Focus on Osteopathy: Osteopathic Manipulative Medicine for Inflammatory Skin Diseases

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Dear Members of the AOCD,

Welcome to another issue of the Journal of the American Osteopathic College of Dermatology (JAOCD). The JAOCD has come a long way. It began as the collective vision of Drs. Jay Gottlieb, Stanley Skopit, and James Del Rosso, who wanted to create a platform to better serve the educational needs of the College. During the years of their dedication and now under the stewardship of Dr. Karthik Krishnamