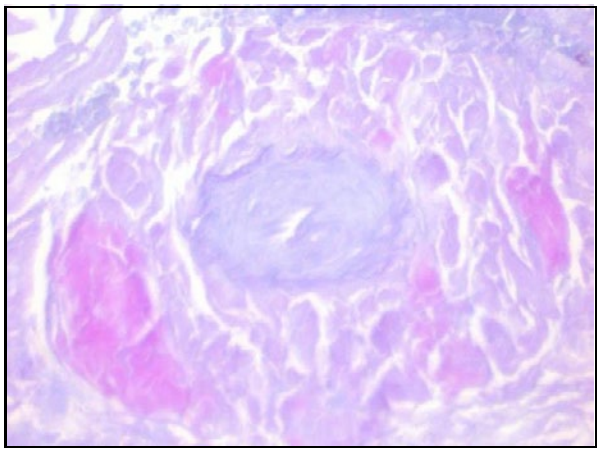








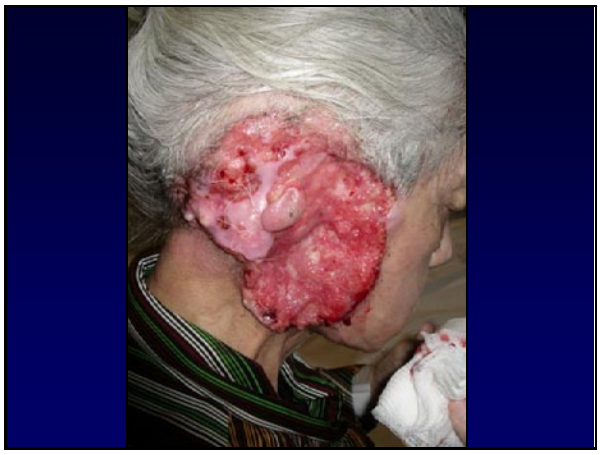




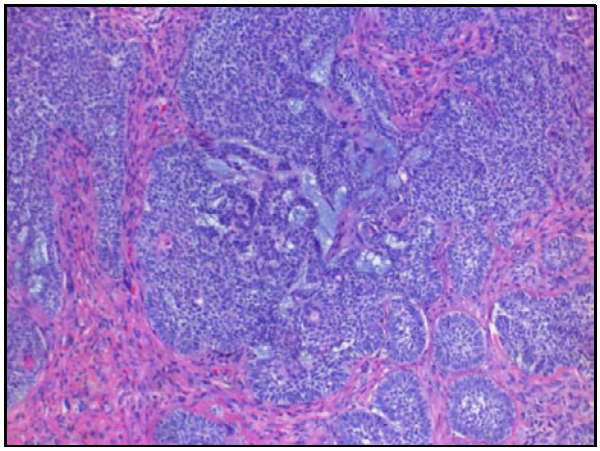
Diagnosis

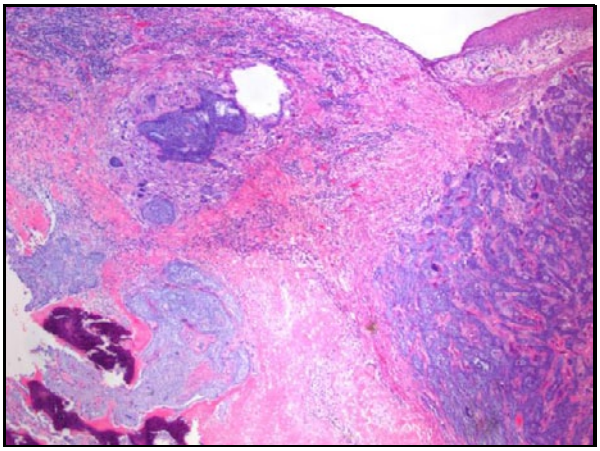
Nodular Amyloid	Soft Tissue Amyloidoma
• Solitary or multiple lesions	Solitary lesion
• AL amyloid	AA or AL amyloid
• Plasma cells +++	Plasma cells +/-
• Amyloid rings	No amyloid rings
• +/- AL systemic	No systemic amyloid
• Amyloid deposits respect normal tissue	Tumoral amyloid replacing normal tissue
• - Foreign Body Giant cells	+ Foreign Body Giant cells
• +/- Calcification	+ Calcification

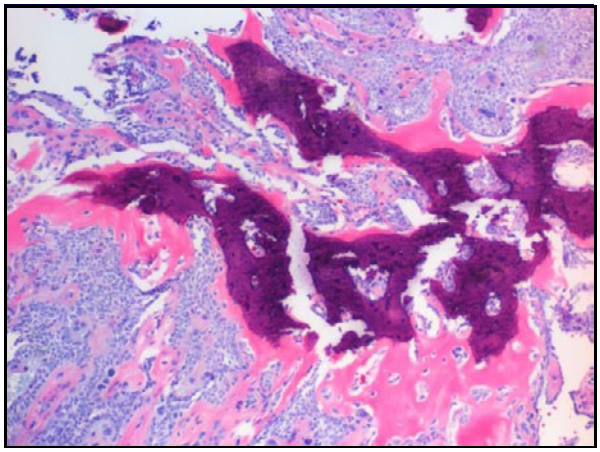
- Int J Dermatol. 2010 Feb;49(2):229-30.
- **Primary localized cutaneous nodular amyloidosis associated with CREST (calcinosis, Raynaud's phenomenon, esophageal motility disorders, sclerodactyly, and telangiectasia) syndrome.**
- Shiman M, Ricotti C, Miteva M, Kerdel F, Romanelli P.



- 85 year old woman
- Location: Right Scalp
- **Giant** ulcerated tumor
- Duration: 7 years
- Clinical diagnosis: BCC, SCC, AFX ?





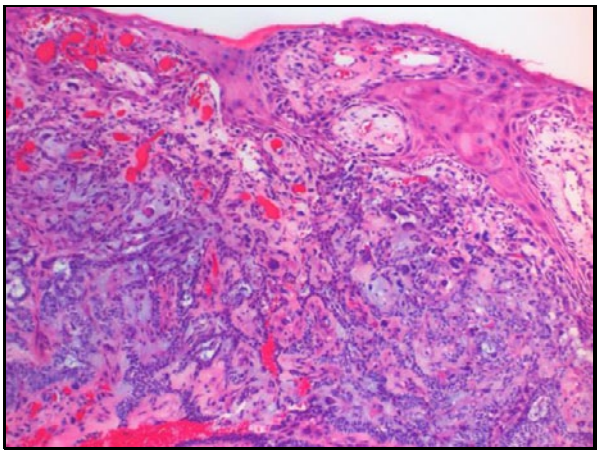


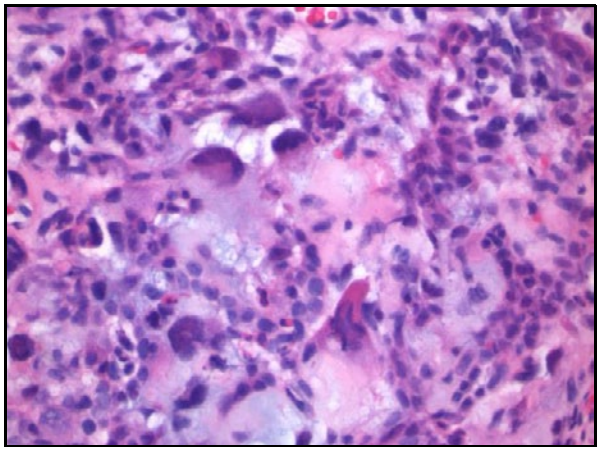
Histopathology

- Biphasic tumor composed of two closely intermingled components.
- The epithelial element consisted of islands of basaloid cells with brisk mitotic grade and dyskeratotic cells representing Basal Cell Carcinoma.
- The stromal component showed cells arranged in fascicular pattern with occasional mitoses, pleomorphism and anaplastic features mainly consistent with fibrosarcoma/osteosarcoma.

Diagnosis

- Primary Carcinosarcoma (Metaplastic Carcinoma) of the skin



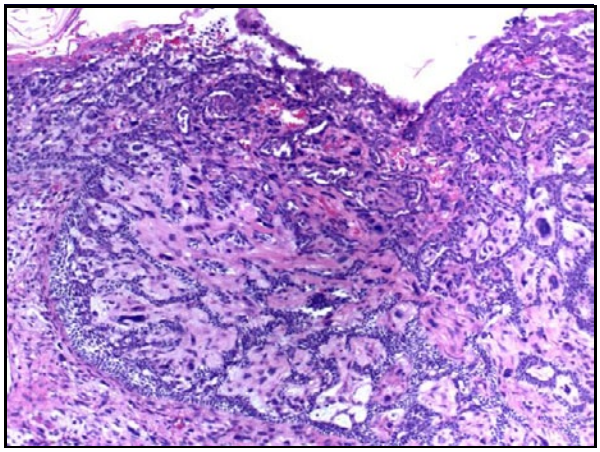


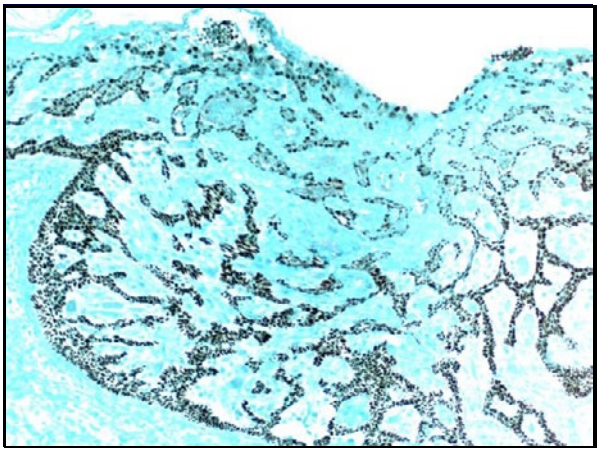
Immunohistochemistry

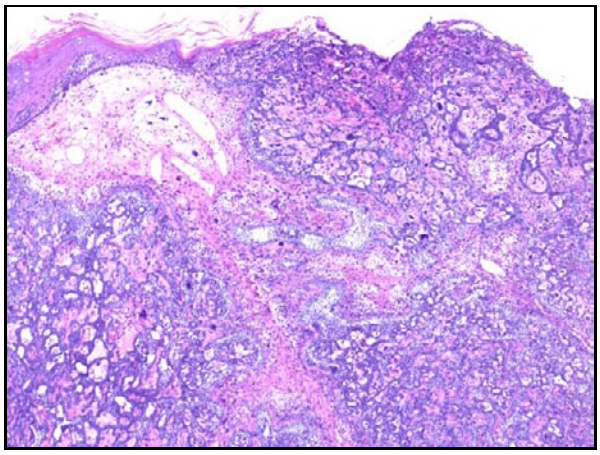
- Basaloid component:
  - positive for Keratin, p63, Ki-67 and p53
  - negative for S-100 and HCD
    (High Molecular Caldesmon)

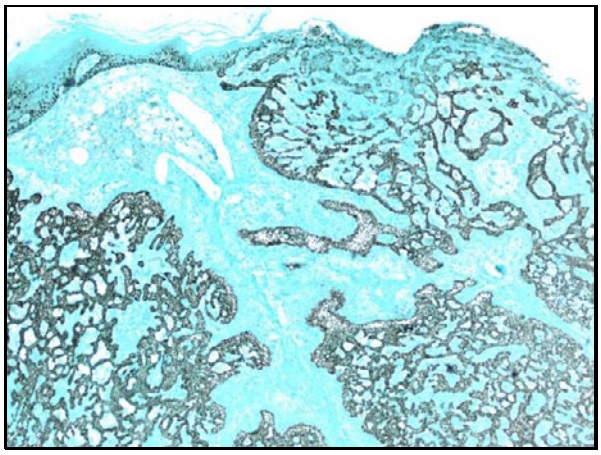
Stromal component:

- Positive (strongly) for p53, keratin (slightly)
- Negative for p63, S-100, and HCD

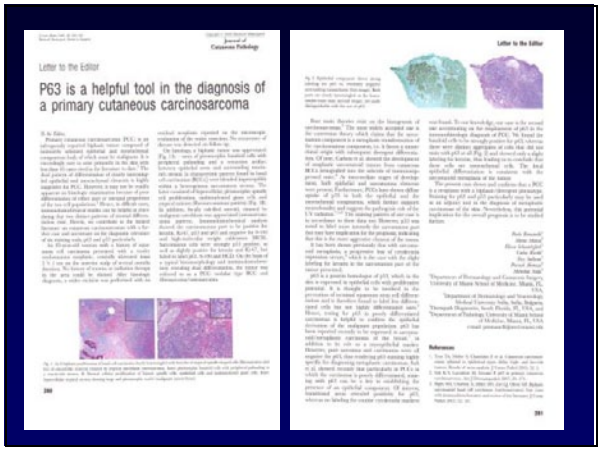








- J Cutan Pathol. 2009 Feb;36(2):280-2.
- **P63 is a helpful tool in the diagnosis of a primary cutaneous carcinosarcoma.**
- Romanelli P, Miteva M, Schwartzfarb E, Ricotti C, Sullivan T, Abenoza P, Nadji M.



Letter to the Editor

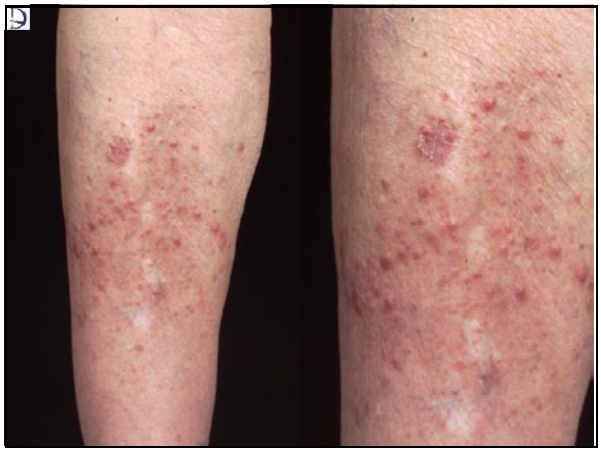
P63 is a helpful tool in the diagnosis of a primary cutaneous carcinosarcoma

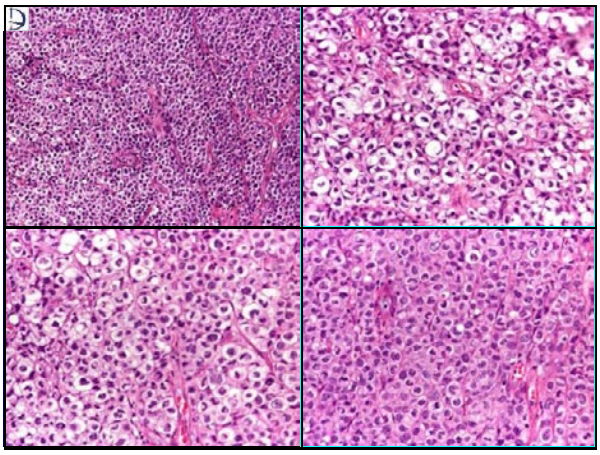
Helmut Kerl, M.D.

Professor and Chairman

Department of Dermatology and Dermatopathology,

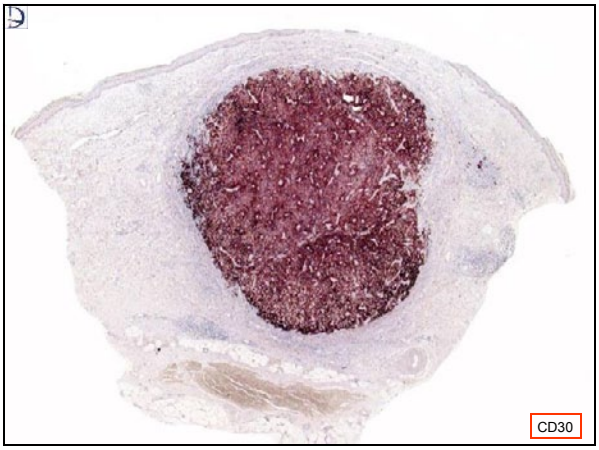
Medical University Graz Austria

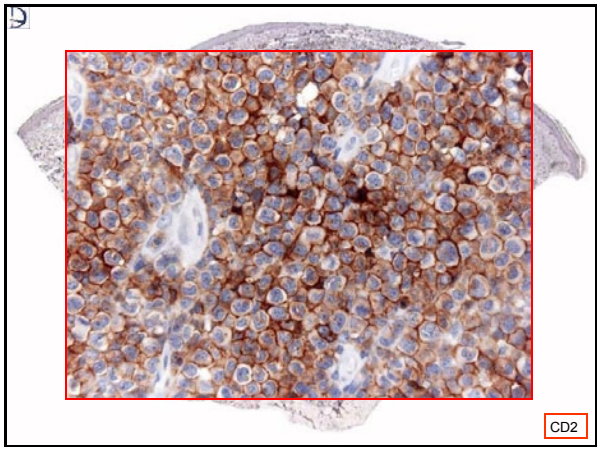




pan-CK-
AE1/AE3-
Vimentin+
S100-
HMB-45-
Melan-A-
CD45 (LCA)-

?





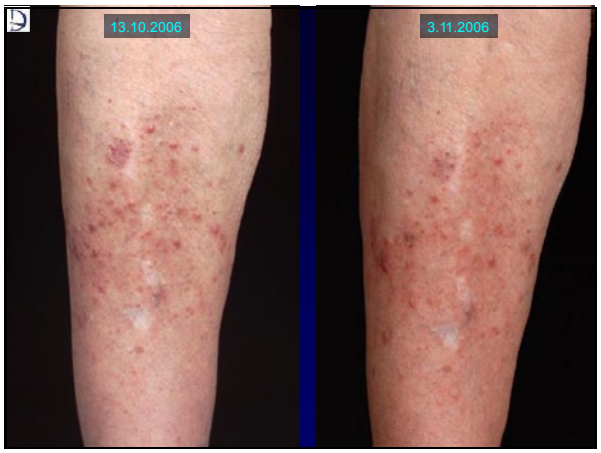
Anaplastic large - cell lymphoma

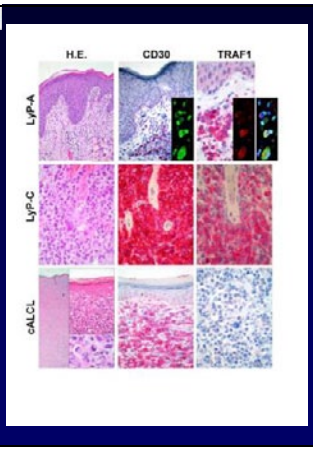
?

Lymphomatoid Papulosis
Type C

Lymphomatoid Papulosis

- Histologic types *(A, B, C)*
- Rare histologic variants *(follicular, syringotropic, etc.)*
- Clinical variants *(regional, ALCL-like, etc.)*
- Represents part of a spectrum of cutaneous CD30+ lymphoproliferative disorders *(ALCL – LyP)*

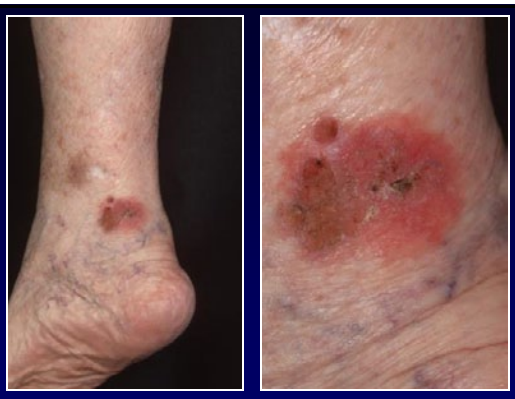




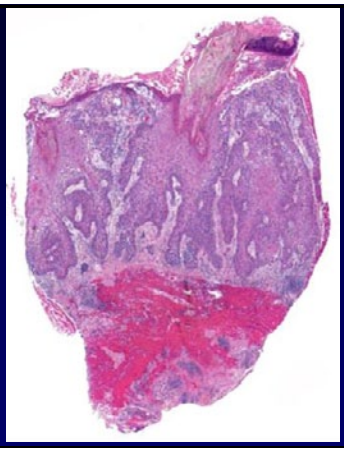
TRAF 1
Tumor necrosis factor receptor-associated factors

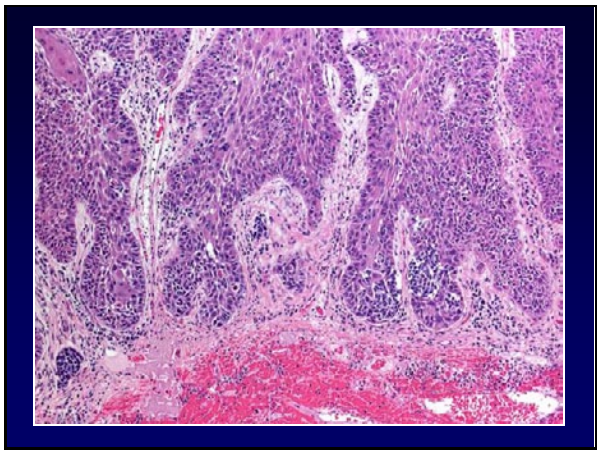
DD: Ly P vs LCAL

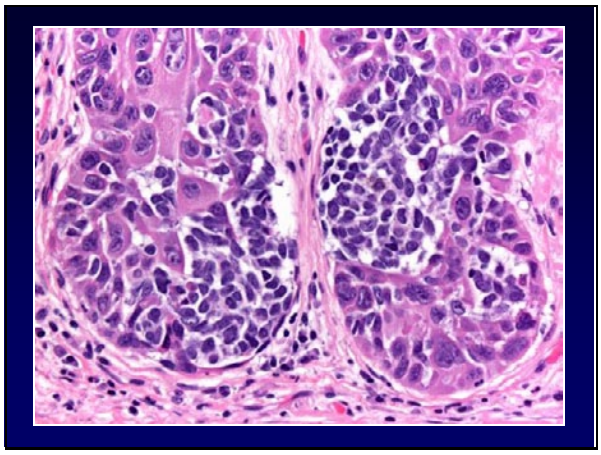
Ch. Assaf, JID 2007

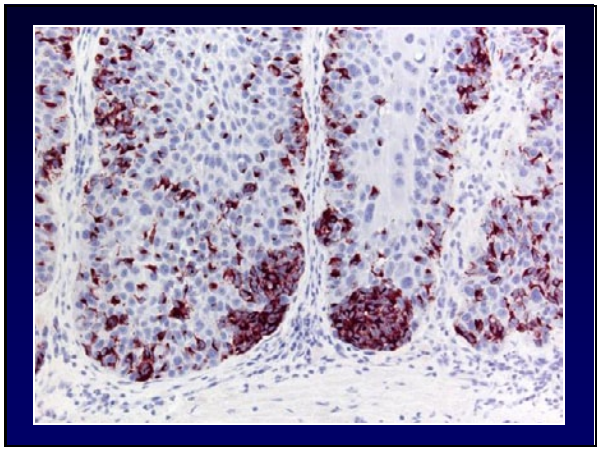


85-year-old woman





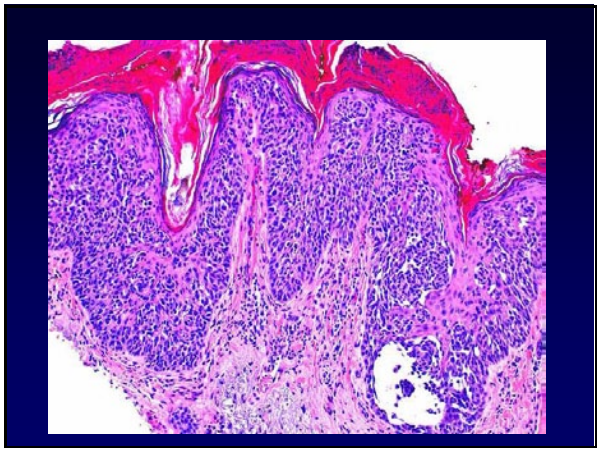


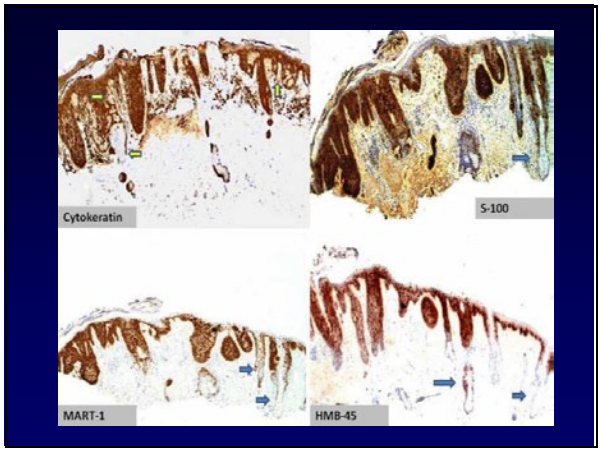


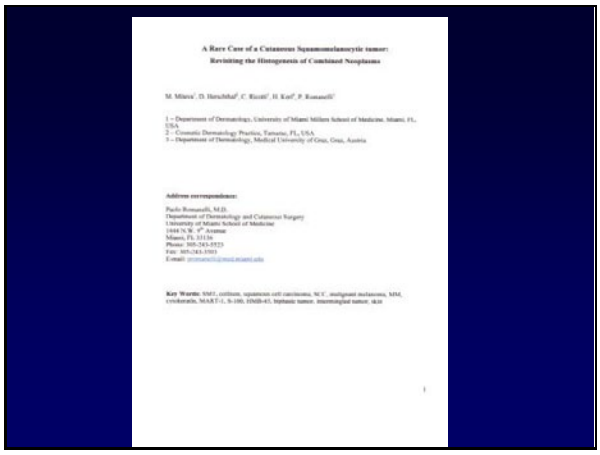
C A M E L

CARCINOMA + MELANOMA

Melanomatous Carcinoma
Squamo-Melanocytic Tumor
Pigmented SCC
Parasitism of SCC by MM
Collision Tumor







A Rare Case of a Cutaneous Squamomelanocytic tumor:
Revisiting the Histogenesis of Combined Neoplasms

M. Miteva[1], D. Herschthal[2], C. Ricotti[3], H. Kerl[3], P. Romanelli[1]

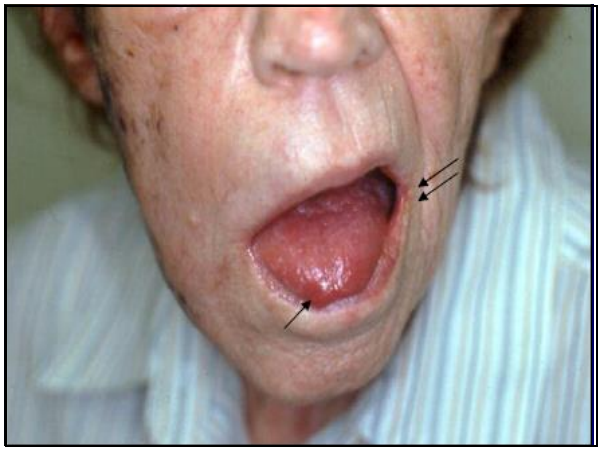
1 – Department of Dermatology, University of Miami Miller School of Medicine, Miami, FL, USA
2 – Cosmetic Dermatology Practice, Tamarac, FL, USA
3 – Department of Dermatology, Medical University of Graz, Graz, Austria

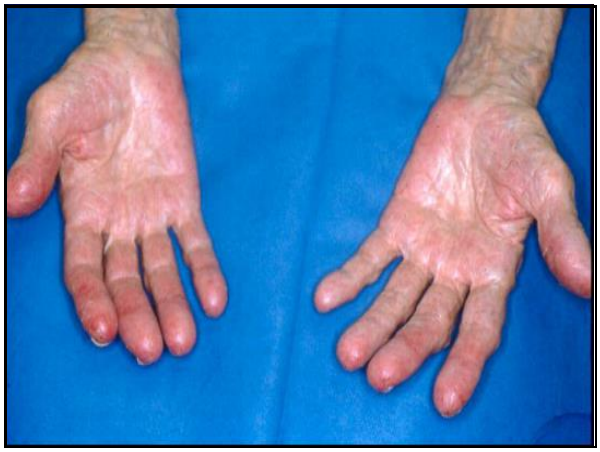
Address correspondence:

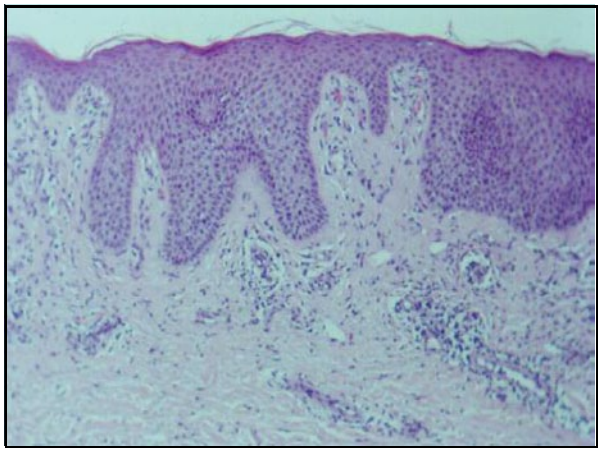
Paolo Romanelli, M.D.
Department of Dermatology and Cutaneous Surgery
University of Miami School of Medicine
1600 N.W. 10th Avenue
Miami, FL 33136
Phone: 305-243-5523
Fax: 305-243-3503
E-mail: promanelli@med.miami.edu

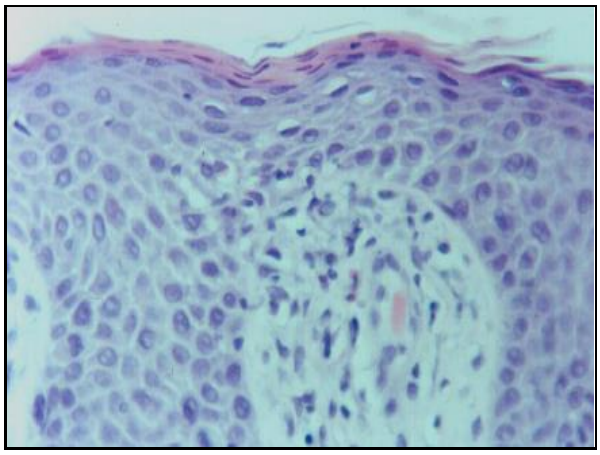
Key Words: SMT, collision, squamous cell carcinoma, SCC, malignant melanoma, MM, cytokeratin, MART-1, S-100, HMB-45, biphasic tumor, intermingled tumor, skin

- Am J Dermatopathol. 2009 Aug;31(6):599-603.
- **A rare case of a cutaneous squamomelanocytic tumor: revisiting the histogenesis of combined neoplasms.**
- Miteva M, Herschthal D, Ricotti C, Kerl H, Romanelli P









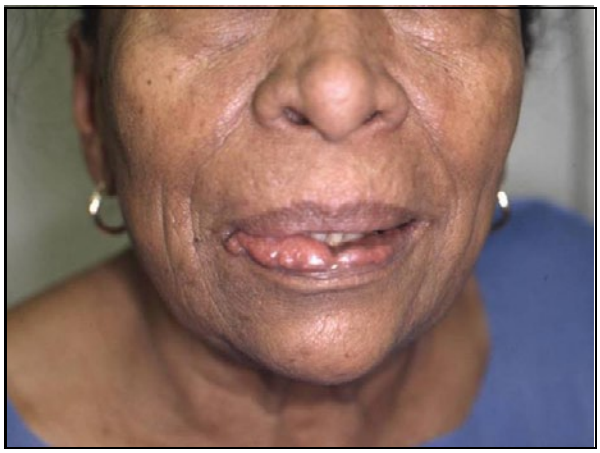
Page 5 of 11 International Journal of Dermatology

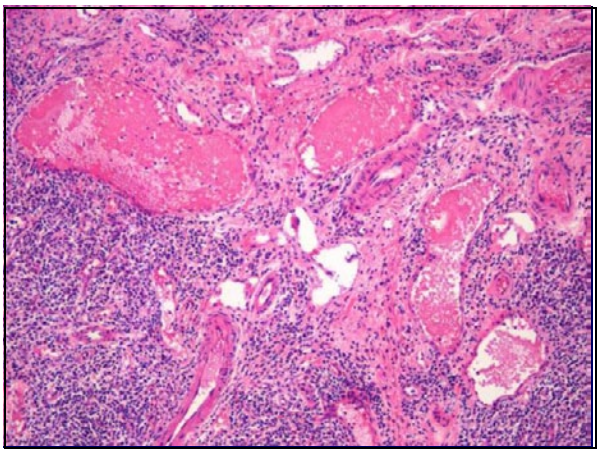
NECROLYTIC MIGRATORY ERYTHEMA ASSOCIATED WITH NONFUCTIONAL ISLIET CELL TUMOR

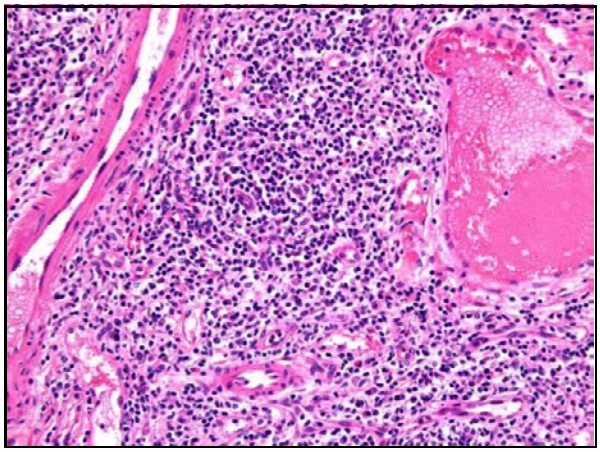
Janelle Vega, MD;[a] Navid Bouzari, MD;[b] Paolo Romanelli, MD;[b] Emma L. Lanuti, BS;[b] Pasquale Benedetto, MD;[c] Andy Green, MD;[b] Franco Rongioletti, MD;[d] Francisco Kerdel, MD[b]

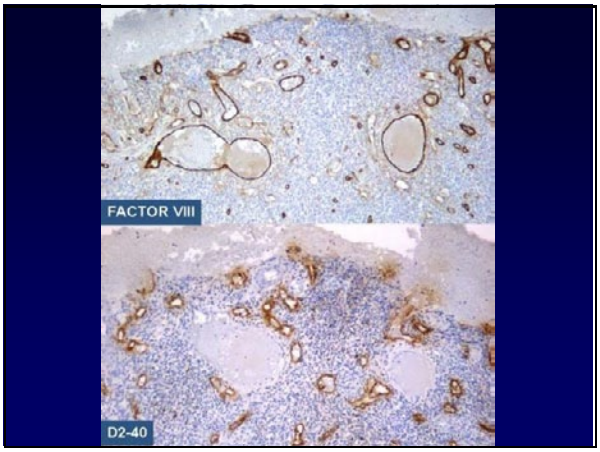
a. University of Florida, School of Medicine
b. Department of Dermatology and Cutaneous Surgery, University of Miami, Miller School of Medicine, Miami, Florida
c. Department of Internal Medicine, University of Miami, Miller School of Medicine, Miami, Florida
d. Section of Dermatology, DISEM, University of Genoa, Italy

Corresponding Author:
Paolo Romanelli, M.D.
Department of Dermatology and Cutaneous Surgery
L. Miller School of Medicine, University of Miami
1444 N.W. 9th Avenue
Miami, Fl 331 36
(e-mail: promanelli@med.miami.edu)









- J Cutan Pathol. 2009 Dec;36(12):1316-22
- **D2-40 highlights lymphatic vessel proliferation of angiolymphoid hyperplasia with eosinophilia.**
- Miteva M, Galimberti ML, Ricotti C, Breza T, Kirsner R, Romanelli P.
- Department of Dermatology and Cutaneous Surgery, University of Miami School of Medicine, Miami, FL 33136, USA

UM Rapid Wound Pathology Service

MILLER SCHOOL OF MEDICINE
UNIVERSITY OF MIAMI

25 US wound healing centers >300 cases

- venous ulcers (31)
- vasculitis (12)
- vasculopathy (10)
- mixed (9)
- diabetic (9)
- carcinomas (7)
- pressure (7)
- hypertensive (6)
- infectious (5)
- calciphylaxis (CUA) (4)
- radiation ulcers (5)
- granulomatous ulcers (3)
- factitial (3)
- others (37) (Amyloidosis, B.Pemphigoid etc)


DERMATOPATHOLOGY LABORATORY

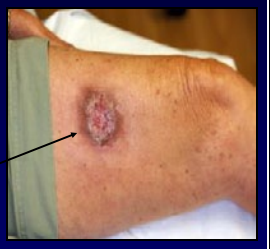
PHYSICIANS AND TOTAL BIOPSIES FROM WOUND HEALING CENTERS

National Healing

Biopsy is a consult with a pathologist
The consultant matters (or the Algorithm matters)

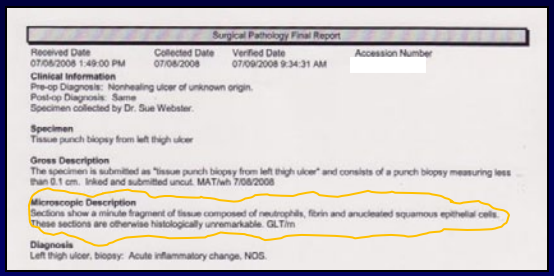
- **65 year old woman from Ohio**
- **otherwise healthy**
- **3 m. h/o a left thigh ulcer, that started as a "pimple which eventually began to drain" unspecific cough and fatigue**
- **3 consequent antibiotics:**
  - Ciprofloxacin
  - Cephalexin
  - Amoxicillin

NO IMPROVEMENT



- referred to a Wound Center
- standard wound care treatment
- Bx: c/w chronic wound
- culture results: no growth
- **wound painful, enlarging**
- **4th antibiotic was initiated**

1st Biopsy Report


Surgical Pathology Final Report

Received Date 07/08/2008 1:49:00 PM
Collected Date 07/08/2008
Verified Date 07/09/2008 9:34:31 AM
Accession Number

Clinical Information
Pre-op Diagnosis: Nonhealing ulcer of unknown origin.
Post-op Diagnosis: Same
Specimen collected by Dr. Sue Webster.

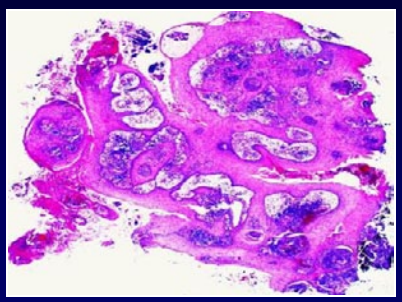
Specimen
Tissue punch biopsy from left thigh ulcer

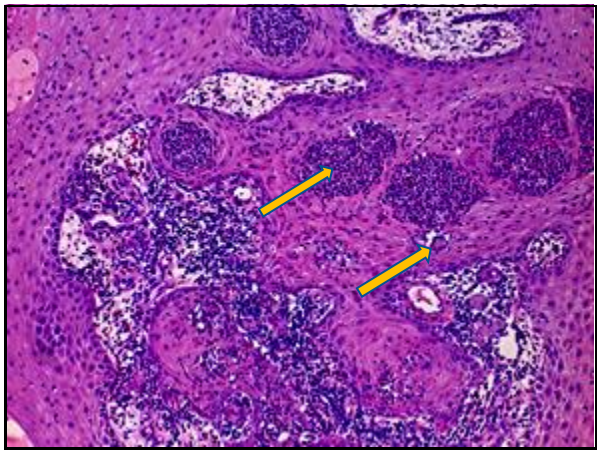
Gross Description
The specimen is submitted as "tissue punch biopsy from left thigh ulcer" and consists of a punch biopsy measuring less than 0.1 cm. Inked and submitted uncut. MAT/wh 7/08/2008

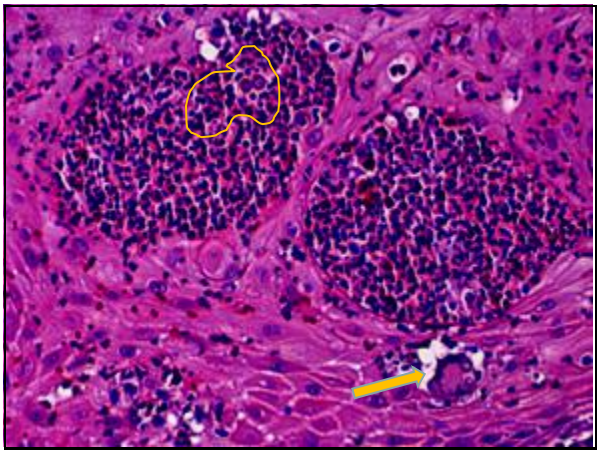
Microscopic Description
Sections show a minute fragment of tissue composed of neutrophils, fibrin and anucleated squamous epithelial cells. These sections are otherwise histologically unremarkable. GLT/rn

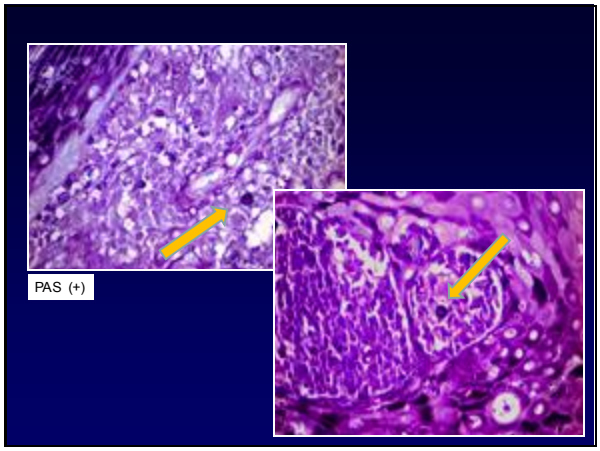
Diagnosis
Left thigh ulcer, biopsy: Acute inflammatory change, NOS.

H&E, low power









Our Report

DIAGNOSIS:

Thigh, Left Anterior

NORTH AMERICAN BLASTOMYCOSIS

Note: The PAS special stain highlights multiple thick-walled spores, some with a broad-based bud. AFB, Fite and B&B are negative.

CLINICAL DATA: MRSA vs. ENVENOMATION DOUBT CA, VASCULITIS, CHECK MARGINS

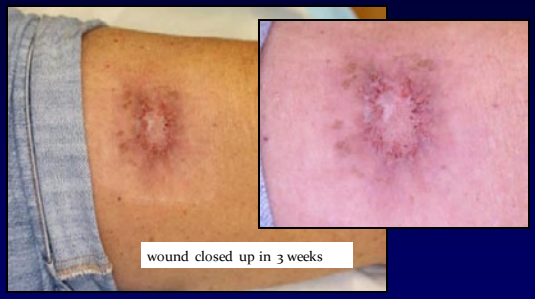
GROSS DESCRIPTION:
Received in formalin is an irregularly shaped fragment of skin measuring 1.7 x 0.5 x 0.4 cm. The specimen is divided into four pieces.

MICROSCOPIC DESCRIPTION:
There is marked pseudoepitheliomatous hyperplasia with multiple intraepidermal neutrophilic microabscesses. Within the neutrophilic abscesses there are thick-walled spores, some with broad-base bud. Within the surrounding dermis there is a diffuse mixed infiltrate of neutrophils, lymphocytes, histiocytes, plasmacells and multinucleated giant cells with no caseation.

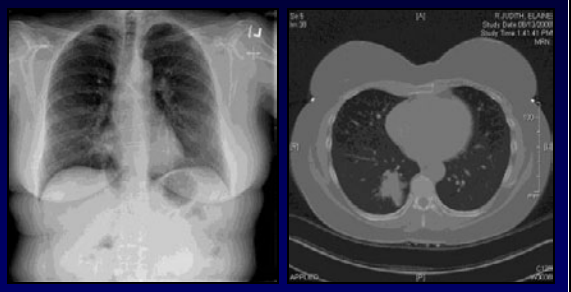
Final Diagnosis performed by
Paolo Romanelli, M.D.
Electronically signed 8/7/2008

- Rapid Wound Pathology Service: North American Blastomycosis
- Patient started on Itraconazole : a systemic regimen for 6-12 months
- CXR and Chest CT ordered (prior to and one month after start of therapy)

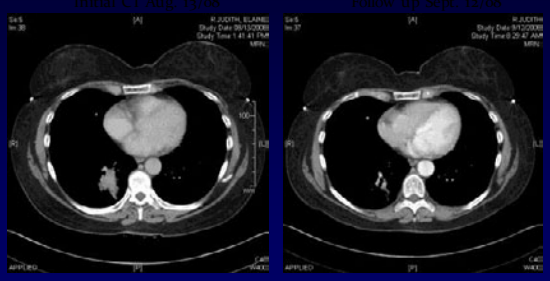
Follow -up Images



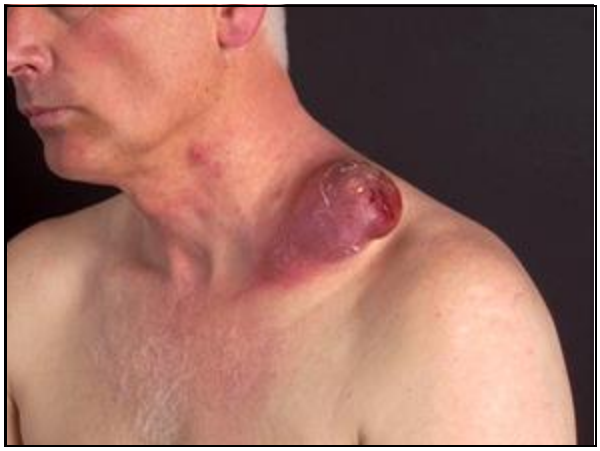
Chest X-ray and CT: R lower lobe process



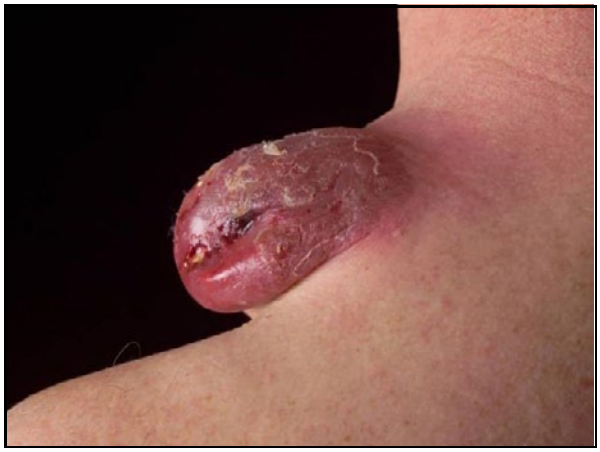
Follow-up CT

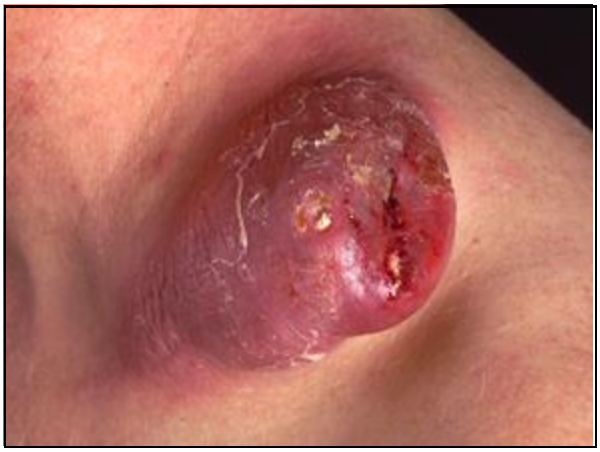


constitutional symptoms resolved completely



- 52-year-old man
- Location: Left clavicular region
- Large ulcerated nodule
- Duration: 7 years
- Clinical diagnosis: Sarcoma?; Lymphoma?





Clinical course

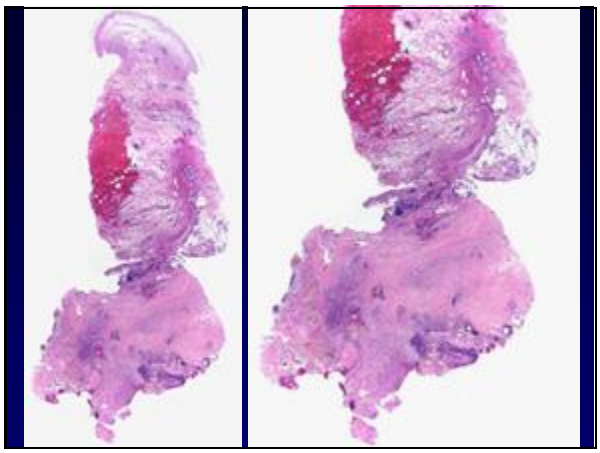
Preceeding total excision:

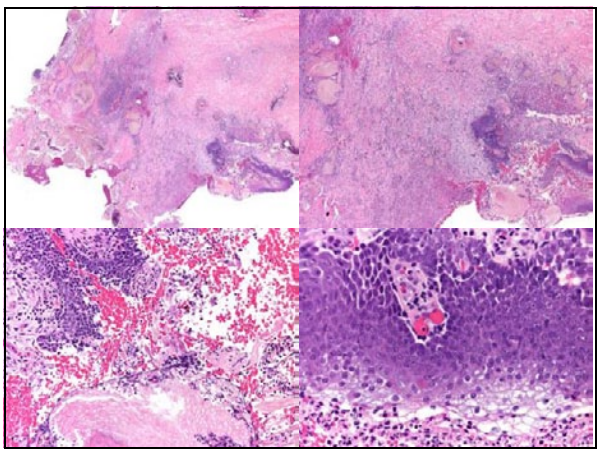
- Skin incisional biopsy
- Sonography
- Computer Tomography (CT)

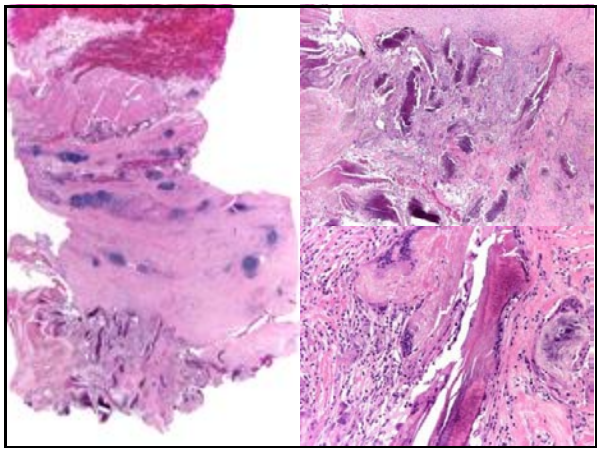
→ Plastic Surgery

Imaging

- Sonography:
  - ulcerated mass with copious calcification
  - hypervascularization at the periphery
- Computer Tomography (CT):
  - large, well-defined tumor (5x5,5x6 cm) with skin ulceration, abundant calcification
  - no bone involvement
  - abnormal left laterocervical lymphnode enlargement (1,4x1,3 cm)







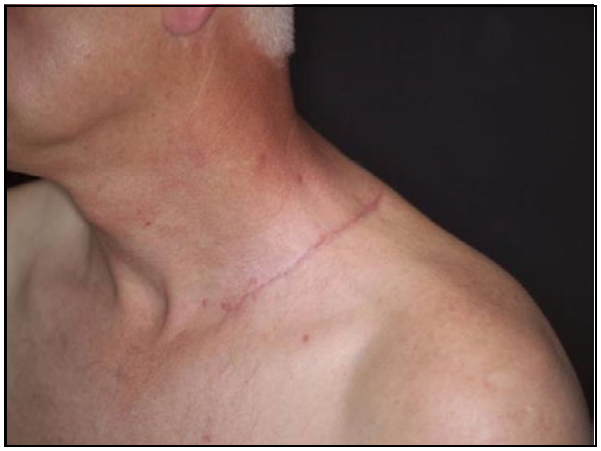
- Histopathologic examination:
  - proliferation of cells resembling basal (matrical) cells of the epidermis and a rather predominant component of ghost (shadow) cells with calcification and metaplastic ossification. No focus to suggest a malignant nature.

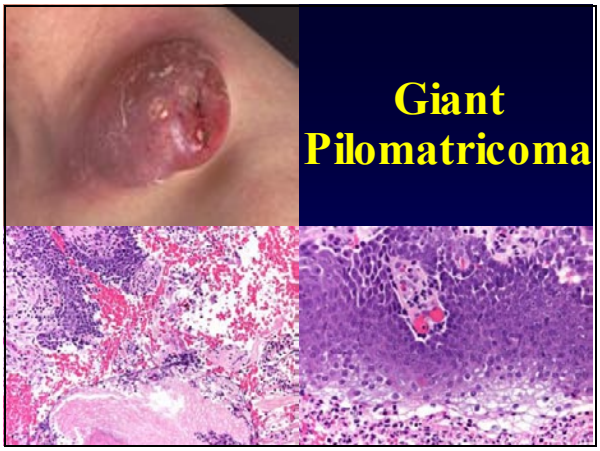
Diagnosis

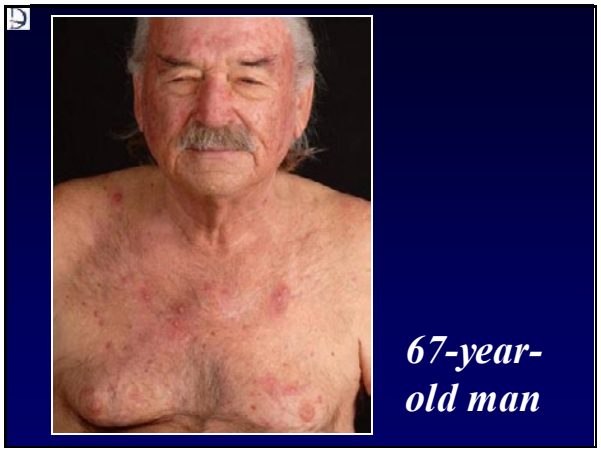
Giant Pilomatricoma

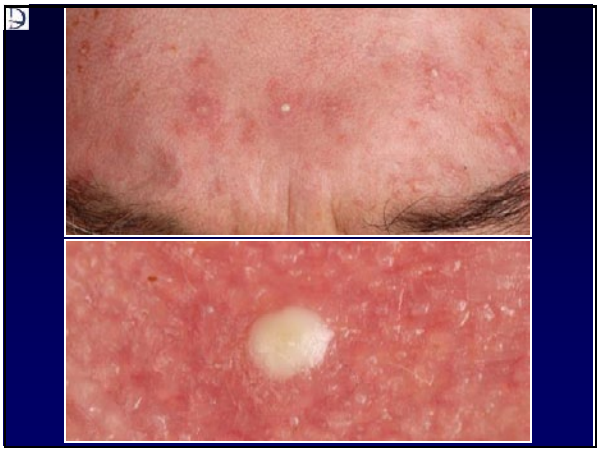
(Giant calcifying epithelioma of Malherbe)

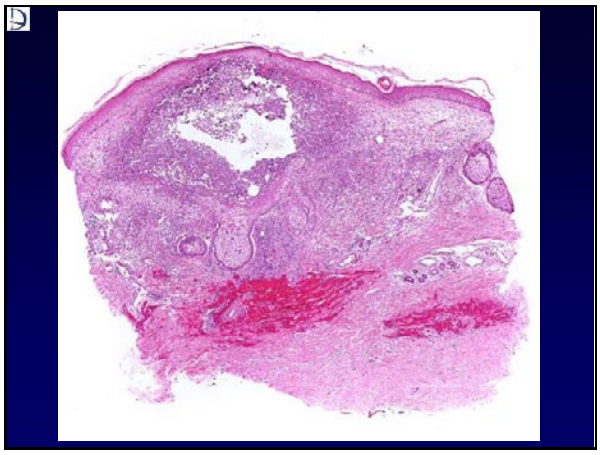
Results after Plastic Surgery

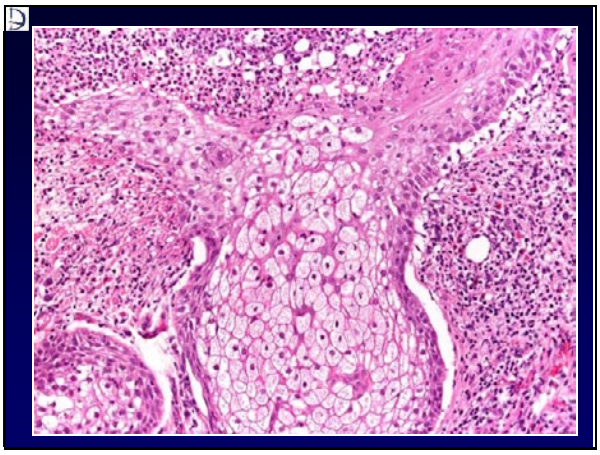


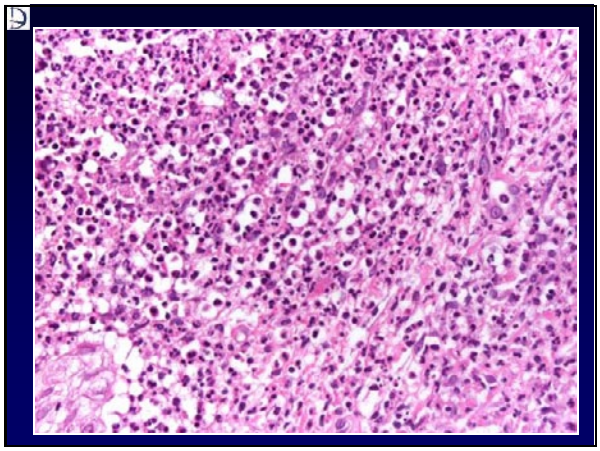




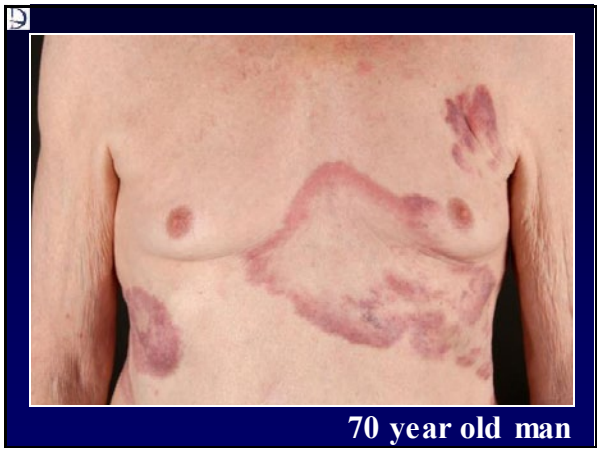




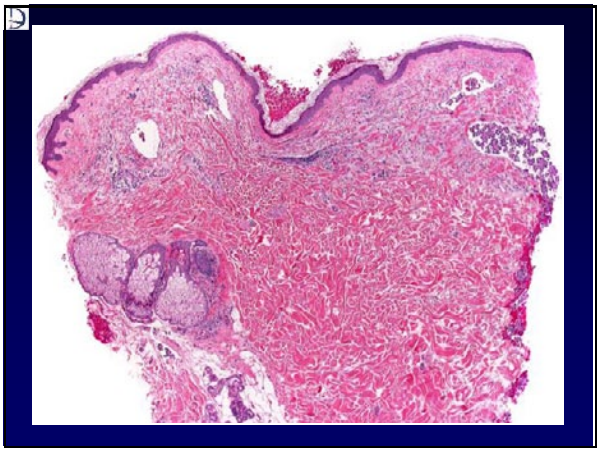


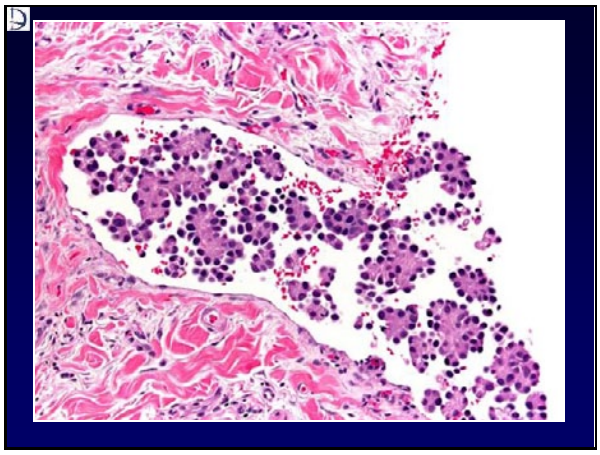


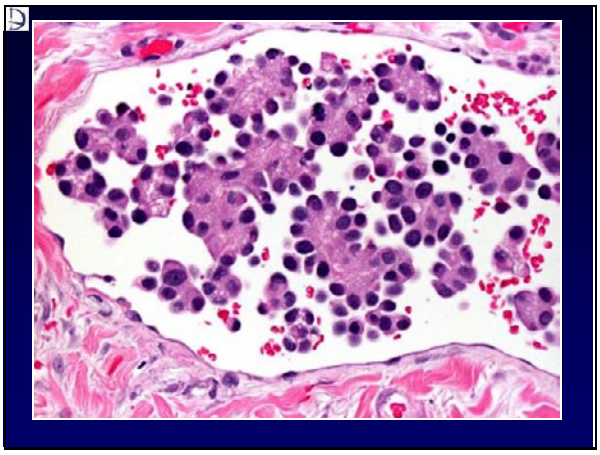
Acneiform eruption induced by Everolimus (Certican®)



70 year old man





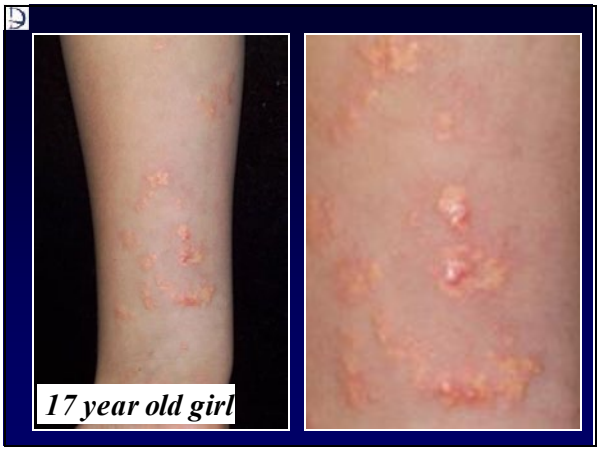


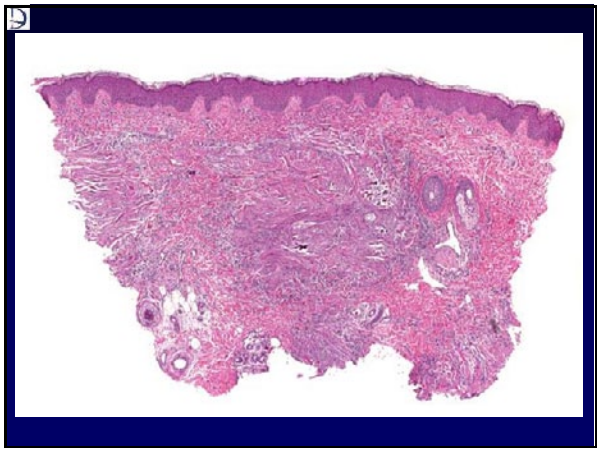
Metastatic carcinoma

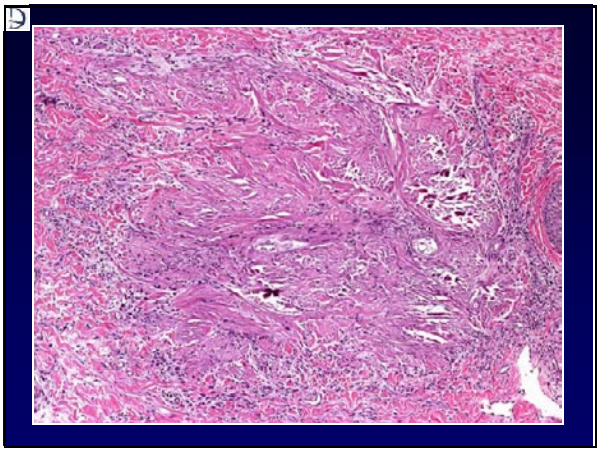
(micropapillary variant)

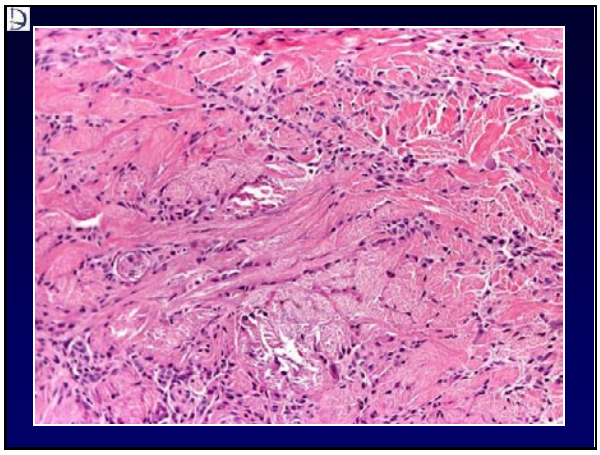
of the

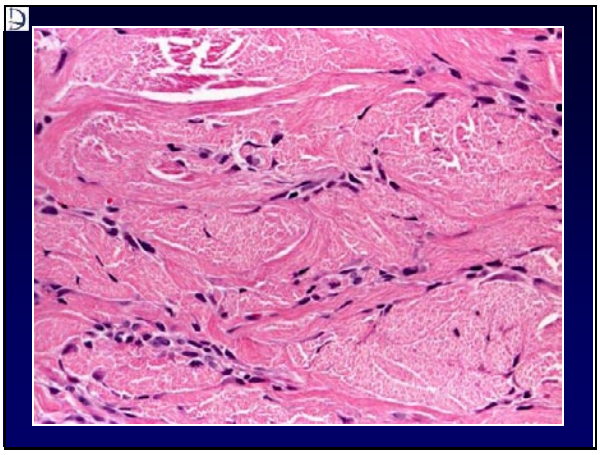
urinary bladder to skin

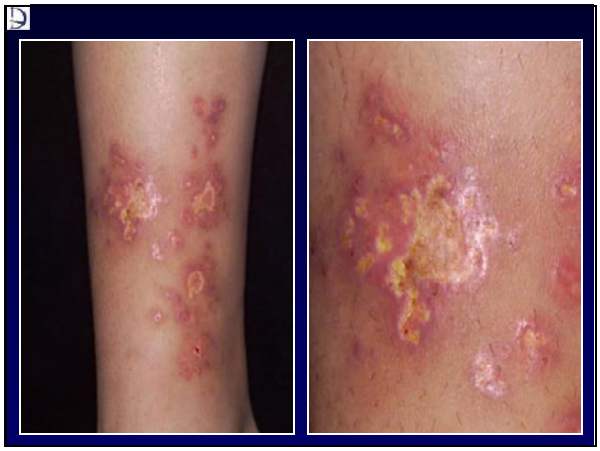


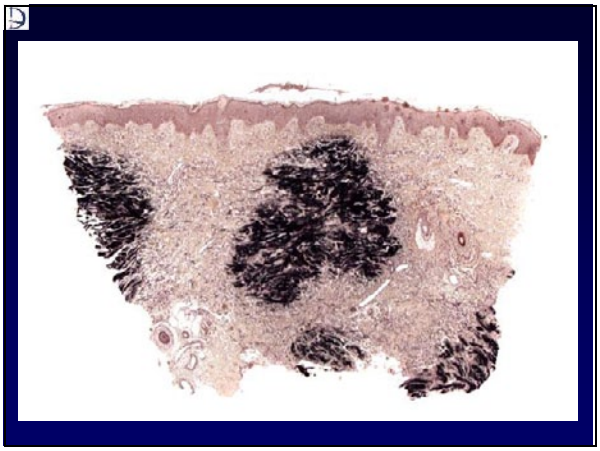












Calcinosis Cutis

Infusion and extravasation of calcium gluconate

UM Rapid Wound Pathology Service

MILLER SCHOOL OF MEDICINE
UNIVERSITY OF MIAMI

25 US wound healing centers >300 cases

- venous ulcers (31)
- vasculitis (12)
- vasculopathy (10)
- mixed (9)
- diabetic (9)
- carcinomas (7)
- pressure (7)
- hypertensive (6)
- infectious (5)
- calciphylaxis (CUA) (4)
- radiation ulcers (5)
- granulomatous ulcers (3)
- factitial (3)
- others (37) (Amyloidosis, B.Pemphigoid etc


DERMATOPATHOLOGY LABORATORY

PHYSICIANS AND TOTAL BIOPSIES FROM WOUND HEALING CENTERS

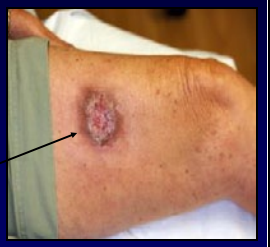
National Healing

Biopsy is a consult with a pathologist
The consultant matters (or the Algorithm matters)

- 65 year old woman from Ohio
- otherwise healthy
- 3 m. h/o a left thigh ulcer, that started as a "pimple which eventually began to drain" unspecific cough and fatigue
- 3 consequent antibiotics:
  - Ciprofloxacin
  - Cephalexin
  - Amoxicillin

NO IMPROVEMENT

- referred to a Wound Center
- standard wound care treatment
- Bx: c/w chronic wound
- culture results: no growth
- wound painful, enlarging
- 4th antibiotic was initiated



1st Biopsy Report

Surgical Pathology Final Report

Received Date	Collected Date	Verified Date	Accession Number
07/08/2008 1:49:00 PM	07/08/2008	07/09/2008 9:34:31 AM	

Clinical Information
Pre-op Diagnosis: Nonhealing ulcer of unknown origin.
Post-op Diagnosis: Same
Specimen collected by Dr. Sue Webster.

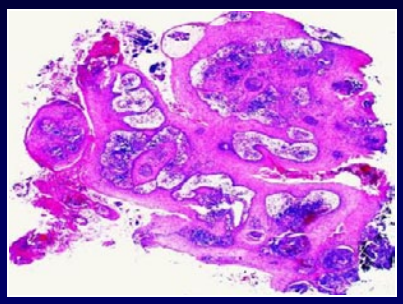
Specimen
Tissue punch biopsy from left thigh ulcer

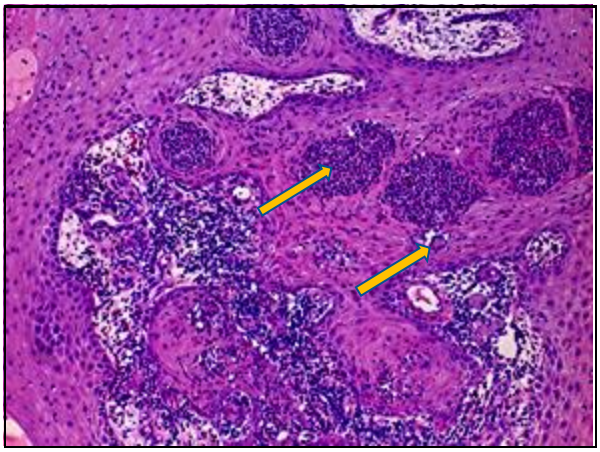
Gross Description
The specimen is submitted as "tissue punch biopsy from left thigh ulcer" and consists of a punch biopsy measuring less than 0.1 cm. Inked and submitted uncut. MAT/wh 7/08/2008

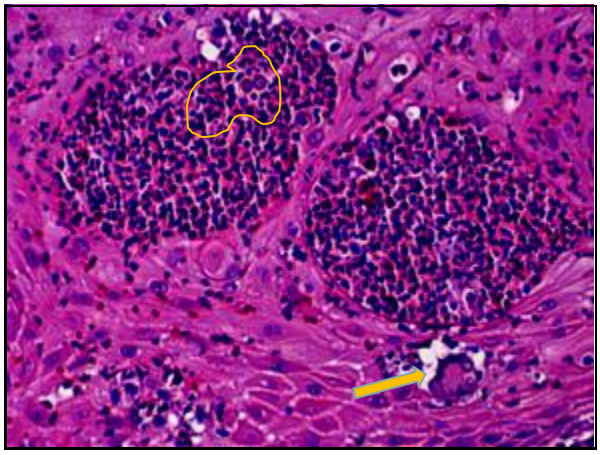
Microscopic Description
Sections show a minute fragment of tissue composed of neutrophils, fibrin and anucleated squamous epithelial cells. These sections are otherwise histologically unremarkable. GLT/m

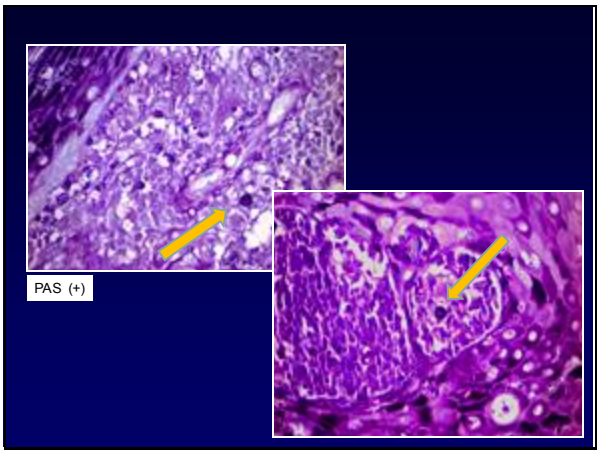
Diagnosis
Left thigh ulcer, biopsy: Acute inflammatory change, NOS.

H&E, low power









Our Report

DIAGNOSIS:

Thigh, Left Anterior

NORTH AMERICAN BLASTOMYCOSIS

Note: The PAS special stain highlights multiple thick-walled spores, some with a broad-based bud. AFB, Fite and B&B are negative.

CLINICAL DATA: MRSA vs. ENVENOMATION DOUBT CA, VASCULITIS, CHECK MARGINS

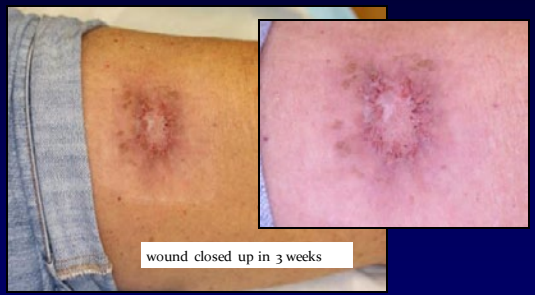
GROSS DESCRIPTION:
Received in formalin is an irregularly shaped fragment of skin measuring 1.7 x 0.5 x 0.4 cm. The specimen is divided into four pieces.

MICROSCOPIC DESCRIPTION:
There is marked pseudoepitheliomatous hyperplasia with multiple intraepidermal neutrophilic microabscesses. Within the neutrophilic abscesses there are thick-walled spores, some with broad-base bud. Within the surrounding dermis there is a diffuse mixed infiltrate of neutrophils, lymphocytes, histiocytes, plasmacells and multinucleated giant cells with no caseation.

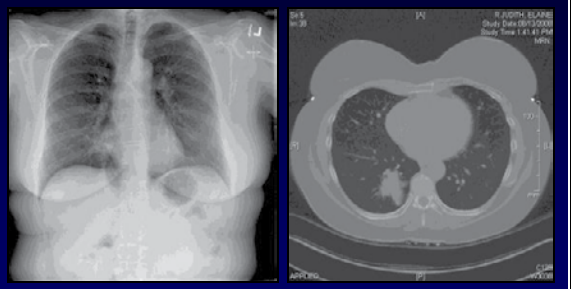
Final Diagnosis performed by
Paolo Romanelli, M.D.
Electronically signed 8/7/2008

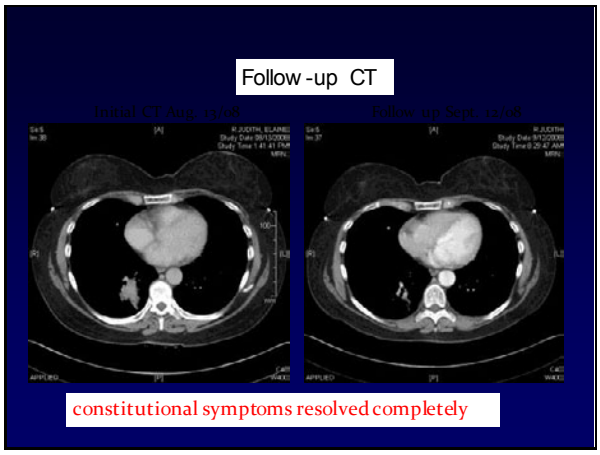
- Rapid Wound Pathology Service: North American Blastomycosis
- Patient started on Itraconazole : a systemic regimen for 6-12 months
- CXR and Chest CT ordered (prior to and one month after start of therapy)

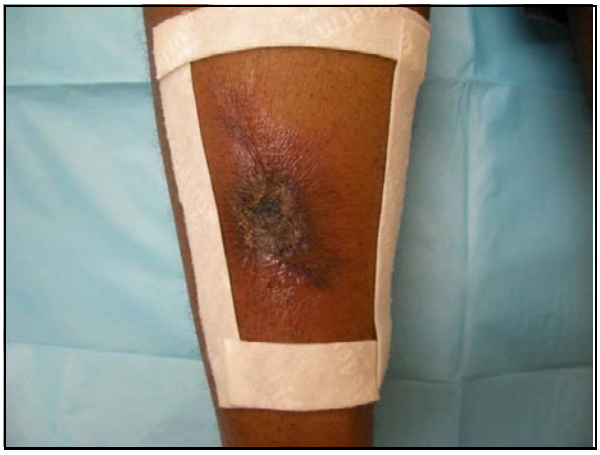
Follow-up Images

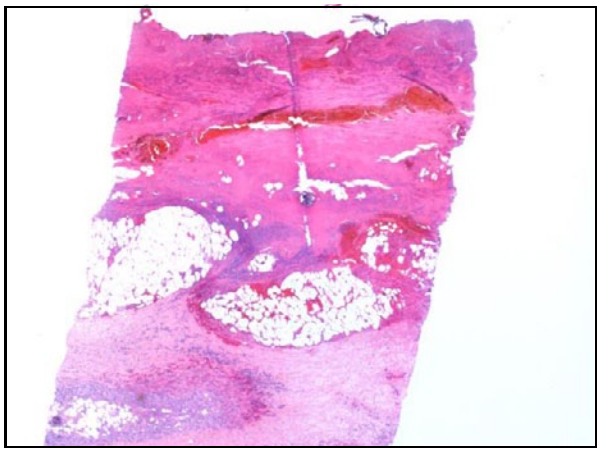


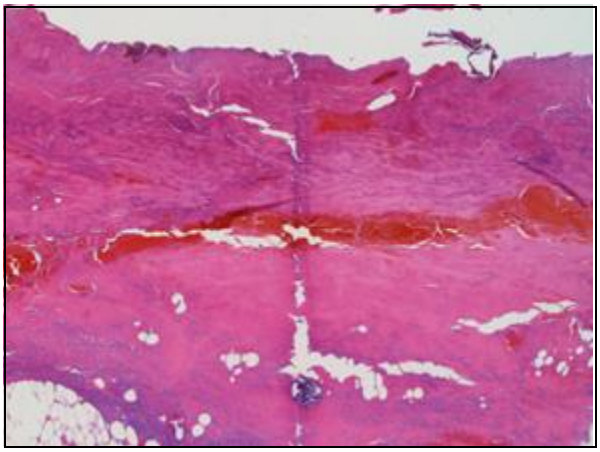
Chest X-ray and CT: R lower lobe process

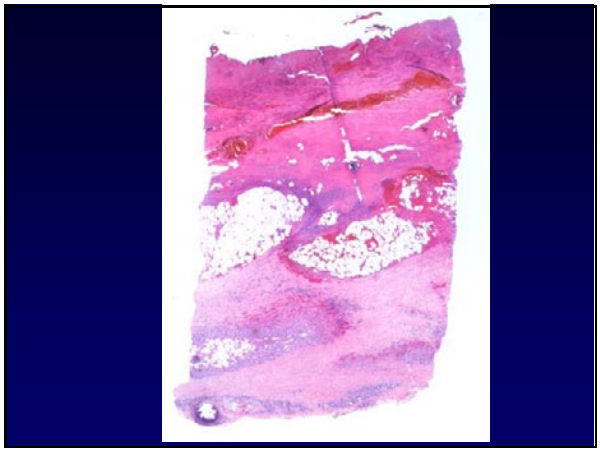


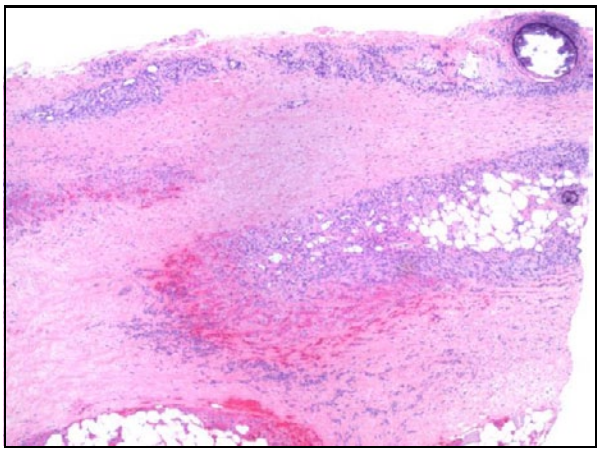

Follow -up CT
Initial CT Aug. 15/08
Follow-up Sept. 12/08
constitutional symptoms resolved completely

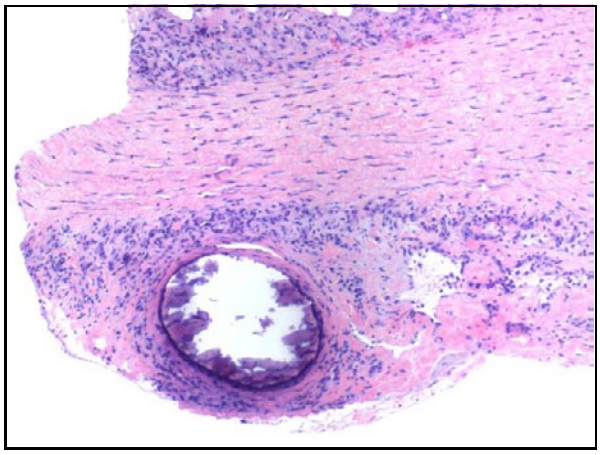


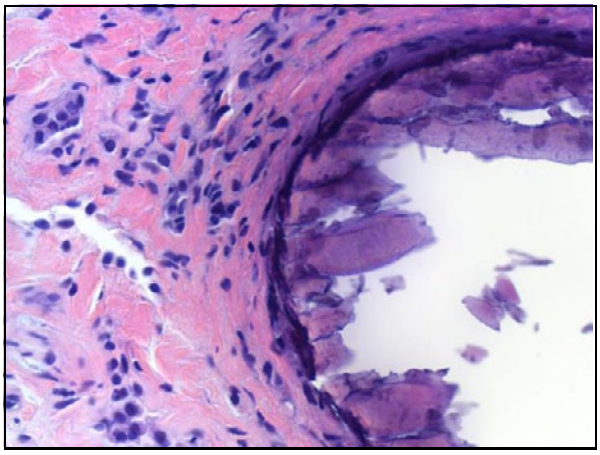












CUA

- Calcific Uremic Arteriolopathy (CUA), also known as Calciphylaxis, is a syndrome of cutaneous microvascular calcification of unknown etiology causing painful violaceous skin lesions.
- These then progress to non-healing ulcers and gangrene.

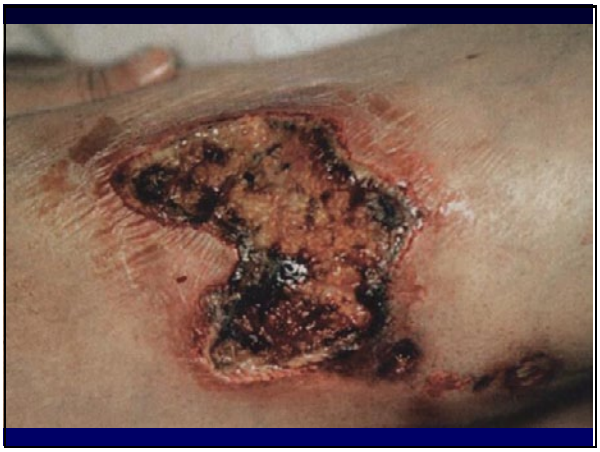
Cutaneous calcification in patients with end-stage renal disease: a regulated process associated with in situ osteopontin expression. Rivet J et al

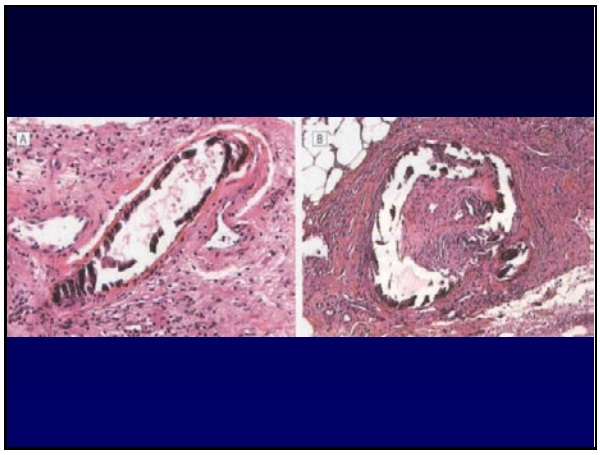
Arch Dermatol. 2006 Jul;142(7):900-6

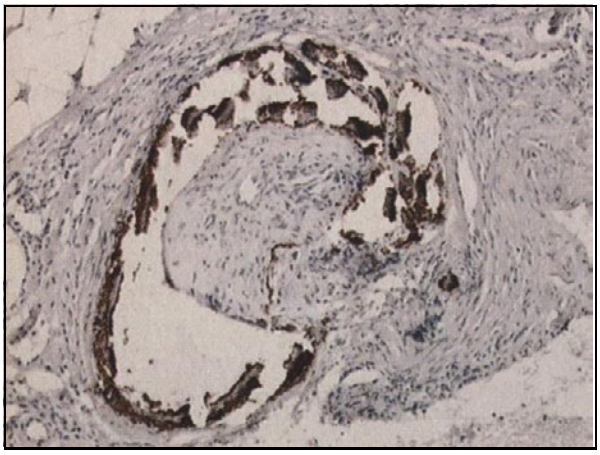
CUA

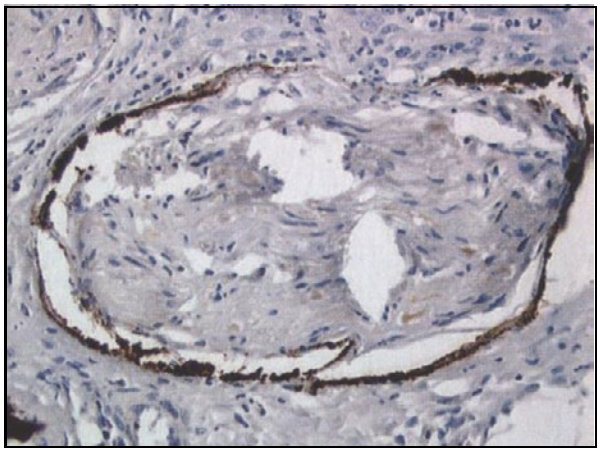
- Osteopontin is a bone matrix protein produced by osteoblasts.
- Although initially isolated from bone, it is localized in many tissues and appears that have increased expression in tissues at risk or known to calcify.

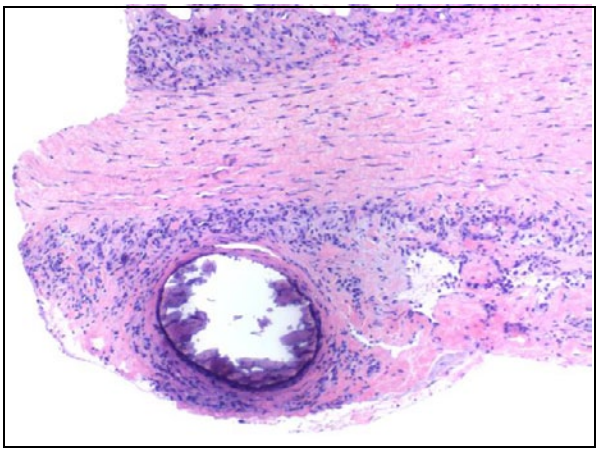
Rittling SR et al. Exp Nephrol 1999;7:103-113

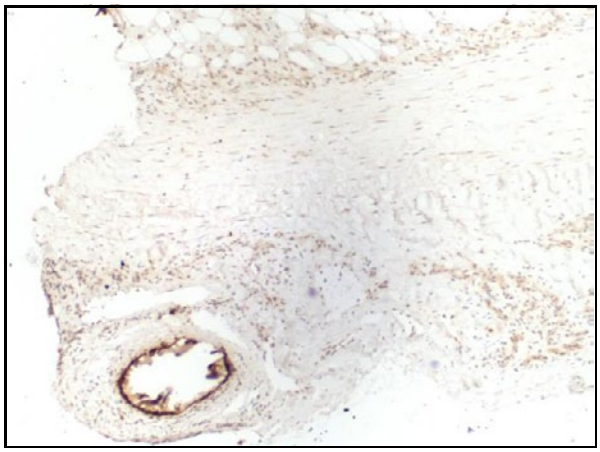


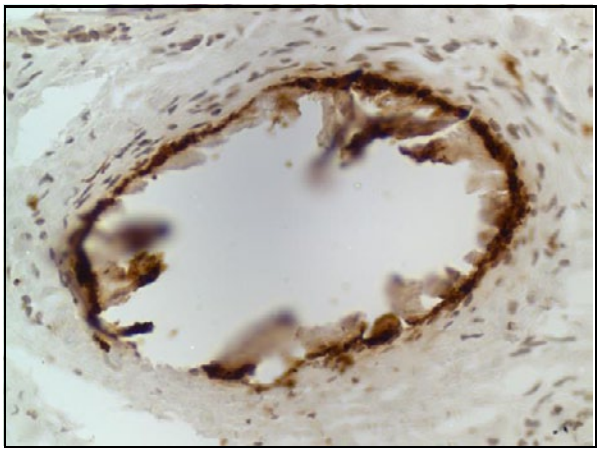

A
B









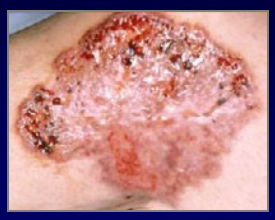


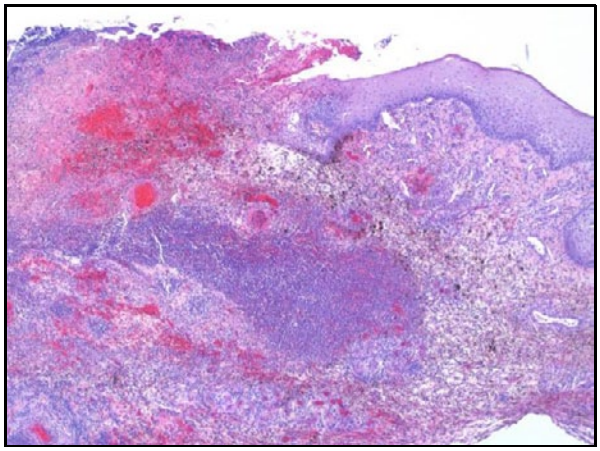
Novel Histopathologic Markers as Diagnostic and Prognostic Tools in Dermatology and Wound Healing

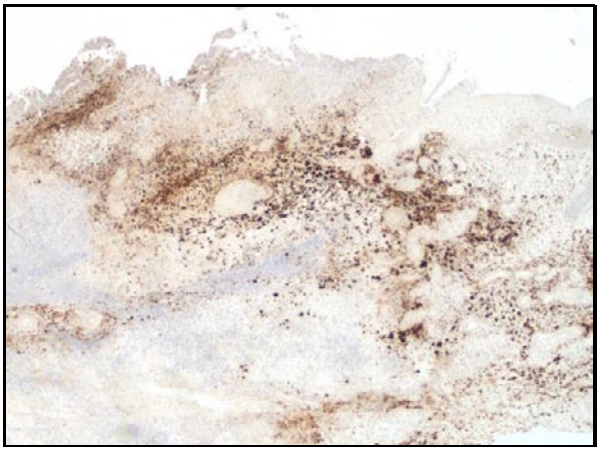
- TNF-alpha
- D2-40
- Mast Cells Tryptase
- Osteopontin
- Collagen IV

Pyoderma Gangrenosum

- Extremely painful
- Cutaneous and mucosal involvement
- Heal with cribriform scarring
- One or many ulcers, may coalesce

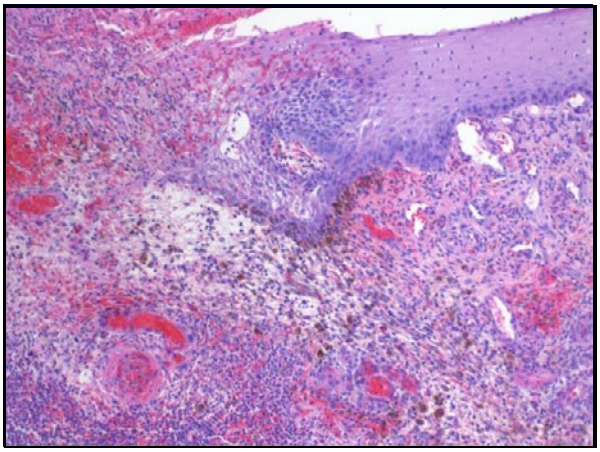


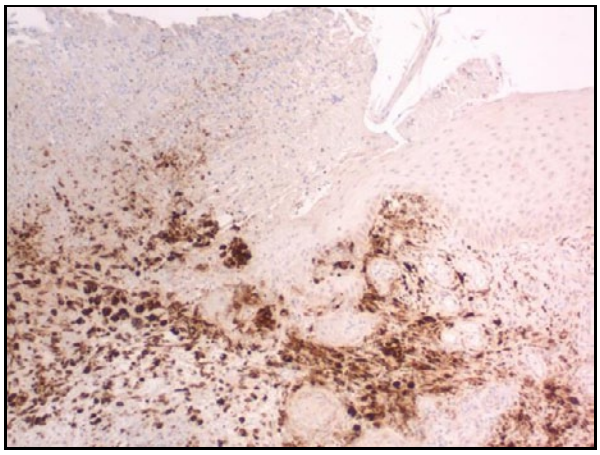




Pyoderma Gangrenosum and TNF-alpha

- Dini V., Romanelli M.,Bertone M. et al Improvement of idiopathic pyoderma gangrenosum during treatment with anti-tumor necrosis factor alfa monoclonal antibody. Int J Low Extrem Wounds. 2007 Jun;6(2):108-13
- Pastor N, et al Pyoderma gangrenosum treated with anti-TNF alpha therapy (etanercept) Clin Exp Dermatol. 2006 Jan 31(1):152-3

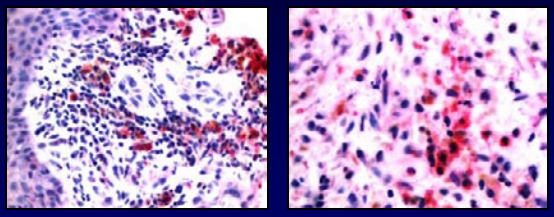




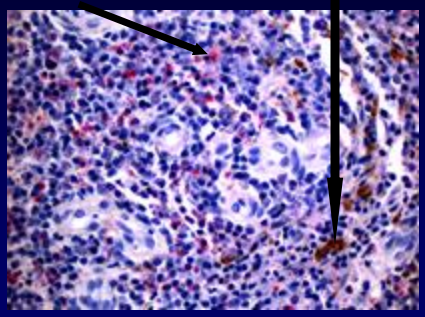
Chronic Wounds and TNF-alpha

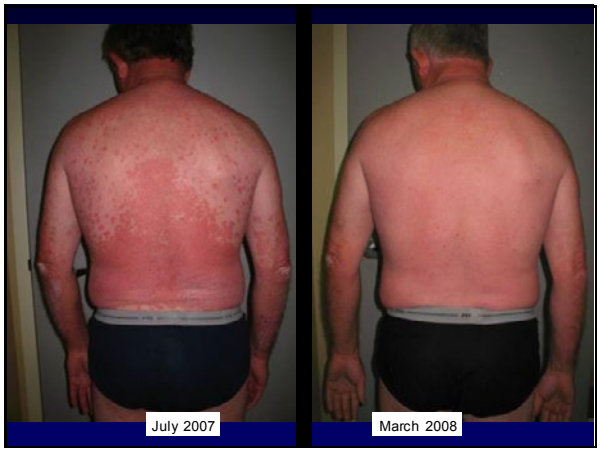
- Streit M. et al Topical application of the tumour necrosis factor-alpha antibody infliximab improves healing of chronic wounds. Int Wound J. 2006 Sep;3(3):171-9.
- Etanercept decreases tumor necrosis factor-alpha activity in chronic wound fluid.
  Wound Repair Regen. 2006 Jul-Aug;14(4):421-6.
- Wallace HJ. Tumor necrosis factor-alpha gene polymorphism associated with increased susceptibility to venous leg ulceration.
  J Invest Dermatol. 2006 Apr;126(4):921-5.

TNFa positive in the macrophages (in red)

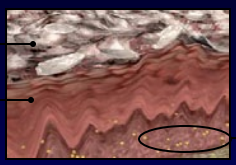


TNFa (red) Hemosiderin (brown)

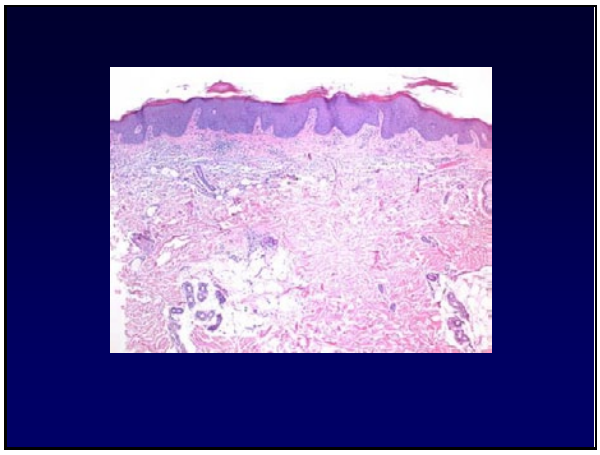


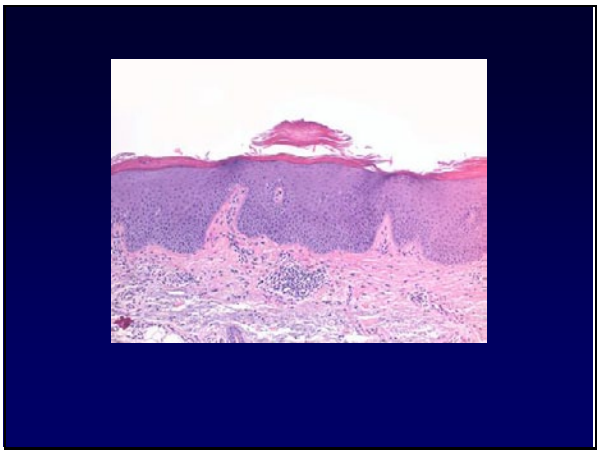


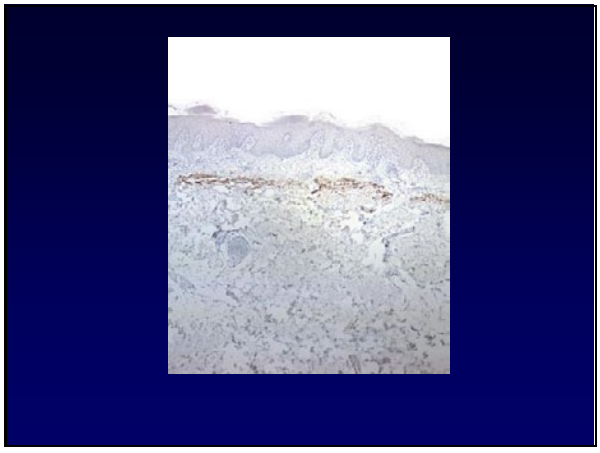
A Natural Process… Goes Awry

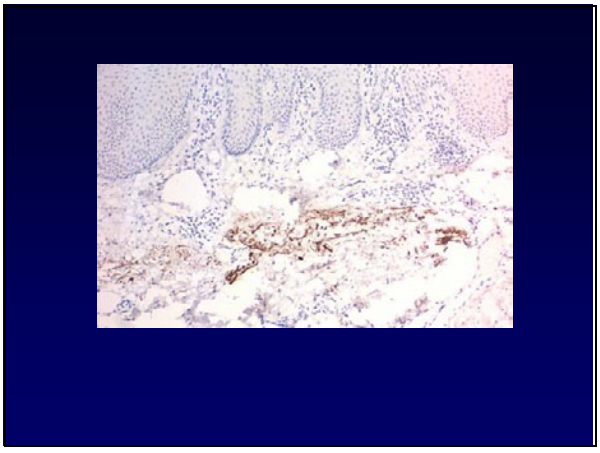


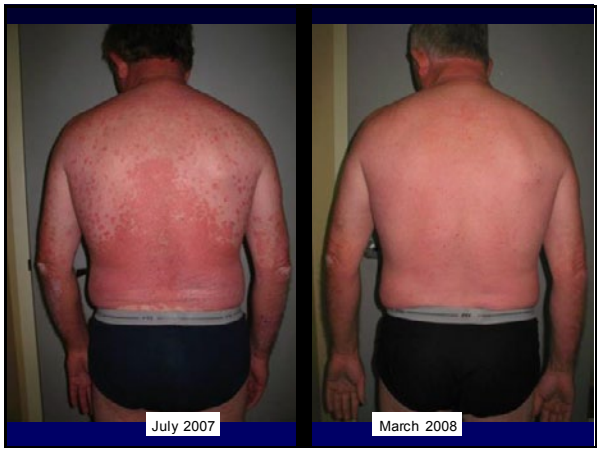
- An elevated level of TNF relative to the body's own unattached
  TNF receptors can lead to increased levels of TNF in the skin, which causes inflammation
- Researchers have found that people with psoriasis often have increased levels of TNF in their affected skin areas

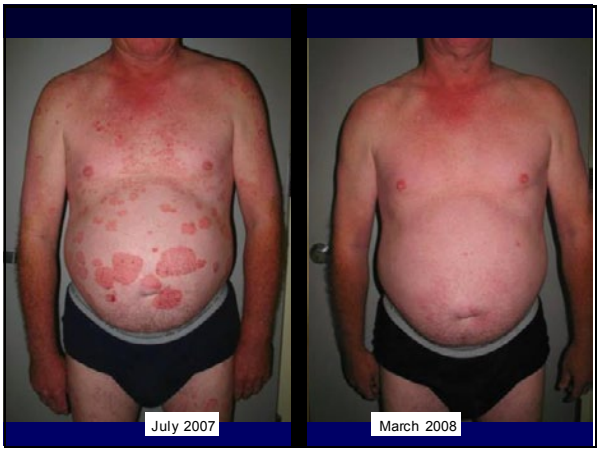


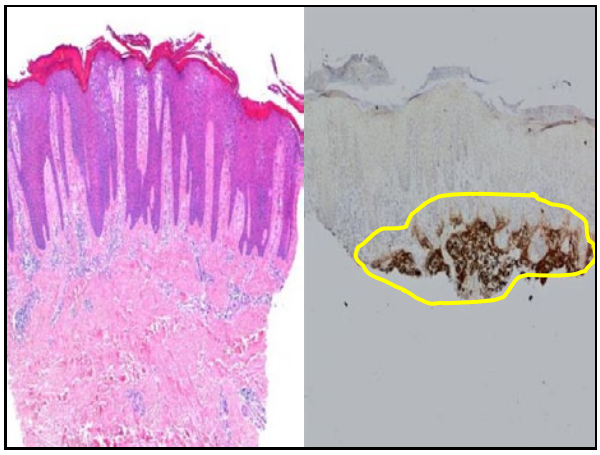


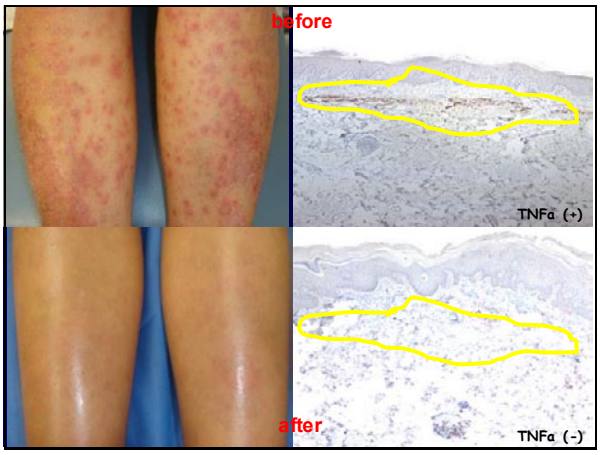





July 2007
March 2008


July 2007
March 2008





Study Evaluating IL-17 Immunohistochemistry in Psoriasis

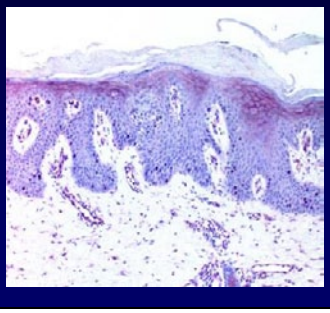
Greg Barron, M.D.
Andrea Maderal M.D.
Alex Villasante
Maria Miteva, M.D.
Paolo Romanelli, M.D.

IRB Protocol # 20100737

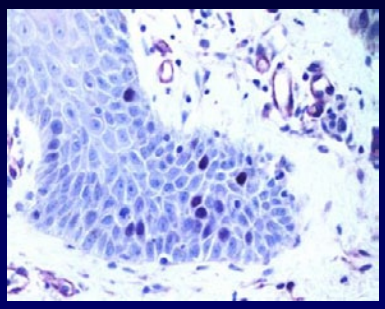
Methods

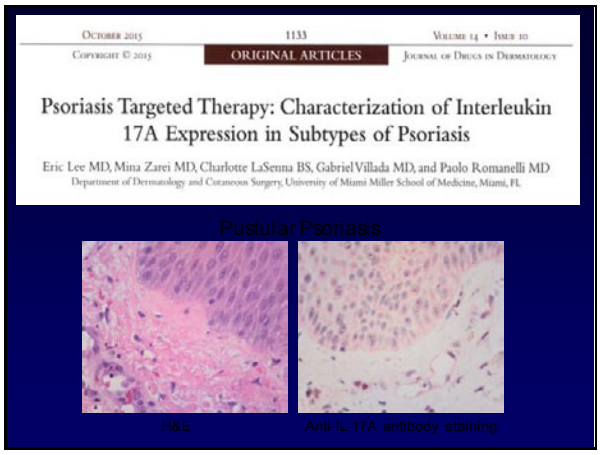
- Institutional Review Board Approval: Protocol # **20100737**
- 10 cases of biopsy proven plaque psoriasis randomly selected from psoriasis data bank
- 5 site matched "normal skin" controls from excision specimens
- Standard immunohistochemistry performed on formalin fixed paraffin embedded tissue sections

Psoriasis-Epidermis



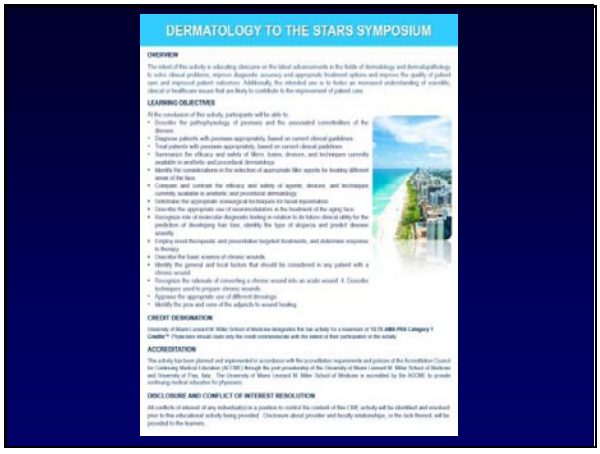
Psoriasis Epidermis (High Magnification)




October 2015 1133 Volume 14 • Issue 10
Copyright © 2015 ORIGINAL ARTICLES Journal of Drugs in Dermatology
Psoriasis Targeted Therapy: Characterization of Interleukin 17A Expression in Subtypes of Psoriasis
Eric Lee MD, Mina Zarei MD, Charlotte LaSenna BS, Gabriel Villada MD, and Paolo Romanelli MD
Department of Dermatology and Cutaneous Surgery, University of Miami Miller School of Medicine, Miami, FL
Pustular Psoriasis
H&E
Anti-IL-17A antibody staining


Thank you
promanelli@med.miami.edu


FIRST INTERNATIONAL MIAMI-PISA
DERMATOLOGY TO THE STARS SYMPOSIUM
APRIL 15 - 17, 2019
Lois Pope LIFE Center
1095 NW 14th Terrace
Miami, Florida 33136
TARGET AUDIENCE
PROGRAM DIRECTORS
Paolo Romanelli, M.D.
Marco Romanelli, M.D., Ph.D.
SCIENTIFIC SECRETARIAT


DERMATOLOGY TO THE STARS SYMPOSIUM
OVERVIEW
LEARNING OBJECTIVES
CREDIT DESIGNATION
ACCREDITATION
DISCLOSURE AND CONFLICT OF INTEREST RESOLUTION


UHealth/University of Miami Miller School of Medicine
Shino Bay Aguilera, M.D.
Gabriella Fabbrocini, M.D.
Ilseh Green, M.D.
Shaka Ho, M.D.
Gianluca Iacobellis, M.D.
Marco Infante, M.D.
Joely Kaufman, M.D.
Robert Kirsner, MD., Ph.D.
Wendy Lee, M.D.
Mariya Mileva, M.D.
Phillip Frost Department of Dermatology
Camillo Ricordi, M.D.
Paolo Romanelli, M.D.
Antonella Tosti, M.D.
Gil Yosipovitch, M.D.
Martin Zaiac, M.D.
Jerry Bagel, M.D.
Valentina Dini, M.D., Ph.D.
Francesca Fornatami, M.D.
Francisco Kerdel, M.D.
Craig Leonardi, M.D.
Teresa Oriangos, M.D.
Massimo Papi, M.D.
Boljan Prodanovich, M.D.
Marco Romanelli, MD., Ph.D.
Franco Rongioletti, M.D.

AARA
Powered by Bendcare

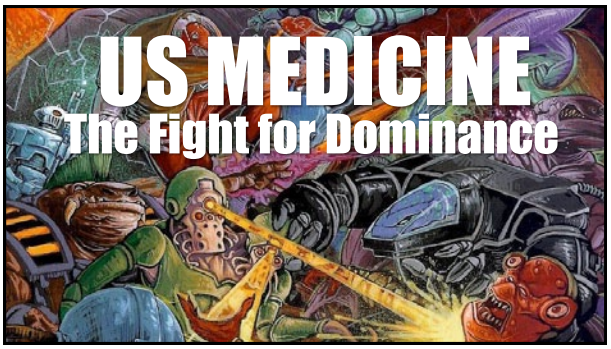
DISCLOSURES

- NONE -

RHEUMATOLOGY PERSPECTIVE ON PSO COMORBIDITIES

HOWARD M. BUSCH DO FACR

PRESIDENT, AMERICAN ARTHRITIS AND RHEUMATOLOGY ASSOCIATES
MEDICAL DIRECTOR OF COLUMBUS REGISTRY



COMORBIDITIES OF PSO

CLASSIC

Symptoms

- COLITIS
- UVEITIS
- ENTHESITIS
- DACTYLITIS
- SPONDYLITIS
- NAIL DYSTROPHY

WHAT ABOUT

Depression
- Stress / sleep / sex disorders

Hypertension

Diabetes
- Obesity

MACE
- MI / Stroke

Metabolic Syndrome

SLEEP DISORDERS IN PSO/PSA

Sleep Studies

- **Incidence of insomnia** in PSO has been estimated from **5.9%–44.8%** identified in 33 studies, where the general population is at 10% and up to 35% with transient insomnia.
- **HOWEVER, incidence of Obstructive Sleep Apnea** is **36–81.8%** compared to general population of 2-4%.
- **In a second study the incidence of insomnia** in PSA was **84%**, PSO **69%** and controls **50%**

Gupta et al, DOI:10.1016/j.smrv.2015.09.003. Wong et al, DOPI: 10. 3899/rheum.161330

IMMUNOLOGY OF SLEEP

Sleep Deficit Associated with:



ULTIMATELY

POOR OUTCOMES AS CYTOKINE UPREGULATION IS RELATED TO ; HYPERESTHESIA, PAIN, FATIGUE AND DEPRESSION

LEVELS
INCREASED TNF alpha IL-1B ,IL-17, CRP, NO, ADENOSINE, AND PGS.

IMPACT ON TARGET ORGANS
IMPACT ON TARGET ORGANS: AN INCREASED LEVEL OF; HTN,CV COMPLICATIONS, METABOLIC DISORDERS AND GENERALIZED PERFORMANCE IMPAIRMENTS

Krajewska-Wodarczyk et al, Rheumatologia. 2018; 56(5): 301-306. Banks S et al, CLIN sleep Med. 2007;3:519-528.

SLEEP IMPACT ON PSO/PSA

SLEEP

Sleep supports the immunoregulatory system

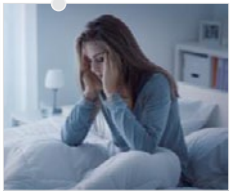
Sleep deprivation leads to a proinflammatory state

Study of 62 PSA , 52 PSO patients. and control group.

Measures
DAS28,FACIT,HAQ, PASI,PSQI,VAS pain

Results
67.7% of PSA, 57.7% of PSO pts and 14.6% controls were found to have poor sleep quality.

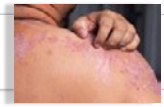
This resulted in worse quality of life and intense fatigue. However, tx with TNF alpha inhibitors led to improvement of sleep quality.



Rheumatologia. 2018 :56(5): 301-306, Gowda et al. J AM Acad Dermatol. 2010;63:114-123

FACTORS THAT APPEARED TO WORSEN SLEEP QUALITY

Factor 01 — PSO; duration of dz, severity of skin lesions, Patients age



Factor 02 — PSA; duration of PSO, TJC, CRP, pain , Pt's age

Rheumatologia. 2018 :56(5): 301-306

STRESS/DEPRESSION AND PSO/PSA

Discomfort from psoriasis may interfere with sleep

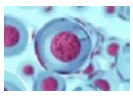
Sleep deprivation may lead to increased stress

Stress may trigger PSO/PSA activation

IMMUNE RESPONSE: Elevation of IL6, MCP1, prostaglandins, There is dynamic change of microglial activation upregulated by IL-1

Kothiwala SK et al. Indian J Dermatol Venereol Leprol .2016 sep-oct, Xu et al,2015 sep 21 doi:10.1186/s12890-015-0102-3
Sing et al PLoS ONE. 2017;12:e0181039

IMPACT OF DEPRESSION ON IMMUNE SYSTEM

01	02	03	04
			
Cytokines down regulate cyp 450 system .	**Up regulation:** NFKB IL6 ,IL8, and type 1 IFN including innate activation of TNF alpha,IL1 b TL R3, TLR 4, as well as CRP AND MCR4:	**They maybe markers of depression and potential predictors of response**	**Polymorphisms** (ie.,TPH2 GENE) have been identified in depression which may be the etiology of treatment failure

Schmidt, et al., Curr Neuropharmacol 2016
Miller et al., role of inflammation in depression: from evolutionary imperative to modern treatment target; 10.137/ doi 10 1038nri.2015.5.vol 16. jan 2016
Gao et al, PLoS One. 2012;7(5):e 36721

PSO IMPACT ON DEPRESSIVE PHENOMENA

SYMPTOMS

Higher rates of depression have been noted in PSO/PSA

Higher risk of sexual dysfunction noted

RESEARCH

Meta analysis of 8 studies evaluating sexual dysfunction in 4039 pts from 1966-2011

RESULTS

48% reported diminished sexual function negatively affecting orgasm, ED, over all decline in function

Depression higher in this group

PSO IMPACT ON DEPRESSIVE PHENOMENA

STUDY

1 STUDY REPORTED:
9% PTS WERE SATISFIED WITH PROVIDERS ATTENTION TO THESE ISSUES

43% FELT PROVIDERS ATTENTION TO SEXUAL MATTERS INSUFFICIENT

STUDY

15 EPIDEMIOLOGIC STUDIES SHOWED PREVALENCE OF SEXUAL DYSFUNCTION RANGED BETWEEN 26%-71%.

CASE CONTROLLED TRIAL SHOWED 53.7% AFFECTED VS 17.5% CONTROLS

RESULTS

AND OF COURSE LOCATIONS OF THE LESIONS HAD SEVERE IMPACT ON SEXUAL DYSFUNCTION

Kurizky et al, Rev Bras Rheumatol. 2012; 52:943-948. Molina et al, J Eur Acad Dermatol Venereol. 2015; 29:649-655

PSO IMPACT ON DEPRESSIVE PHENOMENA

Psoriasis Longitudinal Assessment and Registry (PSOLAR)

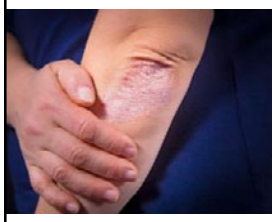
14.7% were depressed
11.1% were anxious
64.7% using alcohol
23% current smokers
32.9% prior use of tobacco

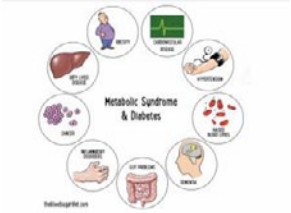
Patients with diminished HRQoL were less likely to adhere to TX
60% with severe PSO had increased lost days at work and decreased work productivity

87% of family members had decreased QOL.

Augustin et al, Expert Rev Pharmacoecon Outcomes Res 2014; 171: 137-147

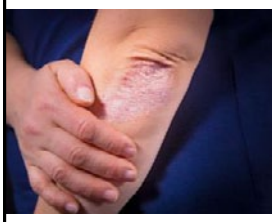
PSO & METABOLIC SYNDROME





Kothiwala SK et al. Indian J Dermatol Venereol Leprol .2016 sep-oct, Xu et al,2015 sep 21 doi:10.1186/s12890-015-0102-3
Sing et al PLoS ONE. 2017;12:e0181039

METABOLIC SYNDROME CONTINUED



Prevalence of metabolic syndrome in PSO

- 140 patients with chronic plaque psoriasis/ 140 controls
- RESULTS: 39.3% with MetS VS 17.1% CONTROLS
- OR=3.13
- SIGNIFICANTLY HIGHER –HTN, ABDOMINAL OBESITY AND DM AND OSA (or=2.87 in @2500 pt meta-analysis)
- TREND : SIGNIFICANT INCREASE IN DM,HTN AND T2D WITH INCREASED SEVERITY AND DURATION OF PSO
- In a pooled meta-analysis-20 countries=1,450,188 total with 46,714 PSO pts-random effects analysis = OR of 2.14

Kothiwala SK et al. Indian J Dermatol Venereol Leprol .2016 sep-oct, Xu et al,2015 sep 21 doi:10.1186/s12890-015-0102-3
Sing et al PLoS ONE. 2017;12:e0181039

PSO & HYPERTENSION

INCIDENCE OF HTN IN PSO—24,285 PTS AGE MATCHED CONTROLS AND 12,502 PSO PTS

PREVALENCE = 38.8% PSO VS 29.1% CONTROLS—p<.001

ANALYSIS Multivariate analysis controlled for DM, SMOKING, AGE , GENDER, NSAIDs

Kothiwala SK et al. Indian J Dermatol Venereol Leprol .2016 sep-oct, Xu et al,2015 sep 21 doi:10.1186/s12890-015-0102-3
Sing et al PLoS ONE. 2017;12:e0181039

IMMUNE REGULATION OF HYPERTENSION

DEFENSE CLASSICAL DEFINITION:"BP >120/80"

DEFENSE ALTERNATIVE DEFN:" HYPERTENSION IS AN AUTOIMMUNE RESPONSE TO ALTERED SELF".

DEFENSE TH1, TH2, TH17, GAMMA INTERFERON, and FOX P3; up regulates ANGIOTENSIN-2 AND MINERALOCORTICOIDS.

Schiffin et al., dept of med, McGill Univ. aug 17 2012

IMMUNE BASIS FOR HYPERTENSION

Proposed Mechanism

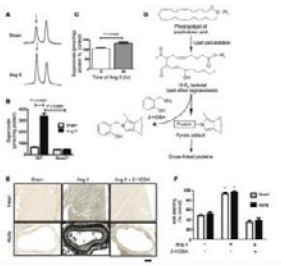
DEFENSE — ISOKETAL ADDUCTS (GAMMA KETOALDEHYDES) ARE FOUND IN HIGH CONCENTRATION IN DENDRITIC CELLS IN PATIENTS WITH HTN.

DEFENSE — 1. OXIDATIVE MODIFICATION OF SELF PROTEINS

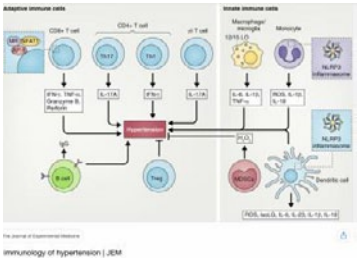
DEFENSE — 2. INCREASES IL6, IL1B, IL23, AND CO-STIMULATORY PROTEINS; CD80-86 , CD8, IFN GAMMA, IL17A, AND PLASMA F2 ISOPROSTANES.

Schiffin et al., dept of med, McGill Univ aug 17 2012

IMMUNOLOGY OF HYERTENSION

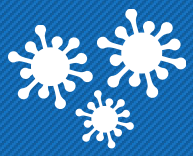


OF CYTOKINE RELEASE IN HTN



immunology of hypertension | JEM

HX OF HYPERTENSION



DEFENSE — IN 2007—HARRISON et al., looked at the role of T cells in HTN in RAG1 DEFICIENT mice.

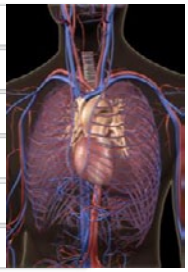
DEFENSE — ANGIOTENSIN 2/DOCA+NACL DID NOT INCREASE BP.

DEFENSE — HOWEVER: SYNGENEIC T CELL TRANSFER ALLOWED MICE TO EXPERIENCE THE HTN.

DOCA=DEOXYCOTICOSTERONE ACETATE
RAG-1 DEFICIENT MICE =NO MATURE B/T CELLS

PSO/PSA AND ENDOTHELIAL DYSFUNCTION

01	GWAS LARGE OVERLAP OF GENES THAT GOVERN CAD and MetS
02	Severe Psoriasis is an independent risk factor for MYOCARDIAL INFARCTIONS in younger patients.
03	RR=1.29 for a 30 yr old with mild dz and 3.10 for severe dz.
04	Prognosis post MI in PSO patient is worse than general population
05	Duration of Disease is an independent risk factor for every additional yr of dz, there is a 1% increase in MACE
06	MACE increased over 3-5 yrs by 36% if PSA was present



Int J Mol Sci. 2018 Jan; 19(1):58.

MARKERS OF ENDOTHELIAL FUNCTION

01 — ICAM, VCAM, E-SELECTIN (ELAM-1), MPO, TMAO

02 — ADMA/SDMA IS INCREASED IN HTN, CKD, DM AND DYLIPIDEMIA AS WELL AS SERVE AS A RISK FACTOR FOR CV DISEASE AND PLAQUE FORMATION

03 — alpha MSH IMPROVES VESSEL RELAXATION VIA NITRIC OXIDE PATHWAYS

EF= ENDOTHELIAL FUNCTION– ADMA/SDMA=ASSYMETRIC/SYMMETRIC DIMETHYL ARGININE (METABOLIC BYPRODUCTS OF CONTINUED PROTEIN MODIFICATION IN HUMAN CYTOPLASM).

STREYER et al.,

EF AND PSO

EVIDENCE FOR INCREASED HOMOCYSTEINE IN PSORIASIS
ELEVATED HOMOCYSTEINE LEADS TO ELEVATED ADMA
TNF alpha elevates ADMA and leads to reduction in NO

ADMA
HAS BEEN STRONGLY ASSOCIATED WITH PASI SCORES

ADMA
IS ASSOCIATED WITH EF

ADMA
MAY PLAY A ROLE IN PATHOGENESIS OF PSO

ADMA
ON THE HORIZON AS A MARKER OF DISEASE ACTIVITY

Bilgic et al. Arch Dermatol Res. 2015 jul;307(5):439-44

RHEUMATOLOGY PERSPECTIVE ON PSO COMORBIDITIES

PSO AND CV DZ WITH TREATMENT

37 PSO PATIENTS AGE 31- NO CVDZ

LAD FLOW MEASURED BY DOPPLER ECHO

MEASURED AFTER 6.3 MOS OF ANTI TNF THERAPY

RESULTS: CFR (CORONARY FLOW RESERVE) INCREASED FROM 2.2 TO 3.02 AFTER THERAPY AND CORRELATED HS CRP AND TNF REDUCTION BUT NOT PASI

FURTHER STUDIES IN PSA DEMONSTRATED THAT ADILIMUMAB REDUCED CAROTID INTIMAL THICKNESS BUT DID NOT CORRELATE WITH LIPID PROFILES

Avgerinou et al Int J. Cardiol. 2011; 151:382-383 Pina et al, J. Dermatol. 2016;43:1267-1272

RHEUMATOLOGY PERSPECTIVE ON PSO COMORBIDITIES

PSO/PSA AND EF

Study
Brezinski et al performed a systemic review that investigated EF dysfunction in PSO/PSA.

Objective
Effect of TNF inhibitors on EF in PSO/PSA

Resuts
- 2261 patients (20 studies) demonstrated:
- Increased arterial thickness
- Impaired endothelial vasodilatation
- Increased carotid intima-media thickness
- Decreased aortic elasticity
- 2/3 studies demonstrated that TNF alpha inhibitors improved EF

Brezinski EA et al. Curr Pharm Des.2014;20(4):513-28

RHEUMATOLOGY PERSPECTIVE ON PSO COMORBIDITIES

REDEFINING DIABETES

Classical Definition

A group of metabolic dzs characterized by hyperglycemia resulting from defects in in sulin secretion, action or both .

Alternative Definition

TYPE 1 DIABETES - IMMUNE DESTRUCTION OF INSULIN PRODUCING CELLS

TYPE 2 DIABETES - IMMUNE SYSTEM IMPAIRING EFFECTOR CELL RESPONSE TO INSULIN.

Kaelmanda et al., the role of TNF alpha in mice with type 1&2 DM; Plos one 7(5) @33254,doi:10.1371/journal.ponc.0033254
DIABETES CARE,26:3160-67,2003

RHEUMATOLOGY PERSPECTIVE ON PSO COMORBIDITIES

DM - B/T CELL CONNECTION

Mice
- Winer et al ,- 2009 – demonstrated that when DIO mice, which were B cell deficient, were subjected to a HIGH cal/fat diets, did not develop insulin resistance
- It was only when the mice were injected with B cells or Ig from obese insulin resistant mice , that they developed manifestations of Diabetes.

Humans
- Winer –studied 32 overweight people with aged matched cohort and demonstrated— those with Insulin Resistance had pathogenic Antibodies.

Mice
- He then went back to his preclinical mice study. He txd the mice with mouse equivalent of anti CD20.
- The CD20 attacked the mature B cells only.

Mice
- After 1 cycle, the mice had a reduction in insulin resistance with near normal metabolism of glucose.

Winer etal ,B cells promote insulin resistance through modulation of T cells and production of pathogenic IgG Abs-Nature Medicine,published online:april 17 2011

FURTHER SUPPORT

Mice
antiCD3 Abs ,IL2 Ig, mut IL15 Ig and rapamycin and alpha 1 Antitrypsin:

Mice
Permanently restored euglycemia to NOD mice.

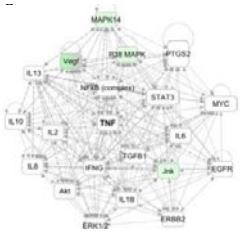
Mice
Reversed gene dysregulation in peripheral lymph nodes and stabilize c-peptide and reduce HbA1C.

Mice
PDE4 inhibitors elevate GLP-1 which lowers serum glucose as well

NOD mice= non-obese diabetic (model for type 1 DM)

Winer etal ,B cells promote insulin resistance through modulation of T cells and production of pathogenic IgG Abs-Nature Medicine,published online:april 17 2011

TNF GENE



Focus Hub genes	Degree	
	Number of Connections	Percentage of Connections
TNF	241	53.00
VEGFA	186	40.97
IFNG	180	39.65
IL6	155	34.14
IL1B	148	32.60
NFKB	139	30.61
MYC	122	26.87
FIBRMPK	106	23.35
IL10	100	22.03
ERK1/2	99	21.81
IL2	98	21.59
STAT3	95	20.93
AKT	95	20.93
JNK	94	20.70
ERBB2	94	20.70
IL13	90	19.82
IL8	89	19.60
PTGS2	86	18.94
EGFR	86	18.94
MAPK14	85	18.72

Kievet, etal.,

TNF ALPHA AS THERAPEUTIC TARGET IN DIABETES

- **New onset T1D/T2D mice:** Control/short course anti TNF
- **Untreated group** remained hyperglycemic despite daily insulin therapy and majority died with in 7 weeks of onset of T1D
- **Anti TNF Group** achieved euglycemia in 22/24 subjects with no deaths.
- **Anti TNF Alpha** has also been shown to ablate a T cell rich islet cell invasion of B cells on biopsy.
- **And in fact...** in 1, 35 pt study-- pts txd with TNF alpha inhibitors There was clear improvement in glycemic control.
- **Txd Group** decrease of FPG by 2.74mmol/L vs .02 mmol/L in control group

Kaelmanda et al., 2012 Cutis 2016 March; 97(3. 235-241.

PSO/PSA AND DM2 Odds Ratio FROM 4 POOLED STUDIES

PSO AND DM= 1.76

PSA AND DM=2.18

SEVERE PSO AND DM= 2.10

THE COMBINATION OF DM AND PSO LED TO MORE MICROVASCULAR COMPLICATIONS THAN DIABETES ALONE.

J. Am.Acad.Dermatol.2015;72:968-977

SO WHAT ELSE?

One Study found that:

- DM undiagnosed in 19% of PSO pts
- HTN undiagnosed in 22% of PSO pts
- Hypercholesterolemia undiagnosed in 30% of PSO pts
- 60% failed to achieve treatment targets for the CV risk factors
- PCPs –only 43% screened for HTN, 11%-dyslipidemia, 27%-DM and 30% for obesity

Kimball et al, J. AM. Acad. Dermatol. 2012;67:76-85-- Parsi et al, J . Am. Acad. Dermatol. 2012:67:357-362.

CIRT AND CANTOS TRIALS

CIRT

CV Inflammation Reduction Trial

- 7000 pts w/o inflammatory disease - TX was placebo or MTX 15-20mg/week –3-5 yrs.
- Results= no change in IL1b, IL6,hs CRP or CV events

CANTOS

Canakinumab Anti-Inflammatory Thrombosis Outcomes study

- 10 ,061 pts with previous MI and elevated CRP (>2 mg/L)
- Canakinumab 150mg/ 3 mos vs placebo-48 mos
- Initial results demonstrate a marked reductions in CV events as well as hsCRP in the active arm –despite elevated lipids

Int J Mol Sci. 2018 Jan; 19(1):58
Ridker et al.N Engl J Med 2019;380:752-62

QUESTIONS

1. DO YOU BELIEVE THAT TREATMENT OF PSO WILL HAVE IMPACT ON COMORBIDITIES OF DM,HTN, SLEEP, DEPRESSION, CV DZ??
2. DO YOU BELIEVE THAT THE COROLLARY IS TRUE?
3. IF SO, HOW CAN WE IMPROVE OUR PATIENT'S OUTCOME??


Thank you

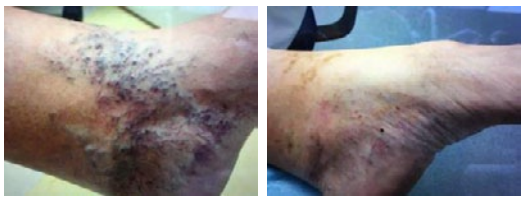
Cutaneous Venous Hypertension

Ronald Bush, MD, FACS
Water's Edge Dermatology
Stuart, Florida

Disclosure

- Minority shareholder in dermaka Skin Care Products, LLC

Why You Are Here Today

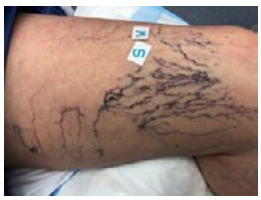


(Bush, 2018)

CEAP

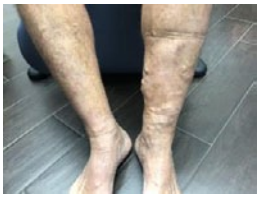
- The CEAP classification consists of categories listed as: C0 to C6.
- Except for categories, C0 & C2, the manifestations of venous disease are confined to the dermal layer
- C2 is varicosities that are subdermal
- There may be isolated skin changes associated with varicosities i.e. eczema

CEAP 1



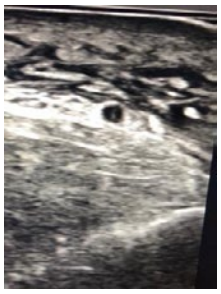
- CEAP 1 is simple venous telangiectasia (Spider Veins)
- The causative factor is transmitted venous pressure with resultant vessel wall dilatation
- Spider veins are located from 300 – 1000 microns below the squamous epithelium

CEAP 2

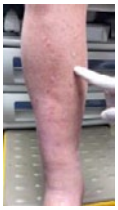


- CEAP 2 is reserved for verification for veins that are subdermal
- Only the valves are abnormal, not the vein itself

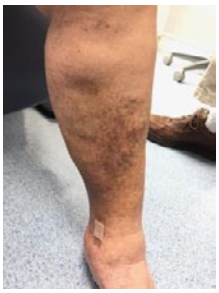
CEAP 3



- CEAP 3 is manifested as edema in the dermal and subdermal tissue

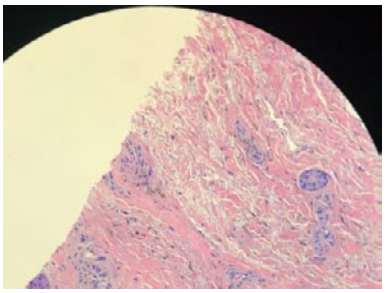


CEAP 4

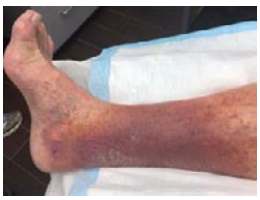


- CEAP 4 refers to stasis changes in the lower leg or signs of chronic venous disease
- Hemosiderin is deposited in the dermal tissue as the result of red cell extravasation

Histology of Skin With Stasis Changes

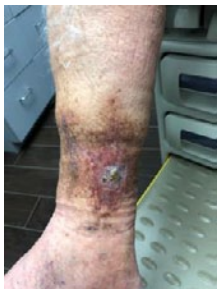


CEAP 5



- CEAP 5 classification if for patients with healed venous ulcer and skin sequalae, secondary to chronic inflammatory process

CEAP 6



- This classification is reserved for patients with active ulceration

Cutaneous Venous Hypertension

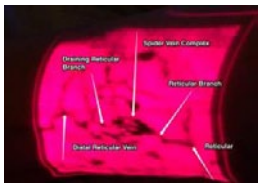
- The manifestations of cutaneous venous hypertension range from:
  - Spider veins
  - Varicose veins
  - Stasis dermatitis
  - Atrophic blanche
  - Venous ulceration
- Most patients seek consultation for spider veins

Cutaneous Venous Hypertension

- Most spider veins are related to an area of venous hypertension
- Reticular veins are the final pathway for transmission of venous hypertension in the majority of patients but not all
- Volume overload in pregnancy is the main etiology of reticular vein dysfunction

Cutaneous Venous Hypertension

- However, reticular veins are usually connected to a deeper source of pathology
- The branches of the reticular complex in the majority of clinical situations, are the final pathway leading to cutaneous telangiectasia



(Bush, 2018)

Cutaneous Venous Hypertension

- The GSV, SSV, AAGSV, and Thigh Extension Branch if incompetent, may transmit abnormal pressure to the skin via an incompetent branch that may or may not connect to a reticular vein
- Refluxing perforators may also transmit abnormal pressure to the skin resulting in cutaneous venous dilatation (Spider Veins)

Cutaneous Venous Hypertension

- Conversely, a refluxing branch may arise from a normal truncal vessel
- This is not an uncommon occurrence
- In this case, the truncal vessel is not treated but only the refluxing vessel that will be discussed later in the presentations

Cutaneous Venous Hypertension

- It is imperative to treat the etiology of the cutaneous manifestation, or one of the following events may happen:
  - Non-Clearance
  - Recurrence
  - Angiogenesis

Cutaneous Venous Hypertension

- The US is indispensible in diagnosing deeper pathology. Use the US at 2 cm depth to trace reticulars to origin of hypertension
- All pathologic pathways will reflux
- Skin illumination only allows visualization to a depth of 2 cm but, is helpful as a mapping aide for reticular veins
- Only an US can determine pathology of the reticular vein

Cutaneous Venous Hypertension

- The etiology of cutaneous venous hypertension must always be alleviated at the time of spider vein treatment

Theories of Spider Vein Formation

- Sommer A, et al, described the 02 & C02 difference between red and blue telangiectasia
- Their conclusion is that all telangiectasia are assumed to be in the capillary bed
- This would involve arterioles in continuity with dilated venous structures
- We do not see this on our histological exams

(Sommer, 1997)

Theories of Spider Vein Formation

- However, our biopsy specimens are limited to 1 mm diameter
- Another theory is the 'Microshunt histology theory'
- Bihari et al, described a theory that many of the telangiectasia are associated with an AV microshunt
- The specimens for study were 2.5 cm by 1.5 cm

(Bihari, 1999)

Theories of Spider Vein Formation

- In a greater percentage of their patients using continuous wave doppler US, they identified arteriole pulsations over spider telangiectasia
- This is only subjective in that arterial pulsations can be heard transmitted from varying depths
- It is a rare event to see pulsatile flow on US when examining telangiectasia except when perforators are present or high flow states are in the reticular branch

Theories of Spider Vein Formation

- However, we have heard multiple transmitted arterial signals that could not be accurately located
- When the etiology of the signals could be located it was usually at a considerable distance below the subdermal layer

Theories of Spider Vein Formation

- Mariani et al, 2000, proposed that all telangiectasia are related to a pathologic perforating vein located beneath the spider vein complex
- In essence, the authors are correct that there is a perforating vein but this is a branch that comes from a reticular vein and not a deeper source

(Mariani, 2000)

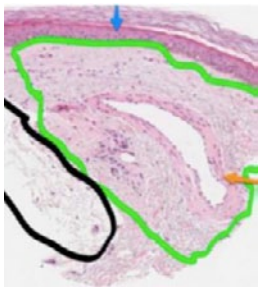
Theories of Spider Vein Formation

- Another interesting point is that the authors report in the 3-year follow-up, there were new spider telangiectasia in 59% of cases
- Only 5% recurred in the previously treated area

(Mariani, 2000)

Why Do Spider Veins Occur?

- What we know based on our clinical and histological studies is that spider veins are secondary to high venous pressure
- The effect of high pressure causes dilatation of the smooth vessel wall of the venules in the reticular dermis



- In all specimens examined the one constant finding in a spider telangiectasia is vessel wall hypertrophy
- ‘’

(Bush, 2014)

Why Do Spider Veins Occur?

- This pressure must be transmitted from a distal source
- We know from US exams in over 500 patients with spider telangiectasia, that all reticular veins associated with spider telangiectasia demonstrate reflux

Why Do Spider Veins Occur?

- Based on US and histological studies of branches and perforators in association with reticular veins, there is always an abnormal valve
- So what occurs is the following:
- For what ever reason; volume overload from pregnancy, genetic induced reflux, etc…there occurs transmission of high venous pressure to the reticular vein

Why Do Spider Veins Occur?

- The reticular veins are conduits of flow and pressure
- Due to incompetent valves in the draining branches, perforators, or volume overload from increased flow, there is a buildup of pressure in the reticular system
- This pressure is transmitted to reticular branches with ultimate dermal perforator involvement

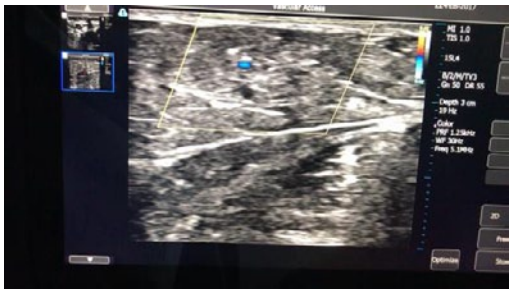
Why Do Spider Veins Occur?

- The length of a spider vein is proportional to the amount of pressure it receives from the subcutaneous circulation

Types of Spider Vein Complexes

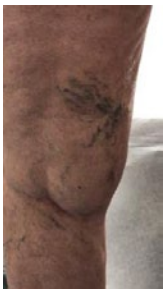
- There are 4 different types of spider veins according to their location and etiology
- The US is indispensable as mentioned before in diagnosing the exact etiology
- One type of complex is that associated with a true perforator from a deeper source

Perforator Leading to Spider Complex



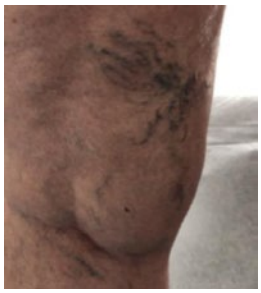
(Bush, 2018)

Perforator Leading to Spider Complex



(Bush, 2018)

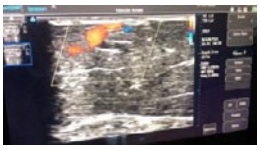
Spider Telangiectasia Associated with a Perforator



- When the spider complex is isolated and dilated, there is always a perforator

(Bush, 2018)

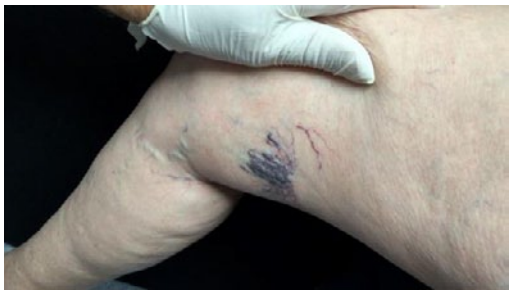
Incompetent Branches From Truncal Vessels



- Second group of spider veins occur from incompetent branches of the GSV, SSV or AAGSV
- Like spider veins associated with perforators there is usually a single isolated large group of spider veins

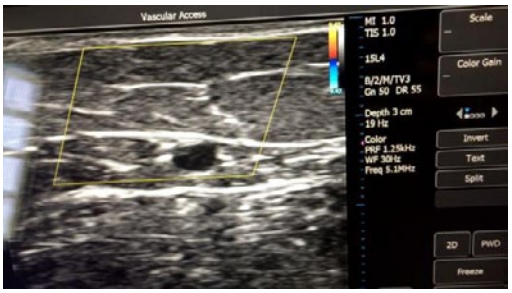
(Bush, 2018)

Case Study: Spider Veins From an Incompetent Branch of the GSV



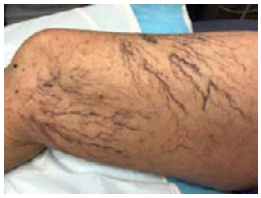
(Bush, 2015)

Case Study: Spider Veins From an Incompetent Branch of the GSV



(Bush, 2015)

Veins Associated with Dermal Perforators



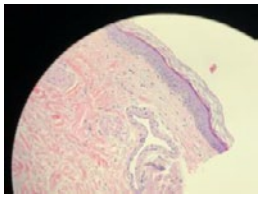
- The third group of common spider vein patterns consist of incompetent reticular veins with a dermal perforator giving rise to the complex
- The reticular veins are abnormal but, always associated with a deeper pathology

(Bush, 2018)

Red Telangiectasia

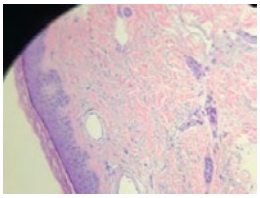
- There are 3 types of red telangiectasia
- Secondary to cutaneous venous hypertension (Most Common) responds to sclerotherapy or heat modalities
- Generalized Essential Telangiectasia (GET)
- Responds poorly to sclerotherapy
- Cutaneous Collagenous Vasculopathy (CCV) responds poorly to sclerotherapy

Telangienctasia Secondary to Venous Hypertension



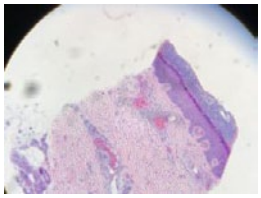
- Vessel wall hypertrophy
- Many endothelial cells located 300 – 500 microns below the squamous layer
- The reddish hue is secondary to smaller blood volume and lack of mixture with large amounts of desaturated blood

GET or CCV?



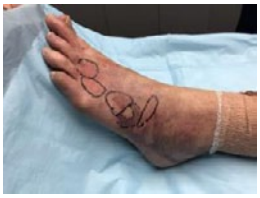
- Components of both are present in this patient
- There is a thickened wall with hylan and not smooth muscle
- Very few endothelial cells are present
- Other vessels show telangiectasia without a thickened wall

GET or CCV?



- This patient had treatment with the V-Beam Laser
- Wave lengths of 590 with either a laser or IPL seemed to be the most effective for this condition

Determining Response of Treatment



- Multiple marked areas represent different energy and pulse duration to find best treatment option

Unloading Cutaneous Venous Hypertension

- 4 Steps to Treating Spider Telangiectasia
- Unload the cutaneous venous hypertension
- Treat the spider vein
- Assess collateral flow
- Minimize sequalae

Unloading Cutaneous Venous Hypertension

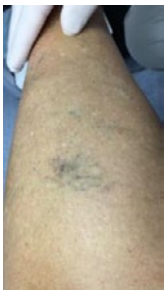
- Identify the source
- Use US
- Trace from complex ➔ reticular ➔ source (Perforator, branch, GSV, AAGSV or SSV)

Unload the Cutaneous Venous Hypertension

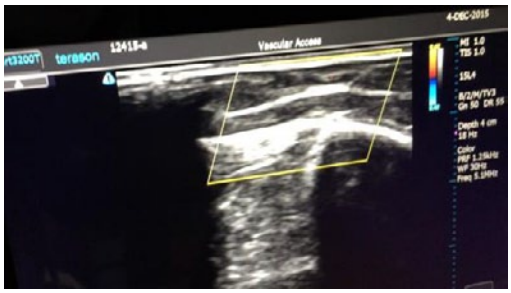
- Surgical – Punch or Phlebectomy
- Chemical – Foam sclerotherapy – USGS or retrograde injection from complex
- Combination of chemical and surgical

Ultrasound Spider Complex

- The following video will demonstrate the actual appearance of a spider complex by ultrasound
- In this video, it was possible to see the branch from the incompetent vein that gives rise to the spider complex
- There is usually a branch from the underlying reticular vein that gives rise to spider complexes

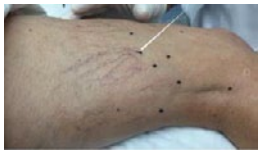


(Bush, 2015)



(Bush, 2015)

Unloading the Cutaneous Venous Hypertension



- The white arrow points to the origin of the spider complex – Where the branch of the reticular becomes superficial
- A punch biopsy at this location unloads the cutaneous hypertension & interrupts the spider telangiectasia

(Bush, 2015)

100 Patients Examined for Origin of Telangiectasia

6. Results

72% of patients had multiple sites of origins of cutaneous venous hypertension. The common sites were lateral thigh (55%), medial thigh (40%), lower leg and ankle (25%), and posterior thigh and calf (11%). 18% of patients had pathology confined to the lateral thigh only with no other patterns of telangiectasia. All telangiectasia could be traced to a refluxing branch of the Greater Saphenous vein (GSV), Small saphenous vein (SSV), Posterior intersaphenous branch, Anterior Accessory Greater Saphenous Vein (AAGSV), or anatomically defined perforators. 30% of patients had co-existing GSV insufficiency as well. 95% of patients with lateral thigh telangiectasia have an associated superior or lower thigh perforator. 95% of medial thigh telangiectasia are secondary to a refluxing branch of the GSV. Telangiectasia of the lower leg and ankle may originate from multiple sources. Telangiectasia of the posterior calf and thigh originate from multiple sources including the SSV, posterior intersaphenous branch or perforators from the popliteal or gastrocnemius vein. Two patients had small AV fistulas as origin of spider complexes usually after previous procedures.

Conclusion

- There is always a source for spider varicosities
- The source may be the GSV, AAGSV, SSV or a perforator
- Find the source and treat with either foam sclerotherapy or phlebectomy (In some cases, thermal ablation)
- Find the end point and unload the spider complex at this level (Where the spider vein branches out or begins)

Conclusion

- Disconnect collateral flow if present
- Treat the spider veins with the appropriate concentration
- When using foam, use dilute concentrations, incise the vein and flush

References

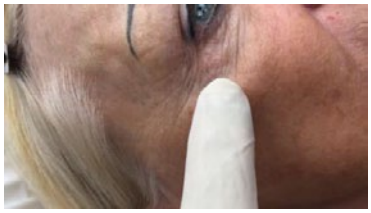
- Bihari I, Magyar E. Microshunt histology in telangiectasias. *Int J Angiol* 1999;8(2):98-101.
-
- Bush, R. (2015). Image retrieved 2015 from http://www.veinexperts.org/
- Mariani F, Bianchi V, Mancine S, Mancini S. Telangiectases in venous insufficiency: Point of reflux and treatment strategy. *Phlebol* 2000;15(1):38-42.
- Sommer A, Van Mierlo P, Neumann H, Kessels A. Red and blue telangiectasias. *Phlebol* 1997;23:55-59.

Treating Peri-Ocular Vein Through the Temporal Vein

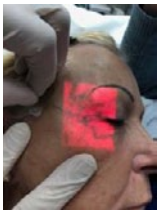
Peri-Ocular Vein

- Patient has large peri-ocular vein
- Using vein illumination the vein & feeding branches are visualized

Peri-Ocular Vein

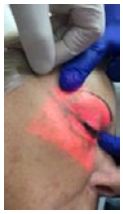


Peri-Ocular Vein

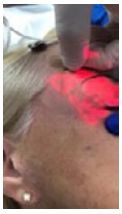


- Using a 27-gauge butterfly, 3 ml of Sotradecol 0.3% is injected

Peri-Ocular Vein



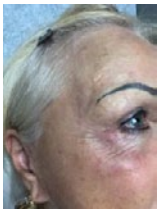
Peri-Ocular Vein



Peri-Ocular Vein

- One month post treatment the venous plexus was obliterated

Peri-Ocular Vein



Evaluation of Clinical and Histological Findings Using Varying Sclerosant Concentrations for the Treatment of Spider Telangiectasia

Histology of Spider Veins After Treatment

- Desired functions of sclerosing agents are destruction of endothelial cells and exposure of subintimal layers to the sclerosant with eventual fibrotic occlusion of the vein
- Undesirable effects of sclerosants are vessel wall necrosis with extravasation of red cells
- The above extravasation leads to inflammatory changes and/or angiogenesis

(McAree, 2012) (Rao, 2005) (Green, 1998)

Sclerosants

- In this study, the sclerosing agents are Sotradecol® and Asclera® (Polidocanol)
- These are detergent agents that act by altering the surface tension around endothelial cells causing lysis
- The subintimal layer is exposed and depending on time of exposure and strength of solution, degradation of smooth muscle wall may occur

Sclerosants

- Evidence of muscle wall damage is visible on microscopic analysis as fibrin replacement of smooth muscle cells
- This phenomenon is desirable if complete necrosis of wall does not occur
- Sub intimal damage is manifested by a ragged appearance of the former lining of the vessel wall

Sclerosants

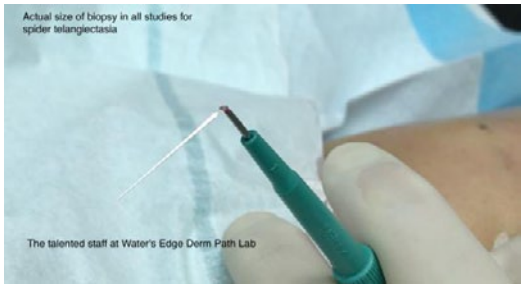
- The best sclerosant concentration will cause total lysis of endothelial cells and subintimal damage with minimal intraluminal debris such as red cells

Evaluation of Clinical and Histological Findings Using Varying Sclerosant Concentrations for the Treatment of Spider Telangiectasia

- This study was designed to correlate histologic findings and clinical results to determine the ideal sclerosant concentration using Sotradecol
- Additional histologic determination of veins treated with Polidocanol were also done
- There may be variability in clinical findings in the same patients using the same concentration for the same size vein

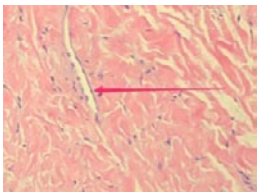
Evaluation of Clinical and Histological Findings Using Varying Sclerosant Concentrations for the Treatment of Spider Telangiectasia

- This variability exists due to the presence or absence of cutaneous venous hypertension
- In this study, all attempts were made to abolish cutaneous venous hypertension prior to treating the telangiectasia
- 1 mm punch biopsies were done at the time of phlebectomy and these biopsies were performed through the treatment site



(Bush, 2018)

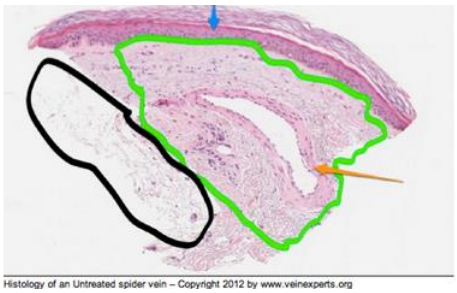
Intradermal Veins



- This specimen is a 1 mm biopsy of a patient with staining
- The red arrow points to a normal vein in the reticular dermis as far as size is concerned
- Note there is no venous wall dilatation

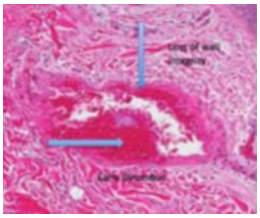
(Bush, 2018)

Untreated Spider Telangiectasia



(www.veinexperts.org, 2012)

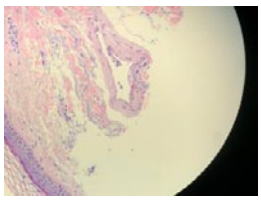
Sotradecol 0.3%



- Note large amount of red cells in lumen
- Wall disruption
- Complete replacement of smooth muscle vessel wall with fibrin
- In this case, angiogenesis is possible

(www.veinexperts.org, 2015)

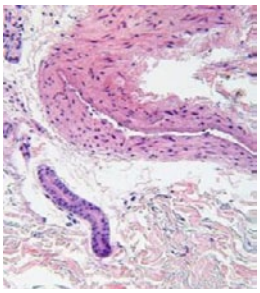
Sotradecol 0.2%



- 100% endothelial cell loss
- Subintimal changes
- Intraluminal debris
- Vein wall replacement with fibrin in some areas

(Water's Edge Dermatology, 2018)

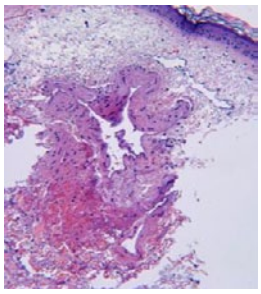
Sotradecol 0.15%



- 100% endothelial cell loss
- Mild subintimal changes
- Upper vessel wall replacement with fibrin

(www.veinexperts.org, 2015)

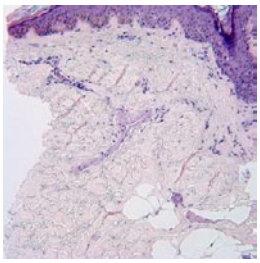
Sotradecol 0.15%



- The same concentration however, from a compounding B pharmacy
- Note the larger amount of intraluminal debris
- Also, thinning of vessel wall inferiorly

(Water's Edge Dermatology, 2017)

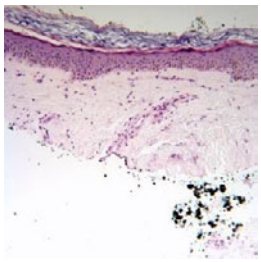
Sotradecol 0.1%



- Complete loss of endothelial cells
- Intact vein wall with no fibrin replacement
- No intraluminal debris

(www.veinexperts.org, 2015)

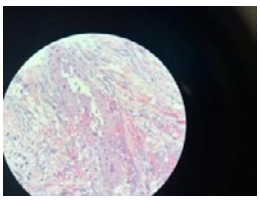
Sotradecol 0.05%



- Incomplete endothelial loss
- No subintimal damage
- Very little histological findings

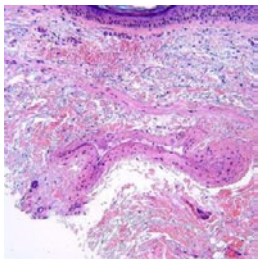
(www.veinexperts.org, 2015)

Polidocanol 0.5%



- Perforation of vessel wall
- Extravasation of RBC's
- This will lead to hemosiderin deposition & prolonged staining

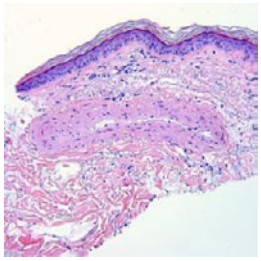
Polidocanol 0.375%



- 100% endothelial cell loss
- Mild subintimal changes
- Minimal intraluminal debris

(www.veinexperts.org, 2015)

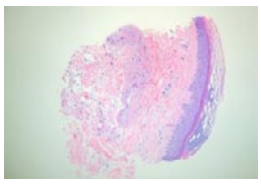
Polidocanol 0.31%



- Complete loss of endothelial cells
- Subintimal damage
- Vessel wall intact with no fibrin replacement
- No intraluminal debris
- The ideal concentration based on histology

(www.veinexperts.org, 2015)

Polidocanol 0.33% ½ NS

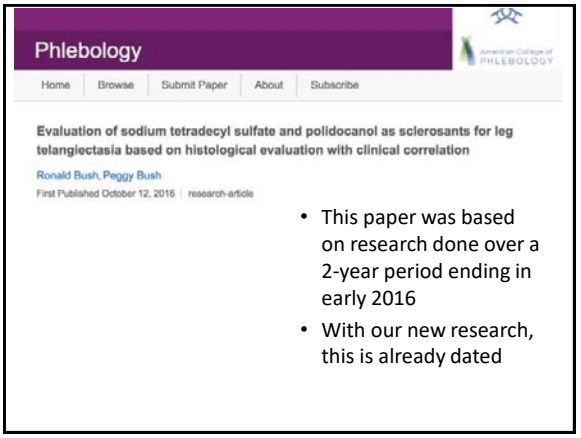


- Note that using ½ NS produces more intraluminal damage
- This is manifested by apposition of the vein walls

(Bush, 2018)

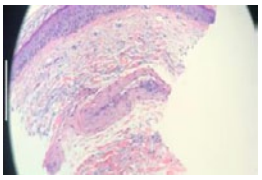
Polidocanol 0.25%

- 50% endothelial loss in 1 mm vein
- No subintimal changes
- Can be tried initially for vessels < 0.5 mm



- This paper was based on research done over a 2-year period ending in early 2016
- With our new research, this is already dated

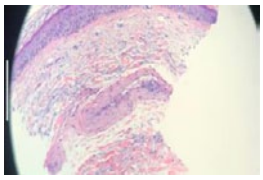
0.1% Sotradecol ½ NS



- Further studies using hypotonic dilutions have revealed that an even better concentration is 0.1% Sotradecol ½ NS as the diluent

(Water's Edge Dermatology, 2018)

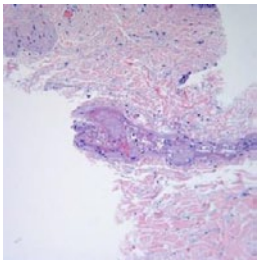
0.1% Sotradecol ½ NS



- We use this concentration for almost all spider veins
- We even use this concentration for foam production in treating spider veins as well
- Prevents refilling

(Water's Edge Dermatology, 2018)

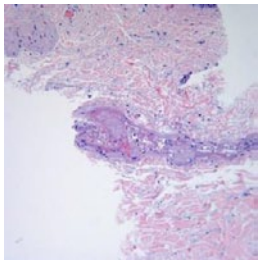
Using Hypotonic Solutions for Dilution



- This image is of a 1 mm spider vein treated with 0.15% Sotradecol diluted with 0.45% saline (10 min post subdermal tumescent)
- Notice that histologically the damage is 2-3 times greater than 0.15% Sotradecol diluted with NS

(Water's Edge Dermatology, 2018)

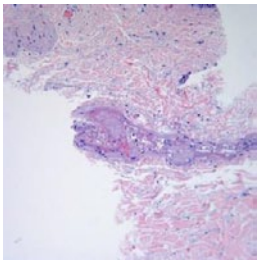
Subdermal Infusion of Tumescent



- Infusion of tumescent subdermally is done quite frequently in our practice
- Within 10 minutes many treated vessels will have intraluminal thrombosis

(Water's Edge Dermatology, 2018)

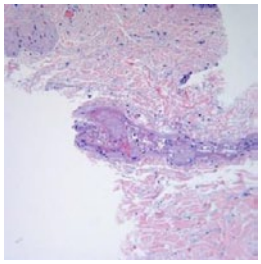
Subdermal Infusion of Tumescent



- By doing tumescent infusion, most collateral flow is ablated & spasm occurs in the vessel itself leading to rapid thrombosis of many of the treated vessels
- Clotting must be removed before completion of procedure

(Water's Edge Dermatology, 2018)

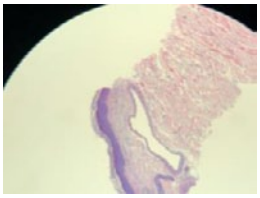
Subdermal Infusion of Tumescent

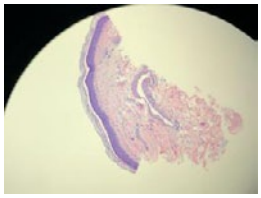


- If you remove the thrombosis by the techniques we show you in this seminar, you will have minimal staining & rapid resolution of the treated complex

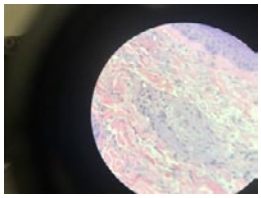
(Water's Edge Dermatology, 2018)

Before & After Subdermal Tumescent



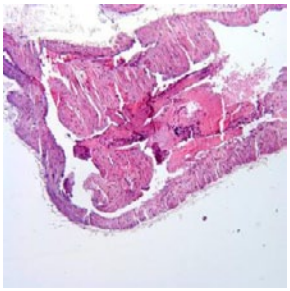


3 Weeks Post Sclerotherapy



- Lumen filled with fibrin
- Vessel wall thickened but, intact
- No inflammation around treated vessel

Sotradecol 0.1% Foam in 2mm Reticular Vein



(Bush, 2015)

Legal Ramifications of Sclerosants

- I think compounding A pharmacies should be totally avoided when purchasing Sotradecol or Polidocanol
- I am aware of many cases of adverse results with these compounds
- Legally, you must have a prescription for each patient and a separate vial labeled specificallly for them

Legal Ramifications of Sclerosants

- If you do not do the above, you are in violation of Federal Law
- Using compounding B pharmacies allows for more margins of safety due to stringent FDA requirements
- However, unless you obtain the sclerosants in small concentrations, you face the problem of sterility with repeated needle sticks into the vial

Legal Ramifications of Sclerosants

- After entry into the vial the solution is no longer considered sterile even though it may be
- Using the FDA approved compounds at the concentrations recommended, most patients can be treated for less than $20/session

Conclusion

- This study provides evidence for appropriate concentrations of FDA approved sclerosants for treating spider telangiectasia's
- Sotradecol and Polidocanol were diluted with 0.9% NS for this study
- Remember, if you use bacteriostatic water to dilute the sclerosant the damage is multiplied by a factor or 2-3

Conclusion

- Ideal concentration is 0.1% ½ NS or 0.15% NS
- This concentration range provides adequate treatment of telangiectasia, desired histological results and minimal post treatment sequelae
- The ideal concentration of Polidocanol for 1 mm spider telangiectasias may be 0.33% diluted with ½ NS

Conclusion

- Polidocanol 0.25% can be used for vessels < 0.5 mm
- Histological findings with Sotradecol foam 0.1%, 0.2%, 0.3% and Polidocanol foam 0.3% are identical

References

- Bush, R. (2015). Image retrieved 2015 from http://www.veinexperts.org/
- Green D. Sclerotherapy for the permanent eradication of varicose veins: Theoretical and practical considerations. *J Am Acad of Dermatol* 1998;38:461-475.
- McAree B, Ikponmwosa A, Brockbank K, et al. Comparative stability of sodium tetradecyl sulphate (STD) and polidocanol foam: Impact on vein damage in an in-vitro model. *Eur J Vasc Endovasc Surg* 2012;43:721-725.
- Rao J, Wildemore JK, Goldman MP. Double-blind prospective comparative trial between foamed and liquid polidocanol and sodium tetradecyl sulfate in the treatment of varicose and telaniectatic leg veins. *Dermatol Surg* 2005;31(6):631-5[discussion 35].

Aestheticveintraining.com

Neutrophilic Vascular Reactions and Selected Autoinflammatory Syndromes

Joseph L. Jorizzo, MD
Professor of Clinical Dermatology
Department of Dermatology
Weill Cornell Medical College
New York, NY - USA

Professor, Founder and Former Chair
Department of Dermatology
Wake Forest School of Medicine
Winston-Salem, NC

Conflict of Interest

Advisory Boards/Honoraria
Amgen

Neutrophilic Vascular Reactions

- Cutaneous small vessel vasculitis
- Sweet's syndrome
- Behcet's Disease
- Bowel-associated dermatosis-arthritis syndrome
- Rheumatoid neutrophilic dermatosis
- Pyoderma gangrenosum

Reference: Jorizzo JL, et al: J Am Acad Dermatol 1988;983-1005

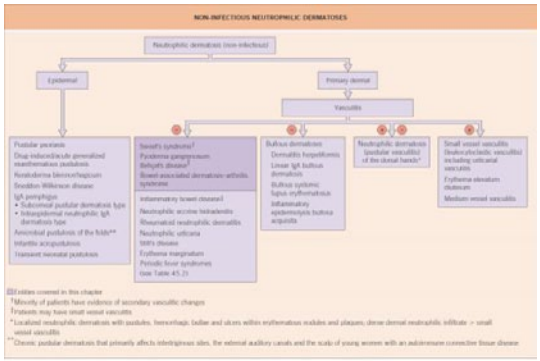


Fig. 27.1 Non-infectious neutrophilic dermatoses. Entities in the darker box are discussed in this chapter.
From Bolognia, Jorizzo & Rapini: Dermatology 2e. © 2008 Elsevier, Ltd.

Possibilities for a patient who presents with a complex medical dermatosis and systemic signs and symptoms:

1. Clinicopathologic diagnosis of dermatosis integrates all findings eg. Sarcoidosis – skin, eye, lungs, etc
2. Clinicopathologic diagnosis reveals a reactive dermatosis – communication with internist or pediatrician will outline underlying medical conditions eg. Vasculitis
3. No direct relationship – eg. Scabies/Fibromyalgia

Step 1. – Clinicopathologic diagnosis- Caution influence of therapy on biopsy and clinical appearance

Step 2. – Assess the extent (internal manifestations of disease)

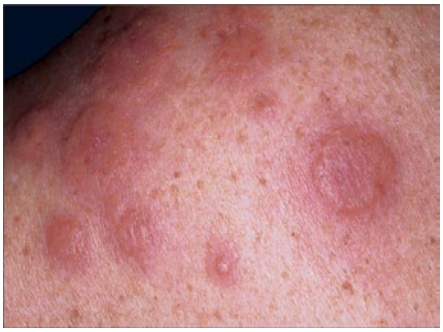
Step 3. – Assess for etiology

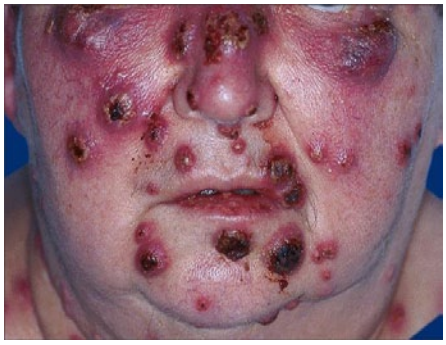
Step 4. - Therapeutic ladder

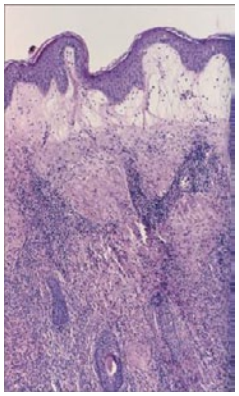
Sweet's Syndrome

Key features

- **Constitutional signs and symptoms such as fever and malaise**
- **Clinically, erythematous plaques are seen; occasionally they are bullous**
- **Histologically, dense perivascular neutrophilic infiltrate, edema and, infrequently, bullae; leukocytoclasia with minimal to no evidence of vasculitis**
- **Associated conditions include infections, malignancies (especially acute myelogenous leukemia), inflammatory bowel disease, autoimmune disorders, drugs and pregnancy**







SYSTEMIC MANIFESTATIONS OF SWEET'S SYNDROME
COMMON (≥50%)
Fever Leukocytosis
LESS COMMON (20–50%)
Arthralgias Arthritis: asymmetric, non-erosive, favors knees and wrists Myalgias Ocular involvement: conjunctivitis, episcleritis, limbal nodules, iridocyclitis
UNCOMMON
Neutrophilic alveolitis: cough, dyspnea and pleurisy; radiographic findings include interstitial infiltrates, nodules, pleural effusions Multifocal sterile osteomyelitis (SAPHO syndrome) Renal involvement (e.g. mesangial glomerulonephritis): hematuria, proteinuria, renal insufficiency, acute renal failure
UNUSUAL/RARE
Hepatitis Acute myositis Aseptic meningitis, encephalitis Pancreatitis Gastrointestinal involvement

Table 26.2 Systemic manifestations of Sweet's syndrome. SAPHO, synovitis, acne, pustulosis, hyperostosis and osteitis.

Sweet's Syndrome Related Articles 2018 alone

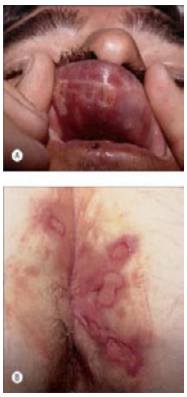
1. Clinicopathologic Expansion: SQ variant (not new); Hands (not new) Hystiocytoid
   Full blown histopathologic LCCV (not new) Insect bite overlap on histopathology
2. Internal Involvement (Sterile neutrophilic lesions) Neuro Sweet's, Upper respiratory tract, Lung)
   Eye – optic nerve, keratitis
3. Etiology
   Many more drugs
   More cancers
   More infections (Sporotrichosis, leprosy, schistosomiasis
   More autoimmune diseases – SLE, throiditis

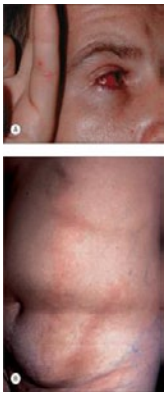
Behcet's Disease

Behcet's Disease

Key Features

- A multisystem, polysymptomatic disease
- Diagnosis is based on International Study Group criteria of recurrent oral ulceration, recurrent genital ulceration, ocular abnormalities (eg. uveitis, retinal vasculitis) and cutaneous lesions
- Cutaneous findings range from sterile papulopustules and palpable purpura to erythema nodosum-like lesions
- Histologically, a neutrophilic angiocentric inflitrate with leukocytoclastic (early) or lymphocytic (late) vasculitis is the characteristic finding





SYSTEMIC MANIFESTATIONS OF BEHÇ ET'S DISEASE

OCULAR (LEADING CAUSE OF MORBIDITY[PLUS])	NEUROLOGIC
•Occurs in 90% of patients; favors men, in whom it is more severe • Can be painful and may lead to blindness • Retinal vasculitis (more frequently associated with blindness) • Posterior uveitis (most characteristic ocular finding) • Anterior uveitis (Fig. 26.18), hypopyon • Secondary glaucoma, cataracts • Conjunctivitis, scleritis, keratitis, vitreous hemorrhage, optic neuritis	•Usually appears later during the evolution of the disease • Associated with a poor prognosis • Acute meningo-encephalitis which may resolve spontaneously • Cranial nerve palsies • Brainstem lesions that can induce swallowing difficulties, laughter and crying • Pyramidal or extrapyramidal signs
JOINTS	**VASCULAR**
•Approximately 50% of patients develop arthritis • In majority (~80% of patients), duration of attacks is <2 months • Mono- or poly-arthritic and non-erosive • Most commonly knees, wrists and ankles	Aneurysmal or occlusive arterial disease • Superficial or deep venous thrombosis
	CARDIOPULMONARY
	•Coronary arteritis, valvular disease, myocarditis •Recurrent ventricular arrhythmias • Pulmonary artery aneurysms
GASTROINTESTINAL	**RENAL**
Abdominal pain and/or hemorrhage may be difficult to distinguish from IBD (see Table 26.12) • Ulcerations* develop within the small bowel (in particular the ileocecal region) as well as the transverse and ascending colon and esophagus; perforation can occur	•Glomerulonephritis

*Resemble aphthae.

Table 26.11 Systemic manifestations of Behçet's disease. IBD, inflammatory bowel disease.

INTERNATIONAL STUDY GROUP CRITERIA FOR THE DIAGNOSIS OF BEHÇ ET'S DISEASE

Major criterion	Required features
Recurrent oral ulceration	Aphthous (idiopathic) oral ulceration observed by physician or patient, recurring at least three times in a 12-month period
PLUS ANY TWO OF THE FOLLOWING MINOR CRITERIA:	
Recurrent genital ulceration	Aphthous genital ulceration or scarring, observed by physician or patient
Eye lesions	Anterior or posterior uveitis; cells in the vitreous by slit lamp examination; or retinal vasculitis observed by ophthalmologist
Cutaneous lesions	Erythema nodosum-like lesions observed by physician or patient; papulopustular lesions or pseudofolliculitis; or characteristic acneiform nodules observed by physician in postadolescent patient not on corticosteroids
Pathergy test*	Interpreted at 24–48h by physician

*Pathergy test is performed on the flexor forearm by obliquely inserting a 20-22-gauge sterile hypodermic needle to a depth of 5 mm ± an intradermal injection of 0.1 ml of normal saline. A positive reaction is defined as the development of a papule or pustule.

Table 26.13 International Study Group criteria for the diagnosis of Behçet's disease[39].

Important Issues Regarding Behcet's Disease

1. Do not overdiagnose complex aphthosis
   Reference: Letisinger JA, McCarty MA, Jorizzo JL. Complex Aphthosis…. J Am Acad Dermatol 2005;52:500-8.
2. Exclude HLA-B27 – associated sacroileitis spectrum disease and/or inflammatory bowel disease
3. Use a therapeutic ladder mucosal/ocular and other major systemic are at polar ends.

Bowel-Associated Dermatosis-Arthritis Syndrome

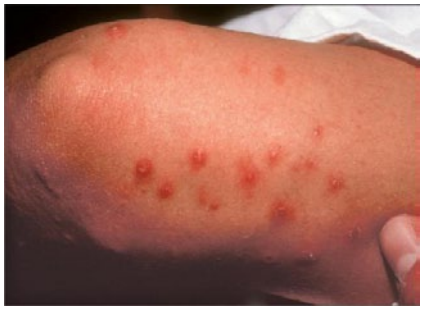
Key Features

- Constitution signs and symptoms are serum sickness-like
- Cutaneous lesions include erythematous and purpuric papules and vesicles as well as nodular panniculitis
- Associated polyarthritis and tenosynovitis
- Histopathology includes dermal nodular perivascular neutrophilic infiltrate with edema and lobular neutrophilic and septal panniculitis
- Bowel bypass syndrome was the preceding condition

  Reference: Jorizzo JL et al. Arch Intern Med 1983;143:457-61

Clinical points regarding Bowel-Associated Dermatosis-Arthritis Syndrome

- Bowel surgery suggests blind loops – evaluate carefully with gastroenterologist
- Inflammatory bowel diseases are important causes of this syndrome.
- While dermatologic therapeutic ladder is useful – management of underlying disease is the focus.



Pyoderma Gangrenosum

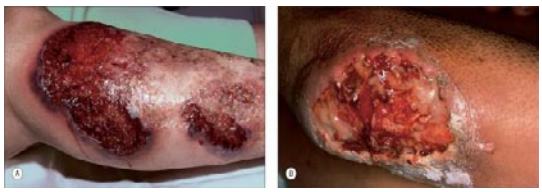
Key Features

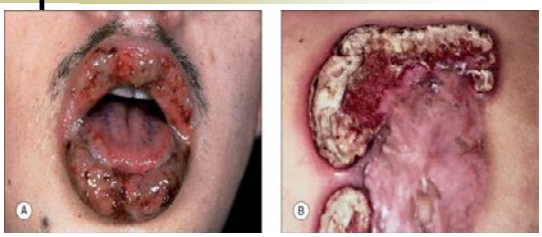
- Four major clinical forms: ulcerative, bullous, pustular, and superficial granulomatous
- Initial lesion is often a pustule on an erythematous base or an erythematous nodule
- Characteristic lesion is an ulcer with a necrotic undermined border; the base may be purulent or vegetative

Pyoderma Gangrenosum

Key Features (Continued)

- Histologically, early lesions are difficult to distinguish from Behcet's lesions
- Associated with inflammatory bowel disease, arthritis, monoclonal gammopathy and other hematologic disorders





PROPOSED DIAGNOSTIC CRITERIA FOR CLASSIC ULCERATIVE PYODERMA GANGRENOSUM
MAJOR CRITERIA
1. Rapid[a] progression of a painful[b], necrolytic cutaneous ulcer[c] with an irregular, violaceous and undermined border
2. Other causes of cutaneous ulceration have been excluded[d]
MINOR CRITERIA
1. History suggestive of pathergy[e] or clinical finding of cribriform scarring
2. Systemic diseases associated with pyodermal gangrenosum[f]
3. Histopathologic findings (sterile dermal neutrophilia, ± mixed inflammation, ± lymphocytic vasculitis)
4. Treatment response (rapid response to systemic corticosteroids)[g]
[a]Characteristic margin expansion of 1 to 2 cm per day, or a 50% increase in ulcer size within 1 month.
[b]Pain is usually out of proportion to the size of the ulceration.
[c]Typically preceded by a papule, pustule or bulla.
[d]Usually necessitates skin biopsy and additional evaluation (see Table 26.8) to exclude other causes (see Table 26.9).
[e]Ulcer development at sites of minor cutaneous trauma.
[f]Inflammatory bowel disease, arthritis, IgA gammopathy, or underlying malignancy.
[g]Generally responds to prednisone (1–2 mg/kg/day) or another corticosteroid at an equivalent dosage, with a 50% decrease in size within 1 month.

Table 26.7 Proposed diagnostic criteria for classic ulcerative pyoderma gangrenosum. Diagnosis requires both of the major criteria and at least two minor criteria[36].

THE DIFFERENTIAL DIAGNOSIS OF PYODERMA GANGRENOSUM
EARLY INFLAMMATORY NON-ULCERATIVE STAGE (PAPULES, PUSTULES, PLAQUES OR NODULES)
•Follicular infections (folliculitis, furuncle, carbuncle of bacterial, fungal or viral origin) • Cellulitis or cellulitis-like lesion (bacterial, mycobacterial or fungal origin) • Insect bite reaction • Cutaneous T- and B-cell lymphomas • Halogenoderma/iododerma or bromoderma) • Reniculitides (inflammatory, infectious, metabolic, neoplastic) • Cutaneous polyarteritis nodosa • Sweet's syndrome (see Table 26.4 for additional entities) • Behçet's disease • Bowel-associated dermatosis–arthritis syndrome
LATER ULCERATIVE OR VEGETATIVE STAGE
•Infections – streptococcal synergistic gangrene, botryomycosis, ecthyma gangrenosum, gummatous treponemal ulcers, cutaneous lesions of the deep mycoses (e.g. blastomycosis, coccidioidomycosis, paracoccidioidomycosis, chromomycosis) and atypical and typical mycobacterial infections • Parasitic infections – leishmaniasis, amebiasis, schistosomiasis • Vascular diseases – ulcerations due to venous hypertension, arterial insufficiency, non-septic emboli, hemoglobinopathies, and thrombosis (secondary to hypercoagulability; see Ch. 105) • Vasculitis – cutaneous polyarteritis nodosa, microscopic polyangiitis, granulomatous vasculitides (Wegener's granulomatosis, Churg–Strauss syndrome, temporal arteritis), autoimmune connective tissue disease (systemic lupus erythematosus, rheumatoid arthritis) and Behçet's disease • Malignancy – squamous cell carcinoma, basal cell carcinoma, cutaneous T- and B-cell lymphoma • Miscellaneous – brown recluse spider bite, ulcerative necrobiosis lipoidica, pemphigus vegetans of the Hallopeau or Neumann type, blastomycosis-like pyoderma, non-healing surgical wound, factitious ulcers, ulcers in patients with Chédiak–Higashi syndrome and leukocyte adhesion deficiency

Table 26.9 The differential diagnosis of pyoderma gangrenosum (PG)[37,39] In a series of 95 patients misdiagnosed with PG, the most common etiologies were vascular (venous or arterial; 28), vasculitis (21), malignancy (16), infection (14) and drug-induced or exogenous tissue injury (13)[39].

Clinical Points regarding Pyoderma Gangrenosum

- Most referred patients have large ulcers; but no inflammation – "Gulliver's sign" (a pterygium)
- Literature is similar to Sweet's regarding expansion of systemic manifestations and etiology
- Re-exclude mimics (diagnosis of exclusion but also contaminants on culture)
- Especially: Wegener's, histoplasmosis, atypical AFB, Sporotrichosis, factitial disease

Neutrophilic Vascular Reactions: Update 2019 Patient Evaluation: Overview

- Confirm clinical diagnosis histopathologically
- Assess extent of disease (less critical then vasculitis)
- Attempt to establish etiology
- Therapeutic ladder

Neutrophilic Vascular Reactions: Update 2019

Etiology

Work with a colleague, generally in internal medicine, to perform sequential evaluations that include history and physical examination not just laboratory tests.

Categories include:

Drugs:(be careful: association does not prove causation!)

Infections: Viral, bacterial, Deep fungal, AFB, other

Disease with immune complexes: Autoimmune connective tissue diseases, other autoimmune, inflammatory bowel disease, autoimmune liver disease, Behcet's disease, malignancy especially myelodysplastic diseases. (Curth's postulates)

Neutrophilic Vascular Reactions: Update 2019 Therapeutic Ladder: Non-ulcerative Cutaneous Lesions

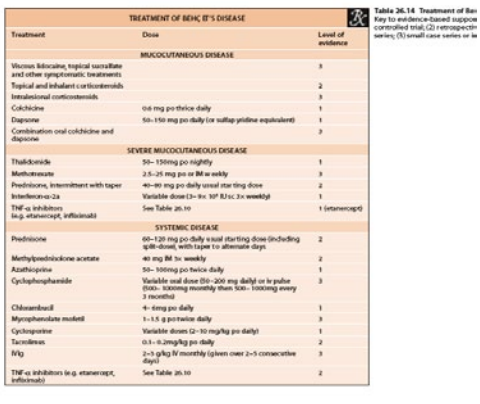
- No Therapy
- Topical therapies
- (access to site of pathology)
- Gradient Support Hose
- Antibiotics
- Pentoxifylline
- Colchicine
- Dapsone/Sulfapyridine
- Combination Colchicine/Dapsone

Neutrophilic Vascular Reactions: Update 2019 Therapeutic Ladder: Ulcerative Cutaneous Lesions or Minimal Systemic Disease

- Various topical (from corticosteroids to dapsone to metronidazole to imiquimod)
- Weekly Pulse Methotrexate
- Prednisone with slow taper
- Thalidomide

Neutrophilic Vascular Reactions Update: 2019 Therapeutic Ladder - More Severe Diseases

- Prednisone alone or in combination (1 or 2 depending on subset)
- Pulse Prednisone
- Azathioprine
- Cyclophosphamide; pulse or daily (1-for larger vessel vasculitis)
- Mycophenolate mofetil
- Chlorambucil
- Cyclosporine
- TNF alpha inhibitors
- IL- 12/23 antagonists
- IL- 1 antagonists
- Leflunomide
- Rituximab (2-Mostly SLE patients with vasculitis)
- Gevokizumab (anti IL-1beta)
- Countless treatments aimed at underlying diseases



Synovitis, Acne, Pustulosis, Hyperostosis and Osteitis (SAPHO) Syndrome

Synovitis, Acne, Pustulosis, Hyperostosis and Osteitis (SAPHO) Syndrome

Key Features

- Presence of aseptic pustular dermatosis and osteoarticular lesions
- Usually a gradual onset of painful, multifocal osteoarticular lesions, especially of the anterior chest and axial skeleton
- The course of osteoarticular lesions oscillates and is protracted, with gradual improvement that can be hastened by anti-inflammatory drugs
- Difficulty in establishing a come genetic association

Selected Auto Inflammatory Syndromes

Selected Auto Inflammatory Syndromes

- PAPA – Pyogenic arthritis, pyoderma gangrenosum, acne (E250k mutation in PSTPIP1 gene on chromosome 15q
  (The proline – serine – threonine phosphatase – interacting protein 1 gene)
- PAPAS – Pyogenic arthritis, pyoderma gangrenosum, acne, and hidradenitis suppurativa
- PASH – Pyoderma gangrenosum, acne, and hidradenitis suppurativa – PTSTPIP1 gene

Selected Auto Inflammatory Syndromes

- The usual approach to managing the neutrophilic disorders and the elements of the follicular occlusion triad (hidradenitis suppurativa, acne conglobata, and dissecting cellulitis of the scalp) are used.
- However a dramatic role for agents which block Ih-1 receptor and reduce the activity of IL-1a and 1b is being reported with anakinra and other agents are being developed

Thursday, April 11, 2019

6:00 a.m. - 7:00 a.m.	Regeneron Sanofi Genzyme Product Theater Palazzo F-G (No CME Awarded)
7:00 a.m. - 7:30 a.m.	*A VIP Approach to Customer Service* **Lawrence Kraska**
7:30 a.m. - 8:00 a.m.	*Osteopathic Approach in Dermatologic Disease* **Suzanne Sirota Rozenberg, DO, FAOCD**
8:00 a.m. - 9:00 a.m.	*New Anti-IL-23 Drugs* **Mark Lebwohl, MD**
9:00 a.m. - 10:00 a.m.	*History of Mohs Surgery* **Leon Kircik, MD**
10:00 a.m. - 10:30 a.m.	Break with Exhibitors Palazzo D
10:30 a.m. - 1:00 p.m.	General Business Meeting
1:00 p.m. - 2:00 p.m.	*Metastatic Carcinoma to the Skin* **Michael Nowak, MD**
2:00 p.m. - 3:00 p.m.	*So Many Drugs, So Little Time: A Therapeutic Update* **James Del Rosso, DO, FAOCD**
3:00 p.m. - 3:30 p.m.	Break with Exhibitors Palazzo D
3:30 p.m. - 4:30 p.m.	*Introduction to Microvascular Head and Neck Reconstruction* **James Azzi, MD**
4:30 p.m. - 5:30 p.m.	*Facial Plastic Surgery* **Jean-Paul Azzi, MD**
6:00 p.m.	Reception Valencia Terrace

A VIP Approach to Customer Service:
Creating an Exceptional Patient Experience…

Lawrence Kraska

April 11, 2019

DISCLAIMER

Currently the CEO of Water's Edge Dermatology.

VIP Customer Service: My Perspective

- Over 30 years of Healthcare Leadership experience.
- Hospitals, Physician Group Practices, Healthcare Staffing, Consulting.
- Lessons from other industries.

VIP Service in Healthcare..?

- Physician Office Visit
- Emergency Room Visit
- Scheduling ANYWHERE
- Parking ANYWHERE
- Insurance Coverage

VIP Customer Service in Other Industries

THE RITZ-CARLTON®

Walt Disney World®
Where dreams come true

Southwest®

Chick-fil-A

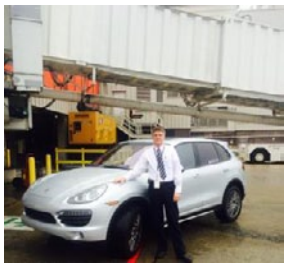
Example #1: Creating a WOW experience

The best ideas often come directly from your customers or patients…

Example:

DELTA

DELTA (Concept Recommended by Customer)



7

Example #2: Empower and reward your staff

The best ideas often come directly from your staff...

Example:

THE RITZ-CARLTON

8

Example #3: The Golf Cart...

Be innovative... Constantly look for ways to improve service.

9

Example #4: Recruit and retain great staff (ROR)

MESSAGE FROM THE OWNER

It's hard to believe we just celebrated two years in the Deerfield Beach community. As we move into our third year, I am making a strategic bet on our people.

We are moving our base pay to $13 an hour by November 5th.

My vision for the restaurant is "A Remarkable Experience Served by Remarkable People." We have some pretty Remarkable People on staff. My hope is that this move will attract more like-minded individuals so that we can fully execute a Remarkable Experience.

Please pass the word along. If you or someone you know may be interested in joining our team at Chick-fil-A Hillsboro & Powerline, they can apply at:

www.PleaseApplyOnline.com/CFAHillsboro

Opportunities for career advancement are plentiful. I'm committed to supporting my team member's professional aspirations both in or outside Chick-fil-A.

10

Example #5: Small touches matter...

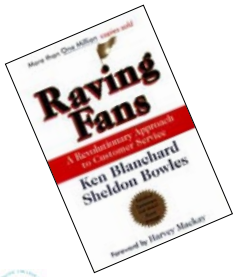
11

VIP Customer Service

- Look for examples of VIP Customer Service in other businesses.
- Great patient care will build your practice. Great service will accelerate your growth.
- Hire, train, and reward your staff.
  - ROR
  - Get feedback from your staff. Reward great ideas.
  - How do we improve patient satisfaction?
  - How do we reduce wait times?
- Attention to details:
  - Front desk.
  - Waiting room.
  - Parking and building appearance.
- Time.
  - Spend time.
  - Be on time.
  - Track wait time.
- Get feedback from your patients.
  - Patient surveys at time of visit.
  - Healthgrades or other star rating surveys.

12

"Raving Fan" Concept:



13

Contact:

Lawrence Kraska

Mobile: 678-315-6086

lkraska@wederm.com

14

Dermatology & Osteopathic Medicine

Suzanne Sirota-Rozenberg, D.O. FAOCD, FAAD
Program director
Department of Dermatology
St. John's Episcopal Hospital

Angela Kim, D.O., MPH, PGY2
Ann Lin, D.O., PGY2

Disclosures

- I have no conflict of interest or any disclosures

Objectives

- Review Osteopathic Principles
- Osteopathic principles in dermatology
- Medical dermatology cases
- Osteopathic Manipulative Medicine
- Dermatology and Osteopathic medicine

Osteopathic Tenets

- Body is a unit; the person is a unit of body, mind, and spirit
- The body is capable of self-regulation, self-healing, and health maintenance
- Structure and function are interrelated
- Rational treatment is based on an understanding of 3 main principles

What are our goals as Osteopathic physicians?

- Seek and address root cause(s) of disease using available evidence-based approaches
- Optimize patient's self-regulating and self-healing capacities
- Provide individualized care plan with emphasis on
  - Health promotion and disease prevention
  - Patient education
  - Patient partnership
- Incorporate palpatory diagnosis and OMM, when appropriate, for well being of patient

Osteopathic principles in Dermatology

Osteopathic Approach in Dermatology	Dermatologic Disease
Osteopathic Manipulative Treatment	
Patients with skin conditions may benefit from osteopathic manipulative treatment as adjunctive therapy	stasis dermatitis, primary hyperhidrosis, brachioradialis pruritis, notalgia paresthetica
Principle 1. The body is a unit.	
Skin disease may affect the mind	acne vulgaris, psoriasis, vitiligo, melasma
The mind may cause or exacerbate cutaneous disease	delusions of parasitosis, trichotillomania, dysesthesia syndromes, pruritis
Principle 2. The body is capable of self-regulation, self-healing, and health maintenance.	
Some skin diseases have an immunologic basis for pathogenesis	psoriasis, atopic dermatitis, vitiligo, alopecia areata
Self-limited skin diseases illustrate the body's ability to heal	pityriasis rosea, granuloma annulare, erythema toxicum neonatorum, lichen striatus
Skin disease can be actively prevented	nonmelanoma skin cancer, melanoma
Principle 3. Structure and function are interrelated.	
Defects in skin structure result in skin disease	bullous impetigo, bullous pemphigoid, pemphigus vulgaris, epidermolysis bullosa variants
Principle 4. Rational treatment is based on an understanding of the 3 main principles.	
Examining the patient as a whole	acne vulgaris, psoriasis, occupational dermatoses, dermatomyositis
Cutaneous signs of internal disease	acanthosis nigricans, recurrent dermatophyte infections, eruptive xanthomas, pruritus

Campbell SM, et al. Dermatology: A Specialty That Exemplifies the Osteopathic Medical Profession. *J Am Osteopath Assoc* 2011;111(5):335–338.

1. Body is a unit; the person is a unit of body, mind, and spirit

Acne vulgaris

Psoriasis

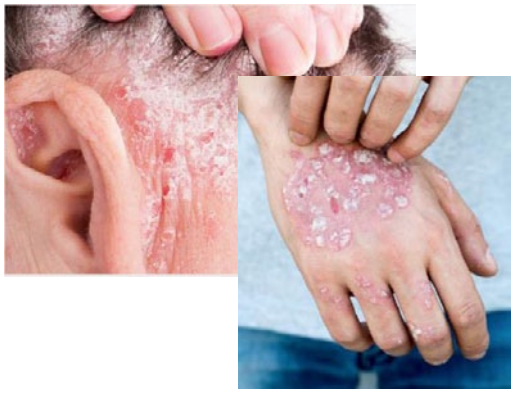
Acne Vulgaris

- Multifactorial
  - Increased sebum production, Follicular hyperkeratinization, Proliferation of Cutibacterium acnes (formerly Propionibacterium acnes), inflammation
  - Drugs, cosmetics, etc
- Comedonal, papular, pustular, cystic types
- Topical and oral retinoids, benzoyl peroxide, topical and oral antibiotics, salicylic acid, spironolactone(off label), oral contraceptives, etc
- Prevent resistance of topical antibiotics by adding topical benzoyl peroxide to the regimen
- → **Scarring and psychosocial stress**
- Prevention and early treatment!!

Acne Vulgaris

Psoriasis

- Chronic, intermittently relapsing inflammatory disease
- Well demarcated erythematous silvery scaly plaques on scalp, elbows, knees, nails, hands, feet, trunk
- Different variants of psoriasis
- Topical steroids and vitamin D analogs, tar based therapy, biologics, etc
- Linked to higher likelihood of suicidal ideation, suicide attempts, and completed suicides (JAAD, Aug 2018)
- Possible new therapy: JAK inhibitors (tofacitinif, baricitinib) (JAAD, Aug 2018



2. The body is capable of self-regulation, self-healing, and health maintenance

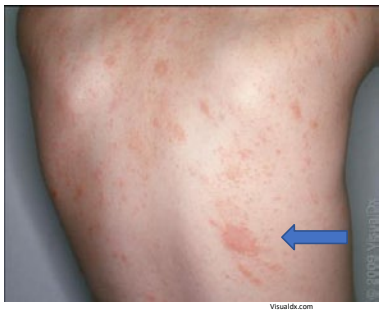
Pityriasis Rosea

Pityriasis Rosea

- Exanthematous disease associated with Human Herpes Virus-6 & HHV-7
- Starts as solitary pink, salmon scaly plaque (herald patch) → spreads in Christmas tree pattern
- Associated with fetal demise if pregnancy women affected within first 15 weeks of gestation

(Drago, et al. JAAD 2008 May;58(5 Suppl 1):S78-83; Drago et al, Dermatology. 2018;234(1-2):31-36.)

Pityriasis Rosea



Visualdx.com

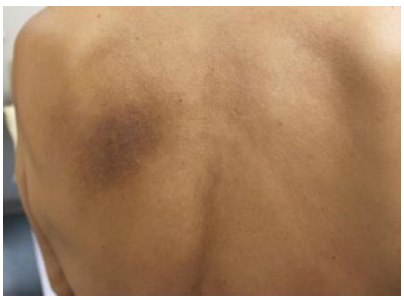
3. Structure and function are interrelated

Notalgia Paresthetica

Notalgia Paresthetica

- Idiopathic (..spinal nerve impingement?)
- Sensory neuropathic syndrome of the midback skin
  - T2-T6 → localized pruritus and dysesthesia (mild→severe)
- Hyperpigmented patch on the scapular/interscapular region
- Unsatisfactory treatment to date
  - Topical capsaicin
  - Gabapentin
  - Botox
  - Physiotherapy/OMM

Notalgia Paresthetica



Primary care dermatology society. http://www.pcds.org.uk

Current therapies to date…

An Bras Dermatol. 2014 Jul-Aug;89(4):570-5.

Efficacy of gabapentin in the improvement of pruritus and quality of life of patients with notalgia paresthetica.

Maciel AA[1], Cunha PR[1], Larsia IO[1], Trevisan E[2].

J Am Acad Dermatol. 1995 Feb;32(2 Pt 1):287-9.

Successful treatment of notalgia paresthetica with topical capsaicin: vehicle-controlled, double-blind, crossover study.

Wallengren J[1], Klinker M.

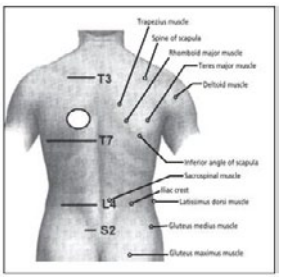
The Cutting Edge

August 2007

Successful Treatment of Notalgia Paresthetica With Botulinum Toxin Type A

Pamela Kirschner Weinfeld, MD

OMM for Notalgia paresthetica

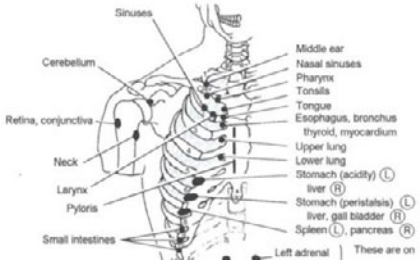


Richardson BS, et al. OMT in the management of notalgia paresthetica. *J Am Osteopath Assoc.* 2009;109:605-608

- **Muscle energy**
- **HVLA**
- **Counterstrain**
- **Chapman's points**

Sahhar, L et al. "Treatment of notalgia paresthetica with manipulative physiotherapy." in Australasian Journal of Deramtology. 2018

Chapman's Points



4. Rational treatment is based on an understanding of the 3 main principles

Whole person approach

Dermatologic manifestation of internal diseases

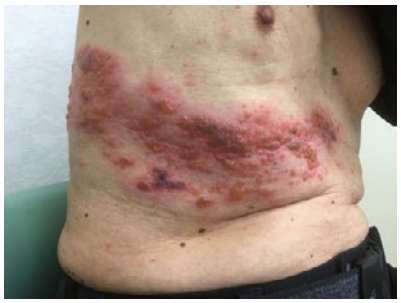
Medical dermatology cases

- Herpes Zoster
- Post herpetic neuralgia
- Stasis Dermatitis
- Elephantiasis Nostra Verrucosa
- Lipodermatosclerosis
- Hyperhidrosis

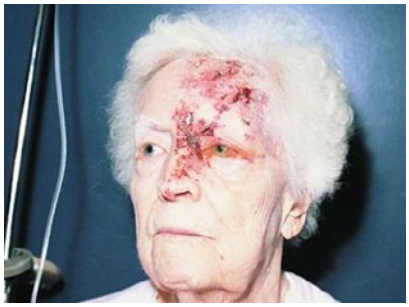
Herpes Zoster Infection (Shingles)

- Reactivation of latent varicella-zoster virus (chickenpox), dormant in dorsal root ganglia
- Transmission by airborne droplets or direct contact with active lesions
- Virus replicates in DRG →ganglionitis →intensified pain down sensory nerve
- Groups vesicles in unilaterna dermatomal distribution
- Typically resolves without sequelae…

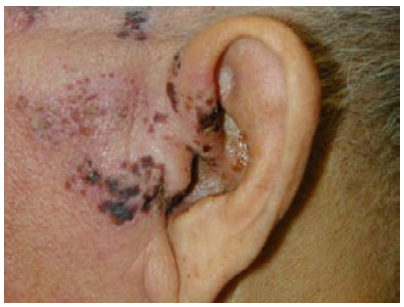
Thoracic spine



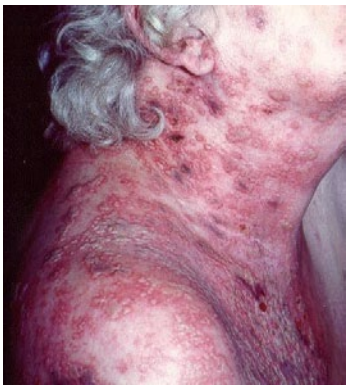
Hutchinson's sign and zoster ophthalmicus



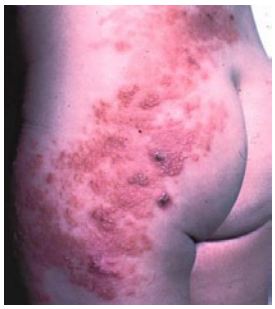
Ramsay Hunt Syndrome



Cervical spine



Lumbar spine



Current pharmacologic therapy

- Immunocompetent/uncomplicated hosts
  - Less than or equal to 72 hours since onset, prescribe one of following:
    - Valacyclovir 1g BID for 7-10days (initial); 500mg BID x 3 days or 1g QD x 5days (recurrent); 500mg or 1g QD (suppressive)
    - Famciclovir 500mg TID for 7 days
    - Acyclovir 800mg Five times daily for 7 days
  - Greater than 72 hours since onset
    - Prescribe antiviral only if ongoing new lesions- indication of ongoing viral replications
    - Otherwise, minimal benefit
- Pregnant women
  - Little evidence for increased risks for complications
  - Treat early herpes zoster
    - Oral acyclovir 800mg five times daily for 7 days
- Immunocompromised hosts:
  - Regardless of time frame of rash presentation
    - **Treat EVERYONE**
    - Rapid initiation of therapy is critical
    - Severe disease: Acyclovir IV therapy for disseminated zoster

Alternative Treatment

Transl Biomed. 2012;3(2). pii: 2.

In vitro antiviral activity of honey against varicella zoster virus (VZV): A translational medicine study for potential remedy for shingles.

Shahzad A[1], Cohrs RJ.

BMC Complement Altern Med. 2009 Aug 12;9:31. doi: 10.1186/1472-6882-9-31.

Acupuncture in acute herpes zoster pain therapy (ACUZoster) - design and protocol of a randomised controlled trial.

Fleckenstein J[1], Kramer S, Hoffrogge P, Thoma S, Lang PM, Lehmeyer L, Schober GM, Pfab F, Ring J, Weisenseel P, Schotten KJ, Marsmann U, Imich D.

OMM in Herpes Zoster

- As adjuvant therapy **AFTER** acute phase to help prevent post herpetic neuralgia
  - Suboccipital decompression to normalize the peripheral nervous system
  - Muscle energy to upper thoracic and cervical regions
  - Rib raising to normalize the sympathetic nerves

Postherpetic Neuralgia

- Most common complication of Herpes Zoster (Shingles)
- Neuropathic pain that persist after the skin lesions have healed

Adjunctive treatments for PHN

Drugs Aging. 1995 Oct;7(4):317-28.

Topical capsaicin. A review of its pharmacological properties and therapeutic potential in post-herpetic neuralgia, diabetic neuropathy and osteoarthritis.

Rains C[1], Bryson HM.

Drugs. 2004;64(9):937-47.

Review of lidocaine patch 5% studies in the treatment of postherpetic neuralgia.

Davies PS[1], Galer BS.

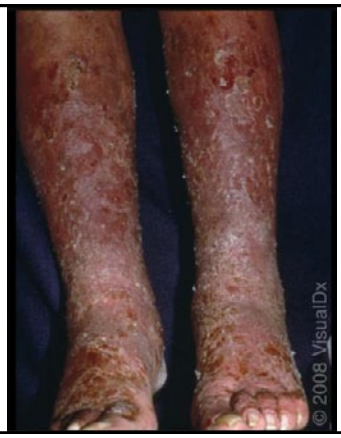
Med Sci Monit. 2010 May;16(5):CS56-61.

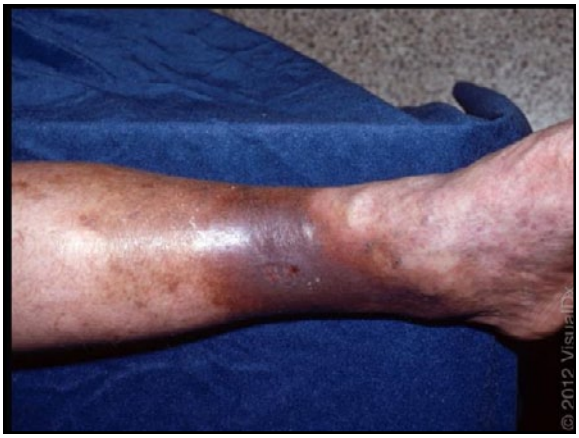
Intravenous administration of vitamin C in the treatment of herpetic neuralgia: two case reports.

Schencking M[1], Sandholzer H, Frese T.

Stasis Dermatitis

- Common in older patients with cardiac insufficiency and venous incompetence
- 2/2 gravity and increased hydrostatic pressure → leaky vessels
- Hemosiderin deposits → hyperpigmentation (MC supramalleolar)
  - pronounced erythema and scaling (MC medial malleoli)
  - May be dry and pruritic
  - May have vesiculation, oozing, and ulcerations





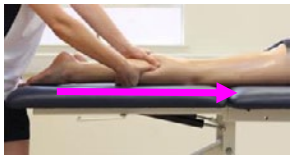
Stasis Dermatitis Management

Medical Management:
- Support stockings (knee high, moderate: 20-30 mmHg pressure)
  - in the morning when leg is least edematous
- Ace wraps
- Leg elevation
- Topical steroids
- Compresses if weeping

OMM:
- **First, open Thoracic inlet!!**
  - Direct or indirect myofascial release
- Lymphatic pump, effleurage
  - May decrease edema and thus improve condition and decrease the incidence of venous stasis ulcers

OMM for Stasis Dermatitis

Open thoracic inlet: superior and medial border of left clavicle via direct or indirect myofascial release



Effleurage: Stroking of appendage from distal to proximal

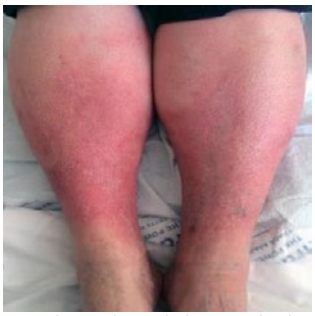
Pedal pump

Pedal lymphatic pump using dorsiflexion, with contraction of the posterior compartment of the lower extremity.

Lipodermato-sclerosis

- Inflammatory disease of the subcutaneous fat 2/2 chronic venous insufficiency
- Unknown pathogenesis
- Erythematous tender plaques, usually on lower extremities
  - Acute: <1 month
  - Subacute: 1 month to 1 year
  - Chronic: greater than 1 year

Lipodermatosclerosis



- Painful, symmetric, red to purple, poorly demarcated, indurated plaques in a stocking like distribution

Lipodermatosclerosis Medical and Osteopathic Management

- Compression therapy
- Stanozolol – androgen and anabolic steroid
- Pentoxifylline – xanthine derivative/anti-inflammatory
- Antibiotics
- ILK
- Foam sclerotherapy
- Danazol

OMM
- Similar to stasis dermatitis
  - Open thoracic oulet
  - Effleurage/Pedal pump
- Can add manual stretching to help the fibrosis

Complementary therapy? $$$

J Am Acad Dermatol. 2011 Nov;65(5):e157-8. doi: 10.1016/j.jaad.2011.06.040.

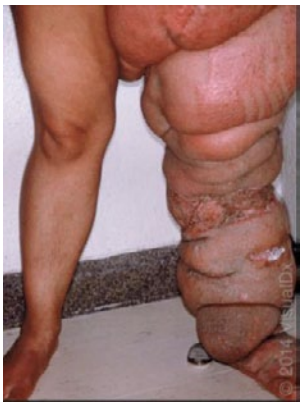
Refractory lipodermatosclerosis treated with intralesional platelet-rich plasma.

Jeong KH, Shin MK, Kim NI.

Elephantiasis Nostras Verrucosa

- Rare complication of chronic obstructive lymphedema
- Pathogenesis:
  - Repetitive streptococcal infections, obesity, poor lymphatic drainage
- Massive constant leg and foot edema with generalized lichenification, hyperkeratotic verrucous plaques, coarsening, corrugation, and fissuring
  - Malodorous
- Treatment is challenging

Elephantiasis Nostras Verrucosa



Medical and osteopathic management

- Similar to stasis dermatitis
  - Support stockings (knee high, 20-30 mmHg pressure)
  - Leg elevation
  - Topical steroids
  - Compresses if weeping
  - Unna boot
  - Surgery
- lymphatic osteopathic manipulation
  - Open thoracic outlet
  - Pedal pump
  - Effleurage

Hyperhidrosis

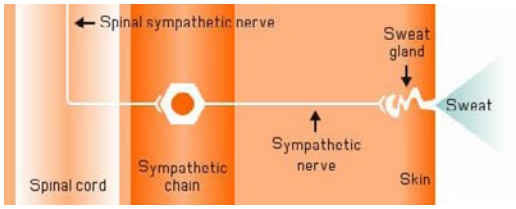
Hyperhidrosis

- Affects 1-5% of population.
- Family history,
- Primary and Secondary causes
- Excessive sweating, typically affecting palms, axilla and soles
  - Cholinergic – excessive thermoregulation
- Somatic dysfunction findings
  - T2-T3 dysfunction

Hyperhidrosis

- Suggested diagnostic criteria for primary focal hyperhidrosis:
  - Focal, visible, excessive sweating of at least six months duration without apparent cause
  - Plus at least two of the following:
    - Bilateral and relatively symmetric
    - Impairs daily activities
    - At least one episode per week
    - Onset before age 25
    - Family history of idiopathic hyperhidrosis
    - Focal sweating stops during sleep

Pathogenesis



Current hyperhidrosis treatment and OMM

- Topical aluminum chloride hexahydrate (Drysol)
- Topical anticholinergics
  - **Newly FDA approved (2018): glycopyrronium cloth wipes (Qbrexza) for primary axillary hyperhidrosis for age >9 yo**
- Oral anticholinergics
- Tap water Iontophoresis
- Botulinum A neurotoxin
- Liposuction and surgical excision (axilla)
- Sympathectomy

OMM

- Suboccipital release, rib sympathetic inhibition

OMM for hyperhidrosis

Suboccipital release

- place fingertips into patient's suboccipital region bilaterally
- apply vertical anterior pressure until occiput rests on palm of hand
- complete with gentle cephalad force on occiput

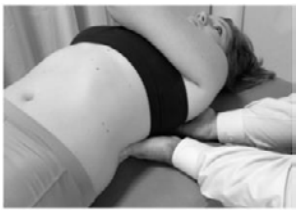
Rib Sympathetic Inhibition Technique

T1-T12

- place hands palms up under throax and apply anteriolateral force on rib angles for >90 seconds
- *<30 sec stimulates sympathetiic ANS!

T12-L2

- place hand with finger pads touching the far side erector spinae and thenar eminance touching the near side erector spinae and squeeze together for >90sec



Osteopathic Manipulative Treatment

- Benefits of OMM for skin conditions as adjuvant therapy
- OMM to address physiologic effects of stress (Emmet et al, JAOA 2018; 118(2):e11)
  - Suboccipital depression → induce parasympathetic
  - Rib sympathetic inhibition → decrease sympathetic tone
- Lymphatic treatment for inflammatory skin diseases (Hibler, JAOCD 2014)
  - Open thoracic outlet/Pedal pump/effleurage

Conclusions

- Instilled in dermatology are osteopathic principles
- multifaceted field
- Whole person approach: body, mind, and spirit
- Think "outside the box"
- Osteopathic manipulation can be an adjunctive therapy that can benefit our dermatology patients

"To find health should be the object of the doctor. Anyone can find disease."

- A.T. Still, MD, DO

Questions?

References:

- Andrews' Diseases of The Skin. Twelve Edition, Saunders Elsevier, 2006.
- Use of Complementary Medicine in Among Outpatients with Dermatologic Conditions within Yorkshire and South Whales, United Kingdom. Baron et. al. JAAD. 2005. Vol 52(4). P589-594.
- Bolognia, Jean, et al. *Dermatology*. Elsevier, 2018.
- Campbell SM, et al. Dermatology: A Specialty That Exemplifies the Osteopathic Medical Profession. *J Am Osteopath Assoc* 2011;111(5):335–338.
- Davies PS, Galer BS. Review of lidocaine patch 5% studies in the treatment of postherpetic neuralgia. Drugs. 2004;64(9):937-47
- Dermatology. Bolognia, Jean et. al, Volume One, Mosby, 2003
- Drago, et al. JAAD 2008 May;58[5 Suppl 1):S78-83; Drago et al, Dermatology. 2018;234(1-2):31-36.
- Ellis C. Notalgia paresthetica: the unreachable itch. *Dermatol Pract Concept*. 2013;3(1):3-6. Published 2013 Jan 31. doi:10.5826/dpc.0301a02
- Emmet et al, OMT to address the physiologic effects of stress.JAOA 2018; 118(2):e11)
- Foundations of Osteopathic Medicine. Robert Ward, Executive Editor, Williams and Wilkins, 1997.
- Forearm Neuropathy and Pruritis, Massey EW, Massey JM. South Med J. Oct 1986: 79(10): P1259-1260.
- Fleckenstein J, et. al. Acupuncture in acute herpes zoster pian therapy (ACUZoster) – design and protocol of a randomized controlled trial. BMC Complement Alternative Medicine. (2009);Agust 12;19:31
- Hibler et al. OMM for Inflammatory Skin diseases. JAOCD. 2014;31:11-3
- Maciel et al. An Bras Dermatol. 2014 July-Aug 89(4):570-5
- *UpToDate*, www.uptodate.com
- Ialtzad A, Cohrs RJ. In vitro antiviral activity of honey against varicella zoster virus (VZV): A translation medicine study for potential remedy for shingles. Translational Biomed. 2012;3(2)
- Osteopathic Considerations in Systemic Dysfunction. Kuchera M and Kuchera W, Greyden Pres, 1994.
- Pottenciha TJ, et.al. Topical amitriptyline-ketamine for the treatment of brachioradial pruritus. JAMA Dermatology. 2013 Feb;149(2):148-50
- Primary care dermatology society. http://www.pcds.org.uk
- Rains C, Bryson HM. Topical Capsaicin. A review of its pharmacological properties and therapeutic potential in post herpetic neuralgia, diabetic neuropathy and osteoarthritis. Drugs Aging. 1995 Oct; 7(4):3127-28
- Richardson BS, et al. OMT in management of notalgia paresthetica
- Sahhar, L. , Howard, M. , Allnutt, K. , Andrews, F. , Bergman, R. and Gin, D. (2018), Treatment of notalgia paraesthetica with manipulative physiotherapy. Australas J Dermatol, 59: 241-243. doi:10.1111/ajd.12701
- Schencking M, Sandholzer H, Frese T. Intravenous administration of vitamin C in the treatment of herpetic neuralgia: two case reports. Medicine Science Monitoring. 2010. May;16(6): CS58-61
- Visualdx.com
- Wallengren J, Klinker M. Successful treatment of notalgia paresthetica with topical capsaicin: vehicle-controlled, double-blind, cross study. JAAD. 1995 Feb;32(2 Pt 1):287-9
- Winhoven SM, Coulson IH, Bottomley WW. Brachioradial pruritus: response to treatment with gabapentin. British Journal of Dermatology
- Weinfield PK. Successful treatment of Notalgia Paresthetica with botulinum toxin type A. The Cutting Edge. 2007; August
- Youtube.com. https://www.youtube.com/watch?v=2y963kkzaf4

THANK YOU, NEXT!

New Anti-IL-23 Drugs

Mark Lebwohl, MD

Sol and Clara Kest Professor
And Chairman
Kimberly and Eric J. Waldman
Department of Dermatology
Icahn School of Medicine at Mount Sinai

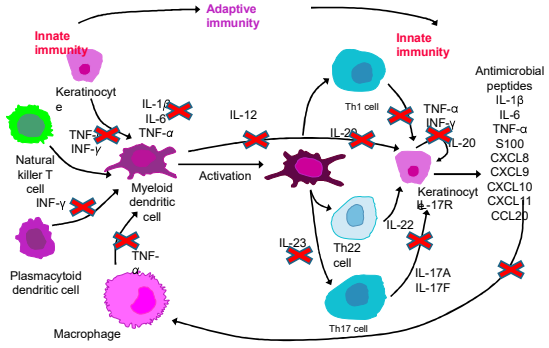
Mark Lebwohl is an employee of Mount Sinai which receives resear
funds from: Abbvie, Amgen, Boehringer Ingelheim, Celgene, Eli Li
Janssen / Johnson & Johnson, Kadmon, Medimmune/Astra Zeneca,
Novartis, Pfizer and ViDac.

Dr. Lebwohl is also a consultant for Allergan, Boehringer-Ingelheim
and Promius.

Anti-IL- 23 drugs: Guselkumab, Tildrakizumab, Risankizumab, Mirikizumab

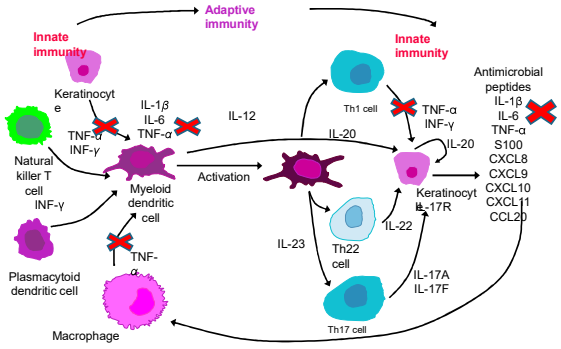
- What are they? How do they work?
- How effective are they?
- Does patient weight affect efficacy?
- Are they safe?
- Patient scenarios where IL-23 therapy might be ideal

Mechanism of Cyclosporine



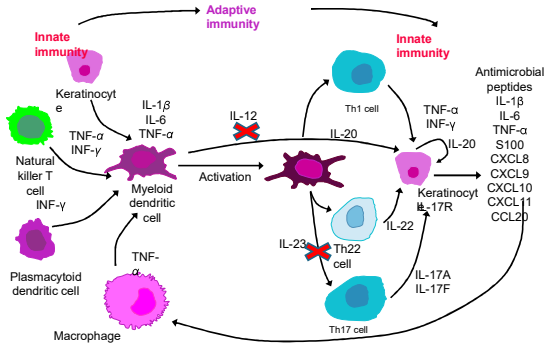
Adapted from: Nestle F, et al, NEJM 2009; 501.

Mechanism of TNF blockers



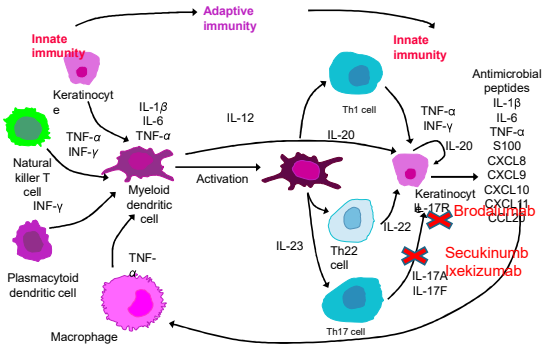
Adapted from: Nestle F, et al, NEJM 2009; 501.

Mechanism of ustekinumab



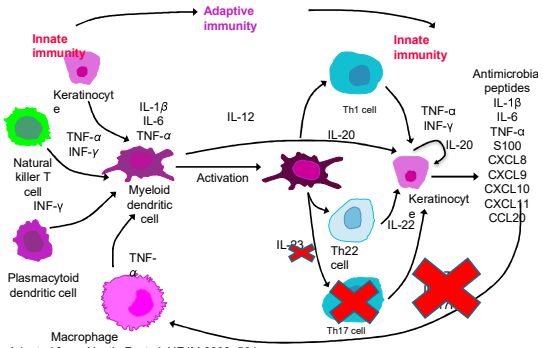
Adapted from: Nestle F, et al, NEJM 2009; 501.

Mechanism of Secukinumab, Ixekizumab & Brodalumab



Adapted from: Nestle F, et al, NEJM 2009; 501.

Mechanism of Tildrakizumab, Guselkumab, Risankizumab, Mir



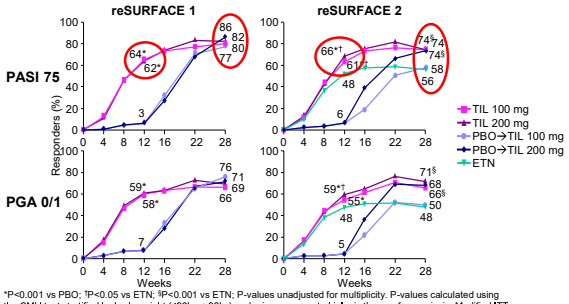
Adapted from: Nestle F, et al, NEJM 2009; 501.

IL-23 blockers – advantages of less frequent dosing

Guselkumab	Tildrakizumab	Risankizumab	Mirikizumab
• 100 mg sc	• 100 mg sc	• 150 mg sc	• 150 mg sc
• 100 mg **w.0,4 then q8w**	• 100 mg **w.0, 4 then q12w**	• 150 mg **w.0,4 then q12w**	• 150 mg x 2 **q4w**

- Tildrakizumab
- Guselkumab
- Risankizumab
- Mirikizumab

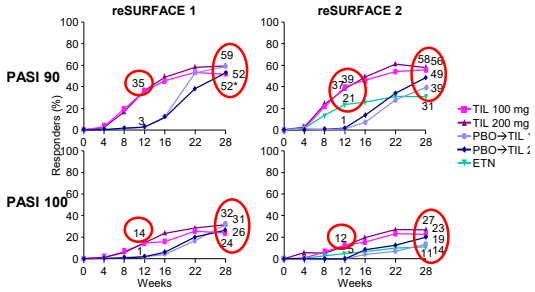
Tildrakizumab-PASI 75; PGA 0/1



*P<0.001 vs PBO; †P<0.05 vs ETN; §P<0.001 vs ETN; P-values unadjusted for multiplicity. P-values calculated using the CMH test stratified by body weight (≤90kg, >90kg) and prior exposure to biologic therapy for psoriasis. Modified ITT population (all randomized patients who received ≥1 dose of study medication). Figure represents observed data only; data shown for Week 12 are based on missing data being imputed as non-responders

Reich K, et al. EADV 2016, D3T01.1I Late Breaker Sponsored by Sun Pharmaceutical

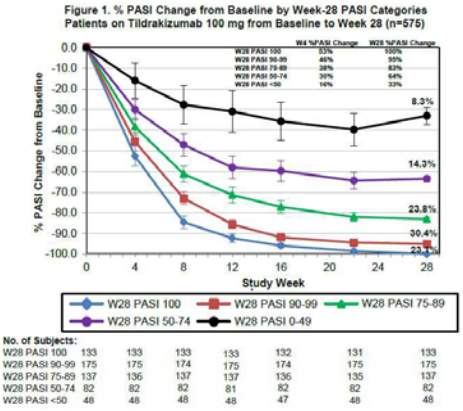
Tildrakizumab-PASI 90 and 100



Modified ITT population (all randomized patients who received ≥1 dose of study medication). Figure represents observed data only; data shown for Week 12 are based on missing data being imputed as non-responders.

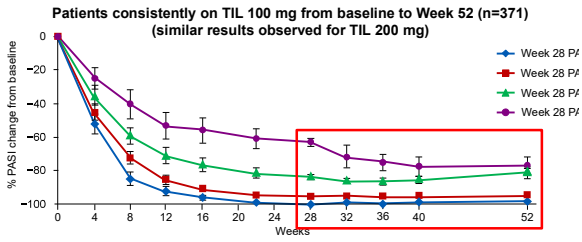
Reich K, et al. EADV 2016, D3T01.1I Late Breaker Sponsored by Sun Pharmaceutical

Tildrakizumab



Blauvelt A, et al. AAD 2018, P6869 Sponsored by Merck Sharp & Dohme Corp, a subsidiary of Merck & Co., Inc.

Post hoc pooled analysis of reSURFACE 1 and 2: PASI change tildrakizumab at Week 52 based on Week 28 response

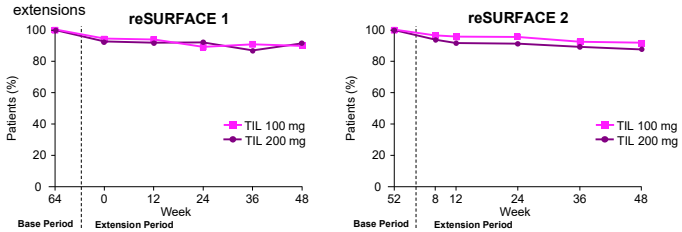


Blauvelt A, et al. AAD 2018, P6869 Sponsored by Merck Sharp & Dohme Corp, a subsidiary of Merck & Co., Inc.

reSURFACE 1 and 2: Maintenance of PASI 75 response levels in 2-year open-label extension

Tildrakizumab

- Eligible patients had to have completed the base studies and have chosen to continue optional extensions

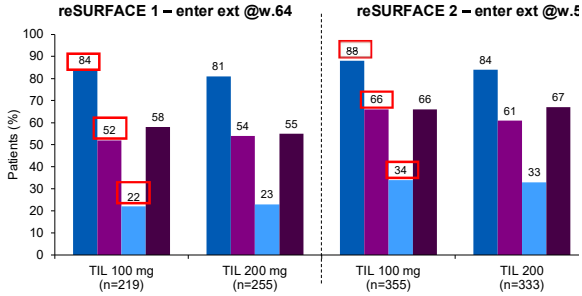


TIL 100: n=	209	203	202	202	197	195	TIL 100: n=347	326	340	341	334	327
TIL 200: n=	218	212	215	214	203	208	TIL 200: n=305	293	301	298	296	293

FAS (full analysis set; subjects with ≥1 dose of extension treatment based on assigned treatment); observed data
Patients entering OLE after 64 weeks (reSURFACE 1) or 52 weeks (reSURFACE 2) were at least partial responders (PASI ≥50). For reSURFACE 1, patients had to have received active drug within 12 weeks of end of base study

Papp K, et al. EADV 2017, D3T01.1H Sponsored by Merck & Co., Inc.

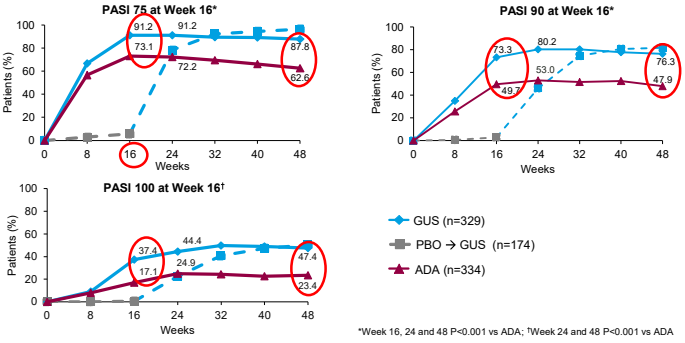
reSURFACE 1 and 2: Overall efficacy after 2 yrs



FAS (full analysis set; subjects with ≥1 dose of extension treatment based on assigned treatment); as observed data
Patients entering OLE after 64 weeks (reSURFACE 1) or 52 weeks (reSURFACE 2) were at least partial responders (PASI ≥50).
For reSURFACE 1, patients had to have received active drug within 12 weeks of end of base study

Papp K, et al. EADV 2017, D3T01.1H Sponsored by Merck & Co., Inc.

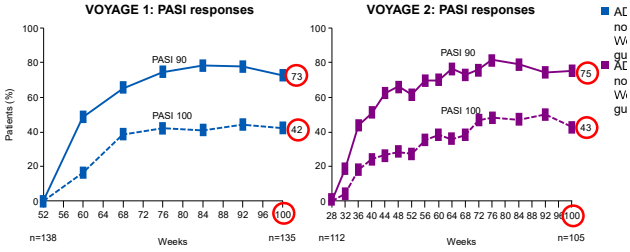
VOYAGE 1: GUS vs ADA in moderate-to-severe psoriasis PASI 75, PASI 90 and PASI 100



*Week 16, 24 and 48 P<0.001 vs ADA; †Week 24 and 48 P<0.001 vs ADA

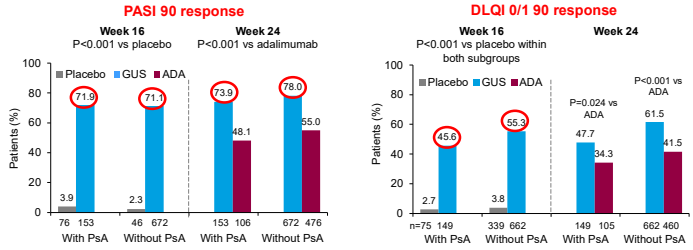
Blauvelt A, et al. EADV 2016, D3T01.1D Sponsored by Janssen Global Services LLC

VOYAGE 1 and 2: Clinical response to guselkumab treatment among adalimumab PASI 90 nonresponders



Griffiths CEM, et al. AAD 2018, P6858 Sponsored by Janssen Research & Development, LLC

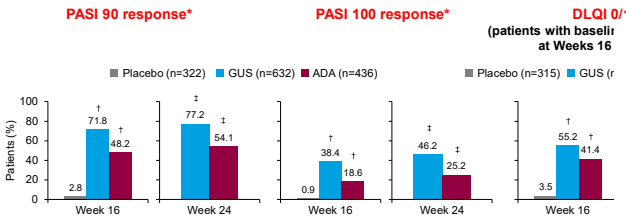
VOYAGE 1 and 2: PASI 90 and DLQI 0/1 responses for guselkumab in psoriasis patients with and without psoriatic arthritis



- PASI response rates are similar in patients treated with guselkumab with or without reported PsA
- DLQI responses are lower in patients with PsA, suggesting that PsA contributes significantly to psoriasis QoL

Kimball AB, et al. EADV 2017; P1828 Sponsored by Janssen Research and Development LLC

VOYAGE 1 and 2: PASI and DLQI responses for guselkumab patients who entered with moderate IGA (3)

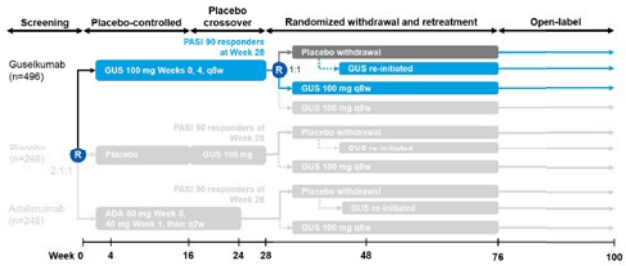


With fewer injections, do patients with moderate disease become candidates for biologics?

*Among patients with baseline IGA score of 3 (VOYAGE 1 and 2); †P<0.001 vs placebo; ‡P<0.001 vs ADA

Griffiths CEM, et al. EADV 2017; P1803 Sponsored by Janssen Research and Development LLC

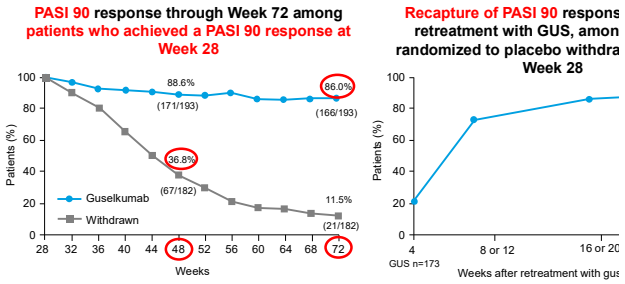
VOYAGE 2: Long-term efficacy of guselkumab after withdrawal and retreatment in patients with moderate to severe psoriasis



Analysis focuses on GUS-treated patients who achieved PASI 90 at Week 28 and were then randomized to placebo withdrawal (with retreatment upon loss of ≥50% of Week 28 PASI improvement) or continued GUS through Week 72

Gordon K, et al. AAD 2018, Late-breaking Research: Clinical Trials; Sponsored by Janssen Research & Development, LLC

VOYAGE 2: PASI 90 responses with maintenance, withdrawa and retreatment with guselkumab through 72 weeks

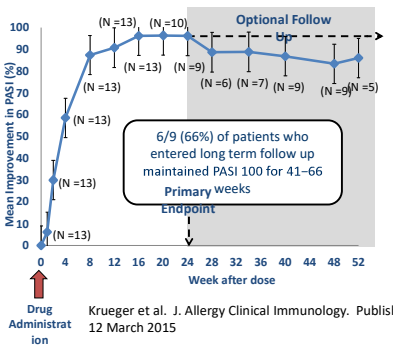


Nonresponder imputation

Gordon K, et al. AAD 2018, Late-breaking Research: Clinical Trials; Sponsored by Janssen Research & Development, LLC

Risankizumab

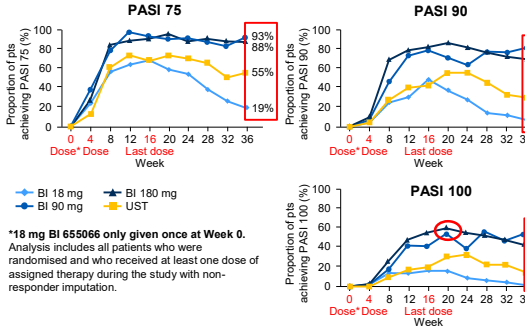
Mean PASI Improvement in Patients Treated with Subcutaneous BI 655066 (0.25 and 1.0 mg/kg)



Krueger et al. J. Allergy Clinical Immunology. Published on line 12 March 2015

24

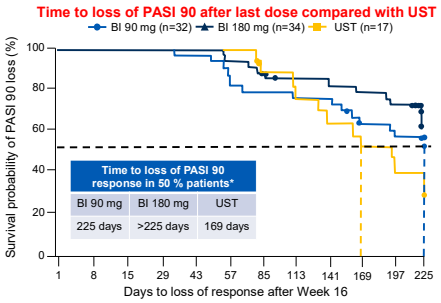
Risankizumab



*18 mg BI 655066 only given once at Week 0.
Analysis includes all patients who were randomised and who received at least one dose of assigned therapy during the study with non-responder imputation.

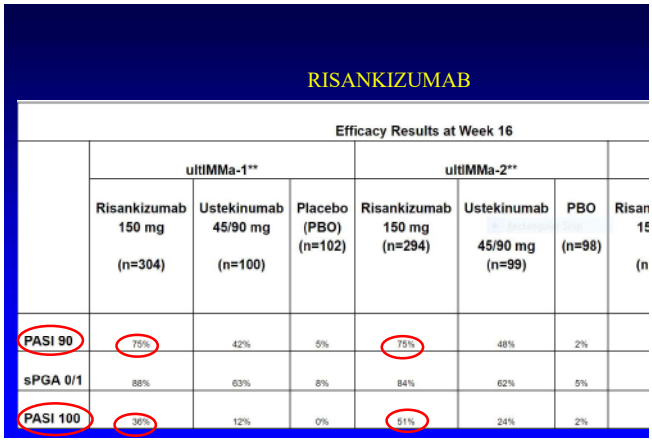
Papp K, et al. EADV 2015, FC03.06 Sponsored by Boehringer Ingelheim

Risankizumab

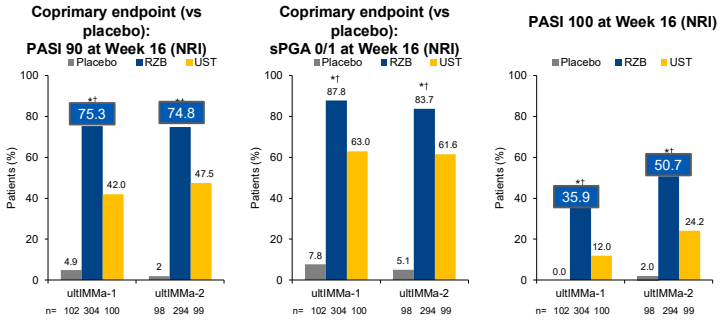


*Statistical analysis not available at time of presentation. Analysis includes all patients who had achieved PASI 90 response at Week 16. Time to loss of PASI 90 response is measured from last dose at Week 16

Papp K, et al. EADV 2015, FC03.06 Sponsored by Boehringer Ingelheim

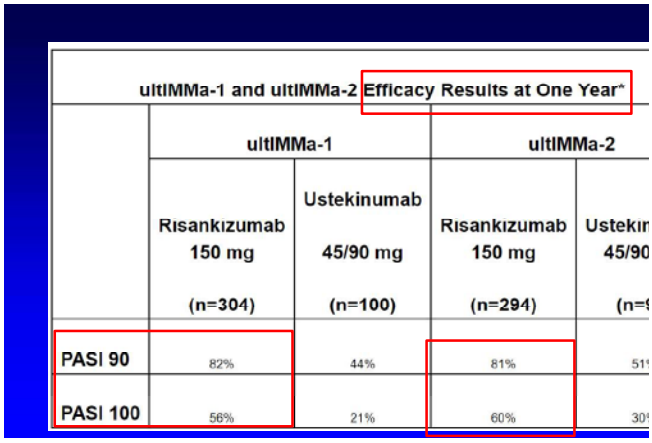


ultIMMa-1 and ultIMMa-2: PASI and sPGA 0/1 responses with risankizumab at Week 16

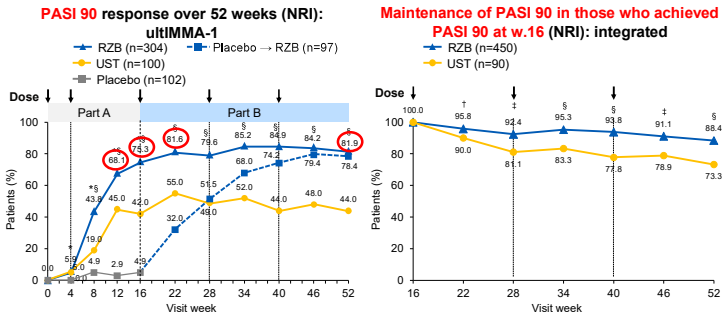


*P<0.001 vs placebo, †P<0.001 vs UST

Gordon KB, et al. AAD 2018, Late-breaking Research: Clinical Trials; Sponsored by AbbVie and Boehringer Ingelheim



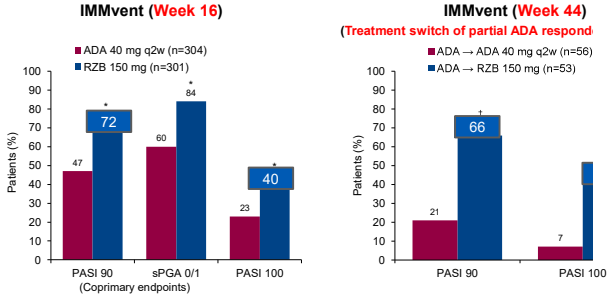
ultIMMa-1 and ultIMMa-2: PASI 90 responses with risankizumab through Week 52



*P<0.001 vs placebo; †P<0.05, ‡P<0.01, §P<0.001 vs UST

Gordon KB, et al. AAD 2018, Late-breaking Research: Clinical Trials; Sponsored by AbbVie and Boehringer Ingelheim

IMMvent Phase 3 trial: PASI 90 & 100 & sPGA responses with risankizumab and adalimumab at Week 16 and Week 44



*P<0.001 vs ADA, †P<0.001 vs ADA → ADA

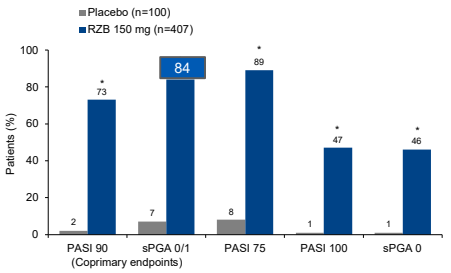
‡Patients originally randomized to ADA with PASI 50 to <PASI 90 at Week 16

Risankizumab Phase 3 psoriasis studies press releases; available at: https://news.abbvie.com/news/press-releases (accessed October 26, 2017)

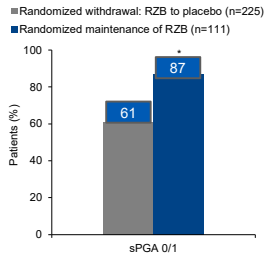
Sponsored by AbbVie and Boehringer Ingelheim

IMMhance: Primary efficacy endpoints at Week 16 and after rerandomization at 1 year

PASI and sPGA 0/1 responses at Week 16 (Period 1)



sPGA 0/1 response at Week 52 (Period 2)

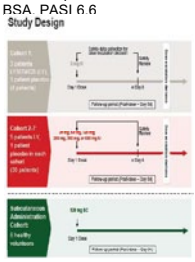


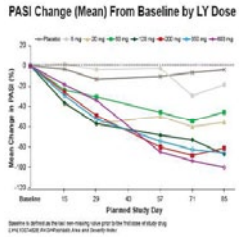
*P<0.001 vs placebo

Risankizumab Phase 3 psoriasis studies press releases; available at: https://news.abbvie.com/news/press-releases (accessed October 26, 2017)
Sponsored by AbbVie and Boehringer Ingelheim

P0456 Safety, efficacy and PK of a p19-directed IL-23 antibody (LY3074828) in patients with plaque psoriasis and healthy subjects

- Phase 1, placebo-controlled, 40 patients, 5 healthy volunteers, 12 weeks; 4% BSA, PASI 6.6

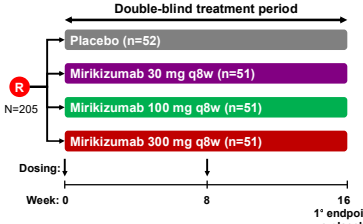




Mirikizumab

Tuttle J, et al. EADV 2016, P0456 Sponsored by Eli Lilly and Company

Phase 2 dose ranging trial of mirikizumab



- Exclusions
  - Nonbiologic systemic therapy or phototherapy within 28 days
  - TNF inhibitors or IL-17 inhibitors within 8 weeks
  - Any IL-23 inhibitor use (including UST)[a]

[a]Previous briakinumab use was permitted

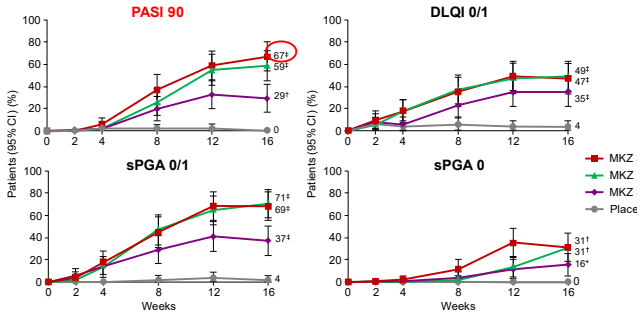
Baseline characteristics

	Placebo (n=52)	Mirikizumab q8w 30 mg (n=51)	Mirikizumab q8w 100 mg (n=51)	Mirikizumab q8w 300 mg (n=51)
Age (y)	46.0 ±12.4	49.2 ±13.3	46.0 ±13.2	47.5 ±13.2
Male	42 (80.8)	39 (76.5)	35 (68.6)	36 (70.6)
Weight (kg) ≥100 kg	89.1 ±22.0 13 (25.0)	91.3 ±19.8 13 (25.5)	86.4 ±15.0 13 (25.5)	87.9 ±21.3 11 (21.6)
BMI (kg/m²)	29.2 ±5.8	30.5 ±6.0	29.3 ±4.9	29.7 ±6.7
Psoriasis duration (y)	18.0 ±9.8	20.4 ±13.5	18.6 ±11.3	18.1 ±12.7
Prior biologics	21 (40.4)	20 (39.2)	21 (41.2)	22 (43.1)
Prior systemic therapy	38 (73.1)	39 (76.5)	41 (80.4)	40 (78.4)
PASI score	19.7 ±7.4	21.0 ±8.4	20.3 ±8.0	18.4 ±6.9
sPGA ≥4	23 (44.2)	18 (35.3)	24 (47.1)	14 (27.5)
% BSA involved	26.4 ±17.5	27.3 ±15.8	26.5 ±16.5	21.3 ±10.3
DLQI	14.1 ±7.2	12.6 ±7.3	12.5 ±5.6	12.7 ±6.6
DLQI 0/1	0	0	1 (2.0)	0

Data are mean ±SD or n (%)

Rich P, et al. AAD 2018, P6131 Sponsored by Eli Lilly and Company

Mirikizumab through Week 16



*P<0.05, †P<0.01, ‡P<0.001 vs placebo. Logistic regression analysis with treatment, geographic region, and previous biologic therapy in the model; N

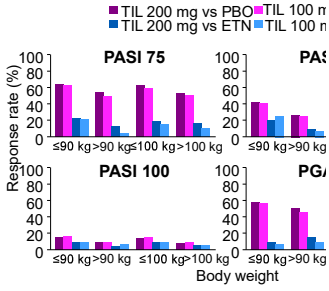
Rich P, et al. AAD 2018, P6131 Sponsored by Eli Lilly and Company

Anti-IL- 23 drugs: Guselkumab, Tildrakizumab, Risankizumab, Mirikizumab

- What are they? How do they work?
- How effective are they?
- Does patient weight affect efficacy?
- Are they safe?
- Patient scenarios where IL-23 therapy might be ideal

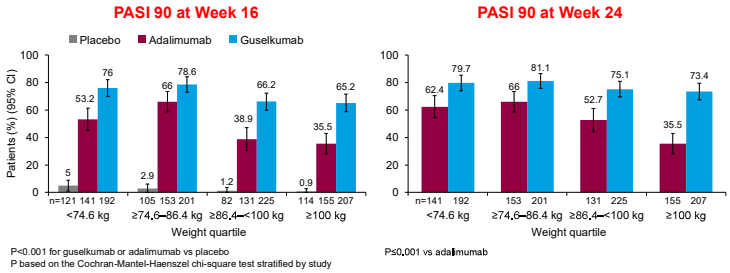
Impact of body weight on efficacy of tildrakizuma weeks in moderate to severe chronic plaque pso

- Pooled analysis from 3 RCTs: reSURFACE 1 and 2 and P05495
- 1º endpoints:
  - reSURFACE 1/2, PASI 75 and PGA 0/1 at Week 16
  - Study P05495, PASI 75 at Week 16
- Randomized patients stratified by body weight (≤90 kg, >90 mg; ≤100 kg, >100 mg
- Authors concluded that PASI and PGA responses were numerically greater in patients with lower vs higher body weight



Scott E, et al. EADV 2017, P1722 Sponsored by Merck & Co., Inc.

VOYAGE 1 & 2: PASI 90 responses with guselkumab and adalimumab stratified by patient weight

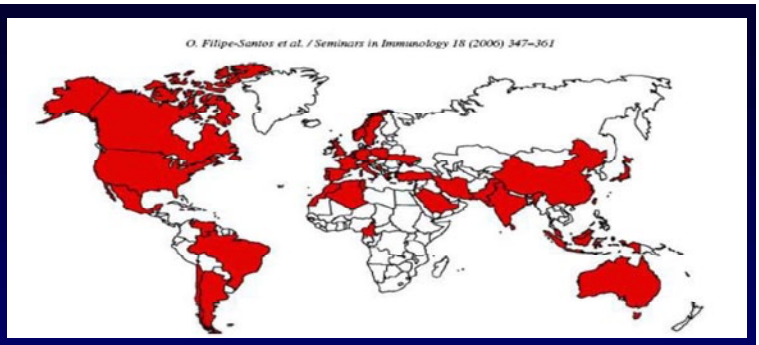


- At high weights, there are lower response rates to guselkumab at the PASI 90 level
- This difference in responses is significantly less evident than with adalimumab

Papp K, et al. AAD 2018, P6729 Sponsored by Janssen Research & Development, LLC

Anti-IL- 23 drugs: Guselkumab, Tildrakizumab, Risankizumab, Mirikizu

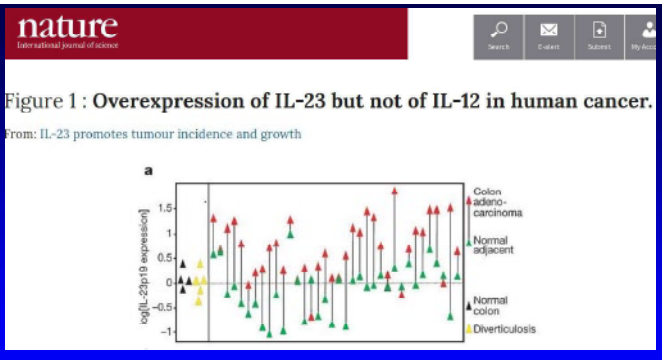
- What are they? How do they work?
- How effective are they?
- Does patient weight affect efficacy?
- Are they safe?
- Patient scenarios where IL-23 therapy might be idea



220 patients with genetic defects in IL12/23-IFNγ circuit

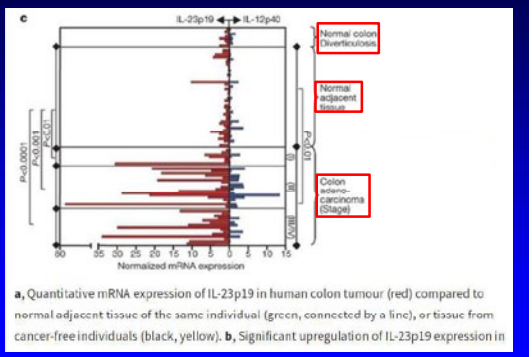
Low penetrance, broad resistance, and favorable outcome of interleukin 12 receptor beta1 deficiency: medical and immunological implications.
Fieschi C,et al.
J Exp Med. 2003;197:527-35.

- 41 patients - IL12 receptor β1 deficiency
- Salmonellosis
- Tuberculosis



IL-23 is increased in colon adenocarcinoma

Langowski JL, et al. Nature. 2006;442:461-465



a, Quantitative mRNA expression of IL-23p19 in human colon tumour (red) compared to normal adjacent tissue of the same individual (green, connected by a line), or tissue from cancer-free individuals (black, yellow). **b**, Significant upregulation of IL-23p19 expression in

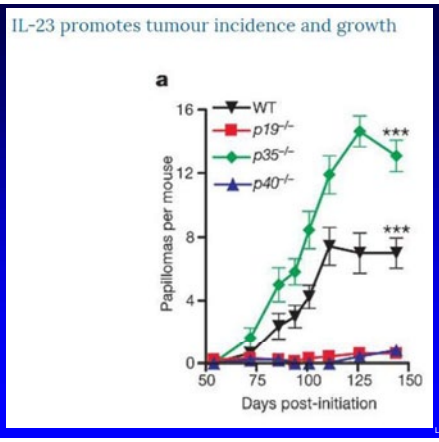
Langowski JL, et

Cancer type	Number of paired (tumour and normal) samples	Fold increase in expression			
		Average	Number >5×	Number >10×	*P*
Colon	36	15.33	23	17	0.0001
Ovarian	32	9.45	12	4	0.0001
Head and neck	44	3.41	11	4	0.01
Lung	114	3.03	20	8	0.0001
Breast	78	2.86	16	6	0.0001
Stomach	64	2.13	9	3	0.001
Melanoma	89	1.47	5	0	0.0001

↑IL-23 in many cancers

Langowski JL, et al. Nature. 2006;442:461-465

Mouse carcinogenesis model



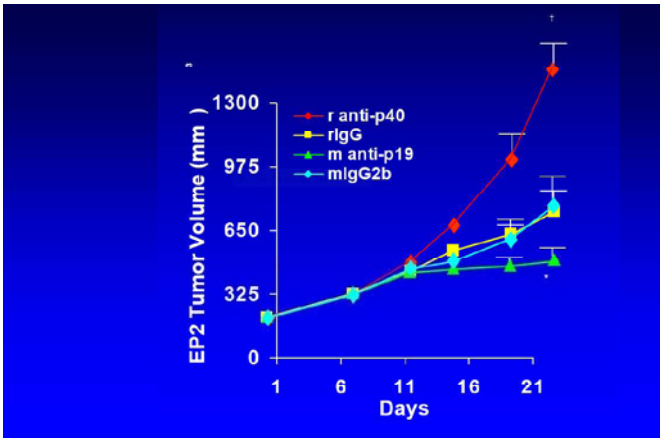
Langowski JL, et

Role of IL-23 in Malignancy

- IL-23 is expressed at increased levels in tumors and decreases cytotoxic T cell tumor suppression
  - IL-23p19$^{-/-}$ mice are resistant to chemical-induced carcinogenesis models and have decreased tumor burden upon tumor transplantation
  - Anti-IL-23p19 therapy leads to protection against tumor formation and growth, as well as increased tumor rejection and elimination
- IL-12 induces proliferation and cytotoxic activity, promoting immune surveillance and antitumor responses
  - IL-12p40 ablation leads to increased tumor incidence and size vs anti-IL-23p19 or control

*$P < 0.05$; †$P < 0.001$.

Langowski JL, et al. *Nature*. 2006;442:461-465.



IL-17 Mediated Inflammation Promotes Tumor Growth and Progression in the Skin

D. He, et al

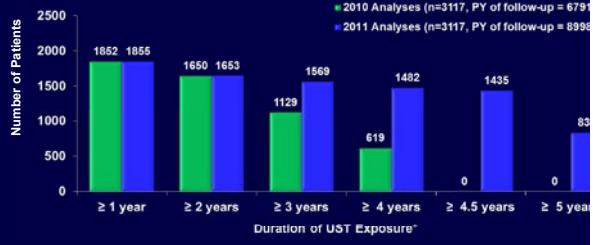
PLoS ONE 2012; 7: 1-9

IL-23→↑IL-17→↑tumor growth

Could blocking IL-17 be protective against cancer?

Ustekinumab Psoriasis Safety Databases: Duration of Patient Exposure Evaluated in 2010 and 2011 Analyses

- The 2011 Analyses included a total of 3117 patients with 8998 PY of follow-up; 47.5% of patients treated for at least 4 years and 26.9% treated for 5 years (median follow-up was 3.2 years)

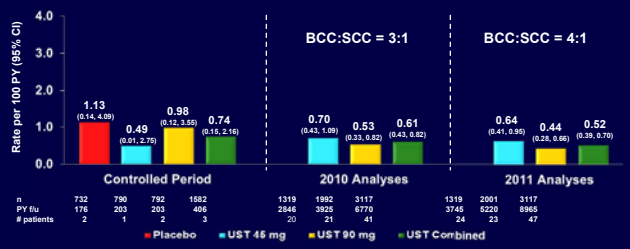


*PBO subjects crossed-over to UST at Week 12, therefore they would only be captured in categories of ≥ 4 years and ≥ 4.5 years of exposure

Papp K., et al. EA

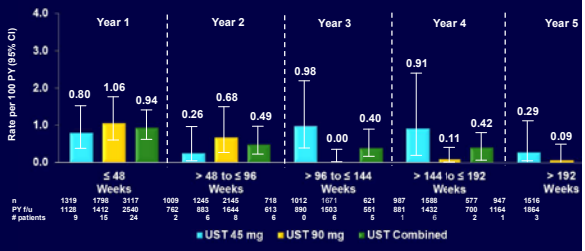
Cumulative Rates of NMSC Through 5 Years of Follow-up

- 47 patients reported NMSCs (3 patients reported both SCC and BCC)
  - 40 had BCC (21 on 45 mg and 19 on 90 mg)
  - 10 had SCC (5 on 45 mg and 5 on 90 mg)



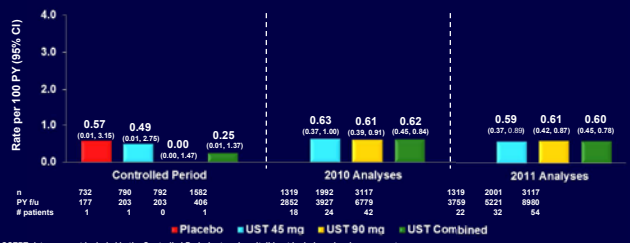
ACCEPT data were not included in the Controlled Period rates since it did not include a placebo comparator.
For PHOENIX 2, patients who were dose adjusted from 45 mg to 90 mg were switched to the corresponding column following dose adjustment.

Rates of NMSC by Year Through 5 Years of Follow-up



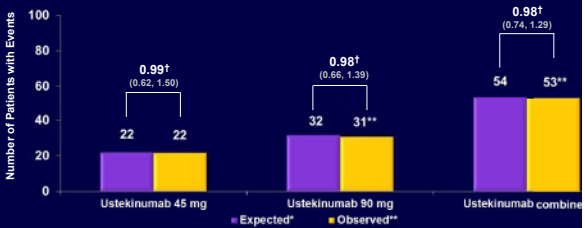
PHOENIX 2 patients who were dose adjusted from 45 mg to 90 mg were switched to the corresponding column following dose adjustment.

Cumulative Rates of Other Malignancies Through 5 Years of Follow-up



ACCEPT data were not included in the Controlled Period rates since it did not include a placebo comparator.
PHOENIX 2 patients who were dose adjusted from 45 mg to 90 mg were switched to the corresponding column following dose adjustment.

Rates of Other Malignancies Through 5 Years of Follow-up Compa with SEER Population

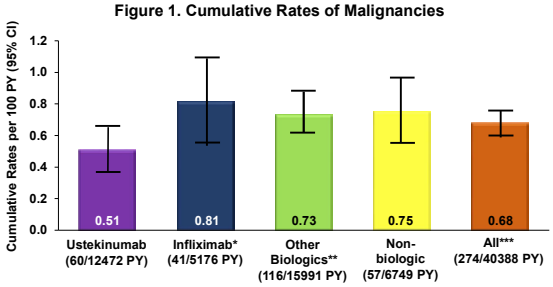


*The expected number of patients with malignancies is based on the SEER Database (2009), adjusted for age, gender, and race.
†Indicates Standardized Incidence Ratio (SIR) with 95% CI.
**Since cervical carcinoma in situ is not captured in SEER, a single case in 90 mg is not included in this analysis.
PHOENIX 2 patients who were dose adjusted from 45 mg to 90 mg were switched to the corresponding column following dose adjustment.

PSOLAR

Results: Age and Gender Adjusted Cumulative Rates of Malignancies (excluding NMSC) per 100 Patient-Years (PY) Based on Any Exposure to Therapy (Figure 1)

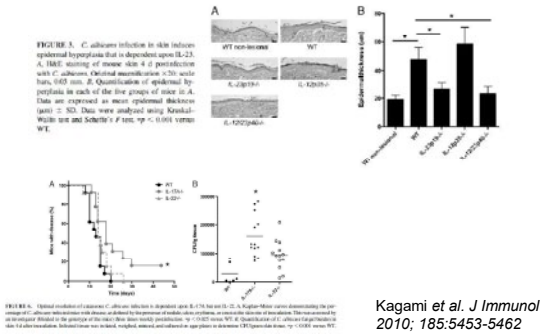
Figure 1. Cumulative Rates of Malignancies



*This group Includes (n=36) patients exposed to golimumab only.
**95.7% (n=4067) are adalimumab &/or etanercept patients, with the remainder exposed to other biologics.
***Adjustment used All population as reference.

Fiorentino D, et al. AAD 2015. P1631.

IL-23 & IL-17A, but Not IL-12 & IL-22, Are Required for Optimal Skin Host Defense against Candida albicans



Kagami *et al. J Immunol 2010; 185:5453-5462*

Inborn errors of human IL-17 immunity underlie chronic mucocutaneous candidiasis.
Puel A, et al.
Allergy Clin Immunol. 2012;12:616-22.

Adverse Events Summary-comparison to placebo reSURFACE 1

Tildrakizuma

Part 1 (Weeks 0-12)

	TIL 200 mg N=308 n (%)	TIL 100 mg N=309 n (%)	PBO N=154 n (%)
≥1 AEs[†]	130 (42.2)	146 (47.2)	74 (48.1)
Serious AEs	8 (2.6)	5 (1.6)	1 (0.6)
Who died	0	0	0
Discontinued[‡] due to AEs	5 (1.6)	0	1 (0.6)
Most common AEs			
Nasopharyngitis	19 (6.2)	23 (7.4)	8 (5.2)
Upper respiratory tract infection	15 (4.9)	10 (3.2)	9 (5.8)
Psoriasis	0	3 (1.0)	8 (5.2)

[†]Subjects who took at least one dose of Part 1 study medication based on the treatment actually received.
[‡]Study medication withdrawn.

Part 2 (Weeks 12-28)

	TIL 200 mg/ TIL 200 mg N=298 n (%)	TIL 100 mg/ TIL 100 mg N=300 n (%)	PBO/ TIL 200 N=72 n (%)	PBO/ TIL 100 N=74 n (%)
≥1 AEs[†]	118 (39.6)	133 (44.3)	29 (40.3)	31 (41.9)
Serious AEs	7 (2.3)	6 (2.0)	1 (1.4)	1 (1.4)
Who died	0	0	0	0
Discontinued[‡] due to AEs	3 (1.0)	1 (0.3)	0	0
Most common AEs				
Nasopharyngitis	12 (4.0)	20 (6.7)	5 (6.9)	4 (5.4)
Upper respiratory tract infection	20 (6.7)	13 (4.3)	0	3 (4.1)

[†]Subjects who took at least one dose of Part 1 study medication based on the treatment actually received.
[‡]Study medication withdrawn.

PBO=placebo; TIL=tildrakizumab; ETN=etanercept.

Adverse Events Summary-comparison to ETN reSURFACE 2

Tildrakizumab

Part 1 (Weeks 0-12)

	TIL 200 mg N=314 n (%)	TIL 100 mg N=307 n (%)	PBO N=156 n (%)	ETN N=313 n (%)
≥1 AEs[†]	155 (49.4)	136 (44.3)	86 (55.1)	169 (54.0)
Serious AEs	6 (1.9)	4 (1.3)	4 (2.6)	7 (2.2)
Who died[‡]	0	1 (0.3)	0	0
Discontinued due to AEs	3 (1.0)	3 (1.0)	2 (1.3)	6 (1.9)
Most common AEs				
Injection site erythema	2 (0.6)	2 (0.7)	1 (0.6)	27 (8.6)
Nasopharyngitis	34 (10.8)	41 (13.4)	12 (7.7)	36 (11.5)

[†]Subjects who took at least one dose of Part 1 study medication based on the treatment actually received.
[‡]A patient on tildrakizumab 100 mg died; patient had alcoholic cardiomyopathy and hepatic steatosis, although adjudication was unable to determine the cause of death.

Part 2 (Weeks 12-28)

	TIL200 mg/ TIL 200 mg N=299 n (%)	TIL 100 mg/ TIL 100 mg N=294 n (%)	ETN/ETN N=289 n (%)	PBO/ TIL 200 N=72 n (%)	PBO/ TIL 100 N=69 n (%)
≥1 AEs[†]	135 (45.2)	135 (45.9)	164 (56.7)	31 (43.1)	37 (53.6)
Serious AEs	6 (2.0)	9 (3.1)	14 (4.8)	2 (2.8)	1 (1.4)
Who died	0	0	0	0	0
Discontinued due to AEs	1 (0.3)	1 (0.3)	3 (1.0)	0	1 (1.4)
Most common AEs					
Nasopharyngitis	42 (14.0)	23 (7.8)	34 (11.8)	3 (4.2)	8 (11.6)
Upper respiratory tract infection	6 (2.0)	5 (1.7)	7 (2.4)	0	0

[†]Subjects who took at least one dose of Part 1 study medication based on the treatment actually received.

PBO=placebo; TIL=tildrakizumab; ETN=etanercept.

Adverse Events of Special Interest During Part 1

Tildrakiz

reSURFACE 1

	n (%)[†]	Difference in % vs Placebo Estimate (95% CI)[‡]	*P*-value
With severe infections[‡]			
PBO	0		
TIL 100 mg	1 (0.3)	0.3 (-2.1, 1.8)	0.480
TIL 200 mg	1 (0.3)	0.3 (-2.1, 1.8)	0.480
With malignancies[§]			
PBO	0		
TIL 100 mg	0	0.0 (-2.4, 1.2)	1.000
TIL 200 mg	0	0.0 (-2.4, 1.2)	1.000
With confirmed extended MACE[‖]			
PBO	0		
TIL 100 mg	1 (0.3)	0.3 (-2.1, 1.8)	0.480
TIL 200 mg	1 (0.3)	0.3 (-2.1, 1.8)	0.480
With drug-related hypersensitivity reactions			
PBO	0		
TIL 100 mg	0	0.0 (-2.4, 1.2)	1.000
TIL 200 mg	1 (0.3)	0.3 (-2.1, 1.8)	0.480

reSURFACE 2

	n (%)[†]	Difference in % vs Placebo Estimate (95% CI)[‡]	*P*-value	Difference in % vs Etanercept Estimate (95% CI)[‡]	*P*-value
With severe infections[‡]					
PBO	1 (0.6)				
TIL 100 mg	0	-0.6 (-3.5, 0.6)	0.161	0.0 (-1.2, 1.2)	1.000
TIL 200 mg	1 (0.3)	-0.3 (-3.2, 1.2)	0.613	0.3 (-0.9, 1.8)	0.318
ETN	0				
With malignancies[§]					
PBO	0				
TIL 100 mg	1 (0.3)	0.3 (-2.1, 1.8)	0.476	0.0 (-1.5, 1.5)	0.989
TIL 200 mg	1 (0.3)	0.3 (-2.1, 1.8)	0.481	0.0 (-1.5, 1.5)	0.998
ETN	1 (0.3)				
With confirmed extended MACE[‖]					
PBO	0				
TIL 100 mg	0	0.0 (-2.4, 1.2)	1.000	-0.3 (-1.8, 0.9)	0.322
TIL 200 mg	0	0.0 (-2.4, 1.2)	1.000	-0.3 (-1.8, 0.9)	0.317
ETN	1 (0.3)				
With drug-related hypersensitivity reactions					
PBO	1 (0.6)				
TIL 100 mg	1 (0.3)	-0.3 (-3.2, 1.3)	0.625	0.3 (-0.9, 1.8)	0.313
TIL 200 mg	0	-0.6 (-3.5, 0.6)	0.156	0.0 (-1.2, 1.2)	1.000
ETN	0				

[†]Subjects who took at least one dose of Part 1 study medication based on the treatment actually received.
[‡]Defined as infection meeting the regulatory definition of a serious adverse event, or any infection requiring IV antibiotics whether or not reported as a serious adverse event, as per the regulatory definition.
[§]Excluding carcinoma in situ of the cervix.
[‖]Includes nonfatal myocardial infarction, nonfatal stroke, unstable angina, coronary revascularization, resuscitated cardiac arrest, and CV deaths that are confirmed as "cardiovascular" or "sudden".
[¶]Based on Miettinen and Nurminen method.
CI=confidence interval; MACE=major adverse cardiovascular event; PBO=placebo; TIL=tildrakizumab; ETN=etanercept.

- Infection rates with TIL treatment were low and comparable to placebo and ETN during the placebo-controlled period
- In the full-trial period (weeks 52/64), exposure adjusted rates remained low for all groups
- Nasopharyngitis was the most common infection in any treatment group

	Placebo-Controlled Period, n (%*)				Full-Trial Period, Exposure-Adjusted Rate†			
	TIL 200 mg	TIL 100 mg	Placebo	ETN 50 mg	TIL 200 mg	TIL 100 mg	Placebo	ETN 50 mg
Infections	(n=708)	(n=705)	(n=355)	(n=313)	(n=1041)	(n=1083)	(n=588)	(n=313)
All infections	155 (21.9)	160 (22.7)	80 (22.5)	74 (23.6)	52.6	48.9	79.5	86.0
Severe infections	2 (0.3)‡	1 (0.1)‡	1 (0.3)	0	1.6	1.1	0.9	2.0
Oral candidiasis	2 (0.3)	1 (0.1)	0	0	0.7	0.2	0	0
Candida skin infections	2 (0.3)	1 (0.1)	0	0	0.7	0.2	0	0
Infections in ≥2% of patients during placebo-controlled period in any treatment group								
Nasopharyngitis	66 (9.3)	78 (11.1)	29 (8.2)	36 (11.5)	22.3	23.3	25.1	41.1
Upper respiratory tract infection	21 (3.0)	13 (1.8)	10 (2.8)	5 (1.6)	9.3	6.3	14.6	7.2
Influenza	6 (0.8)	6 (0.9)	7 (2.0)	0	4.2	3.2	8.7	3.3

*Patients/number of patients exposed
†Patient with events/100 patient years
‡Analyzed as Tier 1 event, $P \geq 0.6$ vs placebo

63

VOYAGE 1: Exposure-adjusted adverse events with guselkumal through 2 years

	Incidence rate per 100 pt-y (events) In patients receiving guselkumab[a]	
	Weeks 0–48 (n=494)	Weeks 0–100 (n=494)
Total pt-y of follow-up	394	847
Median pt-y of follow-up	0.9	1.9
Serious AEs	5.84	6.50
Serious infections	1.02 (4)	0.83 (7)
Malignancy (excluding NMSC)[b]	0.51 (2)	0.71 (6)
MACE	0.25 (1)	0.12 (1)
Deaths	0	0.24 (2)

[a]Includes patients randomized to guselkumab and placebo patients who crossed over to receive guselkumab
[b]n for malignancy is patient-level analysis

- Guselkumab has very high maintenance of response
- Quality of life increases in Year 2: possibly related to stability of disease
- Safety signals remain stable

Griffiths CEM, et al. EADV 2017; D3T01.I Sponsored by Janssen Clinical Research and Development LLC

ultIMMa-1 and ultIMMa-2: Safety of risankizumab from Weeks 0–16

% patients with AE	ultIMMA-1			ultIMMA-2		
	RZB (n=304)	UST (n=100)	Placebo (n=102)	RZB (n=294)	UST (n=99)	Placebo (n=98)
Any AE	49.7	50.0	51.0	45.6	53.5	45.9
Drug-related AEs	11.8	11.0	13.7	9.9	18.2	9.2
Serious AE	2.3	8.0	2.9	2.0	3.0	1.0
Drug-related serious AEs	0.3	3.0	0	0.7	1.0	0
Severe AE	2.0	3.0	4.9	2.4	6.1	1.0
AE leading to drug discontinuation	0.7	2.0	3.9	0.3	0	1.0
Serious infections	0.3	3.0	0	1.0	1.0	0
Active tuberculosis	0	0	0	0	0	0
Latent tuberculosis	0	0	0	0	0	0
Adjudicated MACE	0	0	0	0	0	0
Malignancies	0.3	0	1.0	0.3	0	0
Malignancies excluding NMSC	0	0	0	0	0	0
Deaths (including non treatment-emergent)	0	0	0	0.3[a]	0	0

- Among highest efficacy results reported to date, with impressive durability of response on and off drug. Preliminary safety is encouraging, long-term data are required

[a]1 non-treatment emergent death on Day 189 that occurred after 161 days after last dose of study drug and fell outside of the treatment-emergent window

Gordon KB, et al. AAD 2018, Late-breaking Research: Clinical Trials; Sponsored by AbbVie and Boehringer Ingelheim

Phase 2 randomized controlled trial: Safety of mirikizumab through Week 16

TEAEs (≥5% in any group)

	No. patients with TEAE (%)				
		Mirikizumab q8w			
	Placebo (n=52)	30 mg (n=51)	100 mg (n=51)	300 mg (n=51)	Total (N=153)
TEAEs	25 (48.1)	26 (51.0)	24 (47.1)	24 (47.1)	74 (48.4)
Mild	9 (17.3)	18 (35.3)	9 (17.6)	11 (21.6)	38 (24.8)
Moderate	15 (28.8)	7 (13.7)	14 (27.5)	11 (21.6)	32 (20.9)
Severe	1 (1.9)	1 (2.0)	1 (2.0)	2 (3.9)	4 (2.6)
Death	0	0	0	0	0
Serious AE	1 (1.9)	1 (2.0)	0	1 (2.0)	2 (1.3)
TEAE related to study treatment	7 (13.5)	12 (23.5)	7 (13.7)	9 (17.6)	28 (18.3)
Overall infections	12 (23.1)	14 (27.5)	13 (25.5)	13 (25.5)	40 (26.1)

- 2 (1.0%) patients dis
  the study because of
- Most common TEAE
  viral URTI, URTI, inj
  pain, hypertension, a

- Interesting and impressive preliminary results
- Baseline demographics indicate a more severe psoriasis population

Rich P, et al. AAD 2018, P6131 Sponsored by Eli Lilly and Company

- Patient with medical benefit (e.g. medicare) but incomplete (or no) pharmacy benefit
- Patient with medicare part D who can't afford the donut hole

- Frequent traveler

- Institutionalized patients
- Patients who can't self-inject (e.g. arthritis, Parkinson's)

- Teenager (>17) going off to college
- Children (not approved)

- Women of childbearing potential

Genentech
IN BUSINESS FOR LIFE

April 8, 2009

Dear RAPTIVA Patient,

Re: VOLUNTARY U.S. MARKET WITHDRAWAL OF RAPTIVA® (efalizumab)

Patient safety is a top priority for Genentech. Since September 2008, Genentech has received progressive multifocal leukoencephalopathy (PML), a serious and almost always fatal brain infe caused by a virus, in patients taking RAPTIVA (efalizumab). **Because of the following key as PML and our commitment to safety, Genentech has decided to voluntarily stop selling RA**

- Although we believe that there are many psoriasis patients who benefit from RAPTIVA, t way to know ahead of time who will get PML.
- There is no treatment or cure for PML. People who do live with PML are severely disabl

Reasons to Become a Registry Investigator

- Contribute to education/clinical knowledge of the psoriasis community
- Opportunity to establish a database of your patient population
- Academic recognition and publication opportunities
- Supplement existing insurance fee schedules
  - Site compensation is $400 (including $20 for patient) per Enrollment visit and $300 (including $20 for patient) per biannual Follow Up visit

CORRONA

If you are interested in participating in the Psoriasis Registry as a research investigator, please email psoriasis@corrona.org
or visit www.corrona.org
or call 508.408.5432

CORRONA

METASTATIC CARCINOMA TO THE SKIN

MICHAEL A NOWAK, MD

CONFLICTS

- No conflicts with the content of this lecture

METASTATIC CARCINOMA

- Relatively uncommon in comparison to primary cutaneous carcinomas.
- Requires high clinical suspicion.
- Gender differences.
- Clinical differential diagnosis.
- Histologic differential diagnosis.

METASTATIC CARCINOMA

- Skin metastasis is defined as the spread of malignant cells from a primary malignancy to the skin.
- Originate either from an internal malignancy or from a primary skin cancer (melanoma).
- Skin metastases are encountered in 0.7-9% of all patients with cancer.
- Skin is an uncommon site of metastatic disease when compared to other organs.

METASTATIC CARCINOMA

- Long-time lag between the diagnosis of the primary malignancy and the recognition of the skin metastases.
- Cutaneous metastasis may be the first indication of a clinically silent visceral malignancy.
- Regional distribution of the skin metastasis is related to the location of the primary malignancy and the mechanism of metastatic spread.
- The relative frequency of skin metastasis does not always correlate with the prevalence of the type of primary cancer (ie prostate cancer).

METASTATIC CARCINOMA

- Cutaneous metastasis as the first indication of a internal malignancy.
- Lung.
- Ovary
- Renal

METASTATIC CARCINOMA
Mechanism of Metastatic Spread

- Lymphatic Dissemination:
- Local overlying skin (Breast, Oral Cavity).
- Hematogenous Dissemination:
- Local and/or Distant (Breast, Lung, GI, GU)

METASTATIC CARCINOMA

- Lung carcinoma (24%) is the most common skin metastasis in men (followed by large intestine 19%, melanoma 13%, oral cavity 12%).
- Breast carcinoma (69%) is the most common skin metastasis in women (followed by large intestine 9%).
- The anterior chest and neck region are the areas of greatest predilection in men.
- The anterior chest wall and the abdomen are the most commonly involved sites in women.

Men		Women	
< 40 yr	> 40 yr	< 40 yr	> 40 yr
Melanoma Colon cancer Lung cancer	Lung cancer Colon cancer SCC in the oral cavity Melanoma	Breast cancer Colon cancer Ovarian cancer	Breast cancer Colon cancer Lung cancer Ovarian cancer Melanoma

METASTATIC CARCINOMA

- Histologically, skin metastases usually show features reminiscent of the primary malignancy.
- Poorly differentiated - Carcinoma of Unknown Primary (CUP) - remember melanoma.
- Metastasis to the skin is often a pre-terminal event that heralds poor outcome.

METASTATIC CARCINOMA

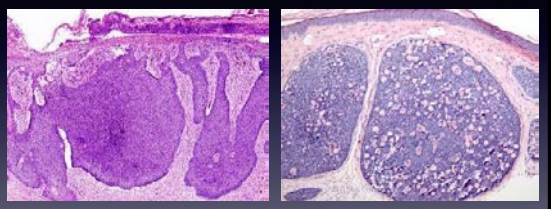
- Benign vs. Malignant
- Primary skin cancer vs. Adnexal
- Primary skin cancer vs. Metastatic
- Adnexal carcinoma vs. Metastatic
- Epidermal involvement, depth/thickness dermis, resemble BCC/SCC, glandular differentiation

METASTATIC CARCINOMA
Benign vs. Malignant

- Size, Symmetry, Circumscription, Depth/Thickness
- Atypia, Mitoses, Differentiation

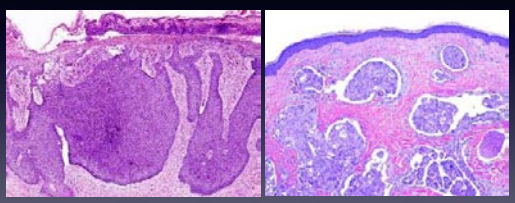
METASTATIC CARCINOMA
Primary Skin Cancer vs. Adnexal Tumor

- Adnexal tumors (Benign and Malignant) usually lack epidermal continuity, involve the deep dermis, look different from a BCC/SCC, frequently display glandular differentiation
- Special stains - identify differentiation



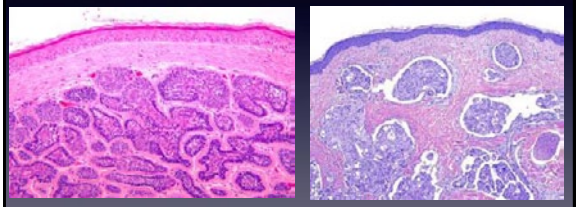
METASTATIC CARCINOMA
Primary Skin Cancer vs. Metastatic

- Metastatic carcinomas usually lack epidermal continuity, involve deep dermis, look different from a BCC/SCC (exception metastatic SCC), frequently display glandular differentiation
- Special stains - identify differentiation



METASTATIC CARCINOMA
Adnexal Tumor vs. Metastatic

- Adnexal tumors (benign and malignant) and metastatic tumors usually lack epidermal continuity, involve deep dermis, look different from a BCC/SCC, frequently display glandular differentiation
- Benign adnexal tumors lack significant cytological atypia and show text book architectural features
- Malignant adnexal tumors show cytological atypia and can have familiar architectural features and/or a remnant benign component
- Special stains - identify differentiation - P63 is key
- Remember melanoma markers!



J Cutan Pathol. 2007 Jun;34(6):474-80.

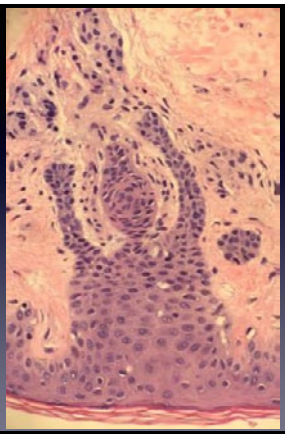
Use of p63 expression in distinguishing primary and metastatic cutaneous adnexal neoplasms from metastatic adenocarcinoma to skin.

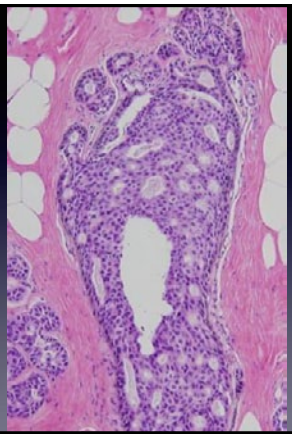
Ivan D, Nash JW, Prieto VG, Calonje E, Lee S, Diwan AH, Lazar AJ.

Department of Pathology, University of Texas - M.D. Anderson Cancer Center

METASTATIC CARCINOMA
Clinical Presentation

- Skin metastases usually appear as non-specific groups of discrete firm painless nodules that emerge rapidly without any explanation.
- They vary in size from so tiny as to be of miliary lesions to as large as goose egg size.
- Some skin metastasis may mimic specific dermatological conditions such as cutaneous cyst, lipoma, dermatofibroma, pyogenic granuloma, hemangioma, papular eruptions, herpes zoster eruptions, morpheaform plaques, alopecia, cellulitis and erysipelas.





METASTATIC CARCINOMA
Carcinoma of the Breast

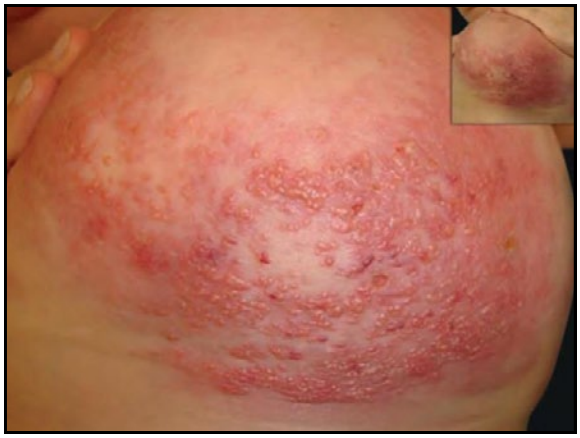
- Inflammatory Metastatic Breast Carcinoma.
- En Cuirasse Metastatic Breast Carcinoma.
- Telangiectatatic Metastatic Breast Carcinoma.
- Nodular Metastatic Breast Carcinoma.
- Alopecia Neoplastica.
- Metastatic Breast Carcinoma of the Eyelid.

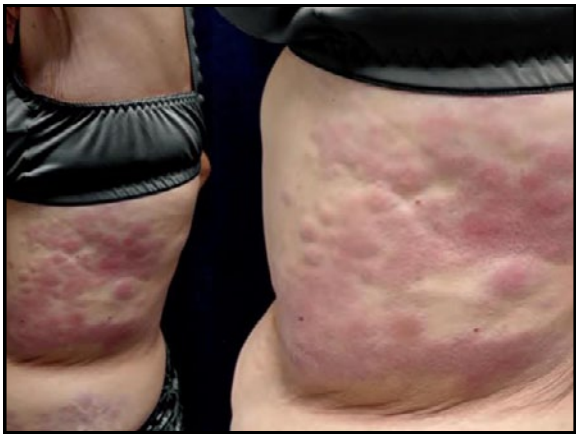
METASTATIC CARCINOMA
Carcinoma of the Breast

- Lymphatic dissemination:
- Inflammatory, En Cuirasse, Telangiectatatic, Nodular including Inframammary Crease.
- Hematogenous dissemination:
- Alopecia Neoplastica and Metastatic Breast Carcinoma of the Eyelid.

METASTATIC CARCINOMA
Inflammatory Metastatic Breast Carcinoma

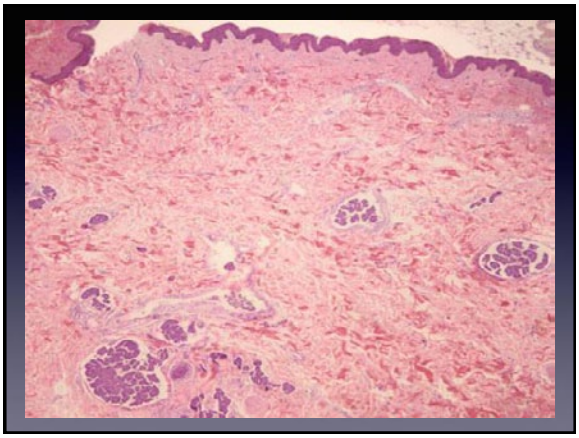
- Erythematous patch or plaque with spreading border involving the breast and adjacent skin.
- Peau d'orange
- Erysipelas-like - aka Carcinoma Erysipeloides





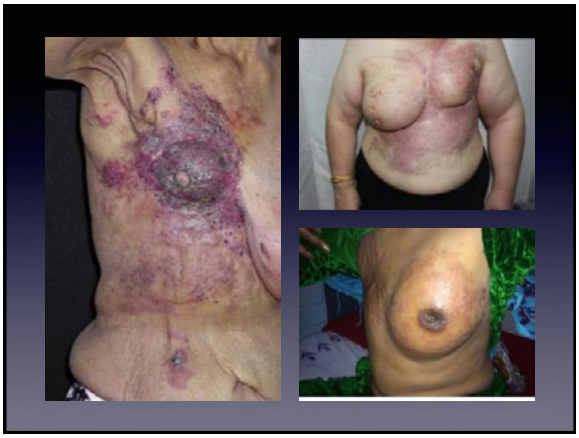
METASTATIC CARCINOMA
Inflammatory Metastatic Breast Carcinoma

- Clusters of tumor cells involving superficial and deep lymphatics (retrograde lymphatic spread into the skin secondary to blockage of deep lymphatics)
- Capillary congestion (clinical erythema/warmth).
- Minimal inflammation.



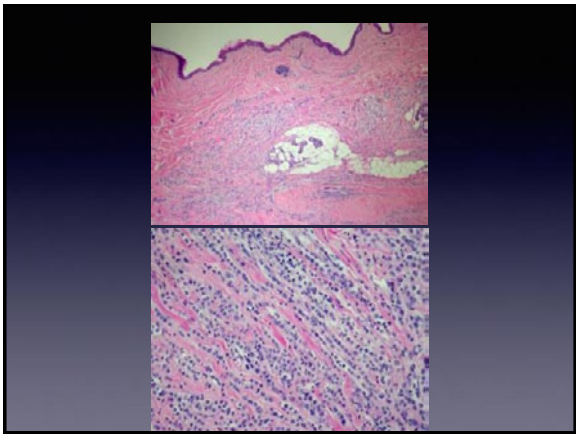
METASTATIC CARCINOMA
En Cuirasse Metastatic Breast Carcinoma

- Cuirass = Armor vest
- Diffuse induration involving skin of the breast.
- Morphea-like.



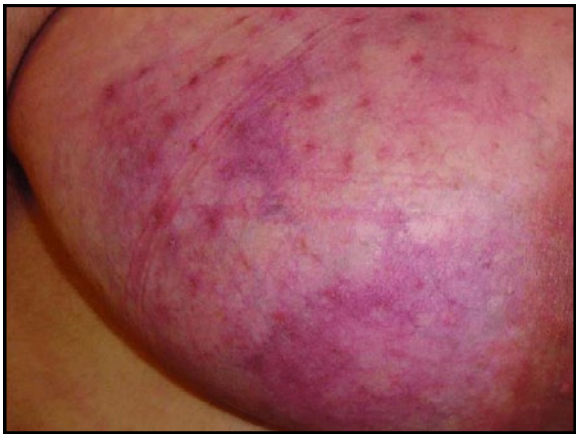
METASTATIC CARCINOMA
En Cuirasse Metastatic Breast Carcinoma

- AKA Scirrhous Carcinoma
- Extensive fibrosis/sclerosis resulting in a rectangular punch biopsy.
- Inconspicuous fibroblast-like tumor cells - both solitary and single rows “Indian filing” between thickened collagen bundles.



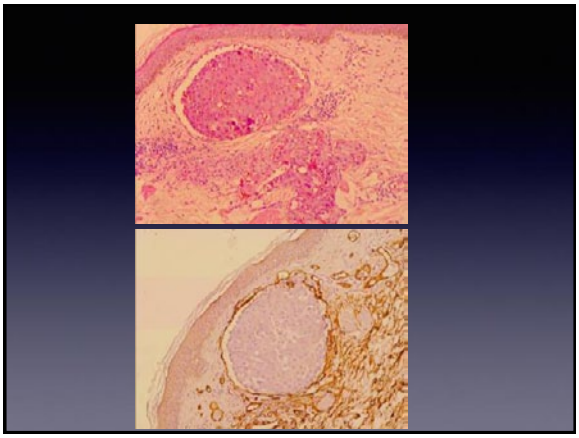
METASTATIC CARCINOMA
Telangiectatatic Metastatic Breast Carcinoma

- Violaceous papulovesicles on skin of the breast.
- Sometimes Lymphangioma circumscriptum-like.



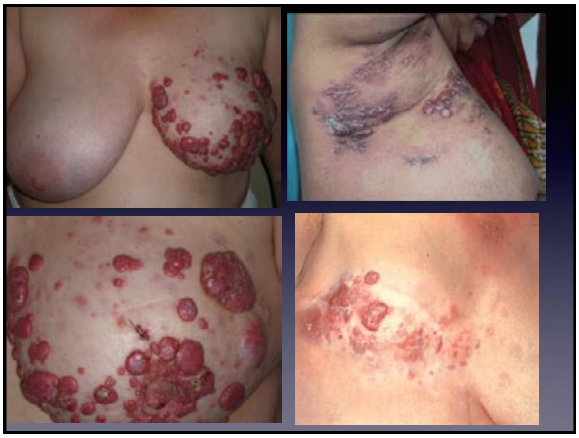
METASTATIC CARCINOMA
Telangiectatatic Metastatic Breast Carcinoma

- Tumor cells involving superficial lymphatics.
- Many prominent congested blood vessels immediately below the epidermis results in the clinical appearance of violaceous “vesicles”.



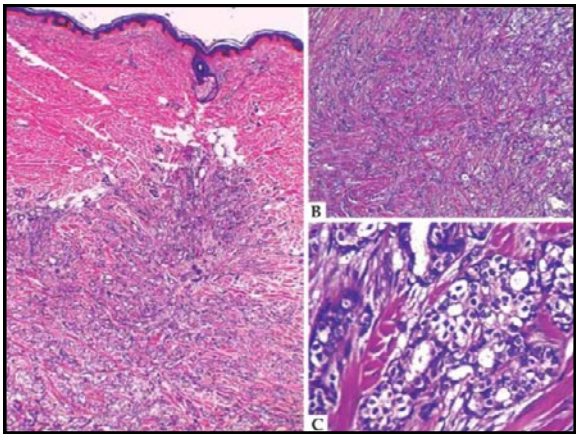
METASTATIC CARCINOMA
Nodular Metastatic Breast Carcinoma

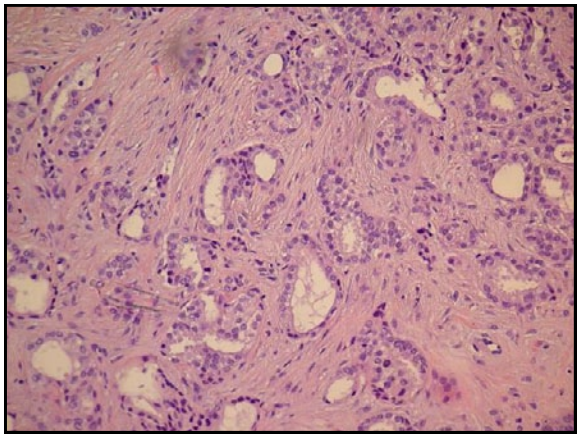
- Multiple firm nodules with or without ulceration
- Inframammary crease frequently in women with large breasts.
- Solitary nodule can mimic primary cutaneous skin cancer.



METASTATIC CARCINOMA
Nodular Metastatic Breast Carcinoma

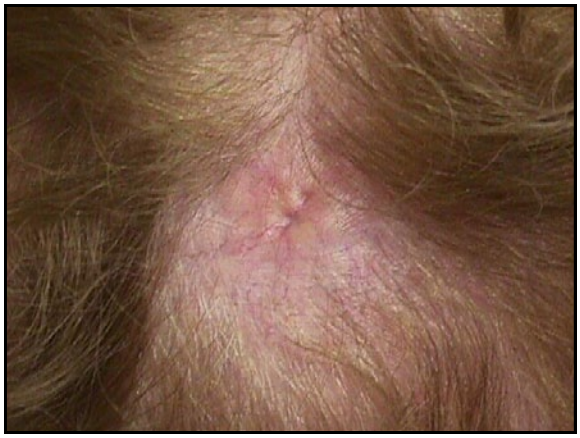
- Variably sized groups of tumor cells throughout dermis without epidermal connection.
- Glandular differentiation.
- Occasionally pigmented.





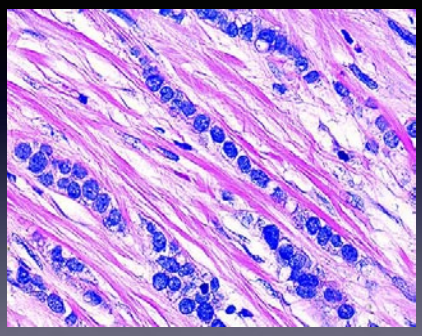
METASTATIC CARCINOMA
Alopecia Neoplastica

- Oval plaques or patches of scalp with hair loss.
- Cicitricial Alopecia vs. Alopecia Areata.
- Hematogenous.



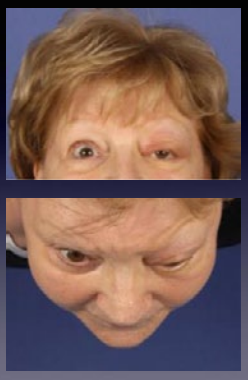
METASTATIC CARCINOMA
Alopecia Neoplastica

- Resembles En Cuirasse (Scirrhous) Carcinoma.
- Extensive fibrosis/sclerosis with rectangular silhouette and reduction of hair follicles.
- Single rows of “Indian filing” tumor cells between thickened collagen bundles.



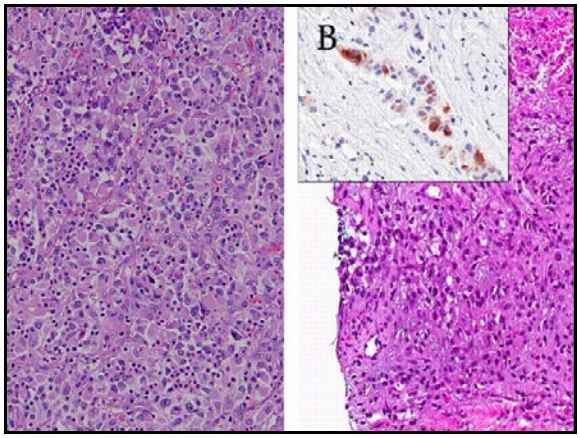
METASTATIC CARCINOMA
Metastatic Breast Carcinoma of the Eyelid

- Painless swelling with induration or a discrete solitary nodule.
- Chalazion vs. sebaceous carcinoma.
- Hematogenous.



METASTATIC CARCINOMA
Metastatic Breast Carcinoma of the Eyelid

- Nodular with glandular differentiation, lacks epidermal connection.
- Prominent histiocytoid appearance can result in misdiagnosis.
- Cytological atypia is present.



METASTATIC CARCINOMA
Immunohistochemical Stains

- Pan Cytokeratin +, CK7 +, CK20 usually negative.
- GCDFP-15 +, EMA +, CEA +
- ER/PR (positive or negative)
- Her2-Neu (positive or negative) - test mets for Her2 "gain"
- GATA3 - very helpful in triple negative breast cancer
- S100, HMB-45

Hum Pathol. 2013 Jul;44(7):1341-9.

GATA3 expression in breast carcinoma: utility in triple-negative, sarcomatoid, and metastatic carcinomas.

Cimino-Mathews A, Subhawong AP, Illei PB, Sharma R, Halushka MK, Vang R, Fetting JH, Park BH, Argani P.

Department of Pathology, The Johns Hopkins Hospital

Clin Breast Cancer. 2009 June ; 9(Suppl 2): S50–S57.

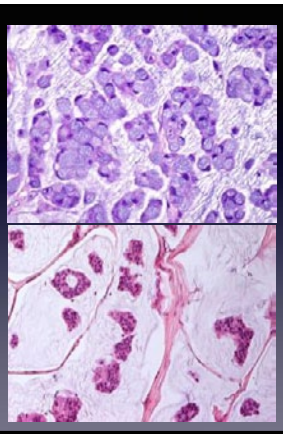
Treatment of HER2-Positive Metastatic Breast Cancer Following Initial Progression

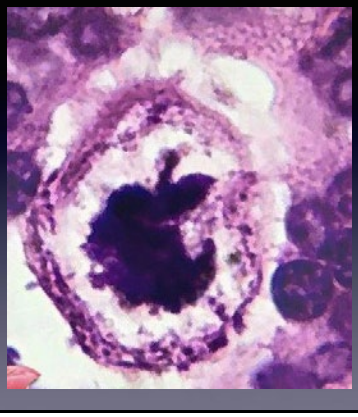
Ingrid A. Mayer

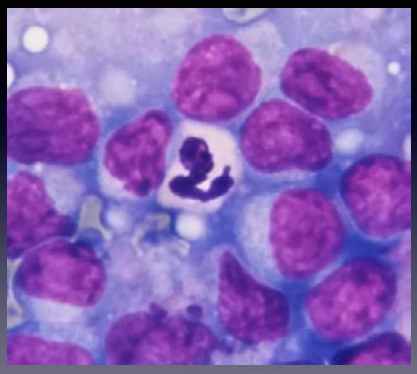
Department of Medicine and Breast Cancer Research Program, Vanderbilt University School of Medicine

METASTATIC CARCINOMA
Carcinoma of the Breast

- Unusual histologic patterns:
- Signet ring cell pattern mimics primary signet ring cell carcinoma (eyelid, CK7+/CK20 +)
- Mucinous carcinoma pattern mimics primary mucinous carcinoma (eyelid, CK7+/CK20-).

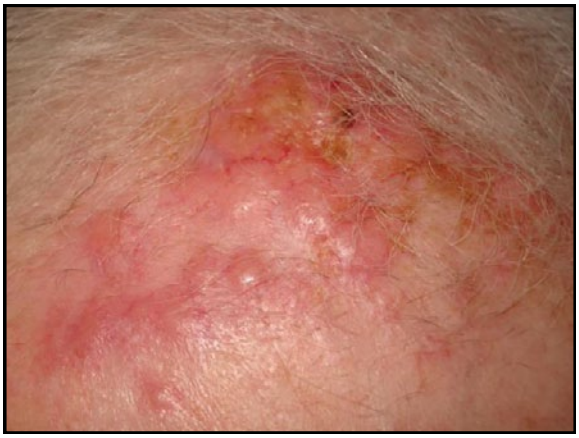


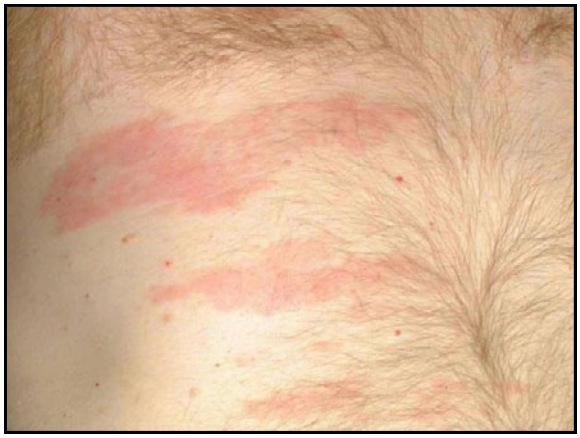




METASTATIC CARCINOMA
Carcinoma of the Lung

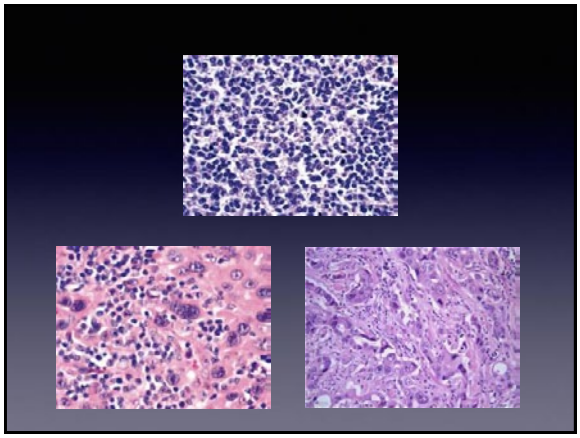
- Most common metastatic carcinoma of the skin in men.
- Most common cause of cancer death in women.
- Localized cluster of papules or nodules on chest wall and back - occasionally solitary.
- Oat (small) cell - skin of the back.





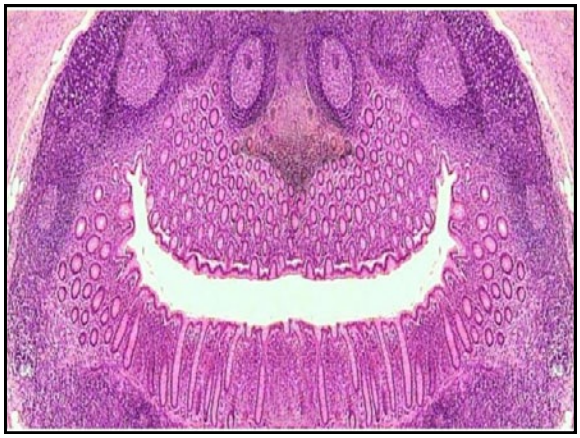
METASTATIC CARCINOMA
Carcinoma of the Lung

- Small cell carcinoma - neuroendocrine.
- Non-small cell carcinoma (Squamous cell carcinoma and Adenocarcinoma)



METASTATIC CARCINOMA
Carcinoma of the Lung

- Small cell carcinoma vs Merkel cell carcinoma.
- Clinical history
- Multiple lesions
- Epidermal involvement
- Immunostains: CEA, CK20, TTF-1

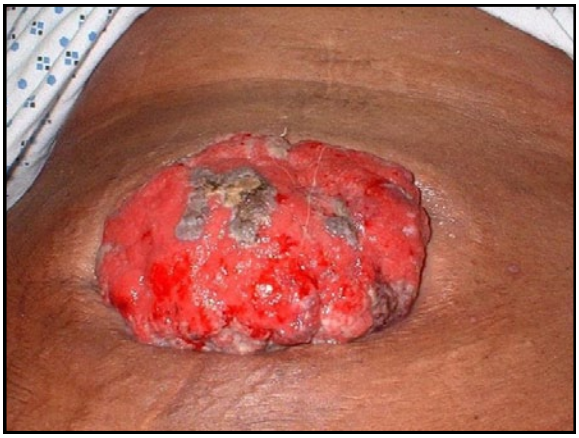


METASTATIC CARCINOMA
Gastrointestinal Carcinoma

- Colorectal carcinoma is the 2nd most common type of primary carcinoma in men.
- Cutaneous metastases usually occur after the primary tumor has been recognized
- Abdomen and perineal area > Head and neck

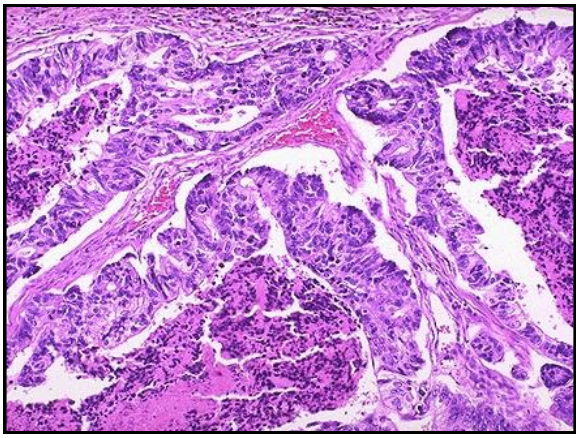
METASTATIC CARCINOMA
Gastrointestinal Carcinoma

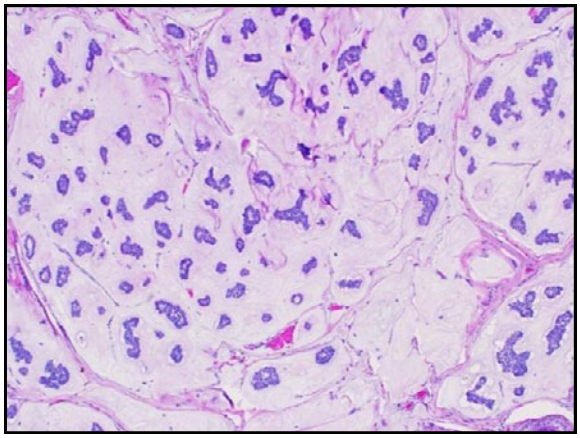
- Gastric carcinoma is uncommon.
- Cutaneous metastases usually occur after the primary tumor has been recognized
- Any site - Umbilical most common



METASTATIC CARCINOMA
Gastrointestinal Carcinoma

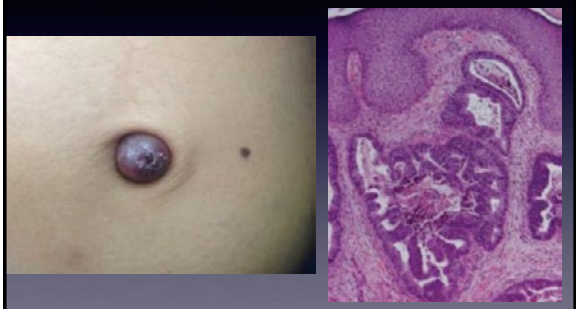
- Histopathology shows glandular differentiation.
- Adenocarcinoma (abortive gland formation)
- Mucinous carcinoma pattern (pools of mucin, Large intestine)
- Signet ring cell pattern (single mucin-laden cells, Stomach)





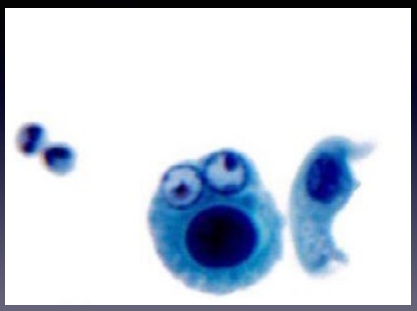
METASTATIC CARCINOMA
Gastrointestinal Carcinoma

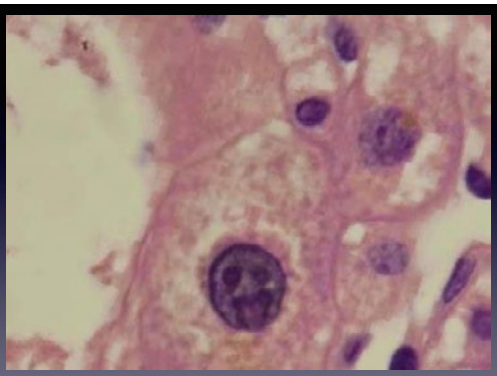
- Special stains
- Mucicarmine, Alcian Blue, Toluidine Blue
- CK20 positive CK7 negative



METASTATIC CARCINOMA
Sister Mary Joseph's Nodule

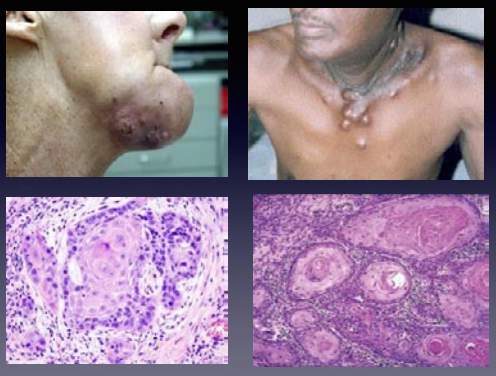
- Gastrointestinal - 52%, colon, gastric, pancreatic
- Genitourinary - 28%, ovarian, uterine
- CUP - Carcinoma of Unknown Primary
- Hernia, endometriosis, keloid, omphalith
- Painful, Poor prognosis, Peritoneal metastases

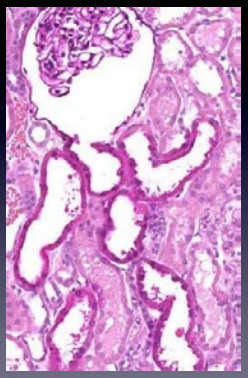




METASTATIC CARCINOMA
Oral Cavity Carcinoma

- Primary - side of tongue or floor of mouth
- Lymphatic spread - face or neck.
- Multiple or solitary nodule(s) +/- Ulceration
- Virtually always Squamous cell carcinoma.
- Deep dermis/subcutis sparing upper dermis except ulcerated lesions - difficult to distinguish from primary cutaneous SCC.



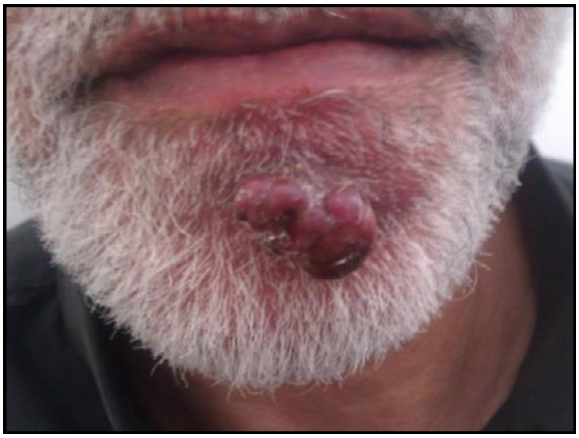


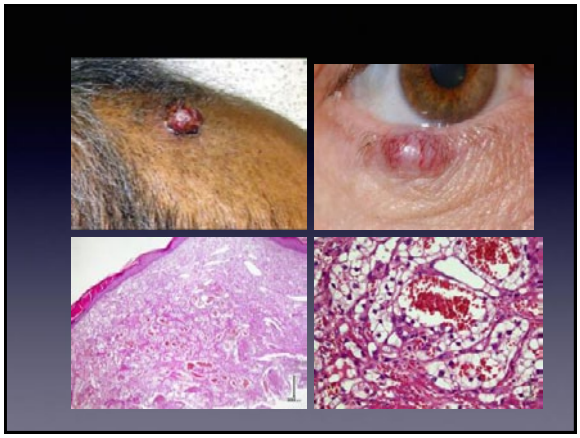
METASTATIC CARCINOMA
Renal Cell Carcinoma

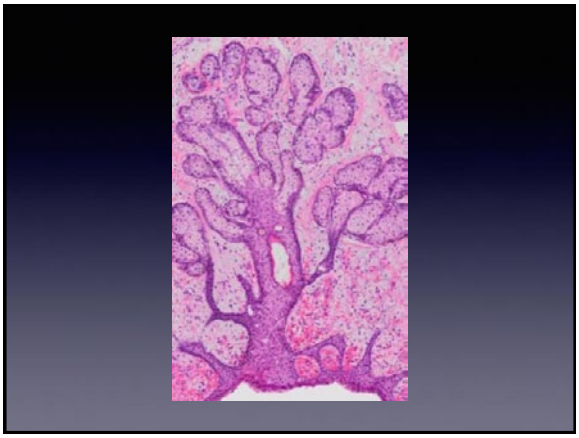
- Head and neck most common.
- Solitary or few nodules - tan-red to violaceous
- First sign or late lesion
- Virtually always in men

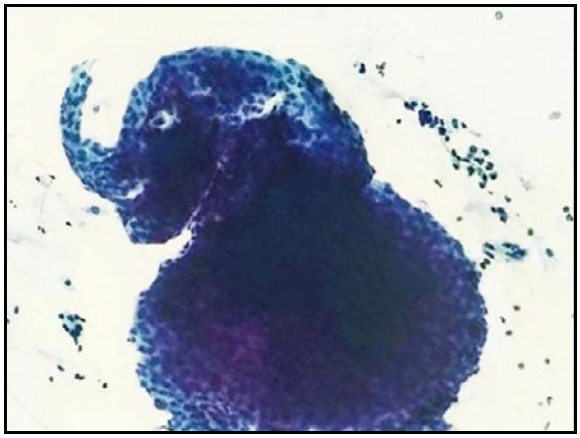
METASTATIC CARCINOMA
Renal Cell Carcinoma

- Clear cell adenocarcinoma
- Vascular
- Glycogen
- CD10 positive



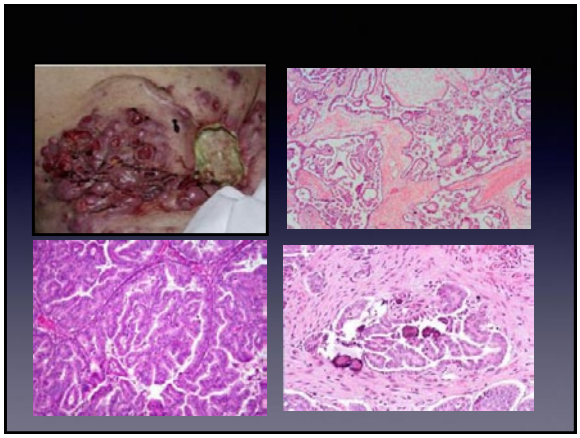


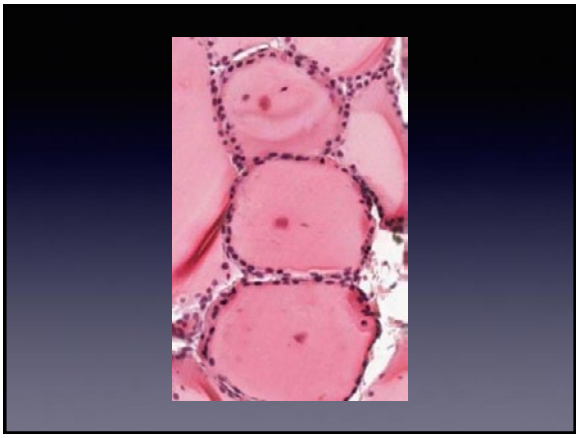




METASTATIC CARCINOMA
Ovarian Carcinoma

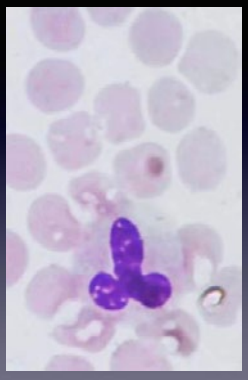
- Abdomen (umbilicus), vulva, back
- Surgical scars
- Papillary Adenocarcinoma - Psammoma bodies
- Mucinous carcinoma
- CK7/CK20-positve

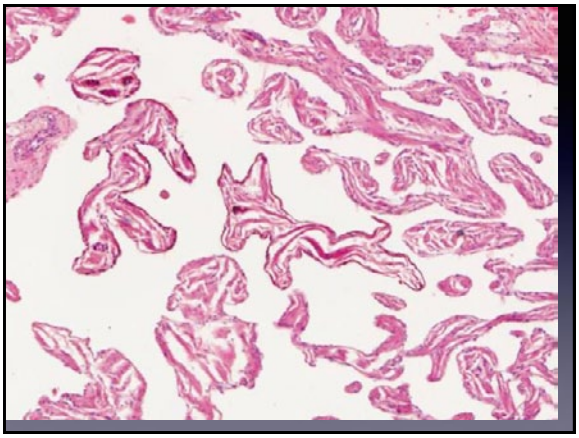




METASTATIC CARCINOMA
Miscellaneous Carcinoma

- Neuroendocrine carcinoma and carcinoid
- Liver
- Thyroid
- Adrenal
- Pancreatic
- Prostate





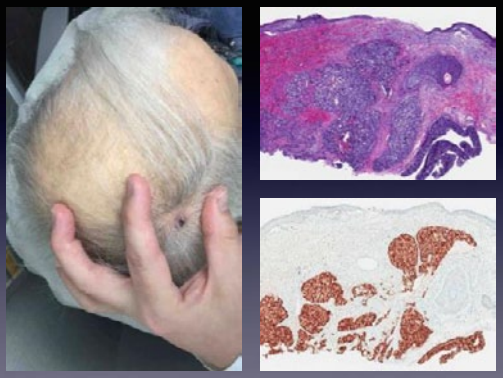
METASTATIC CARCINOMA
Prostate Carcinoma

- Skin Metastases - very uncommon
- Inguinal, thighs, lower abdomen
- Other sites (scalp) rare
- PSA, NKX3.1

Dermatology Online Journal 2018; 24(10).

A novel case of NKX3.1-positive metastatic cutaneous prostate cancer.

Wong JK, Minni JP, Nowak MA



What would I see on a report?

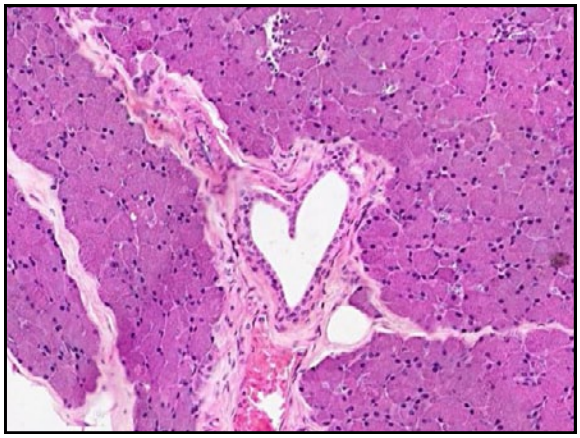
- Carcinoma involving dermis compatible with metastatic carcinoma
- Vascular/lymphatic involvement
- Special stains - P63, etc
- Prognostic studies ER/PR, Her-2-Neu

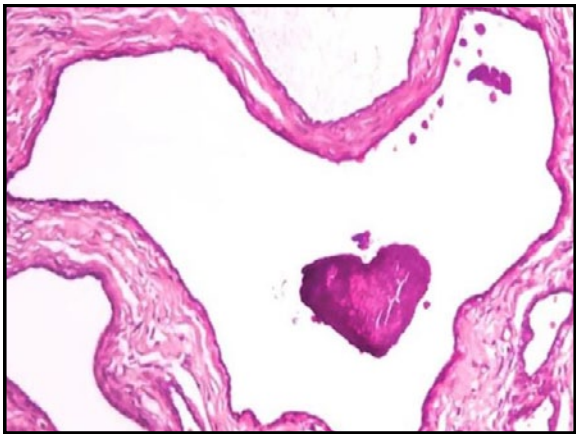
What do I do next?

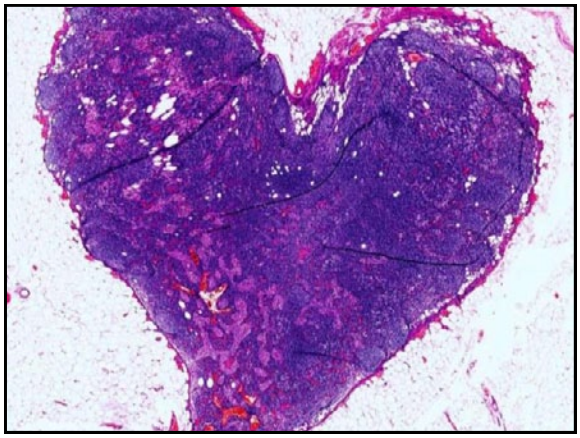
- Very difficult phone call to patient
- Referral to oncologist or back to existing oncologist
- Possible additional biopsy for prognostic markers
- Palliative treatment including simple excision, PDT (Levulan), intralesional chemotherapy, local wound care, etc.

Summary

- Lymphatic vs. Hematogenous
- Gender differences
- Her2 for Breast Cancer
- Merkel - Small cell lung cancer
- Sister Mary Joseph - GI, ovary, pancreatic, renal
- Renal - glycogen in men “Sugarman”
- Prostate - NKX3.1, PSA








Michael Nowak
man2004@comcast.net

SO MANY DRUGS, SO LITTLE TIME…A THERAPEUTIC UPDATE

JAMES Q. DEL ROSSO, DO
Research Director / Clinical Dermatology
JDR Dermatology Research / Thomas Dermatology

Adjunct Clinical Professor (Dermatology)
Touro University Nevada
Henderson, Nevada

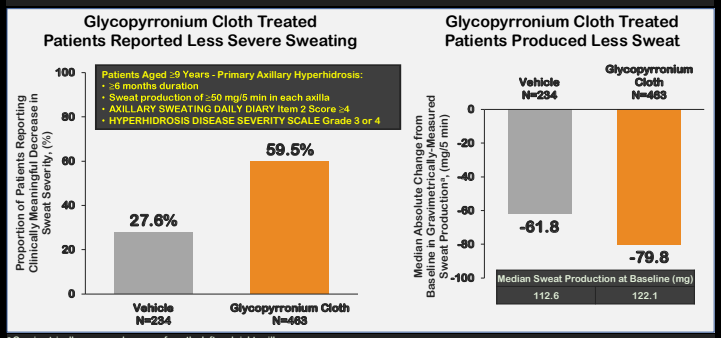
Disclosures

ALMIRALL*^#
ATHENEX*
BIOPHARMX*^
BOTANIX*
CELGENE*^#
DERMIRA*^
ENCORE#
EPI HEALTH*^#
FERNDALE^#
FOAMIX*^
GALDERMA*^#
GENENTECH*#
LEO PHARMA*^#
LA ROCHE POSAY^
NOVAN*^
ORTHO DERMATOLOGY*^#
PFIZER^#
REGENERON*^#
SANOFI-GENZYME^#
SONOMA (INTRADERM)^
SUN PHARMA*^ #
TARO*^#
VERRICA^

* Research Investigator
^ Consultant/Advisor
Speaker

UPDATED 12-24-2018

Glycopyrronium Cloth Applied Once Daily – Axillary Hyperhidrosis
Phase 3 Randomized Controlled Trials (Pooled ATMOS-1 and ATMOS-2)

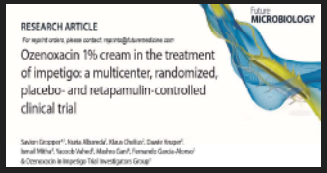


* Gravimetrically-measured average from the left and right axillae
Intent-to-treat (ITT) population, MCMC used to impute missing values; no statistical analysis performed for post-hoc pooled analyses
Glaser DA, et al. *J Am Acad Dermatol.* 2018 Jul 9 [Epub ahead of print]

IMPETIGO/ BACTERIAL SKIN INFECTIONS

Ozenoxacin 1% Cream Twice Daily x 5 Days
New Generation Topical Quinolone – Marked Gram (+) Activity


JAMA Dermatology | Original Investigation
Efficacy and Safety of Ozenoxacin Cream for Treatment of Adult and Pediatric Patients With Impetigo
A Randomized Clinical Trial


RESEARCH ARTICLE
Future MICROBIOLOGY
Ozenoxacin 1% cream in the treatment of impetigo: a multicenter, randomized, placebo- and retapamulin-controlled clinical trial

Multicenter, Double-Blind, Placebo-Controlled Phase 3 Trial (N=411)

Superior Clinical Success vs Placebo After 5 Days of Therapy (54.4% vs 37.9%)

More Rapid Microbiologic Clearance than Topical Retapamulin

Superior Microbiological Success vs Placebo After 2 Days of Therapy (87.2% vs 63.9%)

100% of Drug-Resistant Bacteria Cured/Improved (10/10 Mupirocin-Resistant; 8/8 MRSA)

Rosen T, Albareda N, et al. JAMA Dermatol. 2014.
Gropper S, et al. Future Microbiol. 2014;9(9):1013-1023.

TOPICAL THERAPY for PLAQUE PSORIASIS

Calcipotriene 0.005%-Betamethasone Dipropionate 0.064% (Cal/BD) Foam Use in Psoriasis Patients with Incomplete Response to Biologics ~ Long-Term Management (N=25)

- Open-label, prospective; after ≥24 weeks biologic therapy
  - Persistent areas of plaque psoriasis (≤5% Body Surface Area)
- Cal/BD once daily x 4 weeks THEN twice per week (on 2 consecutive days x 12 weeks
- Assessed Physcian Global Assessment, BSA, BSA x PGA
- Greater improvement in all parameters vs Baseline
- WEEK 4: 76% achieved Target BSA ≤1% and PGA <1
- WEEK 16: 68% achieved Target BSA ≤1% and PGA <1
- Favorable skin tolerability

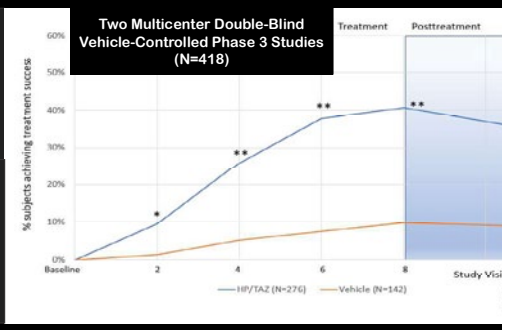
Bagel J, et al. J Drugs Dermatol. 2018;17(8):845-850.

Moderate-Severe Plaque Psoriasis Phase III Trials
Topical Halobetasol 0.01%/Tazarotene 0.045% x 8 Weeks
Evaluation of Investigator Global Assessment (IGA) Results (Pooled Phase 3

IGA
2-Grade Improvement + Clear/ Almost Clear

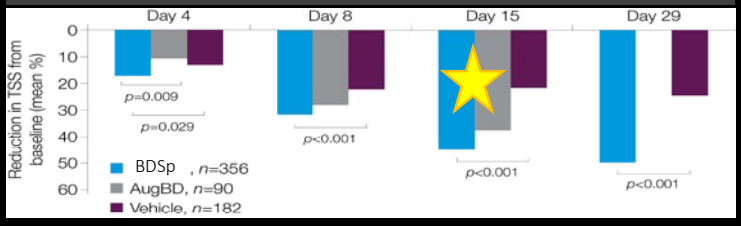
Low Adverse Events
Dermatitis (6.3%) – Stinging (2.6%) – Itching (2.2%)

Two Multicenter Double-Blind Vehicle-Controlled Phase 3 Studies (N=418)



Poster Presentation. Fall Clinical Dermatology. Las Vegas, NV. October 2017.

Moderate Plaque Psoriasis – Target Sign Score
Betamethasone Dipropionate 0.05% SPRAY BID vs Augmented Betamethasone Dipropionate 0.05% Lotion BID vs Vehicle BID



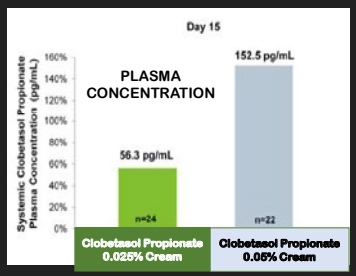
ITT population. Total sign score is defined as the sum of erythema, scaling, and plaque elevation scores

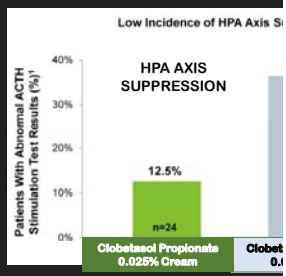
- Reduction in TSS was greater with BDSp at Day 4 (-17.3% vs -10.6%; *P*= .009)
- At Day 4 BDSp was also significantly different from AugBD for both TSS_{60} (13.2% vs 5.6%, *P*= .044) and TSS ≤1 for any sign (13.8% vs 5.6%, *P*= .031)

Fowler J, Hebert A, et al. J Drugs Dermatol. 2016;15(2):154-162.

Clobetasol 0.025% Cream
Pharmacokinetic/dynamic Properties vs 0.05% C

MODERATE TO SEVERE PLAQUE PSORIASIS / TWICE DAILY APPLICATI
N=45 / 20-50% BODY SURFACE AREA





Product Monograph/Data on File, Impoyz Cream, Encore Pharmaceuticls, 2018.

Flurandrenolide Tape (4 mcg/cm²)
for Corticosteroid Responsive Dermatoses

Both occlusive tape alone and steroid incorporated/ occlusive tape inhibit of enzyme activities in psoriatic lesions and normal-appearing skin.

Steroid Tape >> Tape Alone

Halprin KM, et al. Arch Dermatol. 1969;100(3):336-341.

ADJUNCTIVE PHOTOPROTECTION

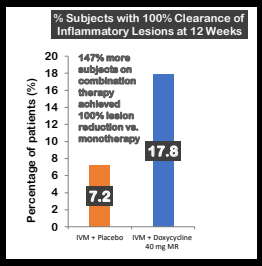
Polypodium Leucotomos Extract (PLE)
New Information of Specific Formulation

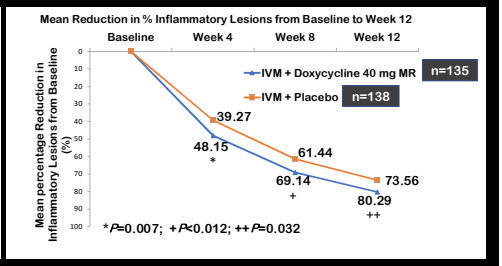
- Analysis of different PLE extracts to determine relative antioxidant content (by HPLC) and ability to prevevent UV damage (Vanillic, Ferulic, Caffeic, Protocatechuic, Others)
  - Results showed marked differences in content between different extract formulations and part of fern used (leaves > root)
  - Specific brand PLE with most efficient photoprotection based on cellular assay testing (ie cell survival, cyclobutane dimers)
- Assessment of oral PLE on Visible Light-induced Pigmentation (VLP)
  - IGA scores do not indicate an effect of PLE on VLP
  - Spectral measurements support an effect of PLE on VLP
  - Preliminary histology results indicate an effect of PLE on visible light induced DNA damage and inflammation

Gonzalez S, et al. Photomedicine. 2018 (in progress). / Mohammad TF, et al. Poster presentation. Henry Ford Hospital, Detroit, MI.

ROSACEA

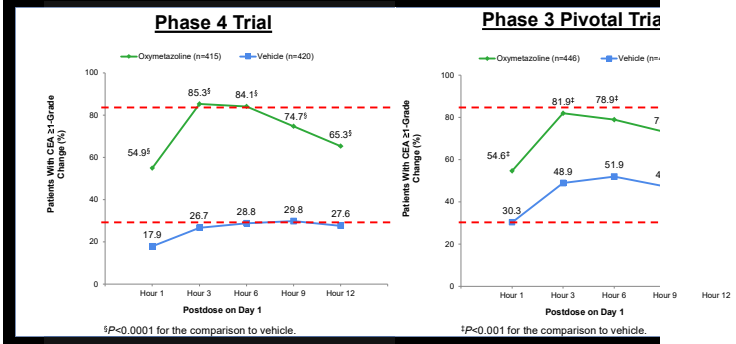
Ivermectin (IVM) 1% Cream + Subantibiotic Dose Doxycycline (Doxy MR 40 mg/day) vs IVM 1% Cream Alone
Severe Rosacea / Mean Lesion Count ~39 / Multiple Prior Therapies





ANSWER Study. Poster Presentation, Fall Clinical Dermatology, Las Vegas, NV, October 2018 / Soolantra Product Information, Galderma Laboratories, Fort Worth, TX.

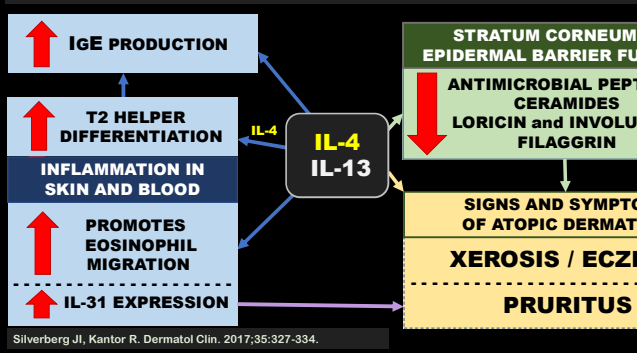
Oxymetazoline 1% Cream: Phase 4 vs Phase 3 Study Out
≥1-Grade Improvement in CEA



CEA, Clinician Erythema Assessment

ATOPIC DERMATITIS

Pathophysiologic Circuits in Atopic Dermatitis (
Role of Interleukin-4 (IL-4) and Interleukin-13 (IL-13



Silverberg JI, Kantor R. Dermatol Clin. 2017;35:327-334.

Safety of Dupilumab for Atopic Dermatitis (AD)
Analysis of Adverse Events / Infection Rates

- Adverse Events reported in 8 clinical trials (4 publications)
- Marked reduction in AD exacerbation
- 54% DECREASED RISK of Skin Infections
- Similar to Negligible Risk of Herpes Simplex Infections (RR 1.21)
- Similar Risk of Upper Respiratory Tract Infections
- Similar Risk of Nasopharyngitis
- Similar Risk of Urinary Tract Infections
- Increased risk for Conjunctivitis (RR 2.64)

Ou Z, et al. International Immunopharmacol. 2018;54:303-310.

Dupilumab in the "Real World"
Emerging Data and Experience with Clinical Uses

PEDIATRIC ATOPIC DERMATITIS

Pharmacokinetics, Safety, and Efficacy of Dupilumab in a Pediatric Population with Moderate-to-Severe Atopic Dermatitis: Results from an Open-Label Phase 2a Trial

Michael J. Cork[1], Diamant Thaçi[2], A. Thomas DiCioccio[3], John D. Davis[3], Qin Zhang[3], Marius Ardeleanu[3], Bolanle Akinlade[3], Neil M.H. Graham[3], Gianluca Pirozzi[3], Ashish Bansal[3]

HAND DERMATITIS

Dupilumab Treatment of Very Severe Refractory Atopic Hand Eczema

Dupilumab for hand eczema.

ALLERGIC CONTACT DERMATITIS

Dupilumab use in allergic contact dermatitis.

DYSHIDROSIS

CASE REPORT

Dupilumab in the Treatment of Dyshidrosis: A Report

BULLOUS PEMPHIGOID

Dupilumab for the Treatment of Recal Bullous Pemphigoid

Am J Clin Dermatol. 2018 Apr;19(2):145-165. doi: 10.1007/s40257-017-0324-7.

Are Biologics Efficacious in Atopic Dermatitis? A Systematic Review and Meta-Analysis.

Snast I[1], Reiter O[1], Hodak E[1,2], Friedland R[3], Mimouni D[4,5], Leshem YA[1,2].

NEMOLIZUMAB (ANTI-IL-31) SQ
- Demonstrated Efficacy for Pruritus (Phase 2)
- Improvement of Pruritus and Dermatitis (52 Weeks)

LEBRIKIZUMAB (ANTI-IL-13) SQ
- Phase 2b Dose Ranging SQ Q4W + TCs x 12 Wks
- 125 mg Q4 Weeks Significantly Greater % Reaching EASI-50 vs Placebo (82.4%%; P=.026)
- Adverse Events Similar to Placebo

FUTURE ???

TRALOKINUMAB (ANTI-IL-13) SQ
- Phase 2b 300 mg Q2W + TCs x 12Wks
- Superior Improvement in EASI and IGA Success vs Placebo
- Improved SCORAD, DLQI, Pruritus
- Response Correlation with Higher IL-31 Biomarkers

LACK OF EVIDENCE SUPPORTING EFFICACY
WITH INFLIXIMAB, RITUXIMAB, OMALIZUMAB, AND USTEKINUMAB

Snast I, et al. Am J Clin Dermatol. 2018;19(2):145-165.
Wollenberg A, et al. J Allergy Clin Immunol. 2018;June 12. pii S0091-6749(18)30850-9. {Epub}.
Kabashima K, et al. J Allergy Clin Immunol. 2018;May 10. {Epub}

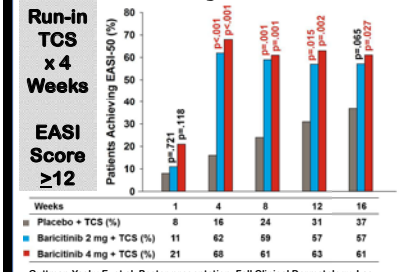
Baricitinib / Moderate-Severe Atopic Dermatitis in
2 MG QD or 4 MG QD + TCS vs Placebo + TCS / 16-Week Phase 2 (

ORAL

Run-in TCS x 4 Weeks

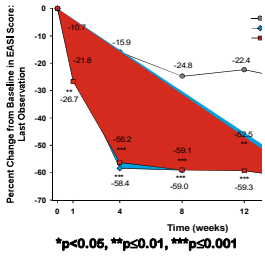
EASI Score ≥12

Primary Outcome
% Achieving EASI-50 at Week 16



Weeks	1	4	8	12	16
Placebo + TCS (%)	8	16	24	31	37
Baricitinib 2 mg + TCS (%)	11	62	59	57	57
Baricitinib 4 mg + TCS (%)	21	68	61	63	61

Change in EASI Sc Over Time (16 We



Guttman-Yasky E, et al. Poster presentation. Fall Clinical Dermatology, Las Vegas, NV, October 2018.

*p<0.05, **p≤0.01, ***p≤0.001

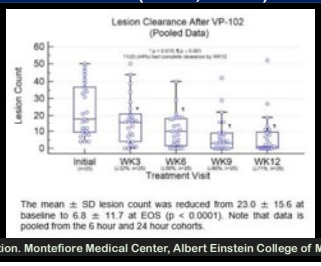
EASI=Eczema Area and Severity Index; MMRM= model of repeated measures; TCS=topical corti

COMMON CUTANEOUS VIRAL INFECTIONS

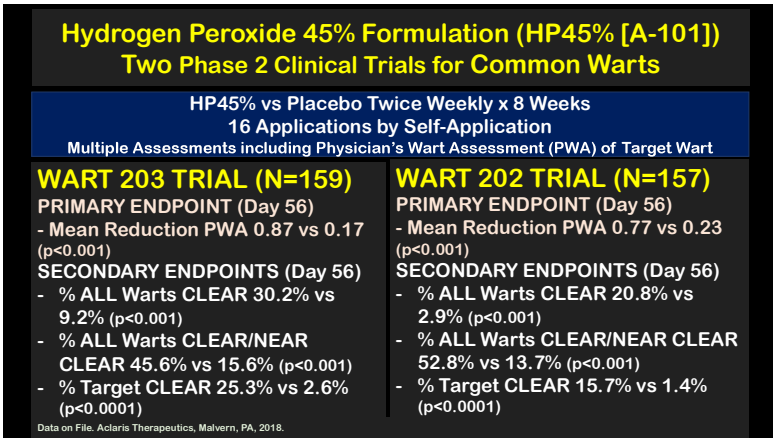
Molluscum Contagiosum
Verruca Vulgaris

Topical Cantharidin (0.7% w/v) Refined Formula
Phase 2 Pilot Study in Molluscum Contagiosum (N
Pharmaceutical Grade / Ether-Free Formulation

12-Week, Open-label Trial; Age 2-17 Years; <50 Lesions
Applied Every 21 Days Up to 4 Treatments or Until Clearanc
Treatment Washed Off at 6 Hours (14/30, 46.7%) or 24 Hours (16/30



Guzman A, et al. Poster presentation. Montefiore Medical Center, Albert Einstein College of Medicine, New York, NY


Hydrogen Peroxide 45% Formulation (HP45% [A-101])
Two Phase 2 Clinical Trials for Common Warts
HP45% vs Placebo Twice Weekly x 8 Weeks
16 Applications by Self-Application
Multiple Assessments including Physician's Wart Assessment (PWA) of Target Wart
WART 203 TRIAL (N=159)
PRIMARY ENDPOINT (Day 56)
- Mean Reduction PWA 0.87 vs 0.17 (p<0.001)
SECONDARY ENDPOINTS (Day 56)
- % ALL Warts CLEAR 30.2% vs 9.2% (p<0.001)
- % ALL Warts CLEAR/NEAR CLEAR 45.6% vs 15.6% (p<0.001)
- % Target CLEAR 25.3% vs 2.6% (p<0.0001)
WART 202 TRIAL (N=157)
PRIMARY ENDPOINT (Day 56)
- Mean Reduction PWA 0.77 vs 0.23 (p<0.001)
SECONDARY ENDPOINTS (Day 56)
- % ALL Warts CLEAR 20.8% vs 2.9% (p<0.001)
- % ALL Warts CLEAR/NEAR CLEAR 52.8% vs 13.7% (p<0.001)
- % Target CLEAR 15.7% vs 1.4% (p<0.0001)
Data on File. Aclaris Therapeutics, Malvern, PA, 2018.

- No financial disclosures

Stars who have aged gracefully…

Others who have not…

What are the Elements of Aging?

Dr. Azzi's "Triad of Aging"

- Textural changes: pigmentation and wrinkles
- Fat and bone re-absorption: loss of facial volume
- Gravity effects: sagging

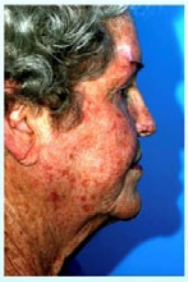
As a baby, we have perfect skin….

- Plump (baby fat)
- Color and tone
- Texture and clarity
- Pore size
- Elasticity

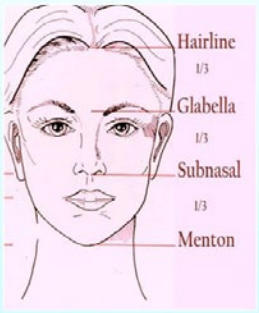
…smooth as a baby's butt.

WHY?
Sun, Environment, and Genetics =

- Uneven skin tone
- Wrinkles and fine lines - dynamic and at rest
- DEEP tissue moves lower with its skin envelope
- Volume loss (bone and soft tissue) with resultant "gaunt" appearance



Rule of Thirds



Rule of Fifths

Treatment of the Aging Face

- Don't Forget the Triad!
- Natural Results generally come from treating:
- Texture with texture
- Volume with volume
- Gravity with gravity

Texture

- Resurfacing
  - Laser
  - Peels
  - Dermabrasion
- Prevention
  - Skin care
  - Neuromodulators

Volume

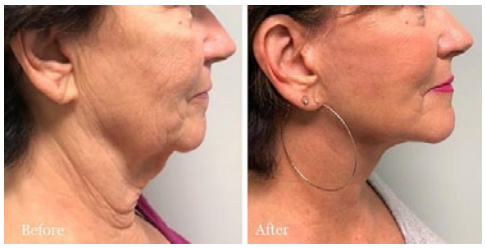
- Fat Grafting
- Implants
- Injectable Fillers
  - Choose the filler wisely
  - Choose the plane wisely

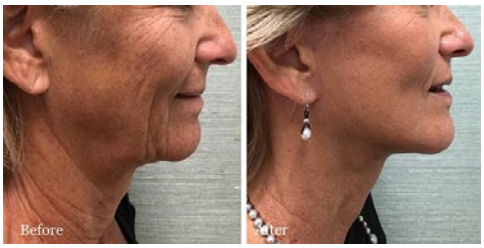
Gravity

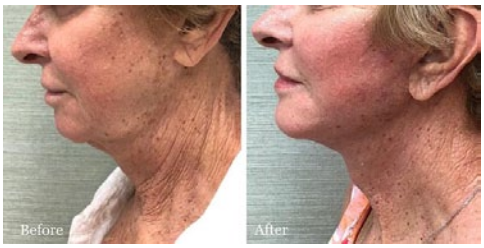
- Lower Face and Neck
  - Deep-Plane Facelift
  - Platysmaplasty
- Eyes
  - Upper and Lower Blepharoplasty
- Lip
  - LipLift

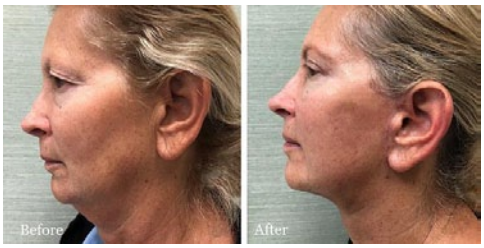
Deep-Plane Facelift

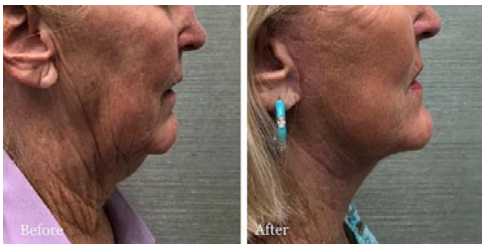
- Natural appearance
- Long lasting
- Quicker recovery
- The actual SMAS and Platysma that have moved over time are addressed directly






Before
After

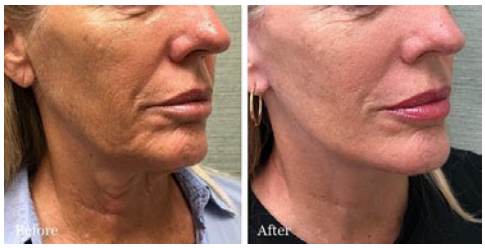

Before
After

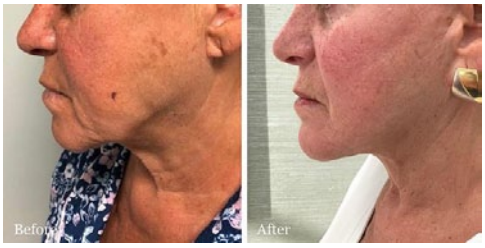

Before
After


Before
After

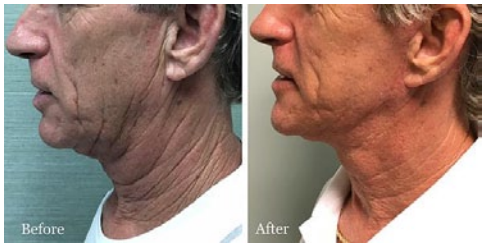

Before
After

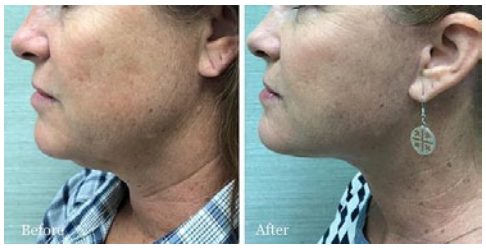

Before
After



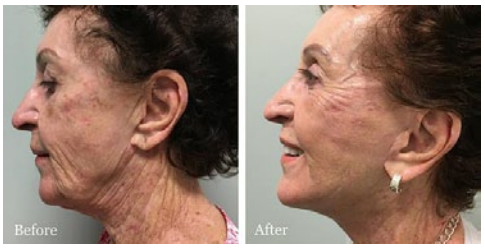


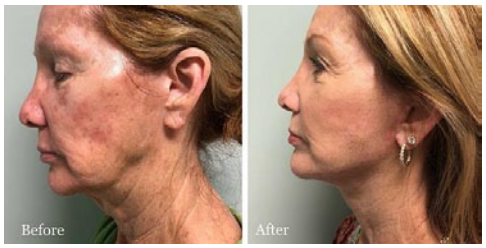
Mini-Facelift





Revisions



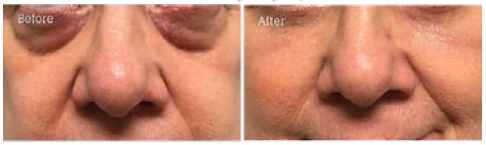


Blepharoplasty

- Upper
- Lower
  - Skin muscle flaps
  - Able to remove and sculpt 3 orbital fat pads
  - Can suspend the midface
  - Can transpose fat
  - Can tailor excess skin and muscle – be careful!

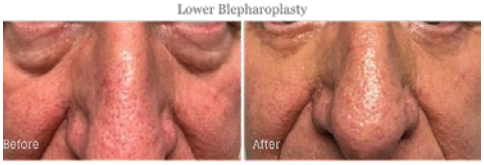
Upper Blepharoplasty

Lower Blepharoplasty

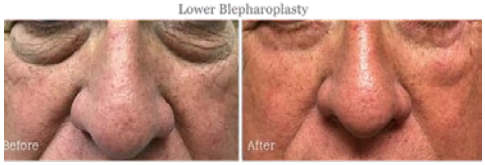


Upper & Lower Blepharoplasty

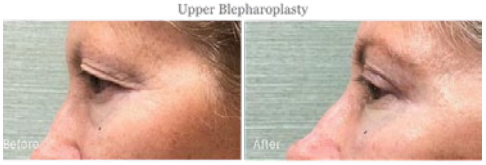
Lower Blepharoplasty

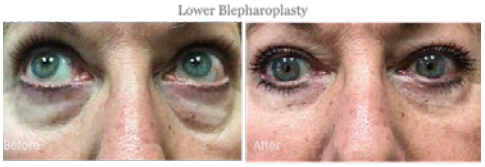


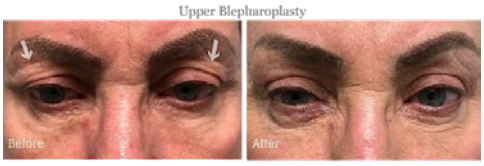
Lower Blepharoplasty



Upper Blepharoplasty

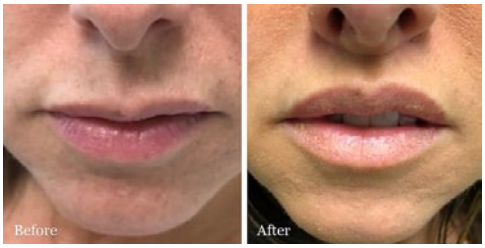


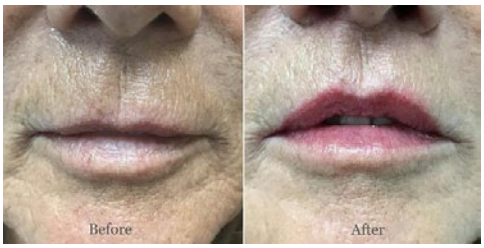


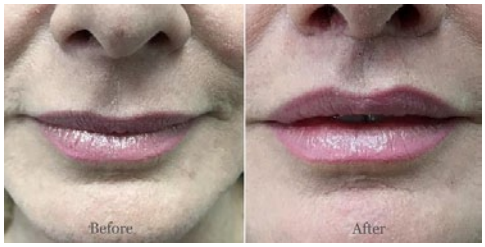


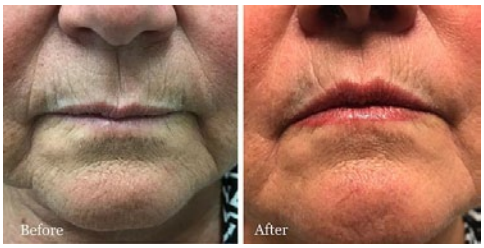
LipLift

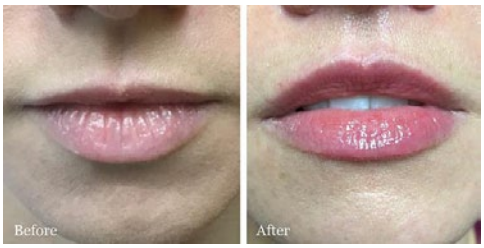
- Relatively permanent
- Natural result
- Can tailor amount of desired lift
- Addresses the cupid's bow and distance from nose to vermilion – things fillers cannot







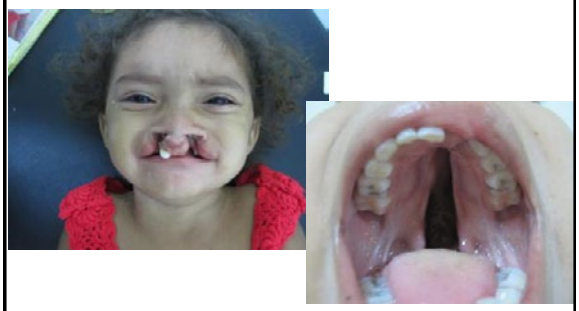




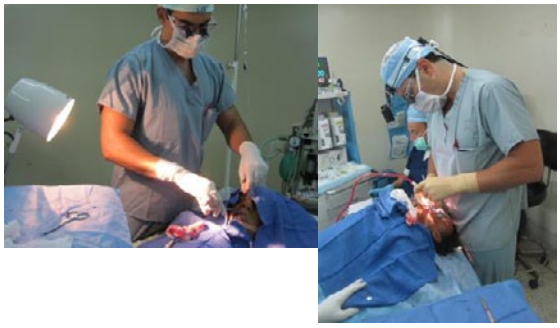
Mission Trips

- Healing the Children Northeast
- HUGS – help us give smiles
- Colombia, Guatemala, Ecuador, Vietnam
- Adding Peru and India
- Microtia, Lips, Palates etc

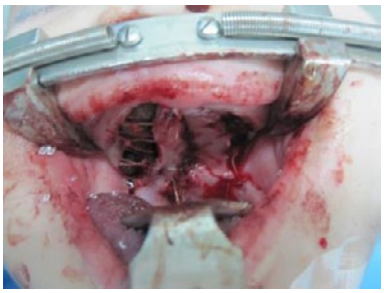
Colombia



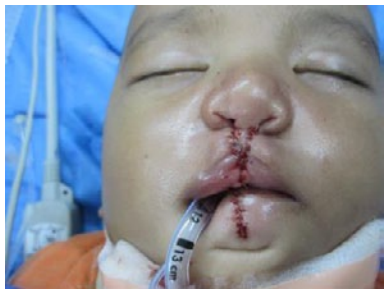
Colombia



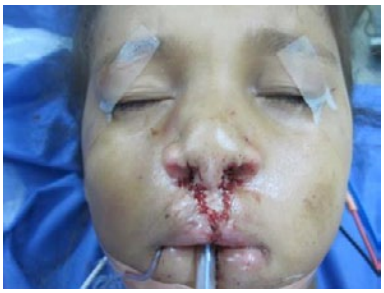
Colombia



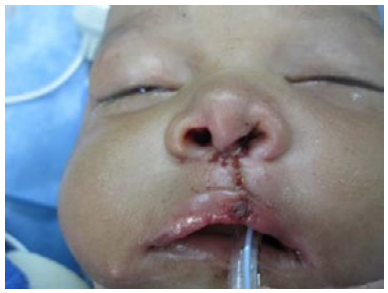
Colombia



Colombia



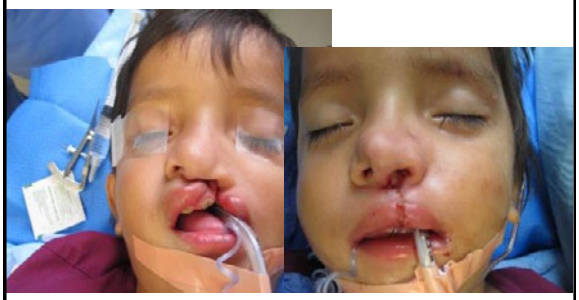
Colombia



Ecuador

Ecuador

Ecuador



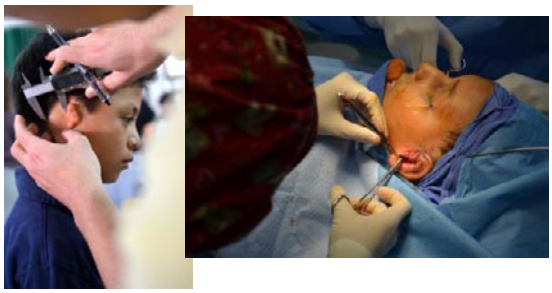
Ecuador - Guayachil

Guatemala

Guatemala

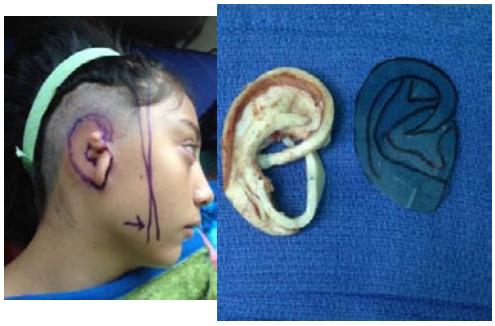
Guatemala

Guatemala

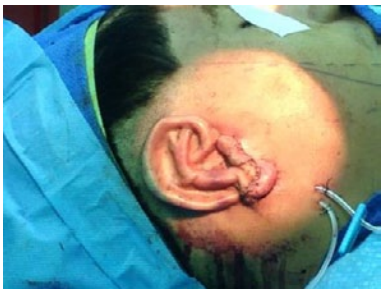


Quito

Quito

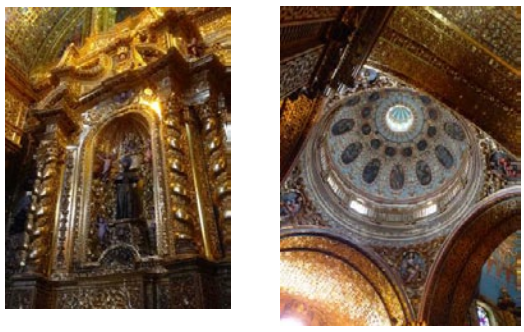


Quito



Quito

Quito



Quito

Hanoi, Vietnam

- I cant find any of my photos from this trip ☹
- So…

Vietnam

Contact Info - Azzi

- JP Azzi:
- doctorazzi@gmail.com
- Office: 561 429-5403
- Cell: 352 871-1015
- www.PalmBeachFacialSurgery.com

Friday, April 12, 2019

7:00 a.m. - 8:00 a.m.	Almirall Product Theater *Introducing Seysara (sarecycline) Tablets* **James Del Rosso, DO, FAOCD and Leon Kircik, MD** Palazzo F-G *(No CME Awarded)*
8:00 a.m. - 9:00 a.m.	*Practical Issues Using Biologics for Psoriasis* **Steven Feldman, MD**
9:00 a.m. - 10:00 a.m.	*Allergy for the Dermatologist* **Michael Wein, MD**
10:00 a.m. - 11:00 a.m.	*The Art of Radiotherapy for Skin Cancer Management* **David Herold, MD**
11:00 a.m. - 11:30 a.m.	Break with Exhibitors Palazzo D
11:30 a.m.	Attendee Free Time

Practical Issues Using Biologics for Psoriasis

Steven R. Feldman, M.D., Ph.D.
Professor of Dermatology, Pathology & Public Health Sciences
Wake Forest University School of Medicine
Winston-Salem, North Carolina

Conflicts/Disclosures

Research, speaking and/or consulting support from Galderma, Almirall, Leo Pharma, Boeringer Ingelheim, Mylan, Celgene, Pfizer, Ortho Dermatology, Abbvie, Janssen, Lilly, Merck, Novartis, Sanofi, Qurient, National Biological Corporation, Caremark, Advance Medical, Sun Pharma, Suncare Research, Informa, UpToDate and National Psoriasis Foundation. I am founder and majority owner of . I am a founder and part owner of Causa Research, a company dedicated to enhancing patients' adherence to treatment.

Objectives

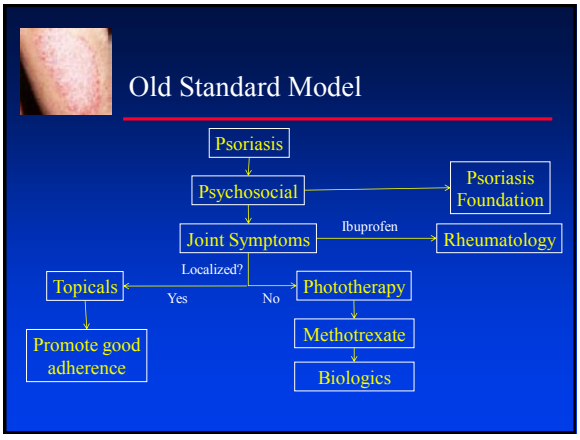
- To describe the psoriasis patient population that should be treated with biologics
  - Treatment goals (targets, comorbidities)
- Features that affect choice of a biologic
  - Efficacy
    - Durability of response
    - Psoriatic arthritis
  - Safety
    - Monitoring
  - Cost
    - Biosimilars
- Getting patients to take the drug

Disclaimer/Warning

- I have mixed feelings about almost everything
- Tendency to be cynical

When to Use Biologics

- When patients need them, not when they don't
  - To achieve high levels of success
- Serious psoriasis, has an impact on patients' lives
  - When the benefit warrants the risk
    - In studies, usually BSA > 10%, PASI>12
    - Approval is for moderate-to-severe, and moderate is >5%
    - Other disabling forms of the disease
  - Not for patients who respond to less risky treatment
    - Phototherapy first when reasonable
      - Office UV, home UV, tanning beds
    - For localized disease resistant to topicals?
      - It may be better to get the patient to use the topicals well first



General Recommendations from AAD Guidelines

- Topicals are reasonable for patients with localized psoriasis
- UVB is safe, effective & cost effective
  - PUVA therapy is very effective but has greater risks
- Methotrexate is effective but has many risks
- Cyclosporine is best used only intermittently
- Acitretin is not immunosuppressive but is teratogenic
- Biologics are safe & effective

National Psoriasis Foundation Algorithms

Treat to Target for Psoriasis

- Patients, NPF Medical Board developed treatment targets
  - 25 psoriasis experts involved
  - Published in the *Journal of the American Academy of Dermatology* (2016)
  - The first treatment targets for psoriasis in the U.S.
  - Set goals for psoriasis treatments will hopefully become a new standard for care

Armstrong AW, et al. (2016). From the Medical Board of the National Psoriasis Foundation: Treatment targets for plaque psoriasis. *Journal of the American Academy of Dermatology*. Advance online publication. doi:

What are the NPF treatment targets for psoriasis?

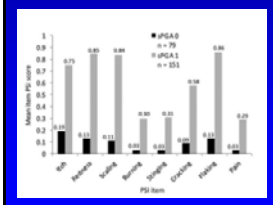
Preferred assessment instrument: **Body Surface Area (BSA)**

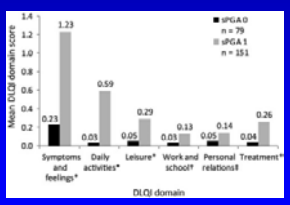
Time Post Initiation	Target	Acceptable
3 Months	BSA ≤ 1%	BSA ≤ 3% - or – 75% Improvement
Every 6 Months	BSA ≤ 1%	

Armstrong AW, et al J Am Acad Dermatol. 2017 Feb;76(2):290-298.

Clearing As A Goal

- Patients do better if you get them completely clear





J Dermatolog Treat. 2016;27(3):224-7

Comorbidities

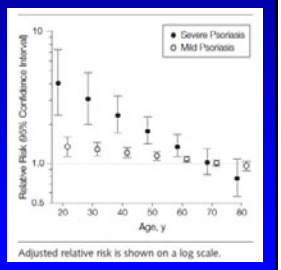
- Psoriasis is associated with many comorbidities
- Hottest research in dermatology

Comorbidity	Exposure	Relative Risk (95% CI)
DM	Mild Psoriasis	1.47 (1.40-1.54)
DM	Severe Psoriasis	2 (1.79-2.22)
NMSC	Psoriasis	7.5 (5.07-11.10)
Melanoma	Psoriasis	6.12 (1.53-24.47)
A fib	Mild Psoriasis	1.22 (1.14-1.30)
A fib	Severe Psoriasis	1.53 (1.23-1.91)
Ischemic Stroke	Mild Psoriasis	1.25 (1.17-1.34)
ischemic Stroke	Severe Psoriasis	1.65 (1.33-2.05)
VTE >=50 yo	Mild Psoriasis	1.26 (1.13-1.42)
VTE >=50 yo	Severe Psoriasis	1.74 (1.32-2.28)
AAA	Mild Psoriasis	1.2 (1.03-1.39)
AAA	Severe Psoriasis	1.67 (1.21-2.32)
Migraine	MIld Psoriasis	1.37 (1.30-1.45)
Migraine	Severe Psoriasis	1.55 (1.29-1.86)
RVO	Psoriasis	1.46 (1.04-2.04)
MI Age 50-60	Mild Psoriasis	1.08 (1.03-1.13)
MI Age 50-60	Severe Psoriasis	1.36 (1.13-1.64)

J Am Acad Dermatol. 2017 Mar;76(3):531-537

Severe Psoriasis is Associated with Myocardial Infarction

- Most impactful publication in my dermatology lifetime
- "As dermatologists care for most patients with severe psoriasis, it is imperative that these patients are screened for CVD risk factors and that they are referred either to a primary care physician or to a cardiologist for management and treatment of risk factors"



JAMA. 2006;296:1735-1741; Drugs (2014) 74:169–182

Number Needed To Harm (NNTH)

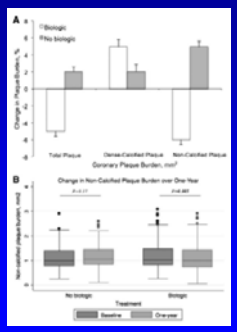
- You would need to see a very large number of patients with psoriasis before, on average, you'd see one more case of comorbidity due to psoriasis

Comorbidity	Exposure	NNTH
DM	Mild Psoriasis	580
DM	Severe Psoriasis	272
NMSC	Psoriasis	1551
Melanoma	Psoriasis	20135
A fib	Mild Psoriasis	1500
A fib	Severe Psoriasis	623
Ischemic stroke	Mild Psoriasis	1320
ischemic stroke	Severe Psoriasis	508
VTE >=50 yo	Mild Psoriasis	1895
VTE >=50 yo	Severe Psoriasis	666
AAA	Mild Psoriasis	13441
AAA	Severe Psoriasis	4012
Migraine	MIld Psoriasis	700
Migraine	Severe Psoriasis	471
RVO	Psoriasis	8801
MI Age 50-60	Mild Psoriasis	2146
MI Age 50-60	Severe Psoriasis	430

J Am Acad Dermatol. 2017 Mar;76(3):531-537

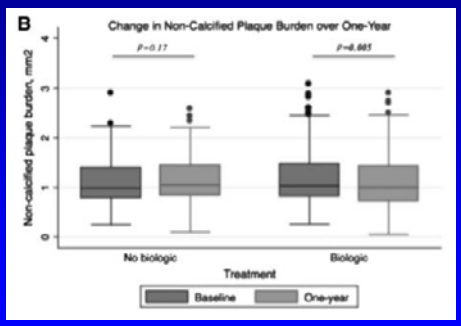
Biologics Improve Coronary Arteries

- Biologic therapy was associated with a 6% reduction in non-calcified plaque burden (P = 0.005)
- Decrease in non-calcified plaque burden in the biologic treated group was significant compared with slow plaque progression in non-biologic treated



Cardiovasc Res. 2019 Feb 5

Change in Plaque Burden



Cardiovasc Res. 2019 Feb 5

Comorbidities in Children!

- Crohn's was 20 times as prevalent in children with psoriasis!
- The incidence was 3 times as high!

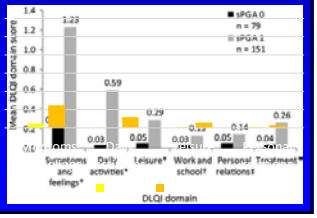
	Psoriasis (N=7,686)		Nonpsoriasis (N=30,744)	
Crohn's prevalence	N=86	11	N=19	0.62
Crohn's incidence	N=14	0.97	N=15	0.29

- 1 in 1,000 children per year with psoriasis developed Crohn's

Pediatr Dermatol. 2019 Feb 21

Clearing As A Goal

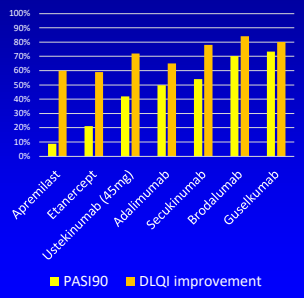
- How much better do patients do if you get them completely clear?
- Symptoms, activities, leisure & relations domains combine 2 questions
- Each on a 0-3 scale
- 1 is "a little"



J Dermatolog Treat. 2016;27(3):224-7

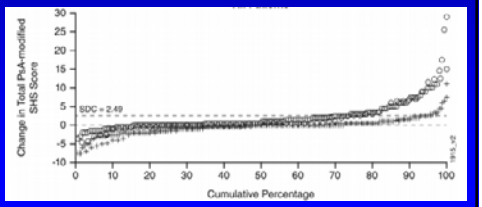
Good Drugs With Lousy Data

- High levels of clearance give statistically better quality of life if you have sufficient sample size to detect the difference
- But even low levels of high improvement are associated with good improvements in patients' quality of life



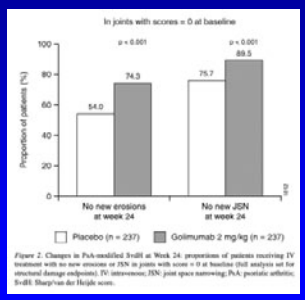
We Have To Address Arthritis?

- Baseline Sharp score: ~35
- Change at 24 weeks: ~2 with placebo & 0.4 with golimumab



Kavanaugh A, J Rheumatol. 2019 Feb 15

Most Don't Progress Without Drug, Some Do Progress With Drug



Kavanaugh A, J Rheumatol. 2019 Feb 15

Which one is best? There may not be one best biologic

- Characteristics vary and are weigh differently in unpredictable ways
  - What may be best for me may not be what a patient would choose
  - How we perceive things is not fixed, either
- My approach: educate patients about options, involve them (as much as they want) in the choice, & guide them to a good decision

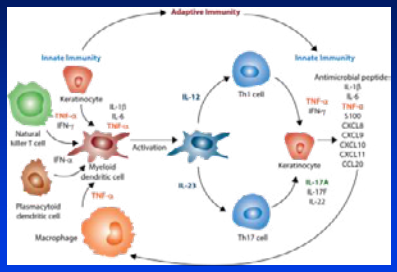
Characteristics of Biologics

- Most effective: not etanercept or ustekinumab
- Most convenient: ustekinumab, tildrakizumab
- Most effective for joints: maybe not ustekinumab
- Most cost effective
  - I've written several papers on this (and have no idea which is the most effective)
- Safest: Very hard to say
  - Anti-IL12 and/or 23 (possibly anti-IL17 drugs)

Dimensions to Consider

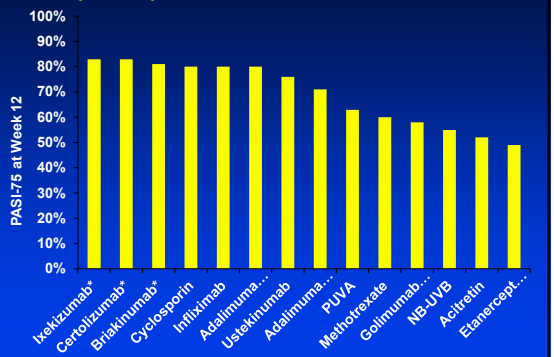
- Mechanism
- Efficacy
  - Durability
  - Psoriatic arthritis
- Safety
  - Monitoring
- Cost
  - Biosimilars
- Adherence

Immunopathology of Psoriasis



CCL: chemokine (C-C motif) ligand; CXCL: chemokine (C-X-C motif) ligand; IFN: interferon; IL: interleukin; NKT: natural killer T cell; Th: T helper; TNF: tumor necrosis factor.
Nestle FO et al. *N Engl J Med.* 2009;361:496-509.

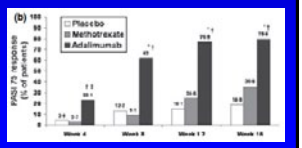
Efficacy of Systemic Treatments for Psoriasis



Biologic vs Methotrexate

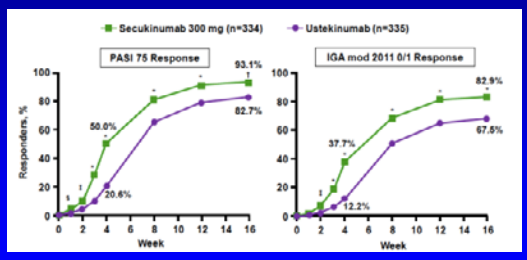
- 40mg every other week of adalimumab
- Methotrexate

Week	0-1	2-3	4-7	8-11	12-15+
Max dose mg/wk	7.5	10	15	20	25



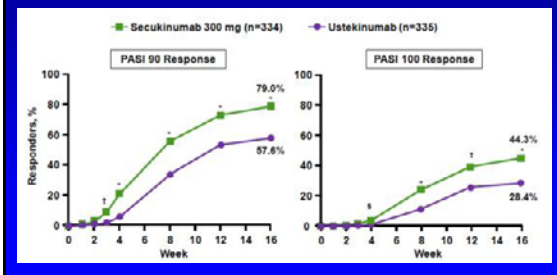
Saurat JH et al. Br J Dermatol. 2008 Mar;158(3):558-66.

Secukinumab vs Ustekinumab



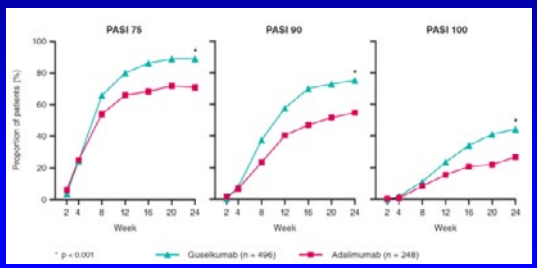
J Am Acad Dermatol. 2015 Sep;73(3):400-9

Secukinumab vs Ustekinumab



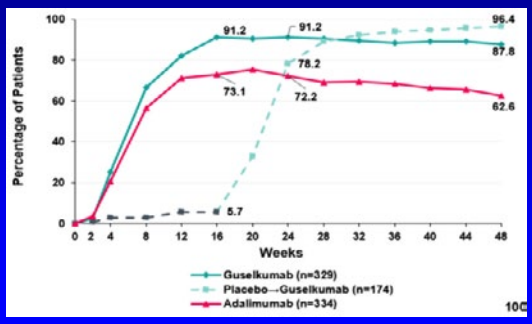
J Am Acad Dermatol. 2015 Sep;73(3):400-9

Efficacy of Guselkumab vs Adalimumab



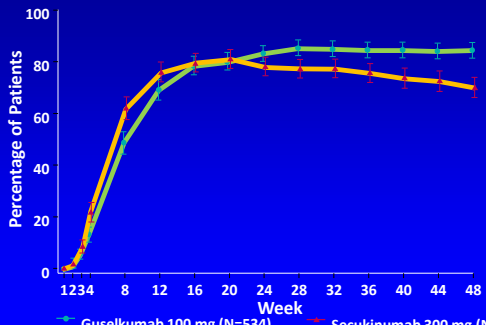
Reich K, et al. *J Am Acad Dermatol.* 2017;76(3):418-431.

Guselkumab vs Adalimumab

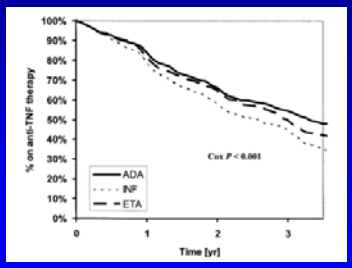


https://www.nice.org.uk/guidance/ta521/documents/committee-papers

Guselkumab vs Secukinumab

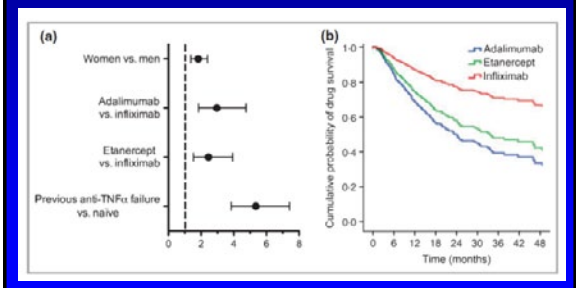


TNF-Inhibitor Treatment Retention



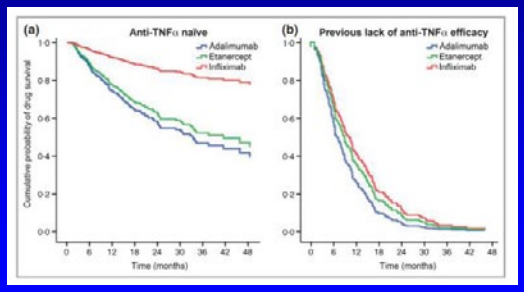
Dupan SM, Arthritis & Rheumatism (Arthritis Care & Research) 2009; 61: 560 –568
Brezinsky, PLoS ONE 7(4): e33486.
Barrera MD, Eur J Dermatol 2008; 18 (6): 683-7

DERMBIO Persistent on Treatment



Br J Dermatol. 2011 May;164(5):1091-6

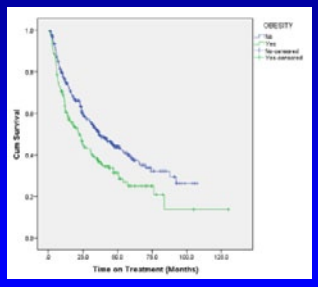
Worse with Previous Failure



Br J Dermatol. 2011 May;164(5):1091-6

ORBIT

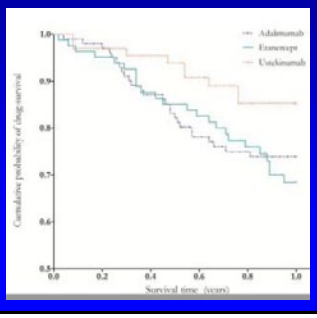
- Worse persistence in obese patients



J Am Acad Dermatol. 2016 Jun;74(6):1066-72

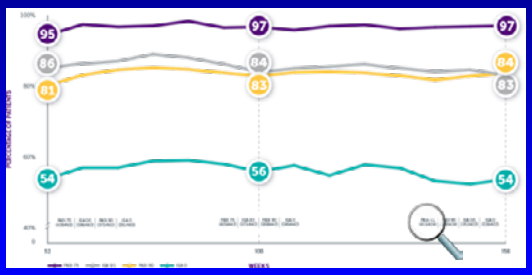
BioCAPTURE: Happy drug survival

- Still on drug
- DLQI<5



Br J Dermatol. 2014 Nov;171(5):1189-96

Interpreting Long Term Response

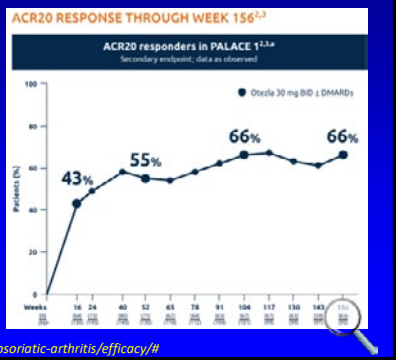


- 424 of 463 = 92%

https://www.tremfyahcp.com/efficacy/open-label-extension-data

As Observed May Be Misleading

- 95 / 150 = 63%
- 66% ACR20 of 63% still in the study = 42%



https://www.otezlapro.com/psoriatic-arthritis/efficacy/#

Managing Psoriatic Arthritis

- Screen for it
  - Can be your pertinent review of systems item
  - Ask about: Joint pain, joint stiffness, back pain
- Refer to rheumatology for evaluation
  - Complete assessment of tenderness and range of motion in joints
  - X-rays to evaluate for joint destruction
  - Comprehensive treatment options

J Dermatolog Treat. 2009;20(6):350-3.

Psoriatic Arthritis Efficacy

	ACR20 at Week 24
Etanercept	50%
Adalimumab	57%
Ustekinumab	42-44%
Secukinumab 300mg	50-54%
Ixekizumab (every 4 weeks)	58%
Guselkumab (every 2 months)	58%
Apremilast (30mg twice a day)	38%

Cochrane Review of Biologic Safety

- Biologics had a higher rate of total adverse events (odds ratio 1.19, NNTH = 30), withdrawals due to adverse events (OR 1.32, NNTH = 37) and risk of TB reactivation (OR 4.68, NNTH = 681) compared to control.
- The rate of SAEs, serious infections, lymphoma, and congestive heart failure were not statistically significantly different between biologics and control treatment.

Cochrane Database Syst Rev. 2011 Feb 16;(2):CD008794.

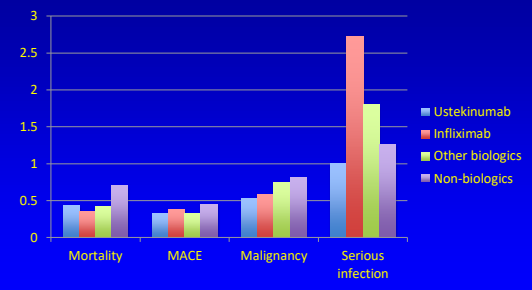
PSOLAR Registry

Table 1	UST (N=3474)	IFX (N=1151)	ETAN (N=1854)	ADA (N=2675)	MTX Non-biologics (N=490)	Non-MTX Non-biologic (N=1610)	All (N=11466)
Age [years], mean ± SD	47.2 ± 13.09	48.5 ± 13.45	48.7 ± 13.65	47.6 ± 13.26	55.1 ± 13.82	50.1 ± 15.82	48.5 ± 13.82
Males, n (%)	1999 (57.5)	655 (56.9)	1038 (56.0)	1505 (56.3)	207 (42.2)	830 (51.6)	6321 (55.1)
Caucasian, n (%)	3002 (86.4)	966 (83.9)	1482 (80.0)	2138 (79.9)	395 (80.6)	1357 (84.3)	9508 (82.9)
BMI [kg/m^2], mean (SD)	31.3 ± 7.17	32.2 ± 8.23	30.4 ± 7.10	31.0 ± 7.00	30.1 ± 6.95	29.9 ± 6.88	30.9 ± 7.23
Duration of psoriasis, years, mean ± SD	19.4 ± 12.80	18.4 ± 12.68	17.4 ± 13.35	17.2 ± 13.07	14.3 ± 14.80	14.3 ± 14.62	17.5 ± 13.43
Physician's Global Assessment (PGA), mean ± SD	2.0 ± 1.25	1.8 ± 1.23	1.9 ± 1.14	1.9 ± 1.22	2.1 ± 1.17	2.3 ± 1.06	2.0 ± 1.21
Psoriatic arthritis (self-reported), n (%)	1134 (32.6)	601 (52.2)	785 (42.3)	1112 (41.6)	140 (28.6)	237 (14.7)	4098 (35.7)
History of treated Infections 3 years prior to enrollment, n (%)	802 (23.2)	350 (30.5)	467 (25.2)	660 (24.7)	116 (23.7)	337 (21.0)	2791 (24.4)

43

Kalb R, et al. AAD 2015. P1643.

Adverse Event Rates



Gottlieb AB et al, J Drugs Dermatol 2014; 13: 1441-48

IL-23 genes protect against IBD

- 3 loss of function mutations in IL-23R linked to protection against the development of Crohn disease and ulcerative colitis in humans
- These 3 IL23R variants cause a reduction in IL23 receptor activation-mediated phosphorylation of the STAT3 & STAT4

THE JOURNAL OF BIOLOGICAL CHEMISTRY VOL. 291, NO. 16, pp. 8673–8685, April 15, 2016

Flares of psoriasis with IBD treatment

- Seen with TNF inhibitors
  - Poorly explained process
  - 21 of 1294 patients with IBD treated with anti-TNF developed drug-induced psoriasis
    - 14 patients with infliximab
    - 7 with adalimumab
  - The onset varied (mean 13±8 doses).
  - Plaque psoriasis (57%), scalp (14%), palmoplantar pustulosis (14%), generalized pustular psoriasis (5%), guttate (5%) and inverse (5%)

J Crohns Colitis. 2012 Jun;6(5):518-23.

Worsening IBD with anti-IL17

- Roughly 1 in 300 patients without screening
- Confirmed in IBD patients
  - 59 IBD patients randomized 2:1 to secukinumab vs placebo
  - Primary end point analysis estimated <0.1% probability that secukinumab reduces CDAI by >50 points more than placebo
  - Secondary showed a significant difference in favor of placebo.

Gut. 2012 Dec;61(12):1693-700

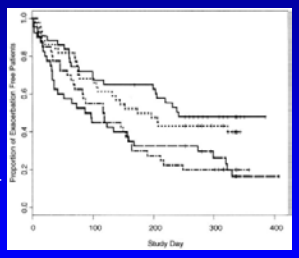
Confirmed with Brodalumab

- Patients randomized receive brodalumab (210, 350, or 700 mg or placebo.
- Study terminated early based on an imbalance in worsening CD in active treatment groups.
- Mean change in CDAI at week 6 was -8.7 (210 mg), -35.4 (350 mg), -0.6 (700 mg), and -28.2 (placebo)
- Brodalumab resulted in more cases of worsening CD in patients with active CD and no evidence of meaningful efficacy.

Am J Gastroenterol. 2016 Aug 2.

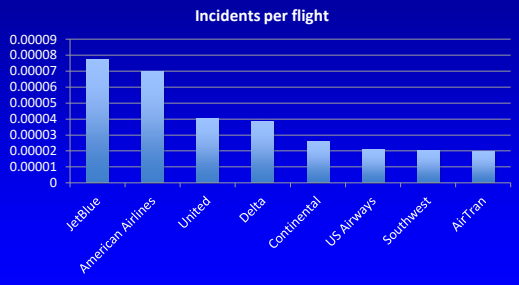
Demyelination with a TNF inhibitor

- Proportion of patients remaining exacerbation free
  - – Placebo ——
  - – Lenercept 10 mg - - - -
  - – Lenercept 50 mg - – - –
  - – Lenercept 100 mg – –

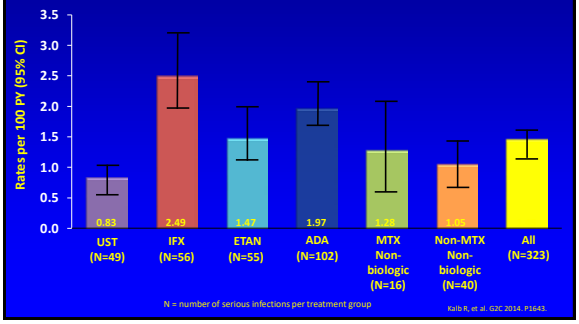


Neurology. 1999 Aug 11;53(3):457-65

Do Safety Differences Matter?

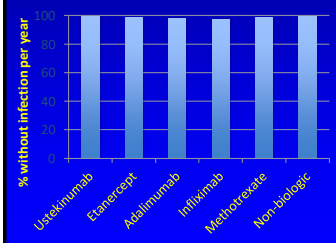


Rates of Serious Infections per 100 Patient-years



No Infection in 99 or 98 out of 100

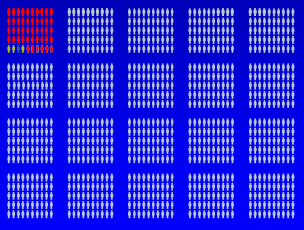
- How patients perceive it depends on how you spin it



Kalb R, et al. G2C 2014. P1643.

Visual communication of numeric information: adalimumab treatment in long-standing RA patients

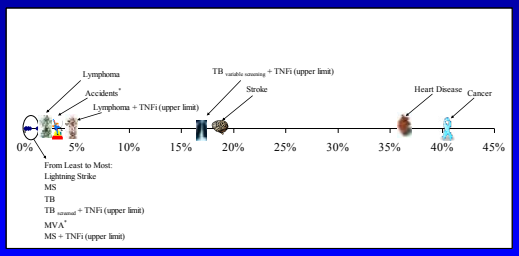
Graphically representing risk in selected patient groups
Risk of selected serious adverse events after one year of exposure in a clinical trial setting



- **All patients exposed to Adalimumab in 1-year period: 1,000 patients**
- **Patients presenting with serious infections: 46 /1,000 patient-years**
- **Opportunistic Infections: 0.9/1,000 patient-years**
- **Tuberculosis: 2.9/1,000 patient-years**

RiskCommunication Tool © John Palling 2002. See www.riskcomm.com.
Burmester GR *et al. Ann Rheum Dis.* 2009;68:1863–1869. 53

Use images to communicate risks in perspective



Kaminska E, et al. Comparing the lifetime risks of TNF-alpha inhibitor use to common benchmarks of risk. J Dermatolog Treat. 2013 Apr;24(2):101-6.

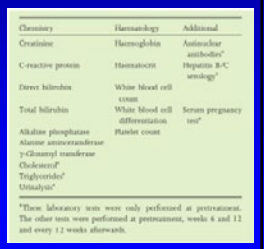
Biologic Monitoring from AAD Guidelines

- "There is no specific guideline or single way of taking care of any patient"
- "There are some tests that many dermatologists obtain in patients with psoriasis before commencing systemic therapies including biologics."
  - Blood chemistries with liver function tests
  - CBC, Hepatitis panel and *TB testing*

Menter A et al. J Am Acad Dermatol. 2008 May;58(5):826-50.
Ahn CS et al. J Am Acad Dermatol. 2015 Sep;73(3):420-8

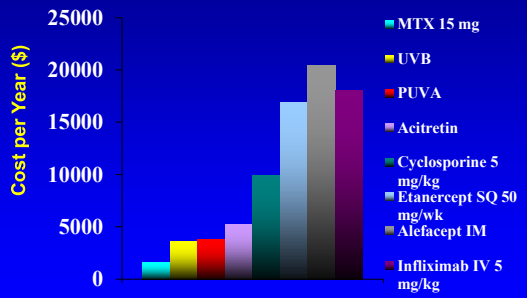
Expected Findings With Lab Testing

- Prospective study over 5 years
- 162 patients treated with etanercept and /or adalimumab
  - 370 patient-years of follow up
- 26% of etanercept and 14% of adalimumab patients had grade 3 or 4 lab abnormalities
- Laboratory abnormalities did not lead to permanent discontinuation of biologic treatment in any patient



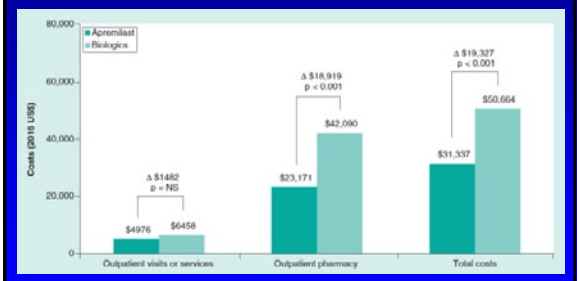
Br J Dermatol. 2011 Aug;165(2):375-82.

Annual Cost of Treatment



Expert Opin Pharmacother. 2003 Sep;4(9):1525-33

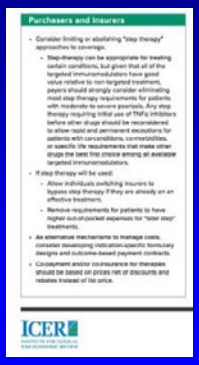
Annual Cost of Treatment



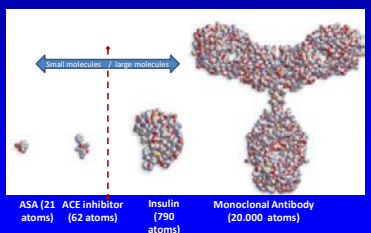
J Comp Eff Res. 2019 Jan;8(1):45-54

Cost

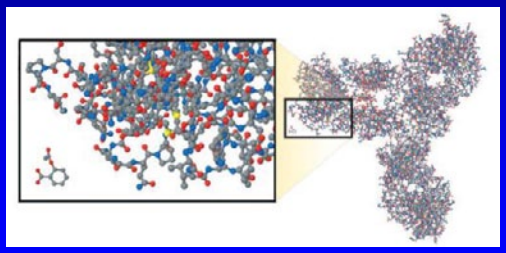
- Doctors often don't know the cost
- The payer does
- ICER suggests that all the treatments are cost effective



Biosimilars: To Complex To Duplicate



Deeper Complexity of Biologics



Etanercept is Not a Single Entity

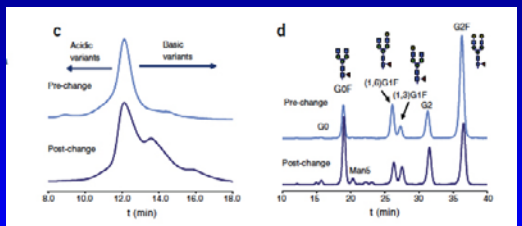
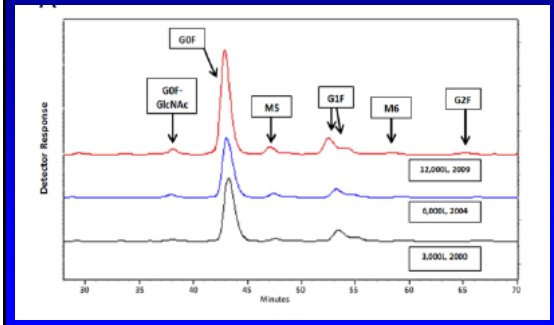
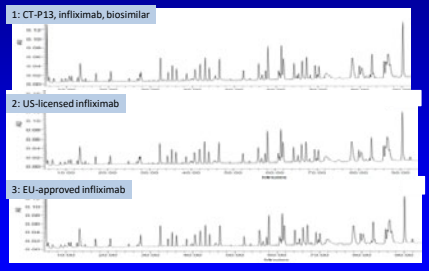


Figure 3 Comparison of the different pre- and post-change batches of Enbrel. (**a**) Relative amounts of basic variants of the pre-change ($n = 6$) and the post-change ($n = 6$) batches as measured by CEX. (**b**) Relative amount of the G2F glycan of the pre-change ($n = 25$) and the post-change ($n = 9$) batches. (**c**) Exemplary CEX chromatograms. (**d**) Exemplary glycan mapping chromatograms.

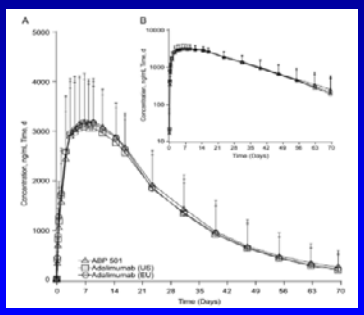
Adalimumab Variation



Primary Structure is the Same

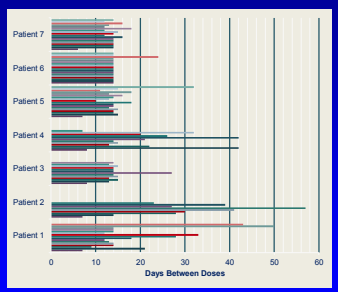


Pharmacokinetics of Innovator and Biosimilar Adalimumab



Kaur P, et al. *Ann Rheum Dis.* 2016 July 27.

Adherence to Biologics



West C, et al. Adherence to adalimumab in patients with moderate to severe psoriasis. Dermatol Online J. 2013 May 15;19(5):18182.

Biologic Adherence

- Assessing adherence
  - "Are you keeping the extra syringes you've accumulated refrigerated like you are supposed to?"
- Putting patients' minds at ease
  - "Biologic? Yes, this is an all-natural anti-inflammatory made in living cells that complements your body's natural healing mechanisms because I like to take a holistic approach to treating skin disease"

Comparison Table

	TNF	IL12 and/or IL23	IL17	JAK	PDE-4
	Etanercept, adalimumab, infliximab, certolizumab (golimumab)	Ustekinumab, guselkumab, tildrakizumab (risankizumab)	Secukinumab, ixekizumab, brodalumab	Tofacitinib	Apremilast
Safety	Some infection, rare MS	Clean	Candida risk Rare IBD	Possible viral reactivation	Diarrhea
Confidence	20 year safety record	3-10 years	3-5 years	Use in rheumatoid arthritis	Limited long term data
Efficacy	Moderate to high	High to highest	Highest	Moderate	Lowest
Convenience	Lots of shots	q2-3 months	Every month	Oral (BID)	Oral (BID)
Cost	Cost to patient may be low, cost to patients may be high				

Give patients the risks & benefits of treatment in writing

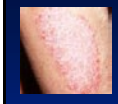
- The National Psoriasis Foundation has terrific resources
- The Systemic Treatment brochure offers an overview of key points on many options

https://www.psoriasis.org/sites/default/files/systemic_treatments_-_biologics_and_oral_tx.pdf

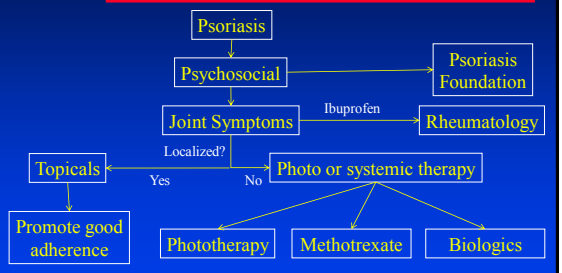
Other National Psoriasis Foundation Resources

- There are Fact Sheets on each of the biologics & a comparison table of all of them
- You can download them at no cost

https://www.psoriasis.org/about-psoriasis/treatments/biologics/resources



Standard Model



Conclusions

- Use biologics for patients who need them
  - Offer the array of biologic options
- Statistically or clinically significant?
  - Comorbidities: demand absolute risk information
  - Efficacy differences
- Long term data: check who stays in the study
- Risk is subjective
  - Monitoring can be minimal or intensive as you see fit
- Give patients confidence & understanding
  - Have them use the medication regularly

Saturday, April 13, 2019

7:00 a.m. - 9:00 a.m.	*Prescribing Laws and Rules Controlled Substances* **Edwin Bayo, JD**
9:00 a.m. - 10:00 a.m.	*Professional Medical Ethics* **Raymond Mosely, PhD**
10:00 a.m. - 10:30 a.m.	Break
10:30 a.m. - 11:30 a.m.	*Florida Laws and Rules* **Jason D. Winn, Esq.**
11:30 a.m. - 1:30 p.m.	*Prevention of Medical Errors* **Arnold Mackles, MD**

Resident Poster Presentations

Type II Cutaneous Meningioma: A Case Report and Discussion
Morgan Arnold, D.O.
Still OPTI/Northeast Regional Medical Center

Adult Onset Henoch-Schönlein Purpura Treated with Colchicine
Katherine Braunlich, D.O.
NSUCOM/Largo Medical Center

The Great Imitator Strikes: A Chancre of Primary Syphilis on the Nipple
Falon Brown, D.O.
OMNEE/Sampson Regional Medical Center

Extra-Nodal Rosai-Dorfman Disease
Soham Chaudhari, D.O.
Texas OPTI/Bay Area Corpus Christi Medical Center

Fractionated Carbon Dioxide Laser Resurfacing as an Ideal Treatment Option for Severe Rhinophyma: A Case Report and Discussion
Victoria Comeau, D.O.
PCOM/North Fulton Hospital Medical Campus

An Unusual Skin Infection with Achromobacter Xylosoxidans
Matthew Crosby, D.O.
MWU/OPTI/Advanced Desert Dermatology

Focal Atypical Lymphoid Infiltrate with CD30 Positivity in a 36-Year Old Male
Alexandria Glass, D.O.
PCOM/North Fulton Hospital Medical Campus

Cutaneous Larva Migrans
Naeha Gupta, D.O.
PCOM/Lehigh Valley Health Network

A Case of Nevoid Basal Cell Carcinoma Syndrome in a 9 Month Infant
Jeffrey Harbold, D.O.
Texas OPTI/Bay Area Corpus Christi Medical Center

Acroangiodermatitis of Mali : A Case Report and Review
Nady Hin, D.O.
LECOMT/Larkin Community Hospital - Palm Springs Campus

Multiple Cellular Neurothekeomas
Megan Jones, D.O.
PCOM/Lehigh Valley Health Network

Localized Cutaneous Leishmaniasis Treated with Observation
Adeline Kikam, D.O.
Texas OPTI/Bay Area Corpus Christi Medical Center

Mohs Micrographic Surgery for Primary Cutaneous Ewing Sarcoma
Raymond Kleinfelder, D.O.
LECOMT/Larkin Community Hospital - Palm Springs Campus

An Atypical Presentation of Langerhans Cell Histiocytosis
Lauren Law, D.O.
SCS/MSUCOM/Botsford Hospital

Blastic Plasmacytoid Dendritic Cell Neoplasm: A Cutaneous Herald
Danielle Lazzara, D.O.
LECOMT/Larkin Community Hospital - Palm Springs Campus

Shades of Acquired Dermal Melanocytosis
Erin Lowe, D.O.
NSUCOM/Largo Medical Center

Alopecia Areata After Bone Marrow Transplant from Alopecia Universalis-Affected Monozygotic Twin
Morgan Mackey, D.O.
MWU/OPTI/Advanced Desert Dermatology

Dermatitis Artefacta Mimicking Pyoderma Gangrenosum
Mitchell Manway, D.O.
MWU/OPTI/Affiliated Dermatology

Rash with Neuropathy Refractory to Medical and Surgical Therapies
Erez Minka, D.O.
Texas OPTI/Bay Area Corpus Christi Medical Center

Small Fiber Neuropathy causing chronic generalized pruritus: Should Dermatologist screen-for it?
John Moesch, D.O.
NSUCOM/Largo Medical Center

Auricular Cartilage Roll Flap
Kevin Myers, D.O.
OPTI-West/Silver Falls Dermatology

Diagnosis of African Tick Bite Fever
Andrew Newman, D.O.
MWU/OPTI/Affiliated Dermatology

Pemphigus Foliaceus: Case Report and Review
Craig Parson, D.O.
OPTI-West/Aspen Dermatology

A Case of Herpetic Sycosis: A Frequently Unrecognized Manifestation of a Common Pathogen
Dahlia Saleh, D.O.
OMNEE/Sampson Regional Medical Center

Successful Treatment of Congenital Oral Melanosis with a 1064/532-nm picosecond Nd:Yag Laser
Shahjahan Shareef, D.O.
OPTI-West/Chino Valley Medical Center

Biosurgery Utilized for Chronic Leg Ulcers in a Patient with Refractory Pemphigus Vulgaris
Mehreen Sheikh, D.O.
LECOMT/Larkin Community Hospital - Palm Springs Campus

Rapid Intraoperative Tissue Relaxation of a Scalp Wound Using a Novel Suture Retention Device
Allison Stoecker, D.O.
OPTI-West/Silver Falls Dermatology

White Fibrous Papulosis of the Neck: An Underrecognized Benign Condition
Rachel White, D.O.
LECOMT/Larkin Community Hospital - Palm Springs Campus

Type II Cutaneous Meningioma: A Case Report and Discussion

Morgan Arnold DO, David Cleaver DO, Nathan Cleaver DO

Northeast Regional Medical Center

STILL OPTI

Introduction

Meningiomas represent the most common intracranial tumors, while cutaneous meningiomas are rare tumors most commonly occurring on the scalp.[1] Cutaneous meningiomas are thought to arise from the herniation of meningeal lining during embryonic development into the dermis and subcutaneous tissue.[2] They are classified into three subtypes; type I tumors arise congenitally, while type II and III tumors represent multipotent mesenchymal/ectopic arachnoid cells and direct extension of an underlying tumor of the arachnoid lining, respectfully.[2,3]

Case

Here we report a 40-year-old female who presented with an enlarging, itchy, painful mass on the posterior mid-parietal scalp (Fig. 1). This lesion had been slowly enlarging over a 2 year period. The patient denied trauma to this area. Past medical history was significant for hypothyroidism and remote seizures. Surgical, family, and social history were non-contributory. On exam, the lesion was firm and poorly mobile with a normal appearing overlying epidermis. Initial differential diagnosis included an epidermal inclusion cyst, pilar cyst and an encapsulated lipoma. The patient elected for surgical removal. Intraoperatively, the lesion was poorly encapsulated, caseous, friable, and non-odoriferous. No communication with the galea aponeurotica or cranium was noted. The specimen was sent for pathological diagnosis.

Histology

Whorls of meningiothelial cells and few psammoma bodies were noted on 4X magnification in Figure 2. On higher magnification (10X), a psammoma body is depicted well in Figure 3. Positive staining with epithelial membrane antigen (EMA) (Fig. 4) and lack of staining with CD34, desmin, factor XIIIa, and pan-keratin (AE-1/AE-3) confirmed the diagnosis of a cutaneous meningioma. Typical histology of meningiomas include meningiothelial cells whorling around focal areas of collagen, and psammoma bodies are often noted. [4]

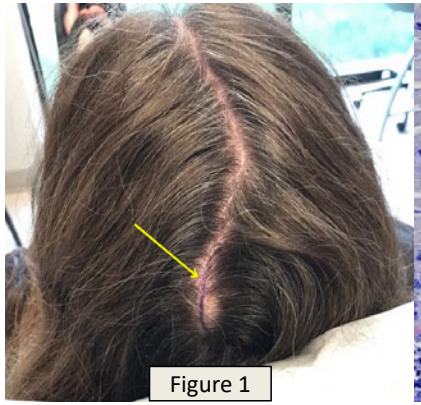


Figure 1

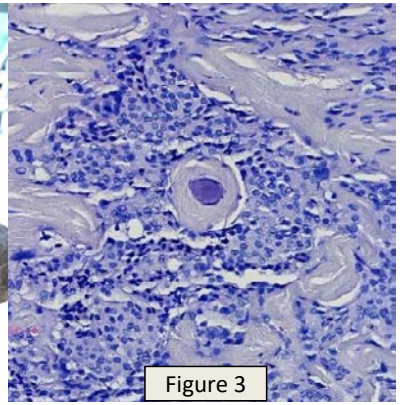


Figure 3

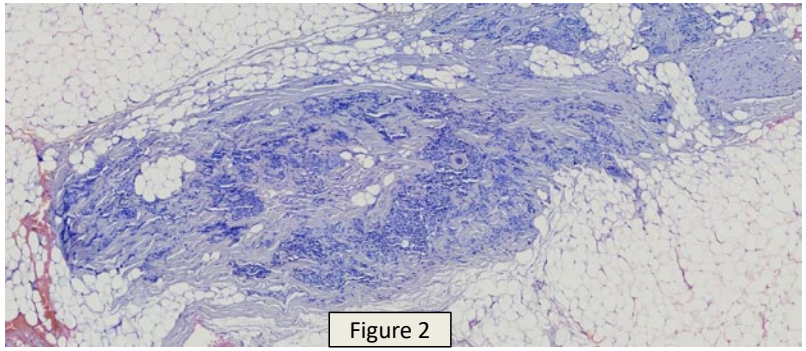


Figure 2

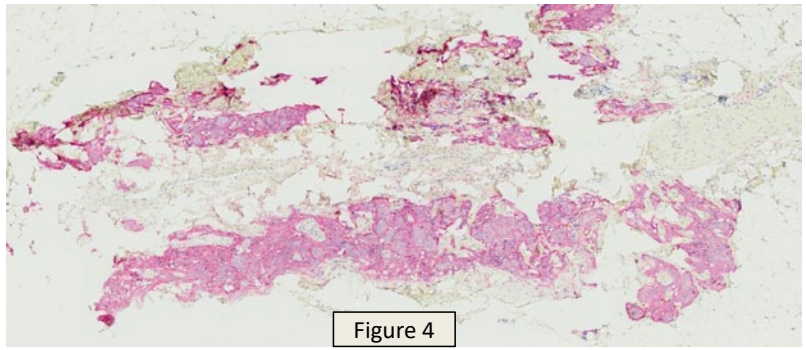


Figure 4

Discussion

Meningiomas constitute 15-25% of tumors of the central nervous system, making them the most common intracranial/intraspinal neoplasm.[2] They are derived from arachnoid membrane cells. Rarely these neoplasms are seen cutaneously. Differential diagnosis of cutaneous meningiomas may include an epidermal inclusion cyst, acrochordon, lipoma, pilar cyst, fibroma, or a vascular lesion. Lopez et. al subclassified cutaneous meningiomas into 3 subsets.[5] Type I lesions occur congenitally and can be distinguished histologically as they tend to have a collagenous stroma. In addition, they tend to be located in the subcutanous fat, while type II and III lesions typically extend into the dermis. [2] Type II lesions are acquired and represent ectopic arachnoid tissue. Type III tumors are also acquired and arise via direct extension of an intracranial meningioma. Distinguishing between type II and III cutaneous meningiomas cannot be made histologically. This differentiation requires neuroimaging to determine if the cutaneous lesion is an extension of an intracranial meningioma, or by lack of infiltration of the tumor to the galea aponeurotica and/or cranium on excision.[3]

Classic histological examination of primary intracranial meningiomas reveal psammoma bodies and meningothelial whorls.[4] These findings are not always appreciated in their cutaneous counterparts, and can pose a diagnostic challenge on behalf of the pathologist. Thus, positive staining with vimentin and EMA are considered diagnostic, while lack of desmin, cytokeratin, CD31, CD34, CD68, and smooth muscle antigen rule out other histological differential diagnosis; including hemangiopericytomas, giant cell fibroblastoma, squamous cell carcinoma, hemangioma, and heterotopic neruogliomas.[6]

Prognosis of cutaneous meningiomas are largely determined based on type. Type I lesions have a favorable prognosis if clear surgical margins are achieved intraoperatively.[6] Type II and type III lesions tend to have a poorer prognosis as these lesions may lack classic histological features of congenital meningiomas as mentioned above. In addition, type III lesions may be inoperable if their intracranial direct extension abuts vital structures.

Currently imaging is recommended prior to surgical excision of known cutaneous meningiomas, as intracranial extension requires removal by a neurosurgeon. Although cutaneous meningiomas represent a rare entity, maintaining a low threshold for biopsy of atypical scalp lesions may be warranted prior to surgical removal.

References

1. Bolognia J, Jorizzo JL, Schaffer JV. (2017). *Dermatology, 4th edition*. Philadelphia: Elsevier Saunders.
2. Kishore M, Kaushal M, Bhardwaj M, Sharma N. Cutaneous Meningioma: A Cytomorphological Diagnosis. *Indain J Dermatol*. 2017 May. 8(3):201-4.
3. Konopinski J et al. Isolated Ectopic Cutaneous Atypical Meningioma of the Scalp: Another Mimicker of Primary Adnexal Tumor. *Am J Dermatopathol*. 2017 Jul. 39(7):545-7.
4. Elston D, Ferringer T. (2019). *Dermatopathology, 3rd edition*. Elsevier Saunders.
5. Lopez DA, Silvers DN, Helwig EB. Cutaneous meningiomas – A clinicopathologic study. Cancer 1974 Sep. 34(3):728-44.
6. Jaiswal P, Jaiswal S, Chakrabarti AM. Primary Type I Cutaneous Meningioma of the Scalp: Cytohistological and Immunohistochemical Features of a Rare Neoplasm. *Asian J Neurosurg*. 2018 Jan. 13(1):110-2.

Adult onset Henoch-Schönlein Purpura, treated with Colchicine

NOVA SOUTHEASTERN UNIVERSITY
LARGO MEDICAL CENTER
GRADUATE MEDICAL EDUCATION
Medical Education in the Sun Coast Tradition

Katherine Braunlich, DO | Taylor Gray, DO | Maheera Farsi, DO | Risa Ross,DO | Richard Miller, DO
Largo Medical Center, Largo, FL

HCA Largo Medical Center
A Teaching Hospital
More Minds Advancing Medicine

INTRODUCTION

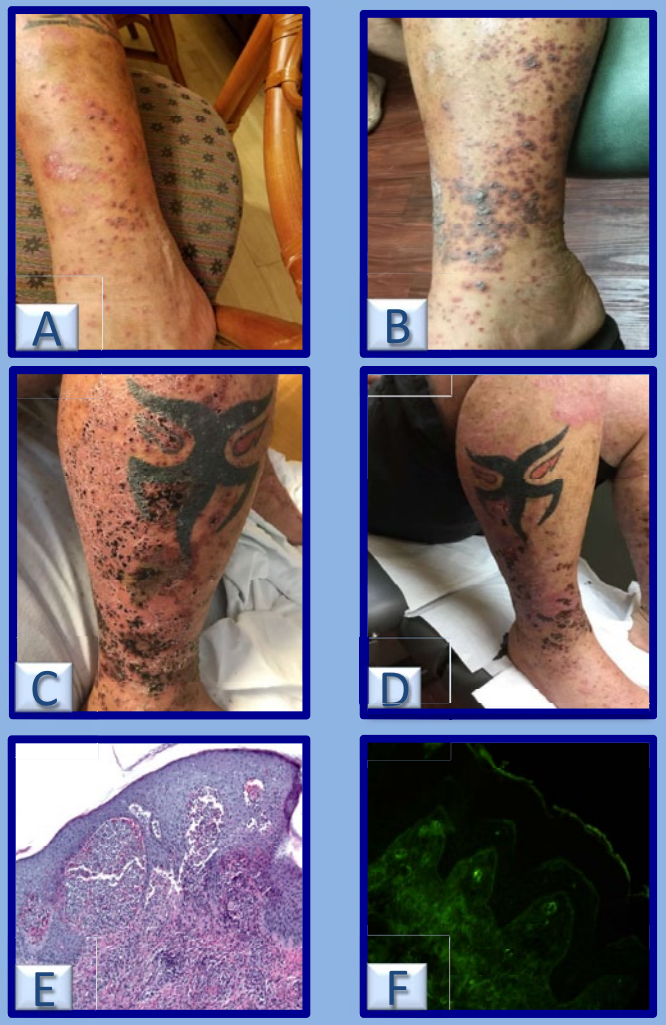
Henoch-Schoenlein Purpura (HSP) is a systemic, IgA mediated autoimmune small vessel vasculitis (IgAV) (1,2,3).
Clinical manifestations include nonthrombocytopenic palpable purpura, arthritis, abdominal pain and nephritis (2).
The **etiology** remains unclear but is associated with bacterial infections, viral infections, medications (quinolones, clarithromycin, acetaminophen, codeine and TNF alpha inhibitors), tumors, alpha-1-antitrypsin deficiency and Familial Mediterranean Fever (3).
Incidence is highest in patients 4-6 years old, however, up to 15% of cases occur in the adult population (1, 4). In adults, HSP tends to have more severe onset with a higher incidence of long term sequelae, in contrast to the more benign course that often occurs in the pediatric population (4). Regardless of age of onset there is a slight male predominance (M:F =1.2: 1.0) and Caucasian populations have the highest incidence (1).

While adult onset HSP has been reported previously, it is diagnosed infrequently. Our case brings attention to the possible development of HSP in individuals utilizing **TNF-alpha inhibitor**s and to the benefit of using **colchicine** as a treatment modality during the acute presentation of HSP.

CASE REPORT

50-year-old Caucasian male developed palpable purpura on his bilateral lower extremities twenty-four hours after arthropod assault in Hawaii. The patient was treated for presumed infection, with Minocycline then Doxycycline, without clinical improvement. Six days after the onset of the lesions, the patient returned from vacation and was evaluated by his dermatologist who obtained 2 punch biopsies (H&E and DIF) and a bacterial culture. At dermatologic follow-up three days later he had developed hemorrhagic bullae and plaques with central necrosis. Bacterial culture had grown group B strep. The patient was prescribed Clindamycin and advised to go to ED. One day later the patient developed arthralgia and edema in his bilateral wrists and hands but denied hematuria or abdominal pain. The following day the patient noted worsening joint pain as well as new onset abdominal pain. Labs included: +ASO, +Hematuria (UA), elevated serum IgA, CBC WNL, compliment WNL. At this point patient met EULAR criteria for Adult HSP and Colchicine 0.6mg daily was initiated. The following day the patient reported significant improvement in joint pain and moderate improvement in abdominal pain. Cutaneous lesions improved significantly over the following month. Biopsy results returned: H&E LCV, DIF: IgA vasculitis.
PMH: Psoriasis (Adalimumab), HTN (Lisinopril)

CLINICAL & HISTOLOGIC FINDINGS



Clinical: Palpable purpura and erythematous plaques with silver scale scattered on bilateral lower extremities (Fig A & B). Hemorrhagic bullae and plaques with central necrosis (Fig C). Significant improvement following treatment with Colchicine (Fig D).
Histopathology (H&E): perivascular infiltrate with neutrophils, karyorrhexis, fibrin deposition within vessel walls and erythrocyte extravasation (Fig E).
Immunohistochemistry (DIF): + vascular deposition with IgA, C3 and Fibrinogen (Fig F).

DISCUSSION

The clinical appearance and disease progression of HSP are not the same in adults and children. Virtually all patients with HSP have palpable purpura, however adults are more likely to present with hemorrhagic lesions, more severe arthritis and have more frequent renal involvement (4). The majority of patients will develop urinary abnormalities within 4 weeks of diagnosis but, it can take months for HSP nephritis to develop (4). **Patients with a diagnosis of HSP should be followed with urinalysis for one year** (1).
Recent research suggests that adult onset HSP is likely underdiagnosed, in part, due to ACR criteria for IgAV including age at onset of under 20 years. Previously unstudied in the adult population, the EULAR/PRINTO/PRES IgAV classification criteria has been shown by one study to have a higher sensitivity and specificity than the ACR criteria when evaluating adult patients for HSP (5). While etiology is often unclear, infections including streptococcal pharyngitis, medications, malignancy, alpha-1-antripyspin deficiency and Familial Mediterranean Fever have been implicated in the development of HSP (1). Recently, several cases of HSP developing in patients on TNF alpha inhibitors have been reported (6). In our case, with elevated ASO titers and use of Adalimumab, it is unclear what exactly initiated the HSP cascade.
Corticosteroids are often the chosen treatment for HSP. Given our patients history of psoriasis we avoided steroids due to the risk of psoriatic flare upon taper. We elected to use low does Colchicine 0.6mg daily due to its reported success in treating cutaneous vasculitis (7). The patient's joint pain and cutaneous findings rapidly improved further supporting the use of this treatment modality in acute episodes of HSP.

CONCLUSION

Adult onset HSP is an uncommon diagnosis that differs in clinical appearance and long-term management from HSP in the pediatric population. This case demonstrates the importance of considering HSP as a diagnosis for adult patients presenting with small vessel vasculitis, and further supports the use of Colchicine as a treatment for patients with HSP.

REFERENCES

1. Sohagia AB, Günturu SG, Tong TR, Hertan HI. Henoch-schonlein purpura-a case report and review of the literature. Gastroenterol Res Pract. 2010;2010:597648.
2. Yang Y-H, Yu H-H, Chiang B-L. The diagnosis and classification of Henoch-Schönlein purpura: an updated review. Autoimmun Rev. 2014;13(4-5):355-358.
3. Chen K-R, Carlson JA. Clinical approach to cutaneous vasculitis. Am J Clin Dermatol. 2008;9(2):71-92.
4. Thong B, Chia F. The Evaluation and Management of Adult-Onset Henoch-Schonlein Purpura. Curr Rheumatol Rev. 2008;4(1):71-75.
5. Hočevar A, Rotar Z, Jurčić V, et al. IgA vasculitis in adults: the performance of the EULAR/PRINTO/PRES classification criteria in adults. Arthritis Res Ther. 2016;18(1):58.
6. Laresche C, Locatelli F, Biver-Dalle C, et al. Severe Henoch-Schönlein purpura complicating infliximab therapy for ulcerative colitis. Cutis. 2017;99(1):E20-E22.
7. Saulsbury FT. Successful treatment of prolonged Henoch-Schönlein purpura with colchicine. Clin Pediatr (Phila). 2009;48(8):866-868.

The great imitator strikes: a chancre of primary syphilis on the nipple

Falon V. Brown, DO [1], Mikél E. Muse, OMS IV[2], James Appel, MD, FAAD[1], Warren White, MD[3]
[1]Department of Dermatology; Campbell University School of Osteopathic Medicine, Buies Creek, NC | Sampson Regional Medical Center, Clinton, NC. [2]Virginia College of Osteopathic Medicine, Blacksburg, VA
[3]Department of Dermatopathology; Coastal Carolina Pathology, Wilmington, NC

Abstract

Syphilis, the "great imitator," presents with a wide range of mucocutaneous and systemic findings. The primary chancre *classically* occurs in the genital region, however up to 6.33% can be extragenital. Among the extragenital chancres reported in the literature, very few occurred on the breast, and of these cases only 5% occurred in men. A 43-year-old healthy man visited our clinic complaining of drainage from the right nipple for one month. Exam was notable for a poorly defined, scaly erythematous plaque on the areola with a superficial erosion of the nipple. The rapid plasma reagin (RPR) titer was found to be 1:32, with positive anti-treponemal antibodies. Histopathological examination of the biopsy specimen revealed variable acanthosis of epidermis with dense underlying superficial, deep perivascular and interstitial infiltrate surrounding benign bundles of smooth muscle. The infiltrate was composed of abundant lymphocytes, plasma cells, and rare eosinophils. Immunohistochemical staining for *Treponema pallidum* revealed numerous spirochetes scattered within the inflammatory cell infiltrate throughout the dermis. Based on these findings, the patient was diagnosed with an extragenital chancre of primary syphilis on the nipple. With a resurgence in the incidence of syphilis, it is important to remind practitioners of the more unusual presentations of this disease.

Introduction

- Syphilis is known for its ability to mimic innumerable conditions. This condition is often misdiagnosed due to the wide variety and transient nature of cutaneous, mucocutaneous, and systemic manifestations which vary greatly depending on the stage of presentation.
- The World Health Organization estimates that each year there are over 11 million new cases of syphilis. With the incidence continuing to rise in the United States at an alarming rate, the US Preventative Task Force updated screening recommendations in 2016 to include screening asymptomatic, nonpregnant adults and adolescents at increased risk for infection.[1,2,3]
- Primary syphilis refers to inoculation with *T. pallidum* and manifests as a localized cutaneous chancre at the site of contact, classically occurring in the genital region. However up to 6.33% of primary chancres can be extragenital. Among the extragenital chancres studied, 5.1% occurred on the breast with only 5% of those on the breast occurring in men.[4,5,6]
- We present one of the first reported cases of a male with primary syphilis on the nipple in the United States.

Case Description

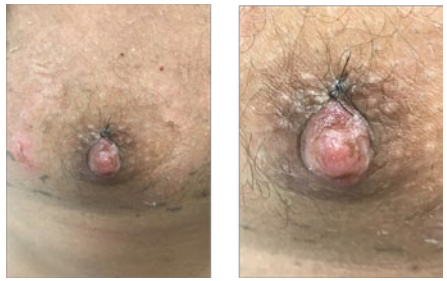


Figure 1. Right nipple and areola. Photographed 2 days after 4 mm punch biopsy of nipple and areola after partial treatment with topical ointment.

- A 43-year-old man presents as referral from outside physician with complaint of drainage from right nipple for one month (Figure 1).
- He reports mild inflammation, pruritis, tenderness to touch and an 'odd sensation' of warmth of the right nipple, but denies overt pain. Patient denies known history of trauma to the area or repeated microtrauma from friction. Denies personal or family history of atopy.
- At follow up, the patient's sexual history remained ambiguous. Attempt to gain further insight into the etiology of this case was made, however patient was unable to recall any sexual encounter involving his breast or nipple.

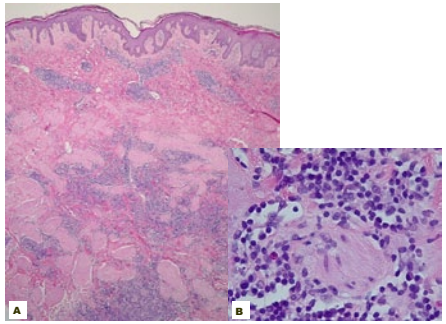


Figure 2. Cutaneous syphilis. A. Acanthotic epidermis with overlying hyperkeraosis of stratum corneum. **A.** Dense superficial & deep perivascular and interstitial infiltrate noted (H&E, original sections at 25X). B. Infiltrate composed of lymphocytes, plasma cells, and rare eosinophils (H&E, original sections at 640X).

- **Past medical history:** Gout
- **Family medical history:** Breast cancer (mother)
- **Physical exam:** Erythematous, ulcerated, plaque with serosanguinous drainage and crusting at the 12 o'clock position of nipple. Tenderness with palpation noted. No palpable axillary or supraclavicular lymphadenopathy noted. No penile ulceration was found.
- **Differential diagnosis:** Nipple eczema, erosive adenomatosis of the nipple, mammary Paget disease or primary breast carcinoma.
- **Pathology**: Punch biopsy demonstrated hyperkeratosis of stratum corneum. The epidermis is variably acanthotic with mild spongiosis focal exocystosis of few lymphocytes within spongiosis. A dense superficial & deep perivascular and interstitial infiltrate surrounding benign bundles of smooth muscle consisting of lymphocytes, plasma cells, and rare eosinophils (Figure 2) was also noted.
- **Staining:** Modified Steiner and immunohistochemical staining for *T. pallidum* revealed spirochetes (Figure 3). Periodic Acid-Schiff with diastase (PAS-D) negative for fungal elements. Acid cytokeratin (CAM5.2) negative.

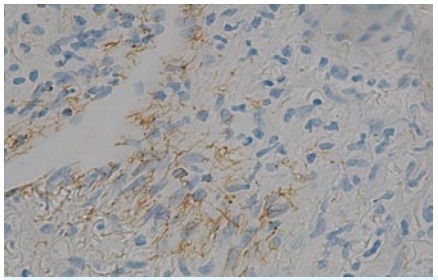


Figure 3. Cutaneous syphilis. Immunohistochemical staining for *T. pallidum* revealing spirochetes.

- **Laboratory results**
  - RPR titer: 1:32 (reactive)
  - *T. pallidum* antibodies: positive
  - HIV screen: Non-reactive
  - Chlamydia/GC DNA probe: Non-reactive
  - HCV Antibody: Non-reactive
- **Diagnosis:** Primary syphilitic chancre of the nipple
- **Management**: Case reported to health department. Patient referred for completion of treatment with Benzathine penicillin 2.4 million units IM x1 as soon as possible due to shortage and unavailability in our clinic.

Discussion

- According to the CDC, there has been a dramatic increase in the incidence of primary and secondary syphilis in the U.S.
  - In 2016, a total of 27,814 cases reported 8.7 cases per 100,000 population spanning equally across all regions of the country.
    - An increase of 17.6% compared to 2015
    - An increase of 74.0% compared to 2012
  - Initially, increase in incidence was associated with men who have sex with men. However, most recent data reveals an increased incidence in women as well.[7]
- Extragenital chancres can occur at any site of inoculation including oral (lips, tongue, palate), perianal, breasts/nipple, conjunctiva, neck, abdomen, intrascapular region, arms, palms, fingers or thighs.[5,6]
- Extragenital primary syphilitic chancre of the nipple is an exceedingly rare manifestation of primary syphilis.
- Historically, primary syphilitic chancre of the nipple was associated with wet nurses resulting from mucous patches in the mouths of congenitally syphilitic infants.[4]
- Fewer than 10 cases have been reported in modern literature. Most cases are associated with sexual encounter involving oral contact, especially biting, of the nipple.[8,9,10]

Conclusion

- Patients who present to a dermatologist with syphilis are more likely to demonstrate unusual or advanced forms of this condition.[11]
- Practitioners must be aware of unusual presentations and maintain a high index of suspicion of syphilis in order to make this diagnosis.
- Early recognition and a low threshold for testing is important to limit disease spread.[11]

References

1. Cossman JP, Fournier JB. Frequency of Syphilis Diagnoses by Dermatologists. JAMA Dermatol. 2017 Jul 1;153(7):718-719. doi: 10.1001/jamadermatol.2017.0460. PubMed PMID: 28467547; PubMed Central PMCID: PMC5817456
2. Pastuszczak, M., & Wojas-Pelc, A. (2013). Current standards for diagnosis and treatment of syphilis: selection of some practical issues, based on the European (IUSTI) and U.S. (CDC) guidelines. *Advances in Dermatology and Allergology/Postępy Dermatologii i Alergologii*, *30*(4), 203–210. http://doi.org/10.5114/pdia.2013.37029
3. United States Preventative Services Task Force. Syphilis Infection in Nonpregnant Adults and Adolescents: Screening. https://www.uspreventiveservicestaskforce.org/Page/Document/UpdateSummaryFinal/syphilis-infection-in-nonpregnant-adults-and-adolescents?ds=1&s=syphilis. Accessed September 14, 2018.
4. Deaver, J. B., McFarland, J., Herman, L. *The breast- its anomalies, its diseases, and their treatment*. Philadelphia, PA: Blakiston's Son &. Co; 1917.
5. Chapel, T., Pinnamaneni, P. et al. "extragenital syphilitic chancres." J AM ACAD DERMATOL 13: 582 -584, 1985.
6. Lleó, M, et al "Atypical Cutaneous Manifestations in Syphilis". Actas Dermosifiliogr. 2016;107(4):275-283.
7. Centers for Disease Control and Prevention. 2016 Sexually Transmitted Disease Surveillance. https://www.cdc.gov/std/stats16/syphilis.htm. Accessed September 1, 2018
8. COh, Y. , Ahn, S. , Hong, S. P., Bak, H. and Ahn, S. K. (2008), A case of extragenital chancre on a nipple from a human bite during sexual intercourse. International Journal of Dermatology, 47: 978-980. doi:10.1111/j.1365-4632.2008.03617.x
9. Sim JH, Lee MG, In SI, et al. Erythematous Erosive Patch on the Left Nipple—Quiz Case. *Arch Dermatol*. 2010;146(1):81–86. doi:10.1001/archdermatol.2009.335-a
10.hiu H, Tsai T. A Crusted Plaque on the Right Nipple. *JAMA*. 2012;308(4):403–404. doi:10.1001/jama.2012.7538
11.Thakrar P, Aclimandos W, Goldmeier D, Setterfield JF. Oral ulcers as a presentation of secondary syphilis. Clin Exp Dermatol. 2018 Jul 23. doi: 10.1111/ced.13640. [Epub ahead of print] Review. PubMed PMID: 30039628.

Extra-nodal Rosai-Dorfman Disease

Chaudhari S[1,2], Sedrak M[3], Hohnadel M[4], Lin R[1,2]

1: Bay Area Corpus Christi Medical Center, Corpus Christi TX ; 2: Dermatology Clinic of McAllen, McAllen TX; 3:Sagis Dermatopathology Laboratory, Houston TX; 4:Rio Grande Dermatology Clinic, Brownsville TX

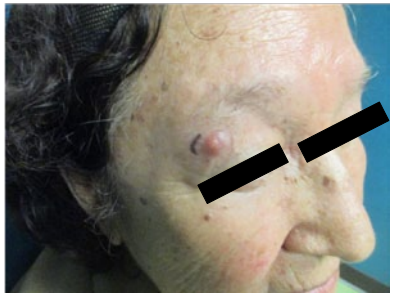
Introduction

Rosai-Dorfman disease (RDD), or sinus histiocytosis with massive lymphadenopathy, is a rare, self-limiting histiocytosis, commonly presenting with bilateral painless cervical lymphadenopathy. The estimated incidence of RDD in the United States is 100 cases per year[1]. The disease mainly affects adolescents and young adults with a slight predilection for males and African Americans[2], with a poorly defined pathogenesis. Although painless bilateral cervical lymphadenopathy is characteristic, extranodal sites are involved in about 40% of cases[3]. Rarely is extranodal involvement the sole manifestation of the disease[5].

Case Presentation

A 75-year-old Hispanic female presented to a South Texas dermatology clinic for evaluation of two, asymptomatic, subcutaneous nodules that had appeared within the last six months. Review of systems was negative for malaise, weight loss, night sweats, joint pain, or recent travel. On physical exam, a 0.9 cm x 0.9 cm erythematous nodule was noted on the right inferior eyebrow. No epidermal changes were appreciated; however, a central area of yellow debris was visualized. A similar appearing 0.5 cm x 0.5 cm papule without central yellow debris was present on the left lateral orbital rim. No cervical lymphadenopathy was appreciated on palpation. CBC was unremarkable except for a Hgb of 10 g/dL. Biopsy of the right inferior eyebrow revealed a nodular infiltrate within the dermis, composed of lymphocytes, histiocytes, and plasma cells. Most of the histiocytes had abundant, clear to faint pink cytoplasm, and there was evidence of emperipolesis. GMS and AFB stains were negative for fungi and acid fast organisms, respectively. Immunohistochemical stains for CD1a were negative, while staining for S100 protein revealed decoration of the histiocytes. The morphology and immunohistochemical profile were consistent with Rosai-Dorfman disease.

Clinical Photographs



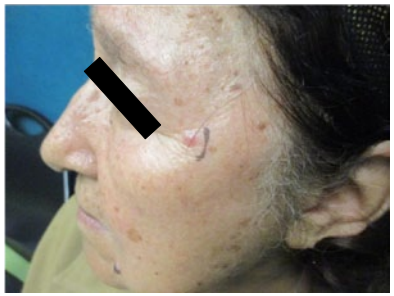


Figure 1 & 2: erythematous subcutaneous nodules visible on left and right side of face

Histology Photographs

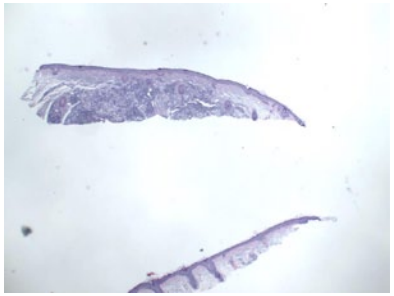
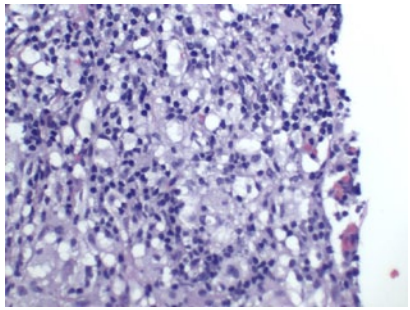


Figure 3: sea of histiocytes and lymphocytes visible on scanning magnification



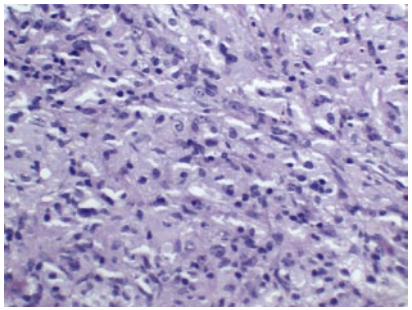


Figure 4 & 5: Numerous histiocytes and lymphocytes demonstrate emperipolesis in both specimens

Discussion

Histologically, in the lymph nodes and the skin, emperipolesis is a common feature. This is defined as the active, non-destructive engulfment of leukocytes including lymphocytes, plasma cells, and erythrocytes by histiocytes and is considered the histologic hallmark of RDD[8,9]. The lesional histiocytes express both CD68 and S-100 protein while negative for CD1a, which helps differentiate this condition from Langerhans cell histiocytosis (LCH) and Erdheim-Chester disease (ECD)[10]. The histiocytes in LCH have a grooved nuclei and surrounding eosinophils may be present. In ECH, hemophagocytosis is present. Radiologic appearance of RDD can vary from a well-defined radiolucent lesion to a poorly defined mixed lesion with areas of sclerosis[11,12]. The lesion may extend into the surrounding soft tissue, as it is locally destructive [4].

Disease processes that can mimic Rosai-Dorfman disease include xanthomatous lesions, including soft tissue xanthoma and juvenile xanthogranuloma, infectious processes, such as lepromatous leprosy, and lysosomal storage disorders, such as Gaucher disease [13-17]. Except for leprosy, histiocytes in all of these lesions are S100 negative. The macrophages loaded with mycobacteria in lepromatous leprosy are S100 positive; however, clinical presentation and fite staining for mycobacterial organism can aid the diagnosis[16,17]

RDD has a protracted and indolent course. It is generally self-limiting. There is no protocol for the treatment of RDD. Surgical excision for locally destructive and persistent disease is usually curative.

Conclusions

We present a rare care of extra-nodal RDD. Dermatologists should be aware of this condition and check for lymphadenopathy to determine the extend of involvement. Aware of histopathological findings although not unique, can be critical in establishing diagnosis.

References

1. Albini TA, Evans M, See R, Rao NA, Marback E, de Souza MM. Rosai-Dorfman disease: isolated epibulbar masses in two adult patients. *Br J Ophthalmol.* 2005;89(2):241-243.
2. Foucar E, Rosai J, Dorfman R. Sinus histiocytosis with massive lymphadenopathy (Rosai-Dorfman disease): review of the entity. *Semin Diagn Pathol.* 1990;7(1):19-73.
3. Singh NG, Kapila K, Mathur S, Ray R, Verma K. Rosai-Dorfman disease manifesting as multiple subcutaneous nodules. Report of a case with diagnosis on a fine needle aspirate. *Acta Cytol.* 2004;48(2):215-218.
4. Hamza A, Zhang Z, Al-Khafaji B. Solitary extranodal Rosai-Dorfman disease of the mandible: an exceedingly rare presentation. *Autops Case Rep.* 2018;8(3):e2018036.
5. Mantilla JG, Goldberg-Stein S, Wang Y. Extranodal Rosai-Dorfman Disease: Clinicopathologic Series of 10 Patients With Radiologic Correlation and Review of the Literature. *American journal of clinical pathology.* 2016;145(2):211-221.
6. Butler WM, Armstrong WA. Pregnancy and sinus histiocytosis with massive lymphadenopathy. *Annals of internal medicine.* 1985;102(2):278.
7. Alawi F, Robinson BT, Carrasco L. Rosai-Dorfman disease of the mandible. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod.* 2006;102(4):506-512.
8. Rosai J, Dorfman RF. Sinus histiocytosis with massive lymphadenopathy. A newly recognized benign clinicopathological entity. *Arch Pathol.* 1969;87(1):63-70.
9. Humble JG, Jayne WH, Pulvertaft RJ. Biological interaction between lymphocytes and other cells. *Br J Haematol.* 1956;2(3):283-294.
10. Dalia S, Sagatys E, Sokol L, Kubal T. Rosai-Dorfman disease: tumor biology, clinical features, pathology, and treatment. *Cancer Control.* 2014;21(4):322-327.
11. Walker PD, Rosai J, Dorfman RF. The osseous manifestations of sinus histiocytosis with massive lymphadenopathy. *American journal of clinical pathology.* 1981;75(2):131-139.
12. Lehnert M, Eisenschenk A, Dienemann D, Linnarz M. Sinus histiocytosis with massive lymphadenopathy. Skeletal involvement. *Arch Orthop Trauma Surg.* 1993;113(1):53-56.
13. Bertoni F, Unni KK, McLeod RA, Sim FH. Xanthoma of bone. *American journal of clinical pathology.* 1988;90(4):377-384.
14. Lustmann J, Ben-Yehuda D, Somer M, Ulmansky M. Gaucher's disease affecting the mandible and maxilla. Report of a case. *Int J Oral Maxillofac Surg.* 1991;20(1):7-8.
15. Kasper HU, Hegenbarth V, Buhtz P. Rhinoscleroma associated with Rosai-Dorfman reaction of regional lymph nodes. *Pathol Int.* 2004;54(2):101-104.
16. Cuevas-Santos J, Contreras F, McNutt NS. Multibacillary leprosy: lesions with macrophages positive for S100 protein and dendritic cells positive for Factor 13a. *Journal of cutaneous pathology.* 1998;25(10):530-537.
17. Dave S, Nori AV, Thappa DM, Siddaraju N. Leprous osteitis presenting as bone cyst and erosions. *Dermatology online journal.* 2004;10(1):17.

printed by MegaPrint Inc. www.postersession.com

Fractionated Carbon Dioxide Laser Resurfacing as an Ideal Treatment Option for Severe Rhinophyma: A Case Report and Discussion

By Victoria Comeau DO, PGY III,; Marcus Goodman, DO; Mary Margaret Kober, MD; and Christopher Buckley, DO

GEORGIA CAMPUS PHILADELPHIA COLLEGE OF OSTEOPATHIC MEDICINE™

GEORGIA CAMPUS PCOM™

INTRODUCTION

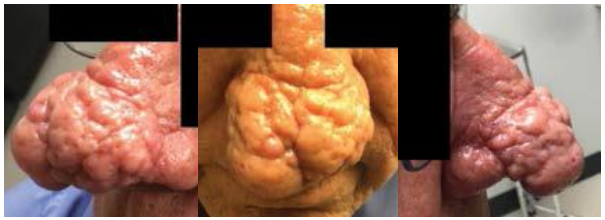
Over the past few decades, severe rhinophyma has remained one of the simplest diagnoses to make, yet is one of the most difficult conditions to treat. Rhinophyma is the progressive hypertrophy of sebaceous units and eventual distortion of facial tissue overlying the nasal region. Multiple theories have been suggested regarding the pathogenesis of rosacea, including dysfunction of the innate immune system, sensitivity to bacterial antigens produced by Demodex mites, and even chronic ultraviolet radiation exposure; however, a lack of consensus remains.[1]

Various treatment modalities have been proposed to treat this disfiguring condition. Historically, topical medications and oral anti inflammatory agents have done little to counteract its unrelenting nature. In more recent years, modern treatment modalities, such as electrosurgery and laser resurfacing, have given hope to patients with rhinophyma, as they produce significant cosmetic results with infrequent adverse effects and minimal downtime.[1,2,4,6,7,8,12]

We present a case of a patient suffering from severe rhinophyma who underwent fractionated CO2 laser resurfacing therapy. This case was selected in an effort to highlight the striking cosmetic and functional improvement our patient experienced. The tolerability of the procedure in combination with the reasonable recovery and dramatic results support the use of fractionated CO2 laser resurfacing in future rhinophyma cases.

METHOD

A 71-year-old man with a longstanding history of rosacea presented to our clinic in search of options to improve the appearance of his enlarging nose. His initial clinical examination revealed telangectasias, significant erythema, and scattered papules with large pores. Severely irregular contour of the nasal architecture was noted as well. Over the next few months he completed a comprehensive topical and systemic treatment regimen including combinations of the following medications: doxycycline hyclate 100mg twice daily, minocycline 105 mg daily, topical metronidazole 0.75% cream, topical ivermectin 1%, topical azelaic acid 15%. Although his overall rosacea clinically stabilized, he demonstrated impressively severe, progressive rhinophymatous changes (Figures 1A–C). He was then referred for fractionated CO2 laser resurfacing.

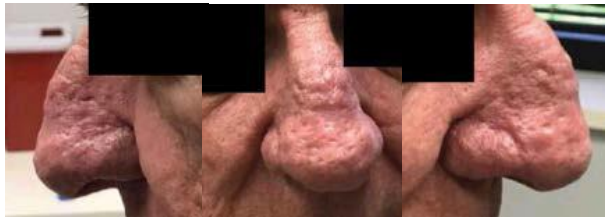


FIGURES 1A–C. Prior to fractionated CO2 laser resurfacing

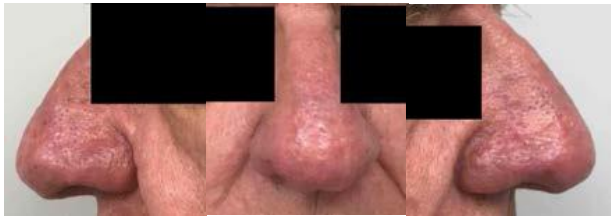
DISCUSSION

The patient underwent initial laser resurfacing in which a dermal optical thermolysis (DOT) fractionated CO2 laser (SmartXide, DEKA Medical Inc., San Francisco, California) was utilized. The panel was set to 30 W with a dwell time ranging from 4,000 to 7,000 microseconds and a pitch of 200 micrometers. Approximately 18 to 20 passes were performed over the highly sebaceous areas of the nose, while the less sebaceous areas were treated with fewer passes. The procedure was tolerated well with no complications. The patient was seen at two weeks postprocedure. A significant improvement was noted. He restarted oral minocycline 105mg daily and topical metronidazole 0.75% cream.

He was seen again at eight weeks postprocedure. A significant improvement was noted in rhinophymatous changes and the patient reported being "very pleased" with his results. He was continued on oral minocycline 105mg daily as well as topical ivermectin. He was started on topical sodium sulfacetamide 9.5% sulfur 5% wash. He also received a single 12-mg dose of oral ivermectin.



FIGURES 2A–C. Twelve weeks after first fractionated CO2 laser resurfacing treatment



FIGURES 3A–C. Four weeks after second fractionated CO2 laser resurfacing treatment

Twelve weeks after the initial fractionated carbon dioxide laser resurfacing treatment, the patient underwent a second treatment. Images were obtained prior to the procedure (Figures 2A–C) Laser settings were as follows: power, 25 W; dwell time, 4,000 microseconds; and pitch, 350 micrometers. Ten to 12 passes were performed on the residual hypertrophic sebaceous tissue, with significant blending into the normal tissue.

At four weeks after the procedure, the healing process was complete and clinical examination revealed remarkable improvement in nasal texture and contour (Figures 3A–C). The patient was very satisfied with the results. The patient has since continued his treatment regimen of oral doxycycline monohydrate 40mg daily and topical sodium sulfacetamide 9.5%/ sulfur 5% wash. Tretinoin 0.05% cream was also added to this regimen. No evidence of unsatisfactory scarring or dyspigmentation was observed at that time.

CONCLUSION

Numerous treatment modalities have been considered to treat the debilitating aesthetic and functional changes of rhinophyma. A review of the current literature reveals a consensus that topical antibiotics, topical retinoids, and systemic antibiotics have proven largely ineffective, leaving surgical intervention, including CO2 laser surgery, as the mainstay of treatment.[1,2,4,6,7,8, 9]

The role of lasers in the treatment of rhinophyma has gained popularity throughout recent years. CO2 laser resurfacing can be performed under general anesthesia or local anesthetic, the latter of which might be preferred by the patient as an in-office treatment option. The literature suggests that laser resurfacing results in minimal bleeding, making it a favorable working environment for the user.[2,4] Unlike many of the alternative treatment modalities, CO2 laser boasts the ability to precisely control the depth of injury.[4] The depth of thermal damage is exact, noted to be 0.5mm below the charred zone in one study involving the use of fully ablative carbon dioxide laser; the bloodless environment also allows for the additional assurance of correct depth as sebum is released from sebaceous glands as a result of the thermal injury.

In addition to satisfactory cosmetic results, other benefits of CO2 laser therapy include rapid reepithelialization starting as early as four days post-procedure, with resolution typically occurring within 3 to 6 weeks post-procedure with relatively mimimal pain.[2,4,6,11] The wide range of reepithelialization is likely attributable to the variation in laser settings, as well as the use of fractionated ablative CO2 laser in some studies, compared with the use of fully ablative CO2 laser in others. In the previously described case series,[12] all three patients were treated with fractionated ablative CO2 laser, with complete reepithelialization occurring within one week post-procedure.[12]

Fractionated ablative CO2 lasers create microthermal zones, leaving uninjured columns of healthy tissue that aid in healing.[1] This process results in faster healing times and fewer adverse effects than traditional fully ablative CO2 laser therapy.10,11,12 In a study performed by Serowaka et al,[11] the authors reported that the fractionated ablative CO2 laser used in the study resulted in an overall "more natural" result. Despite recent significant technological advances in treatment options, rhinophyma remains a challenging condition to treat. Among a multitide of treatment modalities, fractionated CO2 laser resurfacing is an

REFERNCES

1. Bolognia JL, Jorizzo JL, Schaffer JV, et al. Rosacea and related disorders. In: Powell FC, Raghallaigh SN, eds. Dermatology. 3rd ed. China: Elsevier Saunders; 2009: 561–569.

2. Lomeo PE, Mcdonald J, Finneman J. Rhinophyma: treatment with CO2 laser. Ear Nose Throat J. 1997;76(10):740–743.

3. James WD, Berger TG, Elston DM, Neuhaus IM. Acne. In: Andrew's Diseases of the Skin. 12th ed. Philadelphia, PA: Elsevier; 2016: 239–241.

4. Sadick H, Goepel B, Bersch C, et al. Rhinophyma: diagnosis and treatment options for a disfiguring tumor of the nose. Ann Plast Surg.

2008;61(1):114–120.

5. Redett RJ, Manson PN, Goldberg N, et al. Methods and results of rhinophyma treatment. Plast Reconstr Surg. 2001;107(5):1115–1123.

6. Cravo, M, Canelas MM, Cardoso JC, et al. Combined carbon dioxide laser and bipolar electrocoagulation: another option to treat rhinophyma. J Dermatolog Treat. 2009;20(3): 146–148.

7. Fink C, Lackey J, Gradne D. Rhinophyma: a treamtent review. Dermatol Surg. 2018;44(2): 275–282.

8. Rordam OM, Guldbakke K. Rhinophyma: big problem, simple solution. Acta Derm Venereol. 2011; 91(2):188–189.

9. Madan V, Ferguson JE, August PJ. Carbon dioxide laser treatment of rhinophyma: a review of 124 patients. Br J Dermatol. 2009;161(4):814 818.

10. Campolmi P, Bonan P, Cannarozzo G, et al. Highlights of thirty-year experience of CO2 laser use at the Florence (Italy) department of dermatology. ScientificWorldJournal. 2012;2012:546528.

11. Serowka KL, Saedi N, Dover JS, Zachary CB. Fractionated ablative carbon dioxide laser for the treatment of rhinophyma. Lasers Surg Med. 2014;46(1):8–12.

12. Meesters AA, van der Lindent M, De Rie MA, Wolkerstorfer A. Fractionated carbon dioxide laser therapy as treatment of mild rhinophyma: report of three cases. Dermatol Ther. 2015;28(3):147–150.

13. Madan V. Dermatological applications of carbon dioxide laser. J Cutan Aesthet Surg. 2013;6(4): 175–177.

An Unusual Skin Infection with Achromobacter Xylosoxidans

Matthew S Crosby, DO, PGY-3, Angelo A. Petropolis, MD, Keliegh S Culpepper, MD, Vernon T. Mackey, DO

Advanced Desert Dermatology & Cochise Dermatology, Peoria & Sierra Vista, AZ

ABSTRACT

Achromobacter xylosoxidans is an emerging pathogen primarily seen in immunocompromised patients. It is a non-fermentative, gram negative bacterium that has developed multi-drug resistance and is capable of forming biofilms on medical products.

We present the case of a 50-year old immunocompetent, type I diabetic female with a five-month history of tender lump at an attachment site for her insulin pump. Incision and drainage of the lump produced 10 cc of purulent material that was cultured and grew Achromobacter xylosoxidans.

The culture was resistant to multiple antibiotics, but was susceptible to trimethoprim/sulfamethoxazole. After surgical incision and drainage, extirpation of the surrounding granulomatous material, and a 10-day course of trimethoprim/sulfamethoxazole the patient had no signs or symptoms of infection.

This case of a granulomatous abscess formation with Achromobacter xylosoxidans in an immunocompetent patient demonstrates further emergence of this bacteria as a potential pathogen, not only in immunocompromised individuals, but in any patient with an indwelling catheter.

HISTORY OF PRESENT ILLNESS

A 50-year old Caucasian female presented with a five-month history of a sore, tender, red lump on her right superior buttock. Five months earlier the patient used this area to attach the infusion set for her insulin pump. The infusion set was left in place for seven days as opposed to the two or three days recommended by the device manufacturer. A firm, slightly tender lump formed, similar to previous indurations that had developed from use of her insulin pump. This lump, however, began to enlarge, became soft, and was intermittently warm and red. Although, the area was sore and tender, she never had any significant pain associated with it. She also denied any fever, malaise or other systemic symptoms.

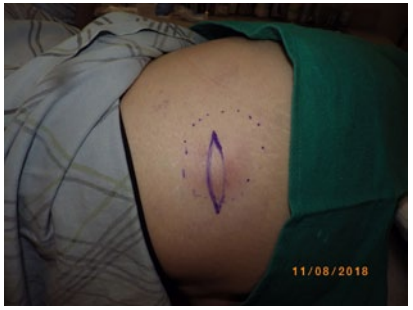
Past medical history is significant for type I diabetes mellitus diagnosed at age 9, hypertension, asthma, gastroesophageal reflux disease, allergic rhinitis, migraines, depression, hidradenitis suppurativa that was treated with surgical excision, and recurrent vaginal yeast infections usually after taking oral antibiotics.

Surgical history is significant for hidradenitis suppurativa excisions at bilateral inguinal folds, bilateral carpal tunnel release, tubal ligation, abdominoplasty, and cholecystectomy.

Current medications include insulin aspart, mometasone furoate, inhaled fluticasone, pantoprazole, cetirizine, spironolactone, duloxetine, sumatriptan, fluconazole, topiramate, and enalapril.

PHYSICAL EXAMINATION

Physical exam revealed a soft, tender, erythematous subcutaneous mass with no visible punctum or overlying epidermal change on the right superior buttock, measuring 5.5 by 7.0 cm in diameter.



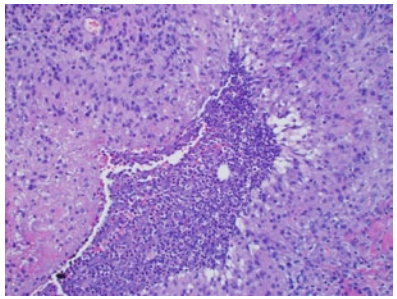
The clinical differential diagnosis included subcutaneous fat necrosis, epidermal cyst and an abscess.

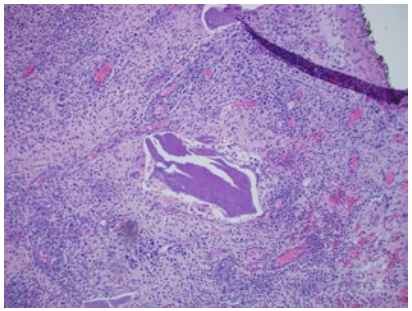
MANAGEMENT & CLINICAL COURSE

The patient was scheduled for excision of the mass the day after presenting to the clinic. Upon incision approximately 10 mL of thick purulent liquid was drained from the lesion. A sample was sent for gram stain, aerobic and anaerobic culture and sensitivities. Necrotic appearing adipose and fibrotic tissue was dissected and extirpated through an elliptical incision, and was submitted for pathology.

PATHOLOGY

Histologic findings showed a subcutaneous defect with palisaded granulomatous inflammation and sclerosis. There was no detection of microorganisms with Gomori Methenamine Silver stain, tissue gram and acid-fast stains. There was a focus of acellular material embedded within the inflammation.





The gram stain of the purulent material showed few white blood cells and rare gram-negative bacilli. Culture grew moderate Achromobacter xylosoxidans resistant to cefepime, cefotaxime, and gentamicin; susceptible to ceftazidime, imepinem, levofloxacin, piperacillin, and trimethoprim/sulfamethoxazole.

MANAGEMENT & CLINICAL COURSE CONTINUED

The patient was prescribed sulfamethoxazole/trimethoprim 800 mg/160mg PO BID for 10 days. The patient tolerated the procedure and the antibiotics well. The patient had normal levels of immunoglobulin A, G and M and a negative HIV screening test. She healed well from the surgical procedure and has had no recurrence of symptoms.

DISCUSSION

A. xylosoxidans is a non-fermentative non-spore forming, motile, gram negative, aerobic, catalase and oxidase positive flagellate bacterium. It is an emerging pathogen that was first isolated in 1971 from patients with chronic otitis media.[1] Since its recognition it has been documented to cause a variety of infections including abdominal, urinary tract, ocular, pneumonia, meningitis, osteomyelitis, endocarditis, bacteremia and skin and soft tissue infections.[2,3] Those affected are usually immunocompromised, have hematological disorders, or have indwelling catheters.[4]

Strains of A. xylosoxidans have shown resistance to multiple antibiotics. Among the antibiotics that A. xylosoxidans has shown resistance to are penicillins, cephalosporins, carbapenems, aminoglycocides, macrolides, fluoroquinilones and trimethoprim-sulfamethoxazole.[3]

A. xylosoxidans has been documented to form biofilms on plastics, including on contact lenses, urinary and intravenous catheters, and reusable tissue dispensers treated with disinfectant solution.[4-6] A resent study has demonstrated that A xylosoxidans is even capable of biodegradation of plastic using the plastic as its sole source of carbon.[7]

Our case illustrates an indolent infection with A. xylosoxidans forming a granulomatous abscess at the site of an insulin pump that was left in place for 7 days in an immunocompetent patient. There are numerous reports of infections with A. xylosoxidans in patients with urinary or intravenous catheters. To our knowledge this is the first report of an insulin pump as the source of such an infection. It is possible that the subcutaneous focus of acellular material described on the pathology report represents a partially biodegraded piece of the insulin pump catheter that broke off, and was serving as a nidus of infection for A. xylosoxidans. Although multi-drug resistance is common, the culture grown from our patient was susceptible to trimethoprim/sulfamethoxazole, among other antibiotics, and our patient was treated successfully with surgical excision, drainage, and a 10-day course of trimethoprim/sulfamethoxazole.

Physicians should recognize A. xylosoxidans as an emerging pathogen that is able to form biofilms on “disinfected” surfaces, may be resistant to multiple antibiotics and is capable of causing infections with various presentations.

REFERENCES

1. Yabuuchi E, Ohyama A. Achromobacter Xylosoxidans n. sp. from Human Ear Discharge. *Japan J. Microbiol. 1971;* 15:477-481
2. Rodrigues CG, Rays J, Kanegae MY. Native-valve endocarditis caused by Achromobacter xylosoxidans: a case report and review of literature. *Autops Case Rep.* 2017; 7(3): 50–55.
3. Tena D, Martinez NM, Losa C, Solis S. Skin and soft tissue infection caused by Achromobacter xylosoxidans: report of 14 cases. *Scand J Infect Dis.* 2014; 46(2):130-135.
4. Pérez Barragán E, Sandino Pérez J, Corbella L, Orellana MA, Fernández-Ruiz M.Achromobacter xylosoxidans bacteremia: clinical and microbiological features in a 10-year case series. Rev Esp Quimioter. 2018; 31(3): 268–273.
5. Konstantinović N, Ćirković I, Đukić S, Marić V, Božić DD. Biofilm formation of Achromobacter xylosoxidans on contact lens. *Acta Microbiol Immunol Hung.* 2017; 64(3):293-300.
6. Günther F, Merle U, Frank U, Gaida MM, Mutters NT. Pseudobacteremia outbreak of biofilm-forming Achromobacter xylosoxidans - environmental transmission. BMC Infect Dis. 2016; 16(1):584
7. Kowalczyk A, Chyc M, Ryszka P, Latowski D. Achromobacter xylosoxidans as a new microorganism strain colonizing high-density polyethylene as a key step to its biodegradation.

Focal atypical lymphoid infiltrate with CD30 positivity in a 36-year old male

GEORGIA CAMPUS PHILADELPHIA COLLEGE OF OSTEOPATHIC MEDICINE

Alexandria B. Glass, DO, Christopher M. Buckley, DO, Dipti Anand, MD, Evangelos G. Poulos, MD, and Marcus B. Goodman , DO

GEORGIA CAMPUS PCOM

INTRODUCTION

Cutaneous T-cell lymphoma (CTCL) is a term that encompasses various lymphomas derived from transformed T-lymphocytes including mycosis fungoides, CD30 positive T-cell lymphoproliferative disorders, and subcutaneous T-cell lymphoma. The CD30 positive T-cell lymphomas follow mycosis fungoides as the second most common category of CTCLs and account for 30% of all primary cutaneous lymphomas. As the name implies, these disorders share the expression by atypical lymphocytes of CD30, a cytokine receptor that belongs to the tumor necrosis factor receptor family and is involved in the process of tumor cell growth. Disorders in this category are primary cutaneous anaplastic large cell lymphoma (PCALCL), lymphomatoid papulosis (Lyp), borderline disorders, transformed stage mycosis fungoides, and systemic anaplastic large cell lymphoma. Although they possess similar expression of CD30, these disorders can be very different in their clinical presentation and progression.

CASE

A 36-year old Caucasian male presented to the clinic for the evaluation of a new growth under his right arm. He stated the growth began one to two months prior and had progressively increased in size. He complained of tenderness surrounding the lesion but denied recent fevers, chest pain, shortness of breath, gastrointestinal discomfort, rash, and edema. The patient's past medical history was significant only for hypertension, managed with Cozaar, and his pertinent family medical history was negative.

On physical exam, a single ulcerated, erythematous nodule was observed posterolateral to the right axilla with faint erythema surrounding the lesion (Figure 1). A shave biopsy was performed and sent to dermatopathology for evaluation. The patient was prescribed oral doxycycline to treat the possibility of a localized cellulitis.

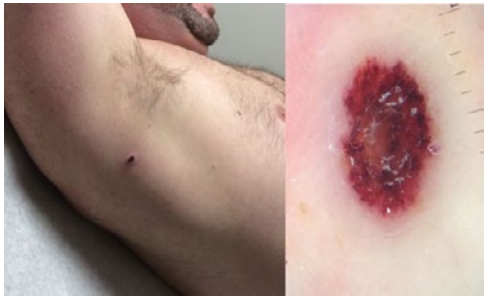


Figure 1. (Left) Lesion on initial presentation. (Right) Dermoscopic view of the lesion.

The histology revealed an atypical T-cell lymphoid infiltrate with CD30 positivity of the dermis, extensive epidermal and dermal necrosis, hemorrhage, and fibrinopurulent exudate. The differential diagnosis included type C variant of lymphomatoid papulosis (Lyp), primary cutaneous CD30 positive anaplastic large cell lymphoma (PCALCL), and metastatic visceral/nodal T-cell lymphoma. Due to the unusual nature of the lesion, the case was referred to the National Cancer Institute for further review. Their report revealed similar findings of an atypical T-cell infiltrate with superficial ulceration and necrosis (Figure 2). Multiple immunostains were performed which showed the lymphoid cells were positive for CD3 and CD4 and negative for CD8. CD20 highlighted some extremely rare B cells. CD30 showed focal and variable positivity. Stains for herpes simplex virus 1, 2, and varicella were all negative (Figure 3). Due to these findings, the possibility of a primary cutaneous CD30 positive T-cell lymphoproliferative disorder could not be ruled out and complete excision was recommended.

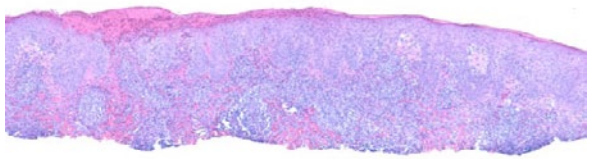


Figure 2. Histology image of the patient's lesion demonstrating focal atypical lymphoid infiltrate.

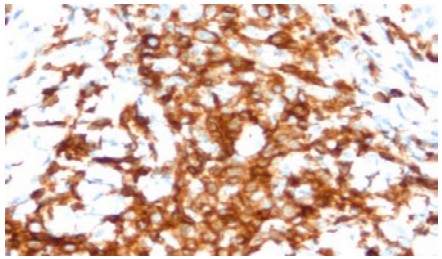


Figure 3. Pathology image showing CD30 positivity

The lesion was excised in the office with resultant clear margins found on pathology. He was then referred to oncology for further workup to rule out a systemic or node-based lymphoma. All additional testing, including full body PET CT scans, were negative. After two and a half years, the patient is doing well and is being followed by oncology for routine monitoring.

DISCUSSION

The findings in this case showed an atypical CD30 positive lymphoid infiltrate; however, the exact diagnosis was inconclusive. The differential diagnosis included primary cutaneous anaplastic large cell lymphoma (PCALCL), lymphomatosis papulosis (Lyp), borderline lesions, cutaneous metastasis from a nodal or systemic ALCL, CD30 positive transformed mycosis fungoides, rare types of CTCL that can occasionally show positivity of CD30, and reactive processes such as drug reactions, arthropod bites and viral infections. The two prominent disorders in the differential diagnosis were PCALCL and Lyp, since they have many overlapping clinical and histological features. The clinical appearance, in conjunction with histology, are used to determine a diagnosis and treatment. After vigilant longitudinal clinical evaluation of the patient, a diagnosis of PCALCL or Lyp can usually be achieved based on clinical behavior. Thus, careful clinical correlation is critical when managing a CD30 positive lymphoid infiltrate.

PCALCL accounts for approximately 12% of all CTCLs. Most patients with PCALCL present with an ulcerated, rapidly growing solitary tumor or grouped nodules. They are most common in the 6th decade of life, are twice as common in males than females, primarily affect adults, and tend to appear on the head, neck, and extremities. Histologically, the tumor is composed of large, anaplastic, pleomorphic lymphocytes with irregular nuclei and abundant cytoplasm arranged in sheets infiltrating the deep dermis and subcutaneous tissue. Over 75% of lymphocytes stain positive for CD30. Treatment for PCALCL includes excising the lesion in its entirety. If the lesion is too large to be excised, radiotherapy should be performed in conjunction. In 10% to 42% of cases, the lesion may partially or completely regress as in Lyp; however, recurrences are common and treatment is necessary for remission. The prognosis is generally favorable, with a 5-year survival rate between 76% and 96%.

Lymphomatoid papulosis (Lyp) is a chronic, recurrent, self-healing, papulonodular skin disorder with debate on whether it is a benign or malignant lymphoproliferative process. Due to its CD30 positivity, presence of abnormal T cells, and similarity to PCALCL, it is most commonly categorized as a low-grade variant of CTCL. There are five distinct (A-E) histological subtypes of Lyp all exhibiting slightly different clinical presentations. Type A is the most common variant and clinically displays the classic papulonodular lesions. Type B is uncommon and generally presents as a mycosis fungoides (MF)-type plaque. Type C presents as a solitary regressing nodule that resembles features of PCALCL.. Type D and E represent more unusual variants of Lyp with Type D appearing as localized erythematous scaly lesions, resembling pagetoid reticulosis. Lastly, Type E, the newest described variant, is the angioinvasive type that has an association with EBV, similar to extranodal nasal NK/T-cell lymphoma. There are multiple treatment options such as psoralen-UVA light therapy (PUVA), low-dose methotrexate, and topical steroids that can help alleviate disseminated or stigmatizing lesions, but no treatment option alters the course of the disease. Therefore, the "wait and see" strategy is an appropriate first-line approach to these patients. Since the main concern is the development of a secondary lymphoma, patients with Lyp should be monitored for life.

CONCLUSION

Based on our patient's history, clinical presentation, and histology findings, our patient likely had a PCALCL. Close monitoring of the patient is being performed and if he develops other lesions in the future, then Lyp type C may be a consideration. Our patient's lesion was excised before adequate time could be given for regression. Regardless of the final diagnosis, this case demonstrated the importance of clinicopathological correlation in evaluating CD30 positive atypical lymphoid infiltrates. This case provides a great learning example of future CD30 positive cases in hopes that further research into the understanding of this process can be accomplished.

REFERENCES

1. Kempf W. Cutaneous CD30-Positive Lymphoproliferative Disorders. Surg Pathol Clin. 2014;7(2):203-28.
2. Kempf W, Kerl K, Mitteldorf C. Cutaneous CD30-positive T-cell lymphoproliferative disorders-clinical and histopathologic features, differential diagnosis, and treatment. Semin Cutan Med Surg. 2018;37(1):24-9.
3. Willemze R. Cutaneous T-Cell Lymphoma. In: Bolognia J, Jorizzo J, Schaffer J, editors. Dermatology. 2. Third ed. China: Elsevier; 2012. p. 2017-36.
4. Kempf W. A new era for cutaneous CD30-positive T-cell lymphoproliferative disorders. Semin Diagn Pathol. 2017;34(1):22-35.
5. Vergier B, Beylot-Barry M, Pulford K, Michel P, Bosq J, de Muret A, et al. Statistical evaluation of diagnostic and prognostic features of CD30+ cutaneous lymphoproliferative disorders: a clinicopathologic study of 65 cases. Am J Surg Pathol. 1998;22(10):1192-202.
6. Kempf W, Pfaltz K, Vermeer MH, Cozzio A, Ortiz-Romero PL, Bagot M, et al. EORTC, ISCL, and USCLC consensus recommendations for the treatment of primary cutaneous CD30-positive lymphoproliferative disorders: lymphomatoid papulosis and primary cutaneous anaplastic large-cell lymphoma. Blood. 2011;118(15):4024-35.
7. Benner MF, Willemze R. Applicability and prognostic value of the new TNM classification system in 135 patients with primary cutaneous anaplastic large cell lymphoma. Arch Dermatol. 2009;145(12):1399-404.
8. Macaulay WL. Lymphomatoid papulosis. A continuing self-healing eruption, clinically benign--histologically malignant. Arch Dermatol. 1968;97(1):23-30.
9. Mori M, Manuelli C, Pimpinelli N, Mavilia C, Maggi E, Santucci M, et al. CD30-CD30 ligand interaction in primary cutaneous CD30(+) T-cell lymphomas: A clue to the pathophysiology of clinical regression. Blood. 1999;94(9):3077-83.
10. Bekkenk MW, Geelen FA, van Voorst Vader PC, Heule F, Geerts ML, van Vloten WA, et al. Primary and secondary cutaneous CD30(+) lymphoproliferative disorders: a report from the Dutch Cutaneous Lymphoma Group on the long-term follow-up data of 219 patients and guidelines for diagnosis and treatment. Blood. 2000;95(12):3653-61.
11. Thomsen K, Wantzin GL. Lymphomatoid papulosis. A follow-up study of 30 patients. J Am Acad Dermatol. 1987;17(4):632-6.
12. Kunishige JH, McDonald H, Alvarez G, Johnson M, Prieto V, Duvic M. Lymphomatoid papulosis and associated lymphomas: a retrospective case series of 84 patients. Clin Exp Dermatol. 2009;34(5):576-81.
13. Christensen HK, Thomsen K, Vejlsgaard GL. Lymphomatoid papulosis: a follow-up study of 41 patients. Semin Dermatol. 1994;13(3):197-201.
14. Gan EY, Tang MB, Tan SH. Lymphomatoid papulosis: is a second lymphoma commoner among East Asians? Clin Exp Dermatol. 2012;37(2):118-21.
15. Salhany KE, Cousar JB, Greer JP, Casey TT, Fields JP, Collins RD. Transformation of cutaneous T cell lymphoma to large cell lymphoma. A clinicopathologic and immunologic study. Am J Pathol. 1988;132(2):265-77.
16. Diamandidou E, Colome-Grimmer M, Fayad L, Duvic M, Kurzrock R. Transformation of mycosis fungoides/Sezary syndrome: clinical characteristics and prognosis. Blood. 1998;92(4):1150-9.
17. Benner MF, Jansen PM, Vermeer MH, Willemze R. Prognostic factors in transformed mycosis fungoides: a retrospective analysis of 100 cases. Blood. 2012;119(7):1643-9.
18. Chen YC, Wu YH. Linear Folliculotropic CD30-Positive Lymphomatoid Drug Reaction. Am J Dermatopathol. 2017;39(5):e62-e65.
19. Saeed SA, Bazza M, Zaman M, Ryatt KS. Cefuroxime induced lymphomatoid hypersensitivity reaction. Postgrad Med J. 2000;76(899):577-9.
20. Piletta PA, Wirth S, Hommel L, Saurat JH, Hauser C. Circulating skin-homing T cells in atopic dermatitis. Selective up-regulation of HLA-DR, interleukin-2R, and CD30 and decrease after combined UV-A and UV-B phototherapy. Arch Dermatol. 1996;132(10):1171-6.
21. Kempf W, Kazakov DV, Palmedo G, Fraitag S, Schaerer L, Kutzner H. Pityriasis lichenoides et varioliformis acuta with numerous CD30(+) cells: a variant mimicking lymphomatoid papulosis and other cutaneous lymphomas. A clinicopathologic, immunohistochemical, and molecular biological study of 13 cases. Am J Surg Pathol. 2012;36(7):1021-9.
22. Fernandez-Flores A. CD30+ cell population in common keratoacanthomas: a study of 21 cases. Rom J Morphol Embryol. 2008;49(2):159-62.
23. Massi D, Trotta M, Franchi A, Pimpinelli N, Santucci M. Atypical CD30+ cutaneous lymphoid proliferation in a patient with tuberculosis infection. Am J Dermatopathol. 2004;26(3):234-6.
24. Cassinaro AM, Malorana A. Verruca vulgaris with CD30-positive lymphoid infiltrate: a case report. Am J Dermatopathol. 2002;24(3):260-3.
25. Leinweber B, Kerl H, Cerroni L. Histopathologic features of cutaneous herpes virus infections (herpes simplex, herpes varicella/zoster): a broad spectrum of presentations with common pseudolymphomatous aspects. Am J Surg Pathol. 2006;30(1):50-8.
26. Werner B, Massone C, Kerl H, Cerroni L. Large CD30-positive cells in benign, atypical lymphoid infiltrates of the skin. J Cutan Pathol. 2008;35(12):1100-7.
27. Chai C, White WL, Shea CR, Prieto VG. Epstein Barr virus-associated lymphoproliferative-disorders primarily involving the skin. J Cutan Pathol. 1999;26(5):242-7.
28. Rose C, Starostik P, Bröcker EB. Infection with parapoxvirus induces CD30-positive cutaneous infiltrates in humans. J Cutan Pathol. 1999;26(10):520-2.
29. Smith KJ, Barrett TL, Neafie R, Tomaszewski MM, Yeager J, Nelson A, et al. Is CD30 (Ki-1) immunostaining in cutaneous eruptions useful as a marker of Th1 to Th2 cytokine switching and/or as a marker of advanced HIV-1 disease? Br J Dermatol. 1998;138(5):774-9.
30. Gallardo F, Barranco C, Toll A, Pujol RM. CD30 antigen expression in cutaneous inflammatory infiltrates of scabies: a dynamic immunophenotypic pattern that should be distinguished from lymphomatoid papulosis. J Cutan Pathol. 2002;29(6):368-73.
31. Hwong H, Jones D, Prieto VG, Schulz C, Duvic M. Persistent atypical lymphocytic hyperplasia following tick bite in a child: report of a case and review of the literature. Pediatr Dermatol. 2001;18(6):481-4.
32. Cepeda LT, Pieretti M, Chapman SF, Horenstein MG. CD30-positive atypical lymphoid cells in common non-neoplastic cutaneous infiltrates rich in neutrophils and eosinophils. Am J Surg Pathol. 2001;25(7):863-8.

Cutaneous Larva Migrans

Naeha Gupta, DO and Richard McClain, MD
Lehigh Valley Health Network, Allentown, PA

Case Presentation

Patient: 14 year-old Caucasian male.

History of Present Illness: The patient presents with a pruritic, red, papular eruption that began on his feet 2 weeks after he came back from a trip to Jamaica. He reports associated pruritus on his bilateral dorsal feet that is worse at night and keeps him awake. The eruption progressed to linear tracks on his feet about four days later. Other children that he was playing with, including his brother and cousin, also have similar lesions. The children report playing on the beach barefoot.

Current Treatment: Ivermectin 12mg PO for 1 day then ivermectin 12mg PO 7 days later

Medical History: None

Social History: High school student, plays basketball, lives with parents and sibling

Medications: Vitamin C 500mg

Physical Examination: Several thin, tense bullae in a serpiginous pattern on the soles, insteps, right lateral foot, left 2nd web space. Several erythematous non-scaly papules bilateral dorsal feet.

Reason for Presentation: Interest

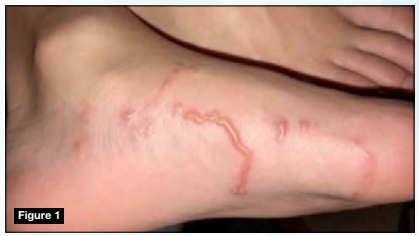


Figure 1: Clinical image of right instep demonstrating serpiginous linear papules and plaques.

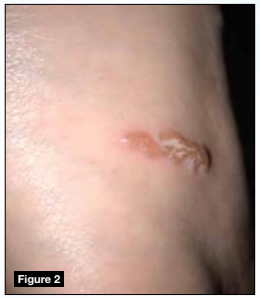


Figure 2: Clinical image of right plantar foot demonstrating a serpiginous linear plaque.

References:

1. Heukelbach, J, Feldmeier H. Epidemiological and clinical characteristics of hookworm-related cutaneous larva migrans. *Lancet Infect Dis.* 2008;8:302-309.
2. Jacobson C, Abel E. Parasitic infestations. *JAAD.* 2007;56:1026-343.
3. Monsel, G, Caumes, E. What's new in travel-associated dermatology? *J Travel Med.* 2015;22:221-324.

Discussion

Cutaneous larva migrans (CLM) is a cutaneous infection which occurs most often in travelers to subtropical regions. CLM is most frequently caused by animal hookworms, including *Ancylostoma caninum and Ancylostoma brazilense* but can also be caused by human hookworms, *Ancylostoma duodenale and Necator americanus.* Adult hookworms reside in the intestines of cats and dogs. The eggs are then shed in the feces and hatch in the soil. The larvae thrive in a warm and humid environment. Thus, CLM is most commonly found in warmer climates, such as Africa, Latin America, and the Caribbean region as well as the Southeast United States.

Transmission occurs with barefoot contact on damp sand or soil contaminated by animal feces. The larvae excrete protease and hyaluronidase allowing passage through the epidermis. While the larvae are able to penetrate into the lymphatic and venous system in animals, they cannot travel further than the skin in human hosts as they lack collagenase enzymes to penetrate the basement membrane zone. Depending on the larvae species, migration can be from a few millimeters to a few centimeters per day. Activity can continue for up to several weeks but the infection is self-limited.

Onset of infection begins with local pruritus and the appearance of papules at the site of entry. Some patients may recall a tingling or prickling sensation within 30 minutes of larvae penetration at the site of exposure. One to five days later, erythematous, serpiginous plaques appear which represent areas of resting larvae. In a small number of cases, vesiculobullous eruptions and folliculitis can occur. Lesions tend to occur on the feet, buttocks, and thighs as well as other exposed areas that come into contact with contaminated soil or sand.

Diagnosis is mostly clinical based on the history of travel to an endemic area and exposure to contaminated soil as well as the pathognomonic serpiginous eruption. Associated itch can be intense enough to disrupt sleep and lead to a bacterial superinfection. Labs and biopsies are generally unnecessary. Eosinophilia can be present but is not specific. Differential diagnosis includes scabies, loiasis, tinea corporis, cercarial dermatitis, and contact dermatitis. However, a good travel history will distinguish CLM from the aforementioned entities.

Treatment can be initiated with oral ivermectin at a single dose of 200ug per kilogram of bodyweight. If that is ineffective, a second dose can be given one week later. However, oral ivermectin is contraindicated in patients less than 5 years old and pregnant or breastfeeding women. Oral albendazole at 400mg daily for a week is an alternative option. Oral albendazole is pregnancy category C with data on use in pregnant women and children less than 2 years being limited. Other treatment options include topical thiabendazole. Prevention is through avoidance of barefoot contact of contaminated soil in endemic areas. Towels do not provide sufficient protection and sun chairs as well as sandals on the beach are advised.

A Case of Nevoid Basal Cell Carcinoma Syndrome in a 9 month Infant

Jeffrey Scott Harbold Jr DO, Carlos Rivera MD, Rick Lin DO FAOCD FAAD

DIAGNOSTIC CRITERIA FOR BASAL CELL NEVUS SYNDROME (BCNS)
Major criteria
1. More than two BCCs or one BCC before the age of 20 years
2. Odontogenic keratocysts of the jaw (proven by histology)
3. Three or more palmar or plantar pits
4. Bilamellar calcification of the falx cerebri
5. Bifid, fused or markedly splayed ribs
6. First-degree relative with BCNS
Minor criteria
1. Macrocephaly (determined after adjustment for height)
2. Congenital malformations: cleft lip or palate; frontal bossing; "coarse face"; moderate or severe hypertelorism
3. Other skeletal abnormalities: Sprengel deformity*; marked pectus deformity; marked syndactyly of the digits
4. Radiographic abnormalities: bridging of the sella turcica; vertebral anomalies such as hemivertebrae and fusion or elongation of the vertebral bodies; modeling defects of the hands and feet; flame-shaped lucencies of the hands or feet
5. Bilateral ovarian fibromas
6. Medulloblastoma

Table 1. Diagnostic Criteria for BCNS. Reprinted from Jean L. Bolognia, Julie V. Schaffer, and Lorenzo Cerroni. Dermatology. 4th edn. 2018:1875

ABSTRACT

Nevoid Basal Cell Carcinoma Syndrome (NBCCS), also known as Gorlin syndrome is an autosomal dominant genodermatosis with a prevalence of 1 in 60,000 people. [1] It can present with a multiple clinical features including musculoskeletal malformations, CNS deformities, medulloblastoma, cardiac fibroma and basal cell carcinoma. Musculoskeletal deformations include jaw keratocyst, craniofacial abnormalities, palmar/plantar pitting and bifid ribs. [2]

Most clinical features manifest in adulthood and rarely present in the pediatric population. The diagnosis can be established with a combination of two major diagnostic criteria and one minor diagnostic criterion or one major and three minor diagnostic criteria (Table 1). [3] In cases where clinical features are inconclusive, sequence analysis of the PTCH1 gene can support the diagnosis.

Management for these patients includes continuous surveillance and treatment of clinical manifestations.

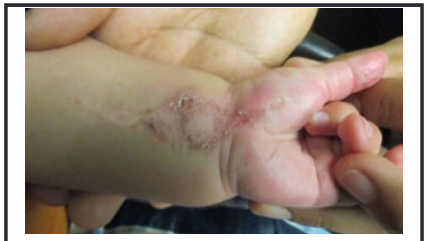


Figure 2. Linear atrophic plaque with annular border and scaling on the flexor surface of the wrist.

CASE PRESENTATION

Our patient is a 9 month old hispanic male with an evolving asymptomatic linear atrophic plaque on the flexor surface of the left wrist extending to the left upper arm. Lesion presented at birth and has recently progressed into a linear pattern towards the proximal arm.

Additional findings on exam includes cleft lip, craniomegaly with frontal bossing, a supernumerary digit of the right foot, and plantar pits. See Figures 3-6.

A 4mm punch biopsy was obtained and histology demonstrated findings consistent with a basaloid neoplasm. The patient was referred to pediatric dermatology where genetic PTCH1 testing was performed and confirmed our suspicion of NBCCS. The patient was referred to pediatric neurosurgery were an MRI head was ordered to evaluate for medulloblastoma. Patient was also referred to ophthalmology and pediatric dentistry. The extra digit was excised by plastic surgery.

Due to the size of the lesion and the age of the patient, topical management was recommended over surgical excision and patient was started topical imiquimod. Strong emphasis was placed on photoprotection including sun avoidance, broad-spectrum sunscreen and ultra-violet protective clothing. The Mother was also educated on the importance of life-long skin evaluations for her child.

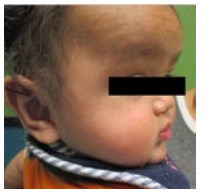


Figure 3. Frontal bossing.

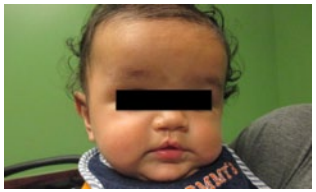


Figure 4. Repaired Cleft Lip.

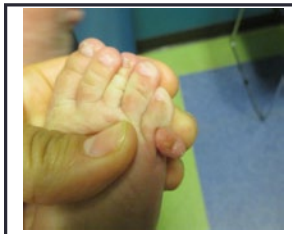


Figure 5. Polydactyly

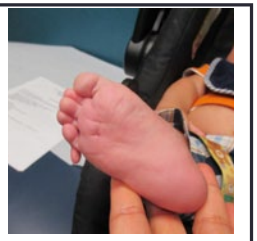


Figure 6. Plantar Pit

DISCUSSION

Management of NBCCS involves a multidisciplinary approach. It requires continuous screening, prevention and treatment of clinical manifestations. Prevention is done by wearing protective clothing in order to minimize UV light radiation exposure, regular use of sunscreen, avoiding excessive exposure to X-rays, and close follow up with a dermatologist for screening.

Referral to dentistry or oral surgery starting at age 8 is recommended every 12-18 months for jaw keratocyst screening, [4] although prolonged X-ray exposure with the use of panoramic dental radiograph (Orthopantogram) should be limited due to increased risk of neoplasm.

Experts recommend performing a brain MRI when patients present with abnormal neurologic findings or changes in head circumference. [5] Surveillance for medulloblastoma is recommended every 4 months until age 3 and every 6 months until age 5. [4] Dermatologic screening is recommended annually until first BCC manifests, then every 6 months or sooner if needed. [3]

Treatment options for BCC in pediatric cases include topical 5-FU, imiquimod and surgical excision. The use of Mohs micrographic surgery is effective for early lesions and can be supplemented with cryotherapy and laser treatment. Radiotherapy is a feasible option when lesions are recurrent, or surgery is contraindicated. [6]

Patients who receive prompt treatment and recurrent screenings may have a favorable prognosis. [7]

REFERENCES

1. Casaroto AR, Loures DC, Moreschi E, et al. Early diagnosis of Gorlin-Goltz syndrome:case report. Head Face Med. 2011;7:2. Published 2011 Jan 25. doi: 10.1186/1746-160X-7-2.
2. Scott C. Bresler, Bonnie L. Padwa, and Scott R. Granter. Nevoid Basal Cell Carcinoma Syndrome (Gorlin Syndrome) Head Neck Pathology. 2016 Jun; 10(2): 119–124. PMID: 26971503
3. Bree AF, Shah MR for the BCNS Colloquium Group. 2011. Consensus statement from the first international colloquium on basal cell nevus syndrome (BCNS). American Journal of Medical Genetics Part A 155:2091–2097. PMID: 21834049.
4. D Gareth Evans, MD, FRCP and Peter A Farndon, MD, FRCP. Nevoid Basal Cell Carcinoma Syndrome. Genereviews. March 2018. PMID: 20301330
5. Foulkes WD, Kamihara J, Evans DGR, et al. Cancer Surveillance in Gorlin Syndrome and Rhabdoid Tumor Predisposition Syndrome. Clin Cancer Res 2017; 23:e62
6. Baker, S, Joseph, K., Tai, P. Radiotherapy in Gorlin syndrome: Can it be safe and effective in adult patients? Journal of Cutaneous Medicine and Surgery Volume 20, Issue 2, March-April 2016, Pages 159-162.
7. Spitz, J. Basal Cell Nevus syndrome. Genodermatoses: A Clinical Guide to Genetic Skin Disorders. Second Edition. 2004, Dec 29.

Acroangiodermatitis of Mali : A Case Report and Review

Nady Hin DO[1], Brad P. Glick DO, MPH[1], Samuel Rubenstein, BS[2]

[1] Department of Dermatology & Cutaneous Surgery, Larkin Community Hospital – Palm Springs Campus; Hialeah, FL
[2] Midwestern University Chicago College of Osteopathic Medicine – Chicago, Illinois

INTRODUCTION

- Acroangiodermatitis of Mali is an uncommon vascular disease of the lower extremity
- It clinically presents as well circumscribed, slowly-evolving, red to violaceous or dusky macules, papules, or plaques on the lower extremities that mimics Kaposi sarcoma(KS), hence the moniker pseudo-KS.
- Herein, we report a case of a 71-year-old Vietnamese male who presented with violaceous papules and nodules on his lower extremity for which he had never been treated by a dermatologist.

CASE REPORT

A 71-year-old Vietnamese male presented for evaluation of multiple erythematous papules and nodules located on his bilateral lower extremity that had initially appeared 10 years prior.

- Initial treatment regimen included 3 weeks of SMZ/TMP by a prior practitioner
- After initial treatment, he returned with rapid progression of his lesions with increasing number and thickness and purulent discharge
- Physical exam: multiple erythematous and crusted violaceous nodules and plaques located bilaterally on the anterior lower extremity (Figure A)
  - Pertinent labs : CBC and CMP within normal Limits. Patient refused HIV testing.
- He underwent two 4-mm punch biopsies on the lower legs
  - Pathology: epidermal hyperplasia and hyperkeratosis with dermal fibrosis, a perivascular lymphocytic infiltrate, and small vessels with thickened vessel walls (Figure C)
  - Vascular slits and CD34 expression were notably absent (Figure D)
- Bilateral Venous Doppler studies showed no evidence of DVT or underlying vascular malformations
- Subsequent treatment
  - Topical Clobetasol applied twice a day
- Within two months of therapy, the patient had alleviation of symptoms and reduction in epidermal changes (Figure B).

CLINICAL IMAGES

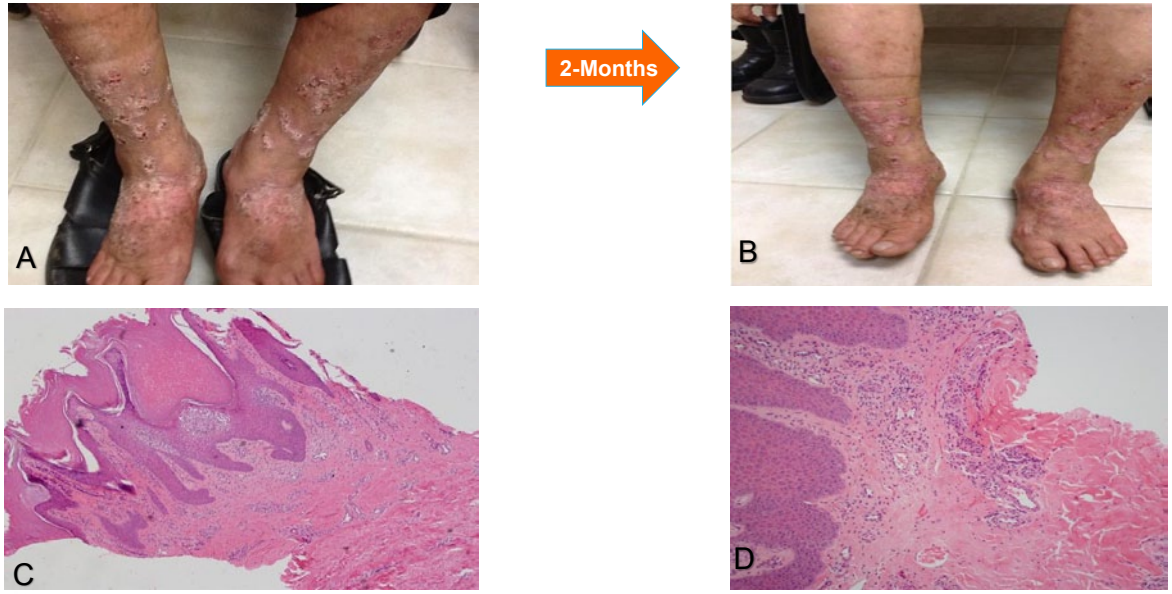


Figure 1: Clinical images of Patient prior to (A), treatment with brentuximab after 2-months (B).
Figure 2: Histologic Images at 40x (C) and 100x (D).

DISCUSSION and CONCLUSION

- AAD is an uncommon condition with less than 100 cases reported that usually occurs in males with a history of venous stasis, hemodialysis shunts, AV malformations, or prosthesis.[3]
- It is also referred to as pseudo-Kaposi Sarcoma due to the clinical and histological resemblance to Kaposi Sarcoma.
- It is hypothesized that AAD is due to alteration of local circulation leading to markedly increased capillary pressure with resultant edema, hypoxia, and neovascularization. [2]
- There is no definitive treatment for AAD. Treatment involves correction of the underlying vascular pathology with the goal of reducing inflammation as well as reducing capillary pressure.[1]
- The reduction in inflammation from the topical steroids likely led to improvement of the lesions.

REFERENCES

1. Horiguchi, Y., Takahashi, K. Tanizaki, H. and Miyachi, Y (2015). Case of bilateral acroangiodermatitis due to symmetrical arteriovenous fistulas of the soles. The Journal of Dermatology. 42: 989-991. Doi: 10.1111/1346-8138.12934
2. Rashkovsky I, et al. Acro-angiodermatitis: review of the literature and report of a case. Acta Derm Venereol (Stockh) 1995;75:475.
3. Walter MR, Lewin MR, Selim MA, Walters RW. Sharply demarcated, erythematous plaques on an amputation stump. Archives of Dermatology. 2009 Dec; 145(12):1447-52. [PMID:20026859]

Multiple Cellular Neurothekeomas

Megan Jones, DO, Nektarios Lountzis, MD, and Joshua Levin, MD

Lehigh Valley Health Network, Allentown, PA

HISTORY OF PRESENT ILLNESS: A 69 year-old Caucasian female presents for evaluation of multiple lesions that have slowly developed on her bilateral dorsal hands and forearms for the last 30 years. The lesions are tender.

MEDICAL HISTORY/SURGICAL HISTORY: Hypertension, partial hysterectomy

FAMILY HISTORY: No family history of similar appearing lesions

MEDICATIONS: Metoprolol succinate ER, vitamin D 2000 units once daily, digoxin, topical conjugated estrogen, aspirin

CURRENT TREATMENT: Punch excisions

PHYSICAL EXAMINATION: Grouped 5-8 millimeter smooth, firm, pink, discrete papulonodules on bilateral dorsal hands and forearms. (Figures 1and 2)

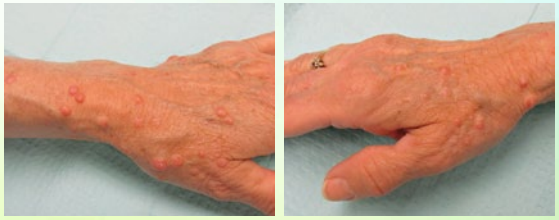
BIOPSY: Advanced Dermatology Associates LTD and University of Washington (AD18-05392, 05/25/2018), Left lateral dorsal hand, left dorsal radial wrist, left lateral distal forearm, right ulnar wrist, right radial wrist: There are similar histologic features in all specimens which are notable for a fascicular, relatively uniform, proliferation of spindled and epithelioid cells with mild atypia in the dermis associated with a myxoid background. The proliferation is relatively well delineated. Immunohistochemical stains demonstrate the cells are negative for SMA. Mart-1, CK5/6, p63, CD31, HMB-45, CD2, EMA, S100, CD45RO, and CD34. CD163 and CD68 highlight background histiocytes. The cells are variably positive for Factor XIIIa, positive for NKI-C3, and weakly positive for NSE. PGP 9.5 is equivocal. A colloidal iron stain demonstrates moderate amount of dermal mucin deposition. (Figure 3)

REFERENCES

1. Mahalingam M, Alter JN, Bhawan J. Multiple cellular neurothekeomas - a case report and review on the role of immunohistochemistry as a histologic adjunct. J Cutan Pathol. 2006;33:51-56.
2. Kelly J, Kristjansson A, Dadras S, Wu Chang M. Multiple, familial cellular neurothekeomas mimicking molluscum contagiosum. J Am Acad Dermatol. May 2015; 301: Ab201.
3. Garcia-Gutierrez M, Toussaint-Caire S, Gonzalez-Sanchez P, Ortiz-Hidalgo C. Multiple desmoplastic cellular neurothekeomas localized to the face of a 16-year-old boy. Am J dermatopathol. 2010;32:841-845.
4. Padgett SN, Walsh SN, Kory MC, Argenyi ZB. Agminated cellular neurothekeoma. J Cutan Pathol. 2011;38:990-993.

TABLE 1. IMMUNOHISTOCHEMICAL PROFILES OF MYXOID AND CELLULAR NEUROTHEKEOMAS.

	Myxoid	Cellular
Immunohistochemical staining pattern	S100 + Collagen type IV + Capsule EMA+	S100-Inconsistently stains for NKI/C3, PGP9.5, MITF, SMA, S100A6



Figures 1 and 2. Clinical appearance of multiple neurothekeomas.

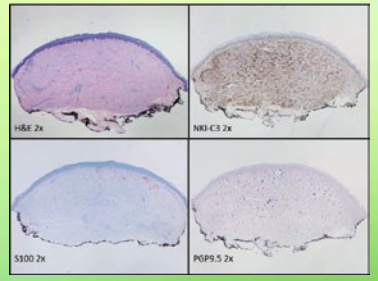


Figure 3. (H&E, 2x): A fascicular, relatively uniform, proliferation of spindled and epithelioid cells with mild atypia in the dermis associated with a myxoid background. (NKI-C3, 2x): Positive. (S100, 2x): Negative. (PGP9.5, 2x): Equivocal.

Neurothekeoma is a rare benign dermal neoplasm of debated lineage with consideration of fibrohistiocytic, neural, or smooth muscle derivation. Neurothekeomas most commonly occur in young females and develop as a solitary, slow growing, asymptomatic papulonodule on the head or neck. Multiple or agminated neurothekeomas are an unusual clinical presentation that have rarely been described.

Histopathologically, neurothekeomas are divided into three subtypes based on the degree of cellularity and mucinous stroma: myxoid, mixed, and cellular. All subtypes are poorly circumscribed plexiform dermal neoplasms that may extend into the subcutis. Myxoid neurothekeomas have abundant stromal mucin with few spindled and epithelioid cells in between fibrous septae. Cellular neurothekeomas are made up of fasciculated spindled and epithelioid cells in a stroma with minimal mucin. The immunohistochemical profile varies depending on the subtype (Table 1). Immunohistochemistry also helps exclude other histopathologic differential diagnoses including melanocytic, fibrohistiocytic, and Schwann cell tumors.

The varied histopathologic appearance and immunohistochemical staining patterns of neurothekeomas are hypothesized to be due to their existence on a morphologic spectrum directly related to nerve sheath maturation. Cellular neurothekeomas representing an undifferentiated variant and myxoid neurothekeomas representing a well differentiated variant. However, others believe that the varied immunohistochemical expression is secondary to their different cytomorphology.

Complete excision of neurothekeomas is both diagnostic and therapeutic. Although neurothekeomas may recur following incomplete removal, benignity is maintained and there are no reports of metastasis. Lastly, no known syndrome has been described in patients who have developed multiple neurothekeomas, but due to the rarity of this condition, it is suggested to follow these patients long term.

LVHN.org Lehigh Valley Health Network

Localized Cutaneous Leishmaniasis Treated with Observation **- A Case Report**

Kikam Adeline, DO[1], Lin Rick, DO[2] Martin, Trey, MD[3] Hohnadel R. Michael, DO[4]
Bay Area Corpus Christi Medical Center, Corpus Christi TX 78412; 2: David Geffen School of Medicine, Los Angeles, CA 90024;
3:Dermatology Clinic of McAllen, McAllen TX 78542, 4: SAGIS Focused Patient Diagnostics, Houston, TX 77092, 5:Rio Valley Dermatology, Brownsville, TX 78520

Abstract

Leishmaniasis is a vector-borne protozoan infection transmitted by the bite of an infected female phlebotomous sandfly. The disease presents in four different forms: visceral leishmaniasis, or kala-azar; cutaneous leishmaniasis; mucocutaneous leishmaniasis; and diffuse cutaneous leishmaniasis. We report the case of a 36 year old Hispanic male trail runner with a painless atrophic plaque to the mid lateral right leg diagnosed as localized cutaneous leishamaniasis with the species identified as L. *Mexicana on tissue culture*. The patient underwent spontaneous resolution of the lesion with no pharmacologic intervention.

Clinical synopsis

A 36 years old Hispanic male presented to outpatient dermatology consult with a chief complaint of a non-painful ulcer to the mid right lateral leg of three months duration that started with itching followed by mild scaling and non purulent exudate a month later. He self-treated the area with neosporin and hebiclens unsuccessfully. He denied other systemic symptoms such as fevers, fatigue and weight loss. Apart from a trip to Cancun, Mexico two years prior, he denied any foreign travel around the time a he first noticed the lesion. His extracurricular activities involved bushy trail running and his last run before developing the lesion was in trails around Houston and Austin. He denied having any immunosuppressive condition or being on immune suppressive medication or therapy.

Case Report (con't)

Exam: Physical exam was notable for a brown solitary atrophic plaque to the right lateral leg with an erythematous center and greyish violaceous outer rim with fibrinous exudate (Fig 1). No swelling, lymphadenopathy, tenderness on palpation or anesthesia to the area was noted on exam. No other ulcers, plaques and patches were present on exam including mucosal surface. The rest of the physical exam was unremarkable.

Laboratory and Diagnostic Findings A 4mm perilesional punch biopsy was obtained from the area. Histopathology analysis of the specimen revealed numerous amastigote present within vacuolized histiocytes, consistent with Leishmaniais on H & E (Fig 2a & 2b). A culture medium of Novy-MacNeal-Nicolle (NNN) was provided gratis from the CDC and another biopsy specimen was obtained from the lesion for invitro culture identification of leishmaniasis and PCR speciation by the CDC. Culture results were confirmatory for leishmaniasis with Leishmania *Mexicana identified* through DNA sequencing.

Intervention: The *L. Mexicana* species is not associated with an increased risk of mucosal leishmaniasis or sever disseminated leishmaniasis in otherwise health individuals. Taking into consideration that the patient's solitary lesion, non immunocompromised state and no other systemic symptoms related to the infection, clinical observation with close follow up and no pharmaceutical therapy was deemed appropriate. Intervention with cryotherapy, topical paromycin and or intralesional pentavalent antimonial was planned should no spontaneous healing of lesion be observed within 6 months.

Response to Treatment: Our patient reported via phone that area healed within three months pf visit with a scar to area. He felt satisfied with outcome and did not think he needed another dermatology visit thus refused re-examination and was lost to follow up.

Figures

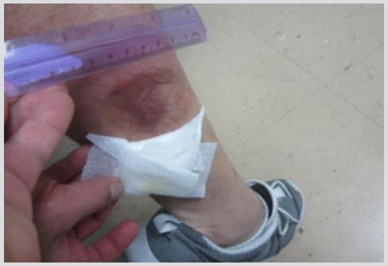


Figure 1: Solitary atrophic plaque to the right mid lateral leg with dark erythematous center and pink outer rim with greyish fibrinoid exudate.

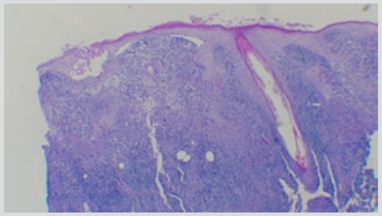


Fig 2a:
On low power there was ulceration of epidermis with ,dense mixed granulomatous dermal infiltrate of lymphocytes, histiocytes, plasma cells, neutrophils, and multinucleated giant cells; occasional caseation necrosis.

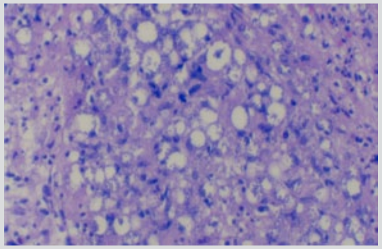


Fig 2b: On high magnification numerous leishmania amastigote organisms present within vacuolized histiocytes with margination around the edge of a clear space in the tissue like flashing lights around the edge of a dressing room mirror commonly referred to as the 'marquee sign.'

Discussion

According to the World Health Organization, leishmaniasis is one of seven most important tropical zoonoses.[8-9] Its manifestations vary in degree of severity depending on the species involved and the immune response of patients.[7] It can present as self-limited skin ulcers to the most severe form where infection can cause multisystem failure secondary to hemorrhage and thrombocytopenia. Our patient presented with the localized cutaneous variant (LCL). Cutaneous Leishmaniasis can be caused by L. *tropica* in the Eastern Hemisphere or L. *Mexicana* in Mexico and Central America. The sandfly, bites usually occur in exposed areas most commonly on ears, nose, upper extremities and ankles.[10] The parasite has an incubation period of 1-4 weeks but may last several years.[11] Initially, it presents with erythematous papules with pruritus in some patients. The lesion size can range from 1 to 10 millimeters. After 48 hours, it converts to a vesicle then into a pustule. Eventually, it may break due to trauma, revealing an ulcer with round borders and sharp edges.[7] The the cutaneous variants can be self limiting based on the variable species of Leishmania. L major, L mexicana complex and cutaneous lesions associated with L donovani complex are usually self-limit within 3 to 6 months; for L braziliensis complex and L tropica, it often takes up to 1 year; and for L *aethiopica* this may range from 6 months to several years.

Diagnosis is usually made by clinical symptoms and epidemiological context. The protozoa can be found on skin scrapings of lesions. Histopathological studies reveal epidermal hyperplasia or atrophy with infiltration of macrophages, lymphocytes and plasma cells with localized necrotic areas.[7] Parasites known as amastigotes, can be found intracellularly within cytoplasmic vacuoles on histiocytes during early stages. During late stages, a lympho-histiocytic infiltrate itis seen within infected macrophages. PCR shows 100% specificity for CL.[7]

There is no general consensus of drug therapies.[12] Treatment options include chemotherapy, cryotherapy, systemic treatments, thermotherapy and local therapy in the form of ointment treatment.[13] Local therapy is reasonable for patients with uncomplicated CL who are not healing spontaneously and/or those pursuing therapeutic intervention. Topical paromycin or intralesional pentavalent antimonial can be used. Some studies describe a combination of miltefosine and thermotherapy has been proven an effective alternative.[14-16]

Conclusions

Management of Leishmaniasis is dependent upon severity of clinical manifestations and strains involved. Clinical observation is a reasonable option for immunocompetent patients with uncomplicated lesions that are healing spontaneously and not associated with MCL such as our patient and should be considered especially in cases where potential side effects to medications is of greater concern and cosmetic appearance of scar is not an issue to the patient.

References

Bahrami F, Harandi AMSources

Bahrami F, Harandi AM, Rafati S. Biomarkers of Cutaneous Leishmaniasis. Frontiers in Cellular and Infection Microbiology. 2018;8:222. doi:10.3389/fcimb.2018.00222.

Contreras I, Estrada JA, Guak H, et al. Impact of Leishmania mexicanaInfection on Dendritic Cell Signaling and Functions. Kelly BL, ed. PLoS Neglected Tropical Diseases. 2014;8(9):e3202. doi:10.1371/journal.pntd.0003202.

Herwaldt BL (1999) Leishmaniasis. The Lancet 354: 1191–1199.

Patino LH, Mendez C, Rodriguez O, et al. Spatial distribution, Leishmaniaspecies and clinical traits of Cutaneous Leishmaniasis cases in the Colombian army. Al-Salem WS, ed. PLoS Neglected Tropical Diseases. 2017;11(8):e0005876. doi:10.1371/journal.pntd.0005876.

Sengupta PC, Bhattacharjee B. Histopathology of post kala-azar dermal leishmaniasis. J Trop Med Hyg 1953;56: 110-6.

Amita Mittal, Vishvabhavan Pandya, Kirti S Parmar, FE Bilimoria. Study of the 2 cases of cutaneous leishmaniasis. Indian Journal of Dermatology. 2005; 50: 233-235.

Torres-Guerrero E, Quintanilla-Cedillo MR, Ruiz-Esmenjaud J, Arenas R. Leishmaniasis: a review. F1000Research. 2017;6:750. doi:10.12688/f1000research.11120.1.

Vargas-Martínez F, Torres-Guerrero E, Quintanilla-Cedillo MR, et al. : Leishmaniasis en México. Academia Mexicana de Dermatología, Colegio de Dermatólogos de Yucatán A. C., Fundación Mexicana para la Dermatología, Universidad Autónoma de Campeche y Secretaría de Salud, México.2013.

Andrade-Narváez FJ, Vargas-González A, Canto-Lara SB, et al. : Clinical picture of cutaneous leishmaniases due to *Leishmania (Leishmania)* mexicana in the Yucatan peninsula, Mexico. *Mem Inst Oswaldo Cruz.* 2001;96(2):163–7. 10.1590/S0074-02762001000200005

Incháustegui A: De la leishmaniosis americana y de la úlcera de los chicleros en México. Tesis, Universidad Nacional de México.1918.

Vera-Izaguirre D, Vega-Memije E, Quintanilla Cedillo M, et al. : Leishmaniasis revisión. *DCMQ.*2006;4(4):252–260.

Mishra J, Saxena A, Singh S. Chemotherapy of leishmaniasis: past, present and future. Curr Med Chem. 2007;14(10):1153–69.

A.Oryan, E.Bemani, S.Bahrami. Emerging role of amiodarone and dronedarone, as antiarrhythmic drugs, in treatment of leishmaniasis. Acta Tropica. Volume 185, September 2018, Pages 34-41.

Reithinger R, Dujardin J, Louzir H, et al. : Cutaneous leishmaniasis. *Lancet Infect Dis.*2007;7(9):581–96. 10.1016/S1473-3099(07)70209-8.

Sundar S, Jha TK, Thakur CP, et al. : Oral miltefosine for Indian visceral leishmaniasis. *N Engl J Med.* 2002;347(22):1739–46. 10.1056/NEJMoa021556

Bhattacharya SK, Jha TK, Sundar S, et al. : Efficacy and tolerability of miltefosine for childhood visceral leishmaniasis in India. *Clin Infect Dis.* 2004;38(2):217–21. 10.1086/380638 .

Mohs Micrographic Surgery for Primary Cutaneous Ewing Sarcoma

Raymond E. Kleinfelder, DO[1], Drew Taylor, MD[2,3], Eduardo Weiss, MD[2,3]

[1]LECOMT/Larkin Community Hospital - Palm Springs Campus, Dermatology Residency Program, Hialeah, FL
[2]Hollywood Dermatology & Cosmetic Specialists, Hollywood, FL
[3]Micrographic Surgery and Dermatologic Oncology Fellowship, Skin Institute of South Florida, Coral Springs, FL

Abstract

Primary cutaneous Ewing sarcoma (PCES) is an exceedingly rare neoplasm with less than 100 cases reported in the literature. Herein we present a case of PCES that developed in a 45-year-old male and was successfully managed with Mohs Micrographic Surgery (MMS) and adjuvant radiation therapy without chemotherapy. The patient has had no evidence of recurrence in the past 24 months of follow-up. We believe this to be the first reported utilization of MMS in the management of PCES.

Case Report

A 45-year-old male presented with a three-month history of an asymptomatic, enlarging lesion on the left anterior shoulder. The lesion was a dome-shaped, red nodule measuring one-centimeter in diameter. Histopathology demonstrated a malignant small round cell neoplasm (Figure 1) with strong, diffuse CD99-positivity. Other immunohistochemical markers, including S100, HMB-45, CK20, CD56, chromogranin, and desmin were all negative, ruling-out entities such as melanoma, Merkel cell carcinoma, and rhabdomyosarcoma. With exclusion of other diagnoses, morphologic and immunohistochemical findings were consistent with Ewing sarcoma.

Upon follow-up (Figure 2A), no lymphadenopathy was noted on examination. Pre-operative positron emission tomography – computed tomography (PET-CT) did not detect any abnormalities in the lymph nodes or internal organs, and bone marrow aspiration was negative for involvement. After ruling-out an internal source of metastasis, the final diagnosis was primary cutaneous Ewing sarcoma (PCES).

The patient was presented with various treatment options, and ultimately Mohs micrographic surgery (MMS) with adjuvant radiation was selected as the ideal therapeutic approach. The patient underwent Mohs with clearance of tumor margins in one stage (Figure 2B). Permanent sections confirmed eradication of the tumor. The defect was repaired in a linear manner (Figure 2C) in order to preserve the architecture for future imaging and potential sentinel lymph node biopsy (SLNB).

Radiotherapy to the tumor bed was performed with a single dose of 55.80 Gy, without concurrent radiation of the ipsilateral axillary and supraclavicular lymph node basins. We elected not to pursue adjuvant chemotherapy due to a lack of systemic involvement and recent reports suggesting that risks of treatment sequelae outweigh the risk of recurrence of tumors that are adequately excised. The patient has been examined every three months and surveyed with an annual MRI for the past two years. The patient has exhibited no evidence of recurrence over the past 24-months post-operatively (Figure 2D). We report the first case of PCES successfully managed with MMS and adjuvant radiation with no evidence of recurrence.

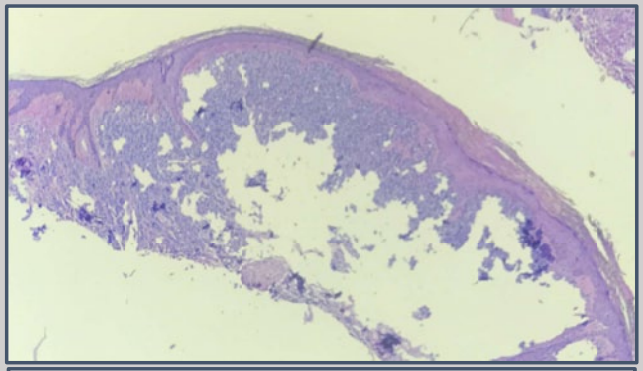
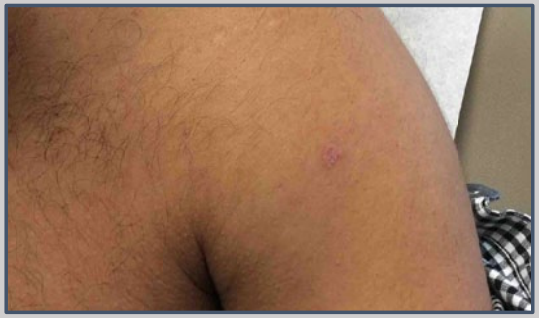
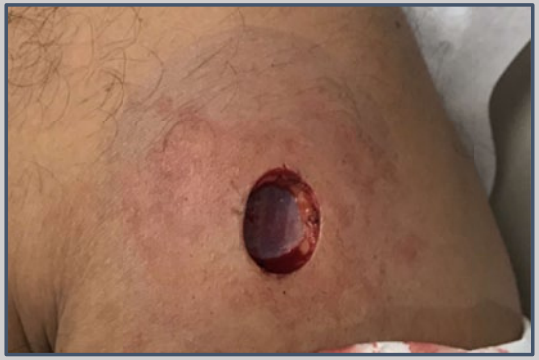
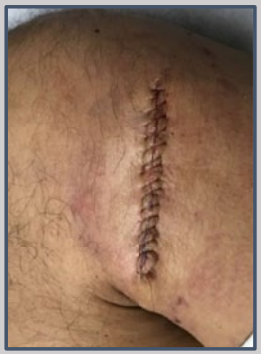


Figure 1: Small round cell tumor, H&E, original magnification X10.







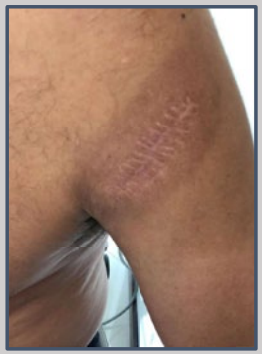


Figure 2: (A) Pre-operative, post-biopsy tumor site , **(B)** Intra-operative, tumor extirpation in one stage, **(C)** Linear closure of defect to preserve architecture, **(D)** Two-year follow-up with no evidence of recurrence.

Discussion

PCES belongs to the family of neuroectodermal tumors that includes Ewing sarcoma, primitive neuroectodermal tumor (PNET), and Askin tumor of the chest wall (1). The osseous form of Ewing sarcoma is the second most common primary bone tumor of children and adolescents. Despite intensive management approaches, Ewing sarcoma of the bone carries a poor prognosis, with five-year survival rates averaging 60.2% (2). In contrast, PCES, while much rarer, carries a more favorable prognosis compared to its osseous counterpart, with ten-year survival rates reaching 91% (1). This difference in prognosis can be attributed to earlier detection and a smaller tumor burden resulting in lower rates of metastasis. Recent studies also suggest that distinct cells of origin and different cooperative mutations may alter the metastatic potential of extraskeletal variants of Ewing sarcoma, though these theories require further analysis (2).

All forms of Ewing sarcoma exhibit similar biology. Tumors are composed of small round basaloid cells that express CD99 – a product of the *MIC2* gene – in a characteristic membranous pattern (3). A chromosomal translocation t(11;22) between the *EWSR1* gene on chromosome 22 and the *FLI1* gene results in a fusion oncogene (1). Notably, this translocation is not specific to Ewing sarcoma; however, after ruling-out other CD99-positive entities, Ewing sarcoma remains as a diagnosis of exclusion.

Given the rarity of PCES, management recommendations have been extrapolated from experience in treating Ewing sarcoma of the bone. First-line therapy is extensive surgical removal followed by several rounds of multi-agent chemotherapy, and adjuvant radiotherapy for inadequately excised tumors (2). Given the dearth of cases and knowledge about PCES, we questioned the utility of such an aggressive strategy in the treatment of a localized cutaneous tumor. A recent publication described a large PCES limited to the foot with no systemic involvement that was successfully excised with 1.5 cm margins and no adjuvant chemoradiation (4). Further, a review of 61 patients by Delaplace, et al. emphasized the increased morbidity and mortality in patients treated with systemic chemotherapy, and suggested a less toxic treatment approach, given the epidemiological and prognostic differences between PCES and Ewing sarcoma of the bone (1). Collier et al. found a 90% survival rate among PCES patients who received excision and chemotherapy, while patients who had excision alone had a survival rate of 85.7% (5). These new data suggest that chemotherapy may not be necessary for tumors that can be managed with local therapy. However, without adequate local control, survival dropped to 66.7% in chemotherapy patients and 0% survival in those without chemotherapy, highlighting the importance of local tumor control (5).

Given these recent data suggesting a more conservative management approach to PCES, we believed MMS to be ideal for our patient. We achieved clearance of tumor margins in one stage and permanent sections confirmed tumor eradication. In concert with oncology, we elected to incorporate a single dose of post-operative radiotherapy to further ensure local tumor suppression. We chose not to pursue chemotherapy given the recent data suggesting that the risk of long-term sequelae of chemotherapy may outweigh the risk of recurrence or metastasis for small tumors that are completely excised.

Conclusions

To our knowledge, this is the first case of PCES successfully treated with MMS. After two years of follow-up, our patient remains disease-free. We believe this confirms our hypothesis that PCES should be approached differently from its osseous counterpart. Further cases will be necessary to determine if MMS is an appropriate therapeutic modality in the management of PCES.

References

1. Delaplace M, Lhommet C, de Pinieux G, Vergier B, de Muret A, Machet L. Primary cutaneous Ewing sarcoma: a systematic review focused on treatment and outcome. Br J Dermatol. 2012;166(4):721-6.
2. Tavakkoli M, Mueller L. Cutaneous Ewing Sarcoma and Ewing Sarcoma of the Bone: Distinct Diseases. Case Rep Oncol. 2018;11(3):729-34.
3. Dagher R, Pham TA, Sorbara L, Kumar S, Long L, Bernstein D, et al. Molecular confirmation of Ewing sarcoma. J Pediatr Hematol Oncol. 2001;23(4):221-4.
4. Grassetti L, Torresetti M, Brancorsini D, Rubini C, Lazzeri D, Di Benedetto G. A peculiar case of large primary cutaneous Ewing's sarcoma of the foot: Case report and review of the literature. Int J Surg Case Rep. 2015;15:89-92.
5. Collier AB, 3rd, Simpson L, Monteleone P. Cutaneous Ewing sarcoma: report of 2 cases and literature review of presentation, treatment, and outcome of 76 other reported cases. J Pediatr Hematol Oncol. 2011;33(8):631-4.

An Atypical Presentation of Langerhans Cell Histiocytosis

Beaumont

Lauren Law DO, Lynn Sikorski DO, Sean Stephenson DO

Department of Dermatology■ Beaumont Hospital, Farmington Hills, MI

INTRODUCTION

Langerhan cell histiocytosis (LCH) is a rare condition occurring predominantly in children and rarely in adults. It is reported to occur in 1-2 cases per million in adults. It is a proliferation of histiocytes and is classified according to the extent systemic involvement. It may appear as a solitary bone lesion or systemic disease. Presentation varies greatly. LCH can affect any organ system and most commonly affects skin, lung and bones in adults. LCH may have a chronic course and can recur after resolution.

CLINICAL CASE

A 61 year-old male presented to the clinic complaining of a “spot”. He stated that it had been present for an unknown duration of time, he had no treatment prior to this visit and he was asymptomatic. His past medical history included hyperlipidemia, coronary artery disease with stent placement, hypertension, eosinophilic esophagitis, and gastroesophageal reflux disease. Current medications included ticagrelor, atorvastatin, and blood thinner of unspecified type. Social history included everyday smoker (5 cigarettes per day) and everyday drinker (1-2 glasses per day).

Physical exam revealed a 6 millimeter violaceous nodule at the left rib cage. A shave biopsy was performed and the specimen was sent for pathological examination.

Histopathological analysis revealed focal Langerhans cell and Langerhans microabscesses within the epidermis. Mixed inflammatory cell infiltrate comprised of epithelioid histiocytoid cells, lymphocytes, and many scattered eosinophils in the dermis. (FIGURE 1, 2) An S100 immunohistochemical stain was performed and labeled many Langerhans cells and Langerhans microabscesses in the epidermis and epithelioid cells within the dermis. (FIGURE 3, 4) A CD1a immunohistochemical stain was performed and labeled Langerhans cells within the epidermis and epithelioid cells within the dermis confirming their origin as Langerhans cells. (FIGURE 5, 6) A Langerin (CD207)immunohistochemical stain was performed and identified birbeck granules. (FIGURE 7, 8) Immunohistochemical staining with CD68 was performed and did not label epithelioid cells. (FIGURE 9, 10)

Patient was referred to Mayo Clinic where he received a positron emission tomography (PET) scan that revealed disease localized to the skin. Patient is not currently on any therapy for the lesions. He is scheduled to follow up at Mayo Clinic in 1 month for a bone marrow biopsy.

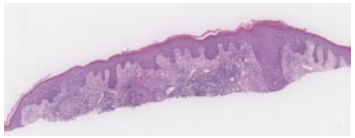


FIGURE 1: Hematoxylin and Eosin Stain at 4x Magnification
Magnification

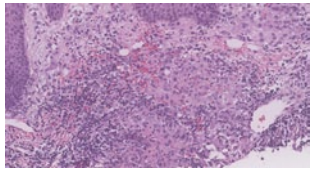


FIGURE 2: Hematoxylin and Eosin Stain at 20x

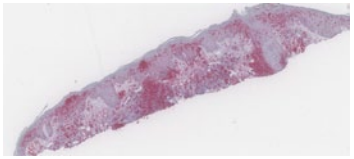


FIGURE 3: S100 at 4x Magnification
Magnification

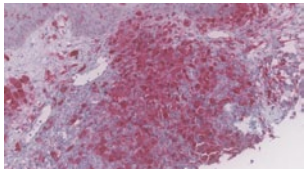


FIGURE 4: S100 at 20x

FIGURE 5: CD1a Stain at 4x Magnification

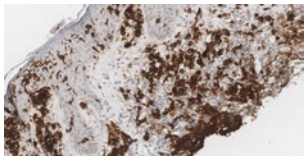


FIGURE 6: CD1a Stain at 20x

FIGURE 7: Langerin (CD207) Stain at 4x Magnification
(CD207) Stain at 20x Magnification

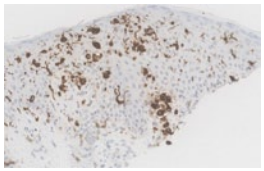


FIGURE 8: Langerin

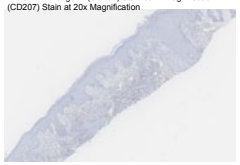


FIGURE 9: CD68 Stain at 4x Magnification
Magnification

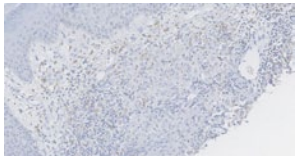


FIGURE 10: CD68 Stain at 20x

CLINICAL SIGNIFICANCE

LCH is a very rare disorder in adults. Classification is based on the number of organ systems involved with one system labeled as unifocal and two or more systems labeled as multifocal. Any organ of the body may be affected and in 33% of cases the skin is involved. Skin lesions may have many different appearances including erythematous to brown papules, nodules, plaques, vesicles, or ulcers on any cutaneous surface, however they are usually painful rather than pruritic. When LCH is detected in a skin biopsy, additional work-up is warranted to evaluate for systemic involvement. This includes complete blood count (CBC), complete metabolic panel (CMP), erythrocyte sedimentation rate (ESR), coagulation studies, full body imaging and referral to oncology. Associations with poor prognosis are mutation in the BRAF V600E gene, involvement of the liver, lungs, spleen and hematopoietic system, and failure to respond to therapy after 6 weeks. LCH may have a chronic course and recur after resolution therefore long-term follow up is imperative.

DISCUSSION

While LCH is a rare disease, it is a potentially fatal disease practitioners need to be aware of. The presentation is often non-specific, but when identified or suspected systemic involvement must be ruled out. In our case the patient had what appeared to be an isolated benign dermatofibroma, however it was LCH. A significant risk of delayed sequelae, leukemia or lymphoma, and mortality have been identified in all ages and therefore identification of the LCH and long-term follow up are vital. Due to the rare incidence of LCH, no clinical trials have been performed on how to guide practitioners. At this time, identifying the disorder and referral to oncology are the standard of practice in dermatology.

REFERENCES

Alikhan, A., Hocker, T. *Review of Dermatology*. Elsevier, 2017.
Arico, M, et al. “Langerhans Cell Histiocytosis in Adults. Report from the International Registry of the Histiocyte Society.” *European Journal of Cancer (Oxford, England : 1990)*., U.S. National Library of Medicine, Nov. 2003, www.ncbi.nlm.nih.gov/pubmed/14556926.
Bolognia, Jean, et al. *Dermatology*. Elsevier Saunders, 2012.
Elston, D., et al. *Dermatopathology*. Elsevier, 2015.
Ma, J., et al. “LANGERHANS CELL HISTIOCYTOSIS IN ADULTS IS ASSOCIATED WITH INCREASED HEMATOLOGIC AND SOLID MALIGNANCIES.” *Hematological Oncology*, 7 June 2017, onlinelibrary.wiley.com/doi/10.1002/hon.2439_200/full.

Blastic Plasmacytoid Dendritic Cell Neoplasm: A Cutaneous Herald

Danielle R. Lazzara, DO[1], Martin Zaiac, MD[2], Brad P. Glick, DO, MPH, FAOCD, FAAD[3]

[1]LECOMT/Larkin Community Hospital – Palm Springs Campus, Dermatology Residency Program, Hialeah, FL
[2]Greater Miami Skin & Laser Center, Miami, FL
[3]Glick Skin Institute, Margate, FL

ABSTRACT

Blastic plasmacytoid dendritic cell neoplasm (BPDCN) is an extremely rare and aggressive hematopoietic malignancy that typically manifests with cutaneous lesions that herald the development of bone marrow involvement and fulminant acute leukemia. Diagnosis is often dependent on recognition of skin lesions, which express the characteristic immunophenotype CD4, CD56, and CD123. Patient prognosis is poor as disease tends to relapse despite initiation of intensive multi-agent chemotherapeutic regimens. Recent FDA approval of CD123-targeted therapy, tagraxofusp-erzs, in treatment-naive and previously treated patients offers promising results per clinical trials and may improve patient survival.

CASE REPORT

A 77 year old Caucasian male presented with a 2 month history of asymptomatic nodules located to the back and a 'bruise-like' patch to the right medial knee. Lesions were reported to rapidly enlarge and disseminate within days of initial presentation. Review of systems was negative for fatigue, fever, chills, night sweats, cough, shortness of breath, chest pain, history of frequent infections, easy bruising/bleeding, or weight loss.

Physical examination was significant for multiple violaceous plaques and nodules scattered to the back and chest (Figure 1). An 8.0 x 6.7 cm infiltrative, violaceous tumor was present on the right medial knee (Figure 2). Total body surface area of involvement estimated to be 1.2%. No lymphadenopathy or hepatosplenomegaly was appreciated.

Histopathology revealed a diffuse monomorphous infiltrate of the papillary dermis composed of medium-sized cells with blastic morphology. Immunohistochemistry (IHC) demonstrated positive staining for CD4, CD56, CD123, TdT, CD43, & CD45. Staining was negative for T cell (CD3, CD5), B cell (CD20, PAX-5), myeloid (MPO), monocyte (CD68, lysozyme), and hematopoietic stem cell (CD117, CD34) lineage markers. EBER in situ hybridization was negative and Ki-67 proliferation index was 10-20%.

CBC and CMP were within normal limits. Patient was extensively worked up for extracutaneous disease including repeat blood work with serum immunofixation electrophoresis and CT Chest, Abdomen and Pelvis with contrast, which were negative for disseminated disease. Bone marrow biopsy was consistent with a concurrent myeloid neoplasm.

Patient will begin tagraxofusp-erzs transfusion therapy.

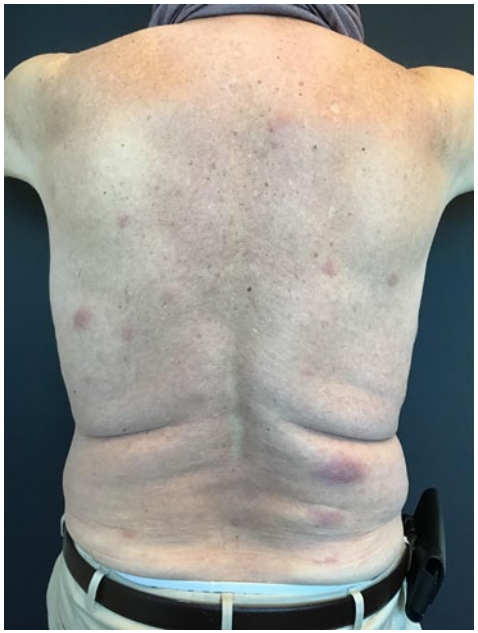


Figure 1. Multiple violaceous nodules to back.

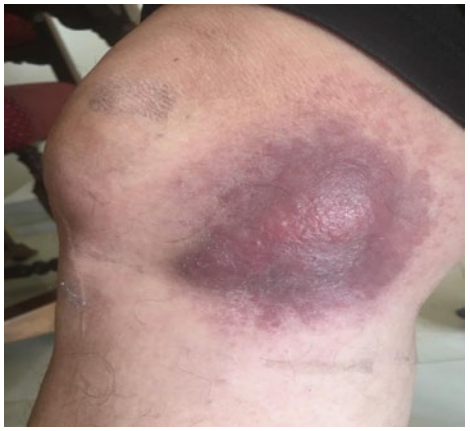


Figure 2. Violaceous indurated tumor to R medial knee

DISCUSSION

BPDCN is estimated to represent <1% of all hematologic malignancies and cutaneous lymphomas (1-3). Less than 300 cases are described in the literature worldwide (2,4). BPDCN most commonly affects elderly, male patients. Initial presentation with solitary or multifocal cutaneous lesions is reported in greater than 90% of affected individuals (4). Lesions appear as 'bruise-like' patches or red-to-violaceous infiltrative nodules that primarily present on the upper trunk or face and rapidly progress in the absence of treatment (1,3). Frequently the disease is already disseminated to the peripheral blood, lymph nodes, and bone marrow at time of diagnosis. BPDCN often co-exists with an underlying myelodysplastic syndrome and will inevitably develop into an acute leukemia. Generally, patients are asymptomatic and rarely exhibit B symptoms (1-4). The characteristic IHC phenotype expressed by BPDCN is CD4, CD56, CD123, TCL1, and TdT (2,3,5). Lineage specific antigen markers for T-cells, B cells, cytotoxic, and myelomonocytic cells are usually negative, with the exception of a few myeloid (CD68, CD33) and T-cell associated antigens (CD2, CD7, CD43, CD45RA) detected in a substantial number of cases. EBV by in situ hybridization are consistently negative (5). Overall patient prognosis is poor, with a median survival of 12-14 months. Due to the aggressive nature of BPDCN, it is imperative that patients begin systemic therapy irrespective of localized or disseminated disease. Unfortunately, there is a lack of consensus on optimal treatment guidelines and few therapeutic options exist. Sustained remission has been achieved using acute lymphoblastic leukemia (ALL)-like protocols followed by allogeneic stem cell transplantation (1,4). To date, bone marrow transplantation has been the only treatment to achieve long-term survival, albeit inconsistently, and many patients are not suitable candidates due to advanced age (2-3). Tagraxofusp-erzs, a diphtheria toxin conjugated to IL-3, targets IL-3 receptor (CD123) and is a promising new treatment for patients diagnosed with BPDCN.

CONCLUSION

It is critical for dermatologists to be aware of the clinicopathologic correlation of BPDCN to better facilitate early diagnosis and initiation of treatment.

REFERENCES

1. Honan AE, Mitchell L, Jury C. Blastic plasmacytoid dendritic cell neoplasm (BPDCN) presenting as bruise-like plaques. J. Am. Acad. Dermatol. 2018;79(3):AB57.
2. Owczarczyk-Saczonek A, Sokołowska-Wojdyło M, Olszewska B, et al. Clinicopathologic retrospective analysis of blastic plasmacytoid dendritic cell neoplasms. Postepy Dermatol Alergol. 2018;35(2):128-138.
3. Petrella JF, Beylot-Barry M, Bagot M, et al. Blastic plasmacytoid dendritic cell neoplasm: clinical features in 90 patients. Br. J. Dermatol. 2013;169:579-586.
4. Allam SH, Collie AMB, Bergfeld WF. Blastic plasmacytoid dendritic cell neoplasm. A case report. J. Am. Acad. Dermatol. 2015;72(5):AB82.
5. Shi Y, Wang E. Blastic plasmacytoid dendritic cell neoplasm. A clfinicopathologic review. Arch. Pathol. Lab. Med. 2014;138:564-568.

Shades of Acquired Dermal Melanocytosis

Erin Lowe DO, Alexa Broderick BS, Richard Miller DO, Michael Heaphy MD

Introduction

- Dermal melanocytoses are distinct melanocytic lesions characterized by a blue-gray discoloration of large portions of the skin.
- Subtypes include a wide variety of congenital and acquired, histologically indistinguishable entities characterized by an intradermal proliferation of fusiform pigment-bearing melanocytes in the absence of melanophages.
- The most frequent dermal melanocytoses are of the congenital type and include nevus of Ota, nevus of Ito, and Mongolian spots. These are usually present at birth and occur most frequently in Asian populations.
- Acquired dermal melanocytoses (ADM) occurring later in life and in non-Asian patients are rare. Herein, we present four unusual cases of ADM.

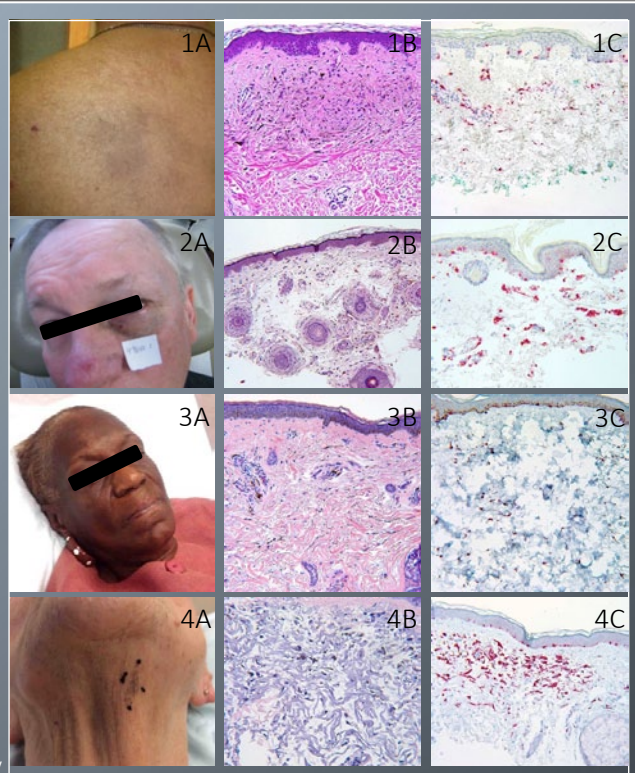
Case Series

1. 57 year-old African American male with acquired dermal melanocytoses of the upper back.
2. 62 year-old Caucasian male with acquired unilateral nevus of Ota with ocular involvement.
3. 73 year-old African American female with acquired bilateral nevus of Ota (Hori's nevus).
4. 73 year-old Caucasian male with "patch-type" blue nevus of the anterior neck.

Discussion

During embryogenesis, melanocytes are found diffusely throughout the dermis. By the end of gestation, these melanocytes have migrated to the dermoepidermal junction. Defect in migration of pigmented neural crest cells result in deep melanin in the skin and associated tyndall effect, appearing clinically as dermal melanocytoses. Such defects usually present at birth or appear within the first year of life, most commonly in Asian individuals. Congenitally acquired nevus of Ota and Ito remain stable throughout life, while Mongolian spots generally regress within a few years.

There are seldom reports of dermal melanocytoses acquired in non-Asian adults. The pathogenesis is uncertain but reactivation of ectopic latent dermal melanocytes has been suggested as a possible cause. The dormant dermal melanocytes may be reactivated by exogenous agents such as solar radiation, local inflammation, trauma, drugs, hormone therapy with estrogen or progesterone, or other yet undefined stimuli. Of note, the individuals presented here were on no medications previously reported to induce ADM.



Four non-Asian patients presented with acquired dermal melanocytosis of varying sites. Photos depict (A) clinical features; (B) H&E stain displaying very sparse but diffuse proliferation of small, spindled, dendritic melanocytes with pigmented cytoplasm splayed between collagen bundles in the dermis; (C) Melan-A stain highlighting ectopic melanocytes in dermis.

Treatment

- Therapy options are the same for congenital and acquired dermal melanocytoses.
- Laser is the treatment of choice, using selective photothermolysis to target the chromophore melanin.
- Q-switched laser surgery with an extremely high power, short pulse duration (nanoseconds) is the preferred waveform because the melanin target molecules are very small with short thermal relaxation times.
- The Q-switched ruby is preferred over the Q-switched alexandrite and Nd:Yag as it emits radiation with Increased absorption and selectivity for melanin.
- Frequency of treatments depends on the pigment intensity. Overall, after 4-8 treatments skin pigmentation is reduced dramatically or removed in 90% of cases, with a less than 1% risk of scarring.
- Less successful treatment methods reported include superficial excision, bleaching agents, chemical peels, and electric cauterization.

References

1. Harrison-Balestra C, Gugic D, Vincek V. Clinically distinct form of acquired dermal melanocytoses with review of published work. J Dermatol 2007 Mar;34(3):178-82.
2. Navarro N, Orland A, Garrido E, Gargia RJ, Ceballos E. Unusual acquired dermal melanocytoses on the trunk. Int J Dermatol. 2008 Mar;47(3):307-8.
3. Rios-Martin JJ, Pinto-Morales W, Marcos-Dominguez A, Gonzalez-Campora R. Acquired nonfacial dermal melanocytosis. Actas Dermosifiliogr. 2011 Sep;102(7):556-7.
4. Rubin A, Van Laborde S, Stiller M. Acquired dermal melanocytosis: appearance during pregnancy. J Am Acad Dermatol. 2001 Oct;45(4):609-13.
5. Kosumi H, Miyauchi T, Nomura T, Suzuki S, Ohguchi Y, Nomura A, Shimizu H. Diagnostic features of acquired dermal melanocytoses of the face and extremities. Clin Exp Dermatol. 2018 Jun 27. Doi: 10.111/ced.13546. EPub ahead of print.
6. Jun JY, Byun HJ, Oh SJ, Oh SH, Park JH, Lee JH. Acquired dermal melanocytoses confined to the hand. Ann Dermatol. 2018 Jun;30(3):380-1.
7. Kok WL, Chen Q, Lee SSJ, Chua SH, Ng SK. A case series of imatinib-induced generalized hypopigmentation and progression of existing acquired dermal melanocytoses. J Dermatolog Treat. 2017 Dec;28(8):762-3.
8. Chen X, Zhang Q, Chen L. Acquired dermal melanocytoses on the back. Clin Exp Dermatol. 2015 Jan;40(1):86-8.
9. Tumbull JR, Assaf C, Zouboulis C, Tebbe B. Bilateral naevus of Ota: a rare manifestation in a Caucasian. J Eur Acad Dermatol Venereol. 2004 May;18(3):353-5.
10. Lee JY, Lee JS, Kim YC. Histopathological features of acquired dermal melanocytosis. Eur J Dermatol. 2010 20(3):345-8.
11. Massi G, LeBoit PE (2014). Histological diagnosis of nevi and melanoma. New York: Springer.
12. Imagawa K, Suzuki S, Fujibayashi M, Kono T, Miyasaka M. Laser Treatment of Dermal Melanocytosis. Researchgate.net. April 2015; 36(1):77-81

ALOPECIA AREATA AFTER BONE MARROW TRANSPLANT FROM ALOPECIA UNIVERSALIS-AFFECTED MONOZYGOTIC TWIN

Morgan Mackey, D.O., PGY-3, V. Thomas Mackey, D.O.
Advanced Desert Dermatology, Peoria, AZ

ABSTRACT

Alopecia areata is an autoimmune disease that leads to non-cicatricial hair loss, and clinically patients are found to have small patches of hair loss on the scalp. It can progress to loss of all the hair on the scalp (alopecia totalis) and even a total loss of hair on the body (alopecia universalis). It can be a chronic disease with relapses that can have a negative impact on the patient's self-esteem, and lead to psychiatric comorbidities.

We report on a case of a 55 year-old female diagnosed with leukemia who later developed alopecia areata after having a bone marrow transplant from her monozygotic twin sister. Her twin sister had alopecia universalis prior to the bone marrow transplant. This represents an uncommon occurrence, and one that demonstrates the frustration commonly encountered in treating alopecia areata.

INTRODUCTION

Alopecia areata is a disease which targets the hair follicles, leading to non-scarring hair loss that can involve parts of the scalp and/or the entire body. The cause of alopecia areata is not fully known, but it is believed to be an autoimmune disease leading to upregulation of inflammatory pathways and destruction of the hair follicle.[1] Alopecia areata is considered to be a T-cell-mediated process with $CD8^+$ T cells being the main cell type that initiates the process. Other cells involved natural killer cells, plasmacytoid dendritic cells, and are T helper and cytolytic T cells that attack the hair follicle leading to its destruction and alopecia.[2] Clinically the hair loss is commonly seen as round or oval patches, and "exclamation point" hairs are often seen at the periphery of alopecia areas.[3] It can progress to hair loss of the entire scalp (alopecia totalis) or to hair loss of the entire body (alopecia universalis). Alopecia areata is associated with other autoimmune and rheumatoid diseases, with atopic diseases, metabolic syndrome, *Helicobacter pylori* infection, lupus erythematosus, iron deficiency anemia, thyroid diseases, psychiatric diseases, vitamin D deficiency, and audiologic and ophthalmic abnormalities being more prevalent in these patients.[4]

HISTORY OF PRESENT ILLNESS

A 55-year-old female presented with a 12-year history of hair loss of the scalp. She was diagnosed with acute lymphoblastic leukemia in 2003. She has a twin sister who was diagnosed with alopecia universalis years prior. Our patient underwent a bone marrow transplant in 2004 with her twin sister being the donor. A few months after the transplant, our patient began having hair loss on her scalp. She denied any pruritus, pain, redness, or rash with the hair loss. She was diagnosed by another dermatologist with alopecia areata. It progressed to involve all of her scalp to the extent of being diagnosed with alopecia totalis. She has been in remission from the leukemia for a few years, but continues to have alopecia areata. During the 14 years of having alopecia areata, she would have exacerbations of the alopecia with significant stresses in her life. She presented to our clinic initially in 2016 with diffuse non-scarring hair loss on her scalp.

Her past medical history also includes hypothyroidism, basal cell carcinoma of the left shoulder, verrucous vulgaris on the right index finger, chronic nausea, and previous surgeries of her left ankle and foot for fractures. She does not smoke, denies drug use, and drinks alcohol seldom.

MANAGEMENT & CLINICAL COURSE

At the time of her presentation to our clinic, she had tried many different therapies over the years in attempts to manage her alopecia. She had already tried topical steroids, topical minoxidil, topical immunotherapy with squaric acid dibutyl ester, and light-based therapy with unsatisfactory hair regrowth. The best response to past treatments was with intralesional injections of triamcinolone (ILIs), although recurrence occurred with significant stresses in her life. She expressed her frustration with failed past treatments and again sought ILIs of triamcinolone. She received multiple ILIs of triamcinolone 5mg/mL every four weeks over the next five months with significant hair regrowth as response to the therapy. Subsequently, there was a gap of time before she returned again with her scalp involved considerably. Again, she sought therapy with ILIs. Lab studies including complete blood count, comprehensive metabolic panel, thyroid stimulating hormone, free T4, free T3, progesterone, estradiol, c-reactive protein, vitamin D levels, lipid panel, antinuclear antibody, and iron studies were normal except for mildly elevated cholesterol level. Discussion was had of other possible treatments that included JAK/STAT pathway inhibitors and other systemic therapies. She denied any other treatments other than ILIs, to which she has a temporary positive response.

DISCUSSION

Alopecia areata prevalence in the United States is ~0.1%. A genetic component in alopecia areata is well documented, with a 10-fold increased risk in first-degree relatives.[1] It has been reported there is a 55% concordance rate in monozygotic twins, indicating both factors of genetics and environment play a role.[5] Other reports have been presented of alopecia areata in twins.[5-7] Similar to this one, there is another case reported of a man who had chronic myelogenous leukemia and received a bone marrow transplant from a brother who had alopecia areata, and the patient went on to develop alopecia areata.[8] Rodriguez et al found alopecia areata concordant in 42% of 19 sets of monozygotic twins, with the average time interval between first onset of alopecia areata in one twin and onset in the second twin being 4.85 years.[5]

This case presents an uncommon presentation of alopecia areata after receiving a bone marrow transplant from the patient's monozygotic twin affected with alopecia universalis. The patient, despite periodic temporary response to ILI treatment, continues to have recurrences of the alopecia areata with significant stresses in her life.

REFERENCES

1. Strazzulaa LC, Wang EHC, Avila L, et al. Alopecia areata: Disease characteristics, clinical evaluation, and new perspectives on pathogenesis. *J Am Acad Dermatol*. 2018; 78:1-12.
2. Simakou T, Butcher JP, Reid S, et al. Alopecia areata: A multifactorial autoimmune condition. *J Autoimmun*. 2019;98:74-85.
3. Bolognia J, Schaffer JV, Cerroni L, eds. *Dermatology*. Fourth Edition. Vol 1. Elsevier Saunders; 2018; 1171-1174.
4. Lee S, Lee H, Lee CH, Lee W. Comorbidities in alopecia areata: A systematic review and meta-analysis. *J Am Acad Dermatol*. 2019;80:466-477.
5. Rodriguez T, Fernandes KE, Dresser KL, Duvic M. Concordance rate of alopecia areata in identical twins supports both genetic and environmental factors. *J Am Acad Dermatol*. 2010;61:525-527.
6. Cole GW, Herzhinger D. Alopecia universal is in identical twins. *Int J Dermatol*. 1984;23:283.
7. Scerri L, Pace JL. Identical twins with identical alopecia areata. *J Am Acad Dermatol*. 1992;27:766-767.
8. Barahmani N, Whaley K, Duvic M. Alopecia areata after allogenic bone marrow transplantation from an affected, human leukocyte antigen-matched sibling. *J Am Acad Dermatol*. 2003;49:1192.

Dermatitis Artefacta Mimicking Pyoderma Gangrenosum

Mitchell Manway, DO[1,2]; Andrew Newman, DO[1,2]; Jason Barr, DO[1,2]
[1]HonorHealth Scottsdale Dermatology Residency Program, Scottsdale, AZ; [2]Affiliated Dermatology, Scottsdale, AZ

HONORHEALTH

HONORHEALTH Academic Affairs

Background

Dermatitis artefacta (DA), also known as factitial dermatitis, is a condition whereby an individual performs self-induced skin damage as a means to consciously or unconsciously satisfy a desire to assume the role of an ill-patient. By definition, this condition should be distinguished from malingering as well as Munchausen syndrome, as those psychological entities possess other unique features and patterns. DA is more common in females, early adults, and those with underlying psychiatric diagnoses or external stressors.

Patients will rarely admit their role and are more likely to actively conceal their involvement in the development of cutaneous manifestations, thus presenting particularly unique and puzzling diagnostic challenges. Various techniques, instrumentation, and chemicals may be utilized by the patient to induce these skin changes, and multiple anatomical sites may be involved, but lesions more often appear within the background of normal skin and are usually within easy reach of the patient. Ulcerations are very common, but other morphologies can present and are only limited by each patients' level of motivation.[1,2]

Case Report

A middle-aged female presented with several large non-healing ulcers on the lower legs and left arm. The patient, who happens to be a retired nurse, stated that the lesions started over 4 months prior to presentation. On physical exam, large, deep, annular ulcerations were seen over the left arm and the bilateral lower legs. The most prominent lesions were noted on the left lower extremity (Figure 1 and Figure 2). Part of the initial work-up included venous and arterial doppler studies which were negative for evidence of vascular disease. The patient was therefore admitted to the hospital floor for non-healing ulcers with a clinical suspicion for pyoderma gangrenosum. She had asserted that in the past she had been diagnosed with inflammatory bowel disease by a gastroenterologist, however, this was not able to be corroborated by the medical team. While in the hospital, she was managed by a multidisciplinary team consisting of specialists in rheumatology, dermatology, and internal medicine. Accordingly, two punch biopsies were performed on lesions revealing a dense superficial mixed cell infiltrate including neutrophils, histiocytes, lymphocytes, and eosinophils dispersed around a significant bed of ulceration. No signs of malignancy were noted on histology. In addition, direct immunofluorescence studies were negative, and a gram stain and bacterial cultures were unremarkable, presenting only mixed normal skin flora. Likewise, specific cultures for fungus including cultures for mycobacterial organisms also proved negative.

After this thorough work-up and given the fact that the histological features were not consistent with pyoderma gangrenosum, a self-inflicted skin disorder was at that time suspected. Hence, a sitter was asked to watch the patient around-the-clock while in the hospital. One week following the initialization of the sitter, the patient's skin had improved dramatically. The patient's son did ultimately discover a bottle of sodium hydroxide accompanied by several vials of suspicious and unlabelled powders in the bedside belongings of the patient. As a result, what was originally thought very likely to be a case of pyoderma gangrenosum was later diagnosed as dermatitis artefacta.

Case Report

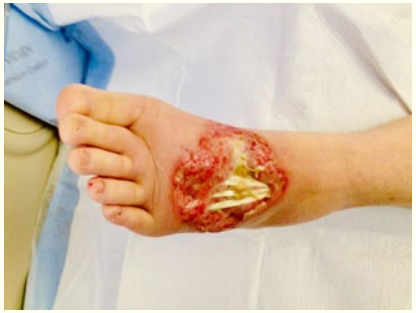


Figure 1. Dorsal foot ulcer clearly revealing muscle tendons

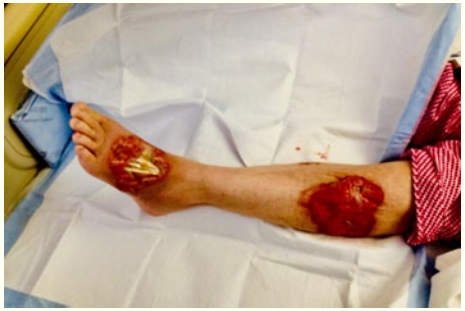


Figure 2. Multiple ulcers of the left lower extremity

Key Points

- **Dermatitis artefacta should be included in the differential diagnosis when skin disorders fail to respond to conventional therapies or when histological/clinical features are atypical.**
- **Patients will likely not admit or be aware of their role in the development of cutaneous manifestations.**
- **Dermatitis artefacta is more common in females, early adults, healthcare workers, and those with underlying psychiatric diagnoses or external stressors.**
- **Treatment of DA can be incredibly difficult, lengthy, and refractory and should involve a multidisciplinary approach including psychiatry/mental health.**

Discussion

Dermatitis artefacta is a diagnosis of exclusion, and thus some index of suspicion is absolutely necessary when testing and work-up yields no viable alternative diagnosis. The patient presented in this case exhibited many insidious but classical features of dermatitis artefacta including lack of supported alternative diagnosis, female gender, morphology of the wounds, as well as experience as a healthcare worker as a retired nurse. Healthcare workers are found to have higher incidence of DA and would likely be more knowledgeable and able to evade immediate detection through more effective means of self-trauma or possess the knowledge to feign a known cutaneous disease such as pyoderma gangrenosum (PG). Not surprisingly, other case reports of DA simulating PG have been reported.[3] Although there are no specific histological features for DA, biopsy and histological evaluation of the edge of a wound will likely provide the ability to rule out other considerations. Likewise, additional testing to rule out other potential causes such as infection, malignancy, or autoimmune etiology should also be performed, but DA should at least be considered sooner rather than later under appropriate circumstances.

Once a diagnosis of DA is assumed, treatment can be incredibly challenging. A nonconfrontational approach and a multidisciplinary team involving mental health professionals is advised and has shown to have beneficial outcomes. [4] That being said, treatment of factitious disease is often unsuccessful.

Initially, patients can be managed with topical treatment modalities including bland emollients, antibiotics, or occlusive dressings which can not only provide diagnostic value, but also physical protection from disease progression. In fact, DA was able to be diagnosed in this case through simple and strict observance of a sitter, physical protection, and barrier restoration. If the patient is receptive, psychiatric medications such as SSRIs or antipsychotics in combination with cognitive behavioral therapy can provide significant value.

References

[1]. Lavery MJ, Stull C, McCaw I, Anolik RB. Dermatitis artefacta. Clin Dermatol. 2018 Nov-Dec;36(6):719-722.
[2]. Rodriguez Pichardo A, Garcia Bravo B. Dermatitis artefacta: a review. Actas Dermosifiliogr 2013;104:854-866.
[3]. Conde Montero E, Sanchez-Albisua B, Guisado S et al. Factitious Ulcer Misdiagnosed as Pyoderma Gangrenosum. Wounds. 2016. Vol 28(2). 63-67 pp.
[4]. Mohandas P, Bewley A, Taylor R. Dermatitis artefacta and artefactual skin disease: the need for a psychodermatology multidisciplinary team to treat a difficult condition. Br J Dermatol 2013;169:600-606.

Rash with Neuropathy Refractory to Medical and Surgical Therapies - a Case Report

Erez Minka, DO[1]; Sarah Minka, DO[2]
[1]Bay Area Medical Center - Corpus Christi, [2]Portland Dermatology

Abstract

Patient was a 63 year old male with an extensive history of worsening neurological symptomatology refractory to medical and surgical care presents with a collection of non-pruritic, erythematous plaques and papules distributed about the proximal upper and lower extremities. This rash had failed anti-fungal and topical over-the-counter medications in the recent past. Biopsy was performed, demonstrating a granulomatous dermatitis with numerous acid-fast bacilli. PCR studies were conducted, verifying the presence of Mycobacterium Leprae. Patient was started on triple therapy with rifampin, clofazamine, and dapsone. At 6-month followup, patient was responding favorably to treatment.

Physical Examination

Visual inspection was performed of the head, neck, torso, and extremities. Patient was alert, oriented, well nourished and was not in any immediately apparent distress. Multiple circinate and geometric erythematous papules and plaques were present, distributed about the proximal upper and lower extremities. Lesional distribution/density appears greater on the left upper extremity than on the remaining 3 extremities. There are no clinically appreciable hair or nail changes on exam. Sensation is in tact to light touch throughout the proximal and distal extremities, and capillary refill is brisk.

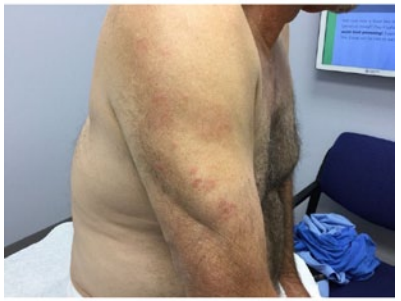


Figure 1. Right proximal upper extremity

Patient Presentation

Our patient was a 63 year old caucasian male rancher, presenting to dermatology clinic complaining about a largely "asymptomatic" yet persistent rash to his bilateral proximal extremities. Patient failed attempts at home remedy with over the counter medications, so he visited his primary care provider. Patient was placed on anti-fungal medications, and there was no improvement. Pertinent history of this patient includes being diagnosed as pre-diabetic, as well as a 6 year history of steadily-worsening peripheral neuropathy. Paresthesias and radicular pain was admittedly prevalent in the upper extremities more-so than lower. Patient was seeing a neurologist for much of this time, yet the symptoms had progressed to a degree that was unmitigated by medical therapies. The patient was referred for surgical decompression of his left cubital tunnel, as well as carpal tunnel, and eventually when symptoms persisted, a single level partial laminectomy and discectomy to decompress a cervical nerve root. At time of presentation, patient already had performed routine bloodwork for his primary care physician, all within normal limits aside from a glucose of 114. Patient denies any history of immunosuppression or constitutional symptoms associated with the presenting rash. He also denies any travel outside of the country.

Diagnosis and Treatment

A 4.0 mm punch biopsy was performed of a papule on the left proximal upper extremity, and the wound was approximated with a 5-0 Chromic gut suture. Differential diagnosis included drug eruption to a recently started lisinopril, tinea corporis, psoriasis, nummular eczema, as well as granuloma annulare.

Initial dermatopathology interpretation of the biopsy demonstrated a superficial and deep lichenoid inflammatory cell infiltrate with both lymphocytes and histiocytes. GMS stain was negative for fungi, treponema immunostain was negative for presence of spirochetes, but there were numerous bacilli visible with Acid-Fast staining. The biopsy specimen was forwarded for PCR analysis to identify the organism. AFB PCR studies confirmed the presence of Mycobacterium Leprae.

Patient was started on multi drug therapy for leprosy, with Rifampin, Clofazimine, and Dapsone. As of 6-month followup, cutaneous lesions have greatly resolved. As is typical with disease course in leprosy, areas of hypoesthesias and neuropathic pain persist. Pain management is being explored with some degree of success. Fortunately, patient denies further progression of neurological symptoms.

Discussion

As we find is true throughout all of medical history taking, it is often times fruitless to inquire about the patient's life without making requests that are exceedingly specific. Despite being asked about traveling and exposure to exotic plants and/or wildlife, it was not until the primary biopsy results returned that the patient was asked about exposure to armadillos. Not only had the patient admitted to handling armadillos several times, he uncovered a history of leprosy in his father. His father has been deceased for over 2 decades, unfortunately, so the history was limited. But as possible as it is that our patient contracted M. Leprae from direct contact with an armadillo, it is equally possible that our patient had inhaled contagious respiratory droplets from his father and became inoculated.
In a case such as this, where neurologic symptoms evolve alone, years before any cutaneous sign of leprosy presents, patients and physicians embark upon a frustrating sequence of trial and error.

Conclusions

Educating primary providers and specialists regarding the presentation of regional infectious disease may allow for the addition of several items to each patient's differential diagnosis. Once considered, these possible diagnoses may guide the physician to ask a specific enough question that not only solves the diagnostic mystery, but also recovers months to years of a patient's life from cycling through the health care system.

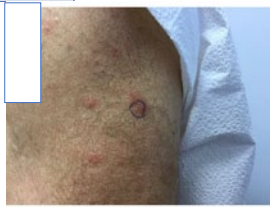


Figure 2. Left proximal upper extremity

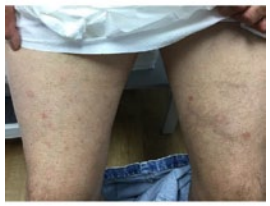


Figure 3. Proximal lower extremities

Contact

[Erez Minka, DO]
[Resident Physician, Dermatology]
[Bay Area Medical Center- Corpus Christi/ Texas OPTI]
[erez.minka@gmail.com]

Small Fiber Neuropathy causing chronic generalized pruritus: Should Dermatologist screen-for it?

John Moesch DO, Matthew Mahoney MD, George Gibbons MD, Richard Miller DO
Department of Dermatology, Largo Medical Center, Largo, Florida

HCA Largo Medical Center A Teaching Hospital — More Minds Advancing Medicine

NSU Nova Southeastern University — Dr. Kiran C. Patel College of Osteopathic Medicine

CASE REPORT

History of Present Illness: A 65 y/o Caucasian female presented to clinic with a two-year history of generalized chronic pruritus. Previous treatment includes Triamcinolone .1% cream and Pramoxine cream for several months without improvement. She also reported electric "shooting" pains and burning in bilateral upper and lower extremities, most severe in the evening.

Past Medical History:
Hypertension, Cholelithiasis, uncontrolled Type II Diabetes, Bladder incontinence

FINDINGS

Physical Exam: Excoriated erythematous urticarial papules and plaques on back, upper arms, and upper thighs with sparing of central back (*Figures 1,2*)

Diagnosis:

- Punch biopsy specimen submitted for H&E *(Figure 3)* revealed a superficial and deep perivascular and interstitial infiltrate with eosinophils
- Neurology performed two punch biopsies which were submitted for epidermal nerve fiber density studies. Frozen sections of the tissue was stained with PGP 9.5, an immunohistochemical stain targeting peripheral nerve fibers. The study showed significantly reduced epidermal nerve fiber density (*Figures 4,5)* consistent with the diagnosis of Small Fiber Neuropathy. *Figure 6* demonstrates normal density of intraepidermal nerve fibers for comparison.

Figure 1

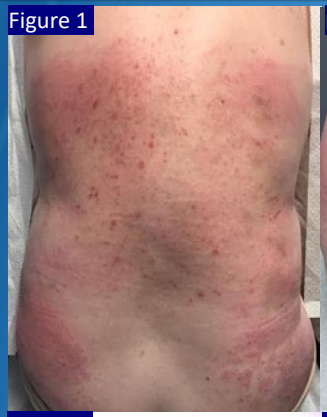


Figure 2

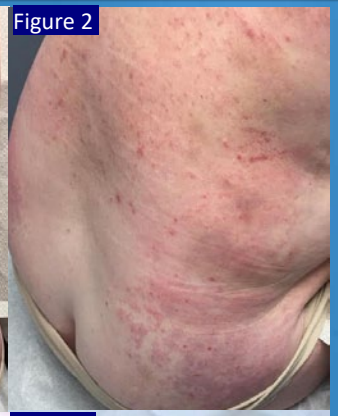


Figure 3

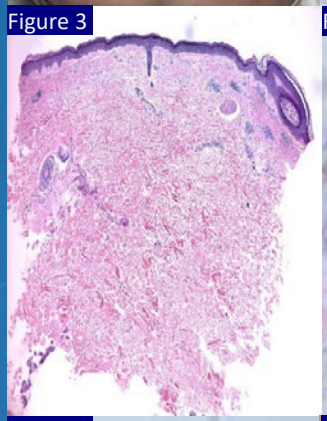


Figure 4

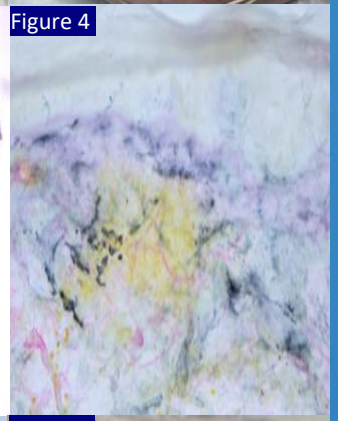
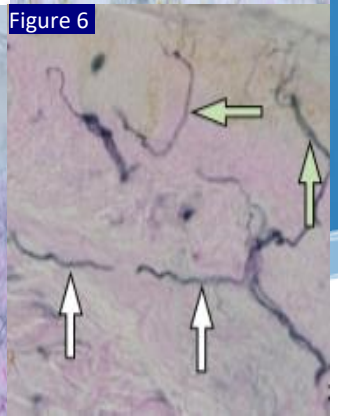


Figure 5

Figure 6



DISCUSSION

- Small fiber neuropathy (SFN) is caused by damage to small, unmyelinated and myelinated fibers in peripheral nerves
- These nerves convey pain and temperature sensations from the skin and mediate autonomic functions. Dysfunctions in these nerve fibers can cause symptoms such as pruritus, numbness, burning, paresthesias, and dysesthesias
- Diagnosis requires examination of the small nerve fibers in the skin using staining with PGP9.5 axonal marker. The standard biopsy sites for diagnosis include the thigh, distal leg, and dorsal foot.
- Epidermal Nerve Fiber Density(ENFD) is a standardized test that measures density of small sensory nerve fibers in the skin after staining with PGP9.5.
- Underlying causes include systemic diseases, the most common being diabetes mellitus or glucose intolerance. Other causes include metabolic syndrome, hypothyroidism, autoimmune rheumatologic disorders such as lupus, vasculitis, sarcoidosis, inflammatory bowel disease, nutritional deficiency (B12,B6,B1 vitamins), celiac disease, Lyme disease, HIV/HCV infection, alcohol abuse, amyloidosis, and drug/toxin exposure. 40% of cases are idiopathic.
- Treatment is aimed at symptom control (gabapentin, topical lidocaine or capsaicin) and treating the underlying cause. Acute onset cases have responded to prednisone.
- Chronification processes may lead to refractory pruritus, thus treatment should be started as soon as possible.

REFERENCES

- Brenaut E, Marcorelles P, Genestet S, Menard D, Misery L. Pruritus: An underrecognized symptoms of small-fiber neuropathies. J Am Acad Dermatol 2015;72:328-32
- Hurliman E, Groth D, Wendelschafer-Crabb G, Kennedy W, Kavand S, Ericson M, Hordinsky M. Small-Fiber neuropathy in a patient with dermatomyositis and severe scalp pruritus. Br J Dermatol. 2017 Jan;176(1):209-211
- Hoeijmakers JG, Faber CG, Miedema CJ, Merkies IS, Vies JS. Small Fiber Neuropathy in Children: Two Cases Reports Illustrating the Importance of Recognition. Pediatrics. 2016 Oct;138(4)
- Voortman M, Fritz D, Vogels O, Eftimov F, Van de Beek Dm Brouwer N, Drent M. Small Fiber neuropathy: a disabling and underrecognized syndrome. Current Opinion in Pulmonary Medicine. 23(5):447–457, SEP 2017

Auricular Cartilage Roll Flap

Kevin Myers, DO (PGY-3), Stephanie Howerter, DO (PGY-5), Whitney Fancher, MD, and William Lear, MD

Good Samaritan Regional Medical Center- Silver Falls Dermatology, Salem, OR

Introduction

Surgical defects of the helical ear present unique challenges to overcome. Depending on the depth and size of your defect you may also have to take cartilage damage into consideration while planning your repair. Other aspects of the repair that require your attention include; auditory function, aesthetics, and patient convenience including hearing aid placement. The authors formulated a novel single stage approach that included a cartilage skin graft to maintain both function and cosmesis.

Case Report

An 86-year-old man presented for Mohs micrographic surgery to treat a biopsy confirmed nodular basal cell carcinoma covering the left scapha. Tumor clearance was achieved after 2 stages and required removal of a large portion of cartilage. The resultant defect was large with missing cartilage and intact posterior auricular skin (figure 1). This left the helical rim with a "sagging" appearance.

A single stage procedure was designed by first making an incision inferior to the original defect to harvest a strip of cartilage from the inferior helical rim (figure 2). A 4mm wide cartilage graft strut was subsequently sutured from the superior antihelix to the remaining helical rim cartilage with PDS sutures (figure 3). The posterior auricular skin was then rolled over the cartilage graft. This construct provided immediate rigidity and prevented collapse of the helical rim. To create a smooth contour of the helical rim, redundant skin was removed overlying the cartilage graft donor area. The helical roll and inferior donor sites were sutured in place with 5-0 Polysorb and 5-0 nylon. A full thickness skin graft was used to cover the remaining defect. (Figure 4) (figure 5). The sutures were removed at two weeks and the patient was seen at five months post op (figure 6).

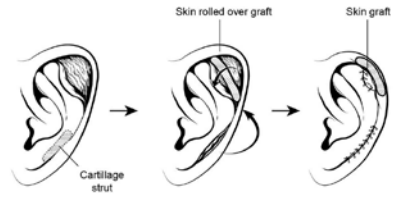


Figure 5

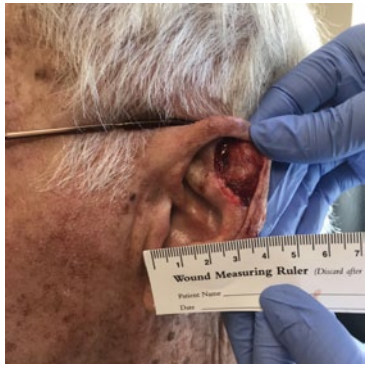


Figure 1

Figure 2

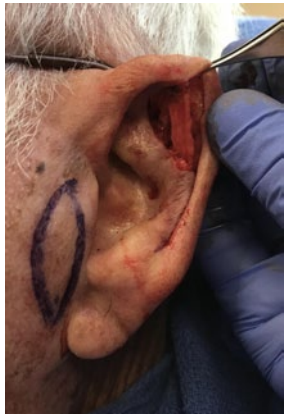


Figure 3

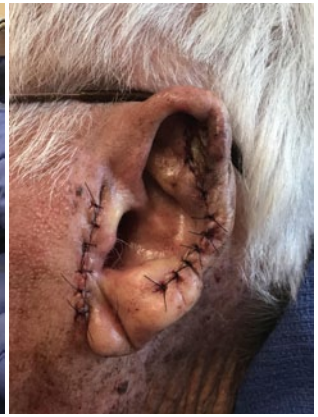


Figure 4

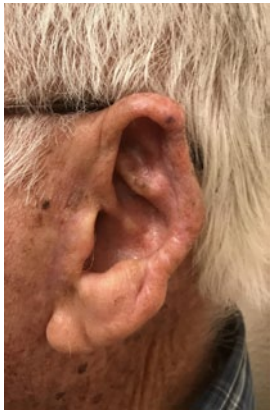


Figure 6

Discussion

When approaching this repair there were several options to consider. Wedge excisions are popular options for defects of the posterior helix. This option, however, is prone to causing several appreciable aesthetic complications including butterfly deformity (pinching the helix into a bi-lobed structure), cupping and webbing[1]. It is especially difficult to avoid altering pinna size, vertical height, and anatomical landmarks using a wedge resection when the defect extends beyond one-fourth of the auricular circumference[2]. Given the size and position of our defect we opted against a wedge resection as we felt it would significantly alter the anatomical and cosmetic appearance of the ear.

A chondrocutaneous advancement flap was another consideration. Helical chondrocutaneous advancement flaps may be used in small defects limited to the helical rim[3]. They have the advantage of providing good color and texture match. Unfortunately, our defect was too large, and this reconstruction would have severely affected the vertical diameter of our patient's ear.

Other staged reconstructive options, including mastoid flap over cartilage were also eliminated due to patients desire to avoid a multi-step procedure.

Our single stage procedure provides an ideal option for repair of larger helical defects that extend through the cartilage but not through the posterior auricular skin. By utilizing an ipsilateral cartilage strip graft along with a skin graft, we were able to recreate the structure of the ear without sacrificing structure or function. Only mild distortion of the helical rim was caused, and overall size compared to the patient's contralateral ear was preserved. The patient reported minimal pain postoperatively and experienced no complications. Thus, this novel approach provides yet another option to dermatologic surgeons faced with the dilemma of helical repair.

References

1. Majumdar A, Townend J. Helix rim advancement for reconstruction of marginal defects of the pinna. Br J Oral Maxillofac Surg. 2000 Feb;38(1):3-7.
2. Armin BB, Ruder RO, Azisadeh B. Partial Auricular Reconstruction. Semin Plast Surg. 2011 Nov; 25(4): 249–256.
3. Radonich MA, Zaher M, Bisaccia E, Scarborough D. Auricular reconstruction of helical rim defects: wedge resection revisited. Dermatol Surg. 2002 Jan;28(1):62-5.

Disclosures

The authors have no conflicts of interest to disclose.

Diagnosis of African Tick-bite Fever

Andrew Newman, DO[1,2]; Dustin Mullens, DO[1,2]; Christine Lin, MD[1,2]; Jason Barr, DO[1,2]; Brook Blumetti, DO[1,2]

[1]HonorHealth Scottsdale Dermatology Residency Program, Scottsdale, AZ; [2]Affiliated Dermatology, Scottsdale, AZ

Academic Affairs

Background

R. africae is the etiological agent for African tick-bite fever (ATBF), the most common tick-borne bacterial zoonosis.[1] There are two known vectors of the disease: the *Amblyomma variegatum* ticks found in Sub-Saharan Africa and West Indies, and the *Amblyomma hebraeum* ticks found specifically in Southern Africa.[2,3]

Unlike other ticks that passively infect their host, *Amblyomma hebraeum* ticks uniquely attract other ticks to the host. Studies have shown that male ticks that are feeding on a non-human host (usually cattle) can emit an aggression-attachment pheromone that attracts other unfed ticks to the host. The presence of the pheromone allows unfed ticks to actively discriminate between hosts on which these parasites have fed successfully (suitable hosts) and those on which they have not.[4] The aggressive hunting nature of the *A. hebraeum* ticks explains the clinical presentation of having multiple eschars and affecting large groups of exposed travellers such as soldiers, leisure safari tourists, game hunters, and foreign aid workers.[2] Another South African spotted fever group Rickettsia, *Rickettsia conorii, is the causative agent for* Mediterranean spotted fever (MSF*) and R. conorii-carrying ticks* exhibit a much less aggressive hunting style than *A. hebraeum* ticks, consequently presenting with a single eschar site. [5]

R. africae has been estimated to have a very high prevalence in Amblyomma ticks (95.2%) and fairly high prevalence of about 4.0-8.6% in travellers coming from rural Southern Africa.[6,12] It has an incubation period of about 5-10 days after inoculation by an infected tick.[7] Clinical signs include fever, generalized maculopapular or papulovesicular rash, fatigue, headache, myalgia, and regional lymphadenopathy. The inoculation eschar, single or multiple, commonly presents on the legs and is accompanied by tender lymphadenopathy of the draining nodes[1,7] More severe symptoms such as, myocarditis and subacute neuropathy have been reported in elderly patients.[8]

Case Report

A 77-year old male presented with a pruritic maculopapular and papulovesicular rash distributed over his upper and lower extremities bilaterally that started 3 weeks prior. He noted he was on a 12-day mission trip in Limpopo, the northernmost province of South Africa, where he was constructing and installing safe toilets to replace areas using dangerous toilet pits. The patient believed he had been bitten by two ticks and noted an eschar on his left lower leg on the third day of the trip. He also noted that he developed a sudden, persistent, and pruritic rash that started on his lower extremities and spread to his upper extremities. He was seen by a US physician on the trip and was given a 7-day course of doxycycline monohydrate 100mg PO BID. About 16 days after his initial symptoms, his exam showed multiple edematous dome-shaped papules 3-6mm in size were scattered over his dorsal feet and ankles bilaterally (figure 1) and an erythematous plaque with a central eschar over the left medial leg (figure 2).

Biopsies were taken from the right shin, left volar forearm, and right fourth finger, all of which revealed histologic findings consistent with a bullous arthropod reaction without any evidence of a vasculitis. Aerobic and anaerobic bacterial cultures taken from the right shin showed no growth. Ten days after the initial biopsies, serum samples and eschar swabs were collected then sent to the Center for Disease Control and Prevention for further testing. The serum Spotted Fever Group IgG IFA (Rocky Mountain Spotted Fever) and African Tick-bite Fever antibodies were negative. However, the cultures from the eschar swab came back positive for *R. africae*.

The patient was given triamcinolone 0.1% cream to apply BID to pruritic lesions for up to two weeks and an additional 7-day course of doxycycline monohydrate 100mg PO BID was given. The skin lesions had fully resolved without scar 7 days after treatment was given.

Case Report

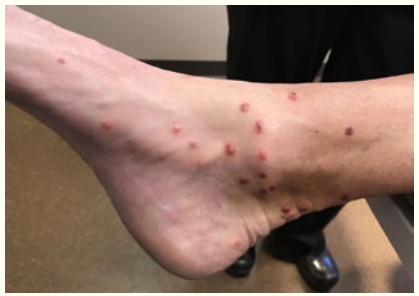


Figure 1. African tick-bites distributed over the right ankle

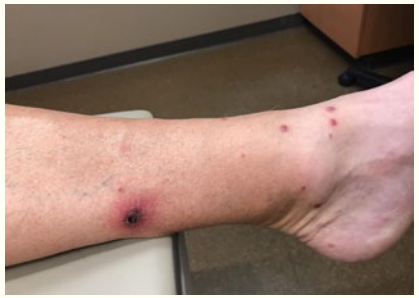


Figure 2. Early eschar forming over the left lower leg

Key Points

- **African tick-bite fever (ATBF) is one of the most common tick-borne bacterial zoonoses.**
- **ATBF should be considered in those with exposure to rural area of Southern Africa in the preceding 2 weeks, particularly when presenting with multiple eschar sites**
- **The *R. africae*-carrying ticks are unique, given their ability to actively attract and hunt their non-human hosts via an aggression-attachment pheromone.**
- **Laboratory diagnosis of ATBF can be challenging due to its high cross-reactivity with *R. conorii* in serological testing and it's delay in seroconversion**

Discussion

Diagnosis of rickettsiosis can occur through serology testing, in which presence of disease-specific antibodies are detected via indirect immunofluorescence assay (IFA) using disease-specific antigens. Antigens from *R. rickettsii* (Rocky Mountain Spotted Fever), *R. conorii* (MSF), and *R.* africae (ATBF) are commercially available for the diagnosis of rickettsiosis. Unfortunately, antigens from *R. conorii* exhibit cross reactivity with *R. africae*, which can confound the diagnosis.[1,11] Another diagnostic dilemma is that serology IFA tests can be less sensitive when done after the initiation of antibacterial treatment. The current hypothesis is that *R. africae* is highly sensitive to doxycycline and the early exposure to the drug prevented the development of detectable titers of reactive antibodies, thus producing a negative serology test.[10] In our patient's case, early exposure to doxycycline explains his negative serology tests.

Due to *R.* africae-carrying tick's aggressive hunting nature, they are associated with multiple eschars and tend to affect a groups of people, especially in rural areas.[4,5] The infection presents with a maculopapular or papulovesicular rash, fatigue, headache, and myalgia. It responds well to tetracyclines, quinolones, and macrolides.[9,11]

ATBF is now one of the most common rickettsial infections in Africa.[12,13] Accordingly, it is incredibly important for travellers to utilize topical repellents containing at least 19.5% diethyl-3-methylbenzamide (DEET) as a preventative measure when traveling to endemic areas.[14]

References

1) *Parola P, Paddock CD, Socolovschi C, et al. Update on Tick-Borne Rickettsioses around the World: a Geographic Approach. Clinical Microbiology Reviews. 2013. Vol 26(4). 657-702 pp.*

2) *Jensenius M, Fournier PE, Vene S, Hoel T, Hasle G, Henriksen AZ, Hellum KB, Raoult D, Myrvang B. Norwegian African Tick Bite Fever Study Group. African Tick Bite Fever in Travelers to Rural Sub-Equatorial Africa. Clinical Infectious Diseases. 2003. vol 36. 1411–1417 pp.*

3) *Parola P, Raoult D, Jourdan J. Tick-borne infection caused by Rickettsia africae in the West Indies. N Engl J Med. 1998. Vol 338. 1391-1392 pp.*

4) *Norval, RA, Andrew, HR, Yunker CE. Phermone-mediation of host-selection in bont ticks (Amblyomma hebraeum Koch). Science. 1989. Vol 243. 364-365 pp.*

5) *Parola P, Raoult D. Ticks and Tickborne Bacterial Diseases in Humans: An Emerging Infectious Threat. Clinical Infectious Diseases. 2001. Vol 32. 897–928 pp.*

6) *Kelly PJ, Mason PR. Transmission of a spotted fever group Rickettsia by Amblyomma hebaeum. J Med Entomol. 1991. Vol 28. 598-600 pp.*

7) *Jensenius M, Fournier PE, Kelly P, Myrvang B, Raoult D. African tick bite fever. Lancet Infec Dis. 2003. Vol 3. 557-564 pp.*

8) *Roch N, Epaulard O, Pelloux I, Pavese P, Brion JP, Raoult D, et al. African tick bite fever in elderly patients: 8 cases in French tourists returning from South Africa. Clin Infec Dis. 2008. Vol 47. 28-35 pp.*

9) *Brouqui P, Baceller F, Baranton G, et al. Guidelines for the diagnosis of tick-borne bacterial diseases in Europe. Clinical Microbiology and Infection. 2004. Vol 10. 1108-1132 pp.*

10) *Fournier P-E, Jensenius M, Laferl H, Vene S, Raoult D. Kinetics of Antibody Responses in Rickettsia africae and Rickettsia conorii Infections. Clinical and Diagnostic Laboratory Immunology. 2002. Vol 9. 324-328 pp.*

11) *Palau L, Pankey GA. Mediterranean Spotted Fever in Travelers from the United States. J Travel Med. 1997. Vol 4. 179-182 pp.*

12) *Maina A, Jiang J, Omulo SA, Cutler Sally, et al. High prevalence of Rickettsia africae Variants in Amblyomma variegatum Ticks from Domestic Mammals in Rural Western Kenya: Implications for Human Health. Vector Borne Zoonotic Dis. 2014. Vol 10. 693-702 pp.*

13) *Jensenius MFournier PEKelly PMyrvang BRaoult D African tick bite fever. Lancet Infect Dis2003;3557-56*

14) *Jensenius MPretorius AMClarke FMyrvang B Repellent efficacy of four commercial DEET lotions against Amblyomma hebraeum (Acari: Ixodidae), the principal vector of Rickettsia africae in southern Africa. Trans R Soc Trop Med Hyg 2005;99708- 711*

Pemphigus Foliaceus: Case Report and Review

Craig Parson, D.O.; Nathan Peterson, D.O.

The above physicians are part of Aspen Dermatology Residency Program in Springville, Utah.

Introduction

Pemphigus foliaceus (PF) is a rare autoimmune blistering disease that can be difficult to diagnose and treat. The disease can be endemic or sporadic with a number of different instigating factors. We present a case of a 73-year-old male who developed PF shortly after treatment with 5-fluoruracil for actinic keratosis and with a distant history of ionizing radiation treatment. The patient proved difficult to properly treat due to his transitory and resistant nature. A short review of PF is also provided.

Case Report

A 73-year-old male presented to our clinic for evaluation of persistent superficial erosions with overlying scale on his upper extremities, trunk, neck, and lateral face that began 3 months previous (Figure 1). The patient had just recently moved and was a new patient to us. At presentation, the lesions on the patient's trunk and upper extremities had a thicker scale than those on his neck and face (Figures 2 and 3). Immediately prior to developing the lesions, the patient was treated with 5-fluoruracil for actinic keratosis on the face and scalp. The patient's medication list included aspirin, clopidogrel, tamsulosin, and atorvastatin. Past medical history is significant for radiation therapy for laryngeal cancer and abdominal aortic aneurysm repair each many years previous.

Three lesional punch biopsies were performed for hematoxylin and eosin staining on chest and upper extremities. Histopathology showed separation of the corneal layer with subtle acantholysis in the granular layer, which favored the diagnosis of pemphigus foliaceus (PF) (Figures 4 and 5). Clinical correlation supported the diagnosis of PF. Direct immunofluorescence, indirect immunofluorescence, and ELISA were not performed due to histological and clinical support of diagnosis, and particularly due to the patient's resistance to further testing.

The patient was started on high-potency topical corticosteroids and a short course of 20mg prednisone that was tapered over a month. By the end of the first month of treatment, he was cleared of nearly all lesions. However, at the next follow up, the patient had a more localized flare up on the neck and lateral face while continuing the topical corticosteroids. The patient was resistant to starting any immunosuppressant medications other than corticosteroids. The patient was started on 1mg/kg per day of prednisone with the plan to taper. The patient is transitory and was soon lost to follow up after starting the new treatment plan.

Discussion

Pemphigus foliaceus (PF) is a member of the chronic blistering pemphigus family that includes other major forms: pemphigus vulgaris (PV) and paraneoplastic pemphigus.1 PF is a rare disease with low prevalence and incidence worldwide.2 PF can be endemic or sporadic. The endemic form, known as fogo selvagem, is found in most commonly in regions of Brazil but can be found in a number of different locations worldwide. Fogo selvagem is believed to be caused by environmental factors. It presents in genetically susceptible children and young adults who are exposed to the bite of black flies, which are a possible vector that precipitates the disease. 1,2 Fogo selvagem presents clinically the same as the sporadic form of PF. While endemic PF presents in children and young adults, sporadic PF typically presents in adults between ages 40 and 60 years of age.2 Both endemic and sporadic PF tend to present equally in men and women.1,2

Pemphigus can be induced by medications, especially thiol-containing drugs such as penicillamine and captopril.2 Our patient reported his first initial flare of PF after using 5-fluorouracil. The patient also reported a history of ionizing radiation for laryngeal cancer. 5-fluorouracil has been implicated as a possible eliciting factor of PF by at least one author but is otherwise undocumented.3 Ionizing radiation and UV exposure have also been documented as possible instigators of pemphigus.2,4,5

PF is an autoimmune condition in which IgG autoantibodies target desmoglein 1 (Dsg1).6,7 The binding of autoantibodies to Dsg1 leads to loss of intercellular connections known as acantholysis.2 Dsg1 is found in greater abundance towards the upper levels of the epidermis, and in lower levels of the epidermis, co-expression of Dsg3 is found.7,8 For this reason, PF tends to develop more superficial bullae, especially compared to PV, which is predominately caused by Dsg3-directed autoantibodies.7,8

PF presents clinically with shallow cutaneous erosions often with overlying scaly crust. Unlike PV, patients do not have mucosal involvement. The lesions are most often found in a seborrheic distribution. The bullae associated with PF are very fragile, often never seen by the provider intact. The Nikolsky sign is commonly positive. Generally, patients are not severely ill but can experience pain and/or burning. PF can rarely be severe, becoming an exfoliative erythroderma. Also occurring rarely, PF can transition to PV. 1,2,9,10

Pemphigus erythematosus (PE, Senear-Usher syndrome) is a localized variant of PF that presents primarily on the malar face and sun-exposed areas. PE is described as having features of both lupus and pemphigus, with some rare patients having positive anti-nuclear antibodies.10 However, pemphigus erythematosus patients have rarely been reported to have both diseases congruently. PE presents identically to PF histologically. 1,2

The histopathology of PF consists primarily of acantholysis of the upper epidermis in the granular layer. Often the stratum corneum is missing due to the fragility of the bullae, but in early lesions can be split from the underlying epidermis.6,11 The location of acantholysis and separation in the epidermis is helpful in distinguishing from PV. PV usually will develop separation lower in the epidermis. 6,11 Direct immunofluorescence (DIF) of perilesional skin shows IgG and C3 intercellular deposition that is more prominent in upper levels of the epidermis. Pemphigus erythematosus differs from PF with DIF showing intercellular deposition of IgG and C3 as well as at the basement membrane. 10 Indirect immunofluorescence with human skin or guinea pig esophagus substrate shows anti-Dsg1 autoantibodies. 1,11 ELISA is sensitive and specific for anti-Dsg1 without requiring skin biopsy.8 DIF, IIF and ELISA help distinguish PF from other forms of pemphigus, bullous impetigo, subcorneal pustular dermatosis, subacute cutaneous lupus, and seborrheic dermatitis.1 ELISA can also serve as a useful tool monitoring disease response to treatment and to help predict flares.8

Treatment for PF can be similar to PV when the disease is widespread. In cases of widespread disease, systemic corticosteroids remain first line, usually with prednisone at 1 mg/kg/day as the initial dose.12 Tapering the dose is based on clinical improvement as well as monitoring circulating anti-Dsg1 levels. Azathioprine, mycophenolate mofetil, dapsone, and cyclophosphamide as adjuvant therapy with systemic corticosteroids or on their own as steroid-sparing options have shown to reduce lesions and aid in remission. 13-16 Rituximab has proven as an increasingly effective adjuvant therapy to pemphigus. 17 Tetracycline with niacinamide has emerged as a useful corticosteroid-sparing medication, showing 90% efficacy in new flares and 60% control with occasional treatment with topical and/or oral corticosteroids. 18 In localized disease, control can be obtained with super-potent topical corticosteroids.1

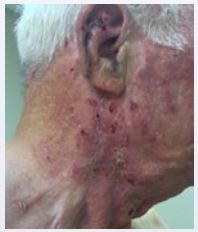


Figure 1. Erythematous plaques with erosions and crusting of the patient's right face, ear and neck.

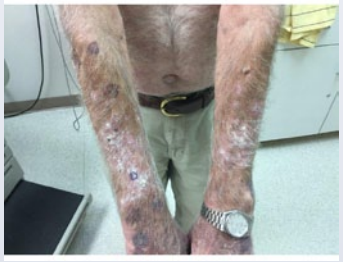


Figure 2. White scaly plaques on patient's bilateral dorsal forearms.

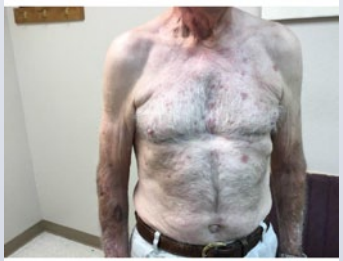


Figure 3. Scattered pink eroded plaques with some overlying crust on patient's chest.

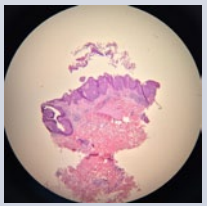


Figure 4. H&E, original magnification 4x

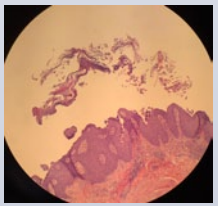


Figure 5. H&E, original magnification 10x

Conclusion

Pemphigus foliaceus is a rare disease that can be difficult to diagnose and treat. Our patient would have benefited by additional studies to confirm the diagnosis of PF and to monitor treatment response based on circulating anti-Dsg1 levels such as found with ELISA. It is also important to recognize the possible but uncommon eliciting factors of 5-fluorouracil and radiotherapy. Due to our patient's refusal for adjuvant immunosuppressive therapy, we will consider treatment with tetracyclines and niacinamide if we are able to regain contact.

References

1. Amagai M. Pemphigus. In: Bolognia JL, Jorizzo JL, Rapini RP, eds. Dermatology. Vol 1. Philadelphia, PA: Elsevier; 2018:494-509.
2. James KA, Culton DA, Diaz, LA. Diagnosis and clinical features of pemphigus foliaceus. Dermatol Clin. 2011;29(3): 405–412. doi:10.1016/j.det.2011.03.012.
3. Callander J, Ponnambath N. Pemphigus foliaceus induced by topical 5-fluorouracil. Clin Exp Dermatol. 2016;41:443-444.
4. Walker A, Favreau T. Localized pemphigus foliaceus. Cutis. 2017;99:E23-26.
5. Cianchini G, Lembo L, Colonna L, et al. Pemphigus foliaceus induced by radiotherapy and responsive to dapsone. J Dermatolog Treat. 2006;17:244-246. doi: 10.1080/09546630600921197.
6. Mahoney MG, Wang Z, Rothenberger K, et al. Explanations for the clinical and microscopic localization of lesions in pemphigus foliaceus and vulgaris. J Clin Invest. 1991;103:461-468.
7. Waschke J. The desmosome and pemphigus. Histochem Cell Biol. 2008;130:21-54. doi: 10.1007/s00418-008-0420-0.
8. Stanley JR, Amagai M. Pemphigus, bullous impetigo, and the staphylococcal scalded-skin syndrome. N Engl J Med. 2006;355:1800-1810.
9. Mihai S, Sitaru C. Immunopathology and molecular diagnosis of autoimmune bullous diseases. J Cell Mol Med. 2007;11(3):462-481. doi:10.1111/j.1582-4934.2007.00033.x.
10. Khachemoune A, Guldbakke KK, Ehrsam E. Pemphigus foliaceus: A case report and short review. Cutis. 2006;78:105-110.
11. Ohata C, Ishii N, Furumura M. Locations of acantholysis in pemphigus vulgaris and pemphigus foliaceus. J Cutan Pathol. 2014;41:880-889. doi: 10.1111/cup.12384.
12. Atzmony L, Hodak E, Gdalevich M, et al. Treatment of pemphigus vulgaris and pemphigus foliaceus: A systematic review and meta-analysis. Am J Clin Dermatol. 2014;15:503-515. doi: 10.1007/s40257-014-0101-9.
13. Martin LK, Werth VP, Villanueva EV, et al. A systematic review of randomized controlled trials for pemphigus vulgaris and pemphigus foliaceus. J Am Acad Dermatol. 2011;65(11):903-908.
14. Singh S. Evidence-based treatments for pemphigus vulgaris, pemphigus foliaceus, and bullous pemphigoid: A systematic review. Indian J Dermatol. 2011;77:456-69. doi:10.4103/0378-6323.82400.
15. Doukaki S, Platamone A, Alaimo R, et al. Mycophenolate mofetil and enteric-coated mycophenolate sodium in the treatment of pemphigus vulgaris and pemphigus foliaceus. J Dermatolog Treat. 2015; 26(1):67-72. doi:10.3109/09546634.2014.880395.
16. Atzomny L, Hodak E, Leshem YA, et al. The role of adjuvant therapy in pemphigus: A systematic review and meta-analysis. J Am Acad Dermatol. 2015; 73(2):264-271
17. Mimouni D, Anhalt JG. In: Lebwohl MG, Heymann WR, Berth-Jones J, Coulson I, eds. Treatment of Skin Disease: comprehensive therapeutic strategies. Philadelphia, PA: Elsevier; 2018: 611-615.
18. McCarty M, Fivenson D. Two decades of using the combination of tetracycline derivatives and niacinamide as steroid-sparing agents in the management of pemphigus: Defining a niche for these low toxicity agents. J Am Acad Dermatol. 2014; 71(3):475-479

A case of herpetic sycosis: a frequently unrecognized manifestation of a common pathogen

Dahlia Saleh, DO[1] Ashley Rice, DO[2] Hannah Pile, OMS-IV[3] Christopher Cook, DO FAAD FAOCD[4], Daniel Zedek, MD[5]
Dermatology Department; Campbell University School of Osteopathic Medicine/Sampson Regional Medical Center

CAMPBELL UNIVERSITY
Jerry M. Wallace School of Osteopathic Medicine

SAMPSON REGIONAL MEDICAL CENTER

Clinical Presentation

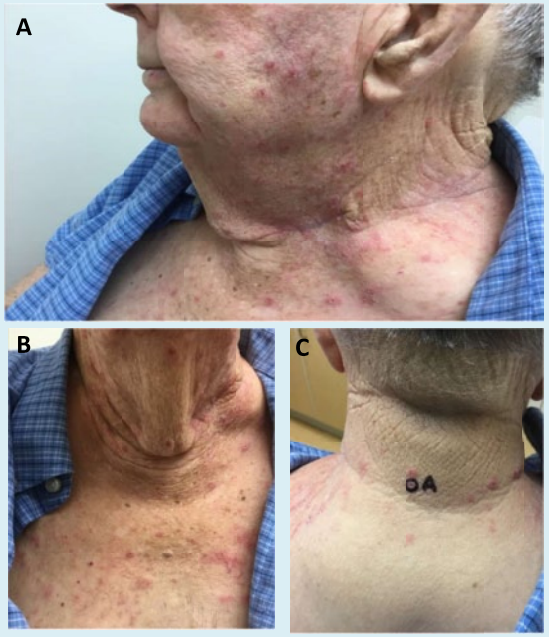


Figure 1 (A, B, and C) Scattered, excoriated papules and vesicles on the bilateral cheeks, neck, and chest of a Caucasian male.

An 84 year old male presented with an eruption on the face, neck, and trunk present for several weeks. He reported itching and burning with no improvement with the use of triamcinolone acetonide cream. Past medical history significant for hypertension, hyperlipidemia, coronary artery disease, COPD, and hypothyroidism. He also reports a history of cold sores. Current medications included aspirin, carvedilol, furosemide, pravastatin, levothyroxine, tamsulosin, docusate sodium, loperamide, milk of magnesia, and an albuterol inhaler. Patient reported daily close razor blade shaving with a straight razor.

Physical examination was remarkable for scattered pink follicular-based papules and vesicles on the bilateral cheeks, neck, and chest **(Figure 1A,B,C)**. There were secondary excoriations overlying the primary lesions.

At time of presentation, the differential diagnosis included folliculitis, allergic/irritant contact dermatitis, drug eruption, neurotic excoriations, arthropod assault, widespread actinic keratoses, or a photosensitive/photoallergic process. A 4-mm punch biopsy was taken from a papule on the posterior neck **(Figure 1C)**.

Abstract

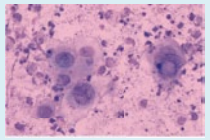
There are few reported cases of herpetic folliculitis in the literature. Herpetic folliculitis represents a rare and frequently unrecognized manifestation of a common pathogen; either varicella zoster virus (VZV) or herpes simplex virus (HSV). When affecting the beard area specifically, it is termed herpetic sycosis. Herein, we present a case of a 3 week long, pruritic and burning pink to red papulovesicular eruption with secondary erosions on the face, neck, and trunk of an elderly male with a history of cold sores. The rash was initially mistaken for an allergic or irritant contact dermatitis and was treated with low and medium potency topical corticosteroids with no improvement. Eventually, a punch biopsy was performed and upon visualizing classic histopathologic findings of a herpes virus infection the patient was diagnosed with herpetic sycosis. While this eruption commonly self-resolves, this patient experienced full recovery following treatment with oral antiviral therapy. This case illustrates the importance of histopathological evaluation and a broad clinical differential diagnosis in the setting of a nonspecific erythematous papulovesicular eruption that is unresponsive to therapy.

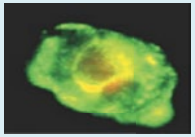
Discussion

- Herpetic folliculitis is most frequently caused by caused by VZV, followed by HSV-1, then HSV-2[1]
- Increased risk in men with a history of recurrent facial HSV who shave closely with a blade razor (herpetic sycosis)[2,5]
- Virus establishes latency in dorsal root ganglia and is able to evade the immune system via several mechanisms, including down-regulating various immunologic cells and cytokines and inducing intracellular accumulation of CD1d molecules in antigen presenting cells (normally, these CD1d molecules are transported to the cell surface, where they stimulate natural killer (NK) cells, promoting an immune response)[1]
- Tzanck Smear **(Fig. 2)** or biopsy revealing multinucleated giant cells are commonly used for diagnosis; other options include direct fluorescent antibody (DFA) assay **(Fig. 3)** , HSV serology (gold standard), or polymerase chain reaction (most sensitive and specific)[3]
- Healthy patients typically self-resolve within 2-3 weeks although clearance may be hastened with antiviral therapy[2]
- In the immunocompromised population, lesions may be widespread or purpuric [4]

Figure 2. Tzanck smear. Multinucleated giant cells present.

This study *cannot* differentiate between HSV and VZV.





Courtesy of 4th edition Dermatology, Bolognia et.al

Figure 3. DFA assay. A keratinocyte infected with HSV fluoresces green.

This study *can* differentiate between HSV and VZV.

The Takeaway

A diagnosis of herpetic folliculitis should be considered in a folliculitis-like dermatosis that is refractory to antimicrobial therapy or topical corticosteroids, especially when a history of prior HSV infection is present.

Histopathological Findings

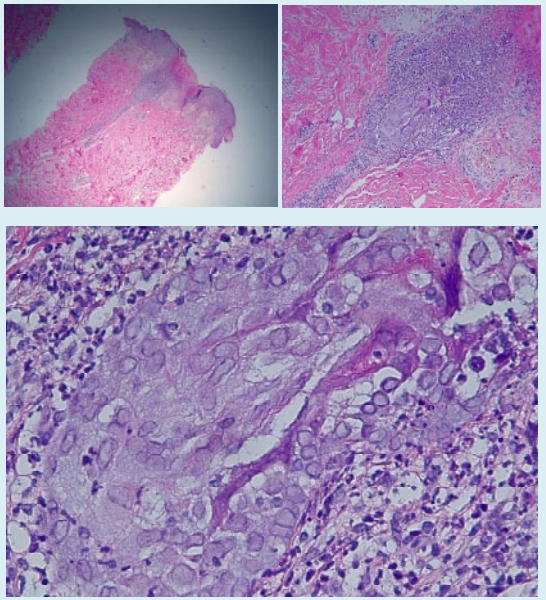


Figure 4. Multinucleated keratinocytes within an area of follicular epithelium. Some of these cells show a "ground glass" nuclear appearance and peripheral margination of chromatin. These may represent either HSV or VZV.
(H&E, original sections at low, medium, and high power)

- On histopathology, partial or complete necrosis of the hair follicle with exocytosis of lymphocytes into the follicular wall and sebaceous gland may be appreciated [1]
- There may be a perivascular and interstitial dermal inflammatory infiltrate that mimics pseudolymphoma or lymphoma[1]
- Multinucleated giant cells, +/- Cowdry A inclusion bodies, herpetic cytopathic effect (peripheral margination of chromatin), and ballooning degeneration of keratinocytes may be seen but not always present [1]**(Fig.4)**

Treatment

A diagnosis of herpetic folliculitis was made. A 7 day course of oral valacyclovir (500mg PO TID) was prescribed with complete clearance of eruption. Alternate regimens include famciclovir 500mg PO TID for 5-10 days or acyclovir 200mg PO q4h for 5-10 days.

References
[1]Yalç T. Herpes folliculitis: clinical, histopathological, and molecular pathologic observations. *British Journal of Dermatology*. 2006;154(4):743-746. Jang K-A, Kim S-H,
[2]Izumi AK, Kim R, Arnold H. Herpetic SycosisReport of Two Cases. *Arch Dermatol*. 1972;106(3):372–374. doi:10.1001/archderm.1972.01620120056012
[3]Ferenczy A, Romanowski B. The laboratory diagnosis of herpes simplex virus infections. *Can J Infect Dis Med Microbiol* 2005;16:92–98. James WD,
[4]Shalgany S, Dabela E, Husain S, Grossman ME. Herpetic zoster folliculitis in the immunocompromised host. *JAAD Case Reports*. 2015;1(1):38-40. doi:10.1016/j.jdcr.2014.11.003.
[5]Choi J-H, Sung K-J, Moon K-C, Koh J-K. Viral folliculitis on the face. *British Journal of Dermatology*. 2000;142(3):555-559.

Successful Treatment of Congenital Oral Melanosis with a 1064/532-nm picosecond Nd:Yag Laser

Shahjahan Shareef, DO[1]; Douglas C. Wu M.D., Ph.D.

[1]Western University of Health Sciences/Chino Valley Medical Center; Cosmetic Laser Dermatology, San Diego, CA

CASE PRESENTATION

Chief Complaint: Brown spots on tongue.

History of Present Illness: Patient is a 22 year old Hispanic female with a lifelong history of hyperpigmentation to the bilateral edges of her tongue. Patient denied any changes in size, color, or morphology. Patient denied any associated symptoms such as itching, burning, pain, bleeding, or tingling. Patient did not try any other treatments in the past for the brown spots on her tongue.

Past Medical History: Patient denied any significant past medical history.

Medications: Patient denied any prescription medications, over-the-counter medications, vitamins, or herbal supplements.

Family History: Patient denied any significant family history. Patient specifically denied any family history of LEOPARD syndrome, Peutz-Jeghers syndrome, Addison's disease, Albrights syndrome or any other hyperpigmentary disorders in the family.

Social History: Patient denied any alcohol, tobacco, illicit drug use, oxidizing mouthwashes or recent travel.

Surgical History: Patient denied any significant surgical history. Patient denied any dental procedures other than routine dental cleaning every 6 months.

Allergies: NKDA, NKA

Physical Exam: Patient is a well-nourished, well-appearing female who presented in no acute distress. On examination, there was discreet macular hyperpigmentation to the bilateral edges of the tongue extending from tip to base (Figure 1). Focal areas of further hyperpigmentation involved scattered papillae throughout. No other oral pathology was noted. A total body cutaneous examination was unremarkable and revealed no other pigmentary abnormalities.

Dermatohistopathology: Due to lifelong history of oral pigmentation and no change in lesion, a biopsy was deferred.

Patient Course/Treatment: After a thorough history and physical a clinical diagnosis of congenital oral melanosis was reached. The patient complained of cosmetic disfigurement and she therefore elected to proceed with treatment and removal. Two treatment sessions spaced 1 month apart were performed with the dual wavelength 1064/532 nm picosecond Nd:YAG laser utilizing a 4 mm spot size, 1.6 J/cm^2, 532 nm wavelength, 375 picosecond pulse duration, and 125 and 83 pulses delivered at a 1-2 Hz repetition rate for the first and second treatment sessions respectively. A mild, instant whitening phenomenon was noted over all treated hyperpigmented areas with the application of each laser pulse. Areas of the tongue that were not involved with hyperpigmentation did not whiten in response to laser exposure. No anesthesia was applied and the patient noted a 2-3/10 pain score. Treatment side effects included a mild erythema and burning sensation to the treated areas that persisted for a period of 3-5 days before complete spontaneous resolution. There was no incidence of peeling, scaling, erosion, ulceration, crusting, or scabbing. Seventy percent clearance was noted after the first treatment session. Two weeks after the second treatment session, 100% resolution of the congenital oral hyperpigmentation was achieved (Figure 2).

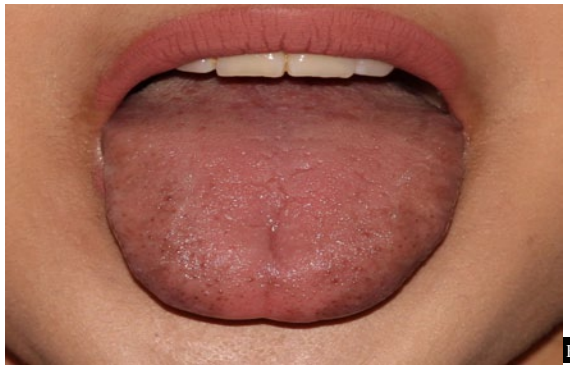


Fig. 1

Figure 1: Congenital oral hypermelanosis. Discrete hyperpigmented patches with focal papillary accentuation are noted to the bilateral edges of the tongue.

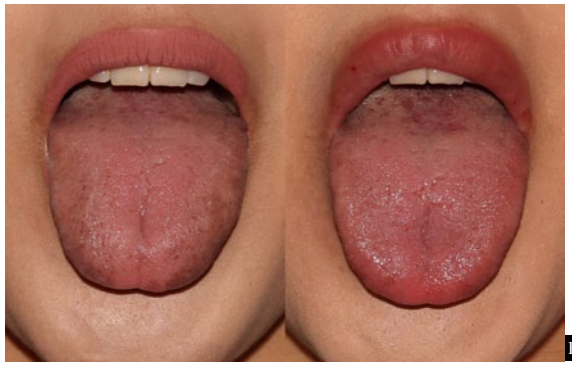


Fig. 2

Figure 2: Complete resolution of the congenital oral hypermelanosis was achieved after two treatment sessions with the 532 nm picosecond Nd:YAG laser.

REFERENCES

1. Guss L, Goldman MP, Wu DC. Picosecond 532 nm Neodymium-Doped Yttrium Aluminium Garnet Laser for the Treatment of Solar Lentigines in Darker Skin Types: Safety and Efficacy. Dermatol Surg. 2017;43(3):456-459.

2. Levi A, Amitai DB, Mimouni D, Leshem YA, Arzi O, Lapidoth M. Picosecond 532-nm neodymium-doped yttrium aluminum garnet laser-a promising modality for the management of verrucous epidermal nevi. Lasers Med Sci. 2018;33(3):597-601.

3. Negishi K, Akita H, Matsunaga Y. Prospective study of removing solar lentigines in Asians using a novel dual-wavelength and dual-pulse width picosecond laser. Lasers Surg Med. 2018;

4. Artzi O, Mehrabi JN, Koren A, Niv R, Lapidoth M, Levi A. Picosecond 532-nm neodymium-doped yttrium aluminium garnet laser-a novel and promising modality for the treatment of café-au-lait macules. Lasers Med Sci. 2018;33(4):693-697.

5. Jerdan K, Hsu JT, Schnurstein E. Successful treatment of Ota nevus with the 532-nm solid-state picosecond laser. Cutis. 2017;99(3):E29-E31.

DISCUSSION

Congenital oral hypermelanosis is a benign hyperpigmentation of the mucous membranes. There is an increase in focal melanin deposition without an increase in the number of melanocytes. It is characterized as a flat macule or patch of brown discoloration of an oral mucosal surface with uniform color and border. Due to congenital oral melanosis' benign and asymptomatic nature, removal is characteristically sought for cosmetic reasons as the hyperpigmentation can be disfiguring. In this report we demonstrate the safety and efficacy of a 1064/532-nm picosecond neodymium:yttrium aluminum garnet (Nd:YAG) laser (Picoway, Syneron-Candela) for the treatment of congenital oral hypermelanosis.

Although the 1064/532-nm picosecond laser was originally developed for tattoo removal, it has since exhibited the ability to treat a variety of benign pigmentary conditions.[1-2] However, this is the first report of successful treatment of congenital oral hypermelanosis with this laser modality. There are several other features that make this case study unique. First, the sensitive mucosal location of the lesion raised potential treatment safety and tolerability issues. Due to the extremely short pulse duration of the 532 nm picosecond laser, much lower fluences (compared with longer pulsed nanosecond lasers) could be applied to achieve treatment efficacy and this allowed for greater treatment safety, minimal downtime and treatment-related side effects, and minimal pain even in the absence of specific anesthetic measures. Additionally, the effectiveness of this laser after just 1-2 treatment sessions highlights the efficiency of the 532 nm wavelength and majority photoacoustic effect in ablating melanin and treating benign melanotic lesions.[3-4]

As has previously been shown, picosecond pulsed laser enables greater fragmentation of melanosomes into melanin particles that are eventually phagocytosed as compared with the previous generation of Q-switched technologies.[5] The 532 nm picosecond laser's high affinity for melanin coupled with its uniquely short pulse duration allows the use of lower fluences to remove melanosomes while causing less nonspecific photothermal damage.[2-3]

In summary, the 532-nm picosecond Nd:YAG laser seems to be a safe and effective treatment option for congenital oral hypermelanosis and is likely the treatment of choice for benign hyperpigmented lesions located on sensitive mucosal surfaces.

Biosurgery Utilized for Chronic Leg Ulcers in a Patient with Refractory Pemphigus Vulgaris

May Sheikh D.O. PGY-3,[1] Francisco Kerdel M.D.[2]

(1) Dermatology Residency Program, Larkin Community Hospital Palm Springs Campus , Hialeah, Florida

(2) Department of Dermatology, Larkin Community Hospital Palm Springs Campus, Hialeah, Florida

Chief Complaint and History

❖A 65 year-old female presented with a two month history of a progressively enlarging rash located over the right eyebrow and back. The patient stated that the rash initially began as a single, non-healing erosion that repeatedly scabbed over with surrounding inflammation. A new lesion near the right eyebrow appeared simultaneously. There was associated pruritis and burning of the affected areas

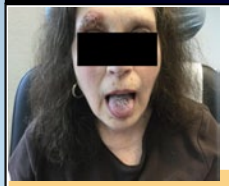
❖Complete ROS was grossly negative and patient denied prior rash

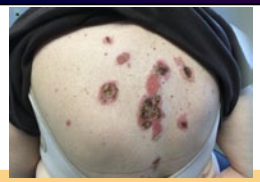
❖PMH: asthma and hyperlipidemia

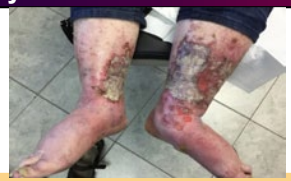
❖ Physical Examination: several flaccid bullae and erosions on the mid-upper back and a single, moist, well-demarcated red plaque with overlying crust on the right eyebrow. Several erosions present on floor of the mouth

❖ Pathology: punch biopsy revealed suprabasilar intraepidermal acantholytic blister consistent with pemphigus vulgaris (PV). DIF consistent with linear/granular IgG deposition throughout the epithelial cell surfaces

Physical Examination







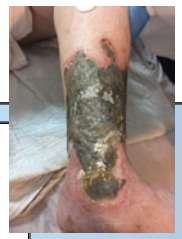
Several flaccid bullae and erosions on upper back; moist red plaque over right eyebrow

Initiated on prednisone 30mg and topical clobetasol 0.05% ointment, lesions progressed to abdomen, scalp, lower extremities, oral mucosa. Patient initiated on mycophenolate mofetil 3g daily and prednisone 40mg daily with little improvement

Patient developed painful, non-healing ulcers of the lower extremities. She required inpatient therapy and biopsies of ulcers showed no distinct etiology. Lesions were cultured for pseudomonas conferring diagnosis of pseudomonas-infected chronic lower extremity ulcerations

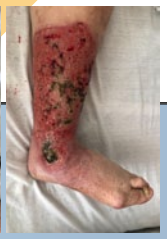
Perilesional maggot therapy, or biosurgery under occlusion was administered twice during the course of inpatient admittance. Following each 48-hour occlusion her bilateral lower extremities markedly improved. Patient continued on mycophenolate mofetil 4g and prednisone 20mg daily to manage PV.

Admission



Treatment 1

Treatment 2



Discussion

Maggot therapy or biosurgery is increasing in popularity for debridement of chronic wounds and enhancement of wound healing.

The maggots have diverse properties including anti-inflammatory, anti-microbial, antibiofilm, and wound healing properties.

Antibacterial activity targets specific organisms such as *Streptococcus A* and *B*, *Staphylococcus aureus, Pseudomonas,* and methicillin resistant *S. Aureus* (MRSA).

Treatment is generally well-tolerated in patients, with reported side effects including venous bleeding

Studies on biosurgery show improvement of tissue oxygenation following debridement for 1-4 days, further elucidating a possible mode of action of this therapy

Further studies are needed to investigate the clinical effects, and possible mechanisms of action of biosurgery; however it proved to be an effective and rapid treatment for our patient's non-healing lower extremity ulcers

References

1. Yan L, Chu J, Li M, et al. Pharmacological Properties of the Medical Maggot: A Novel Therapy Overview. Evidence-Based Complementary and Alternative Medicine. 2018;2018:1-11. doi:10.1155/2018/4934890.
2. Nigam Y, Morgan C. Does maggot therapy promote wound healing? The clinical and cellular evidence. Journal of the European Academy of Dermatology and Venereology. 2015;30(5):776-782. doi:10.1111/jdv.13534.
3. Wollina U, Liebold K, Schmidt W-D, Hartmann M, Fassler D. Biosurgery supports granulation and debridement in chronic wounds - clinical data and remittance spectroscopy measurement. International Journal of Dermatology. 2002;41(10):635-639. doi:10.1046/j.1365-4362.2002.01354.x.
4. Wollina U, Karte K, Herold C, Looks A. Biosurgery in wound healing - the renaissance of maggot therapy. Journal of the European Academy of Dermatology and Venereology. 2000;14(4):285-289. doi:10.1046/j.1468-3083.2000.00105.x.

Rapid intraoperative tissue relaxation of a scalp wound using a novel suture retention device

Allison Stoecker, DO (PGY-3), Stephanie Howerter, DO (PGY-5), and William Lear, MD

Silver Falls Dermatology, Salem, OR

Introduction

Scalp defects present unique reconstructive challenges. When wound edges are difficult to appose, surgeons often employ flaps or grafts. Scalp flaps can be large and result in loss of sensation.[1] Grafts from non-hair-bearing areas can result in poor cosmetic outcomes and may heal poorly if placed over exposed bone.[2] Intraoperative tissue expansion may circumvent large flaps and grafts. Retention sutures may be used for stress-relaxation, but high-tension suture damages underlying skin.[3] We describe the use of a novel suture retention device (SRD) to protect wound edges and provide stress relaxation of wounds, which can then be closed linearly.

Case Report

A 61 year-old female presented with basal cell carcinoma of the right frontoparietal scalp. (Fig 1) The final defect after Mohs micrographic surgery was 4.1- cm by 7.7-cm. (Fig 2) The patient declined repair with a flap or graft. A SRD was used for intraoperative tissue relaxation. First, a USP 1 Nylon retention suture was placed centrally. The suture ends were fed through the SRD and secured with a surgical clamp. (Fig 3) Initial force to approximate the wound edges measured 25.0 N. The suture was incrementally tightened and re-clamped. After 30 minutes, the force reduced 66% to 8.5N. The increased laxity of the scalp skin was also illustrated by a 44% decrease in wound width to 2.1-cm. The wound edges flanking the midline SRD were still difficult to appose. Two more devices were placed on either side of the first SRD. (Fig 4) All retention sutures were incrementally tightened over the next 60 minutes until the wound edges could be easily approximated. (Fig 5) A 4-mm standing cone was removed from the forehead and the defect was closed in a linear fashion using buried 2-0 polydioxanone sutures followed by staples. (Fig 6) There was no dehiscence, necrosis, or infection over the following 14 days of healing.

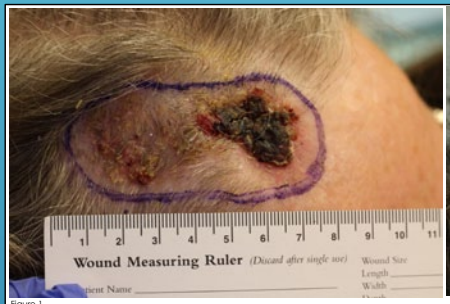


Figure 1

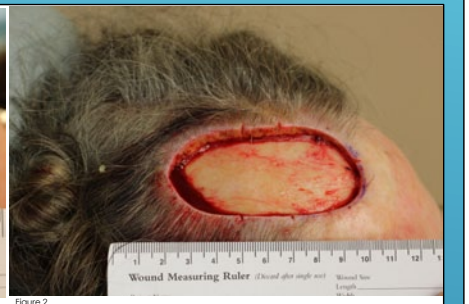


Figure 2

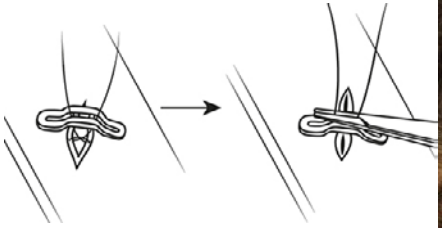


Figure 3

Figure 4

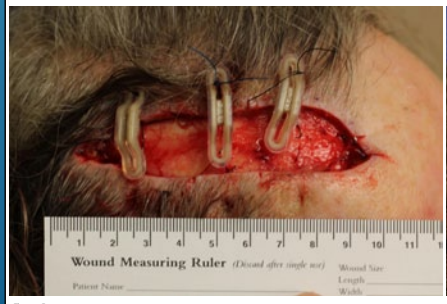


Figure 5

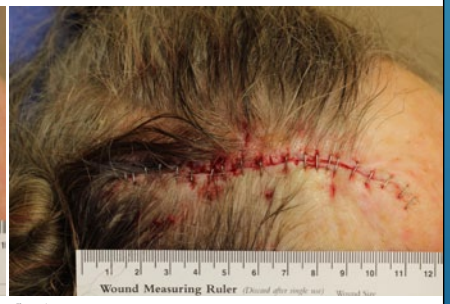


Figure 6

Discussion

Skin is a viscoelastic organ which exhibits load dependent behavior. With repeated cycles of stress and relaxation, collagen fibers reorient and elastic fibers loose their elasticity. This allows for skin elongation over time, known as mechanical creep.[4] Stress-relaxation may allow for direct linear closure of high-tension scalp wounds to avoid large flaps or grafts. This can be accomplished with retention sutures, but excess pressure from suture filaments can cause erosion or ulceration.[5]

Using a SRD may protect the skin from these forces. This device is composed of a semi-rigid insert covered with a softer shell. The core bridge-like structure allows it to withstand the forces of wound closure while protecting wound edges and dissipating pressure on the skin. Using a clamp, surgeons can incrementally place stress on the closure with up to 25N of force without apparent pressure injury to the skin.

In this case, the SRD allowed for 66% reduction in force over the first 30 minutes, and subsequent linear closure of the large defect without undermining, galeotomy, flap, or graft. Further research is necessary to quantify the rate of tissue expansion and limits of force reduction.

References

1. Malone, C. H., McLaughlin, J. M., Ross, L. S., Phillips, L. G., & Wagner Jr, R. F. (2017). Progressive Tightening of Pulley Sutures for Primary Repair of Large Scalp Wounds. Plastic and Reconstructive Surgery Global Open, 5(12)
2. Raposio, E., & Nordström, R. E. (1998). Biomechanical properties of scalp flaps and their correlations to reconstructive and aesthetic surgery procedures. *Skin Research and Technology*, *4*(2), 94-98.
3. Malone, C. H., McLaughlin, J. M., Ross, L. S., Phillips, L. G., & Wagner Jr, R. F. (2017). Progressive Tightening of Pulley Sutures for Primary Repair of Large Scalp Wounds. Plastic and Reconstructive Surgery Global Open, 5(12)
4. Hsu, S., Jamieson, A.M., and Blackwell, J. Viscoelastic studies of extracellular matrix interactions in a model native collagen gel system. *Biorheology*. 1994; 31: 21–36
5. Liu C.M., McKenna J., Griess A. Surgical pearl: the use of towel clamps to reapproximate wound edges under tension. J Am Acad Dermatol. 2004 Feb 1;50(2):273–274.

Disclosures

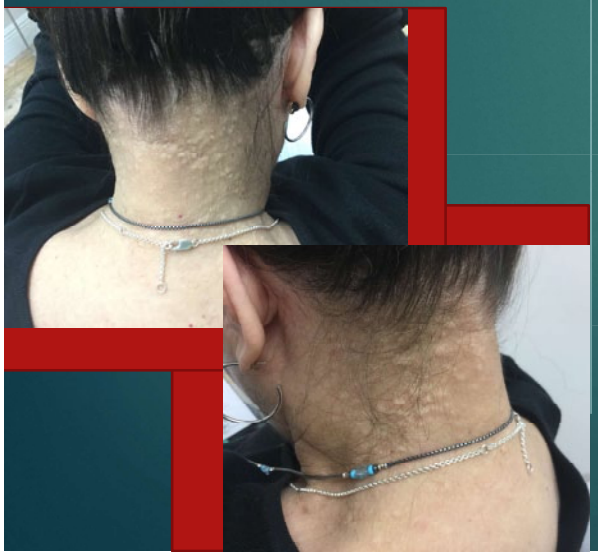
There were no funding sources for this poster. Dr. Lear is co-founder and shareholder in SUTUREGARD™ Medical. The remaining authors have no conflicts of interest to disclose.

White fibrous papulosis of the neck: An underrecognized benign condition

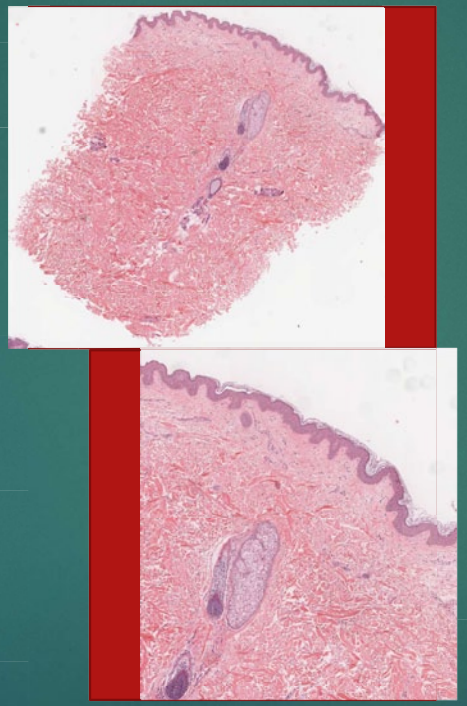
Rachel White DO PGY-4[1], Carlos Ricotti MD[1], Francisco Kerdel MD[1]
[1] Dermatology Residency Program, Larkin Community Hospital
Palm Springs Campus, Hialeah, Florida

Case Presentation

A 71-year-old Caucasian female presented with a five-year history of a worsening rash on her posterior neck. The patient stated the rash started as a single raised bump and spread to include numerous bumps spanning the posterior and lateral sides of her neck. Patient denied associated symptoms including pain or pruritus and a complete review of systems was negative. Patient denied prior treatments. Past medical history included hypothyroidism. Patient denied family members with similar findings. Physical exam revealed numerous 1-3 mm discrete firm monomorphic white papules, some coalescing into plaques, and forming a cobblestone appearance distributed on posterior and lateral neck as seen below.



Pathology



4-mm punch biopsy of posterior neck showed slight thickening of collagen bundles with focal loss of elastin in the papillary dermis and normal appearing epidermis. There was a very sparse interstitial infiltrate of rare lymphocytes and histiocytes.

Discussion

White fibrous papulosis of the neck (WFPN) is a chronic benign condition characterized by isolated or coalescing flesh-colored to white papules on posterior and lateral neck and are often asymptomatic. Histologically, WFPN reveals fibrosis of the papillary and upper reticular dermis. A similar condition, **pseudoxanthoma elasticum-like papillary dermal elastolysis (PXE-PDE)**, is defined by yellow papules on the neck and other intertriginous areas and elastolysis histologically. Recent literature has combined the two conditions due to considerable overlap and renamed the entity, **fibroelastolytic papulosis of the neck (FEPN)**. FEPN is a benign condition most commonly occurring in elderly white females. The pathogenesis is unknown; however, hypotheses relate it to intrinsic skin aging, UV radiation, and free radical damage of elastic fibers. Its incidence is underestimated due to the benign, asymptomatic nature of the disease. It is important to distinguish this condition from pseudoxanthoma elasticum (PXE) which has an indistinguishable clinical presentation. PXE can be excluded by absence of cardiovascular and ocular changes, family history, and characteristic histologic findings of fragmented elastic fibers with calcium deposition. Treatment is aimed at cosmetic improvement; however, there are few reports on effective treatment. Case reports using topical steroids, topical tretinoin, and intralesional steroids have little to no effect. Laser therapy has proven to be the most effective treatment modality. Case reports using fractionated carbon dioxide laser and fractionated 1550-nm erbium laser resulted in clinical improvement.

References

1. Balus L, Amantea A, Donati P, et al. Fibroelastolytic papulosis of the neck: a report of 20 cases. Br J Dermatol. 1997 Sep;137(3):461-6.
2. Ho D, Jagdeo J. Fractionated Carbon Dioxide Laser Treatment of Fibroelastolytic Papulosis With Excellent Cosmetic Result and Resolution of Pruritus. J Drugs Dermatol. 2015 Nov;14(11):1354-7.
3. Lueangarun S, Panchaprateep R. White Fibrous Papulosis of the Neck Treated With Fractionated 1550-nm Erbium Glass Laser: A Case Report. J Lasers Med Sci. 2016 Fall;7(4):256-8.
4. Rongioletti F, Rebora A. Fibroelastolytic patterns of intrinsic skin aging: pseudoxanthoma-elasticum-like papillary dermal elastolysis and white fibrous papulosis of the neck. Dermatology. 1995;191(1):19-24.
5. Shimizu H, Kimura S, Harada T, Nishikawa T. White fibrous papulosis of the neck: a new clinicopathologic entity? J Am Acad Dermatol. 1989 Jun;20(6):1073-7.

Upcoming Meetings:

2019 AOCD Fall Meeting
Omni Nashville Hotel
Nashville, TN
September 24 - September 28

2020 AOCD Spring Meeting
Hilton West Palm Beach
West Palm Beach, FL
February 17 - February 22

2020 AOCD Fall Meeting
Hyatt Centric Magnificent Mile
Chicago, IL
October 8 - October 11

2021 AOCD Spring Meeting
Hilton West Palm Beach
West Palm Beach, FL
February 22 - February 27

2021 AOCD Fall Meeting
Westin Denver Downtown
Denver, CO
October 7 - October 10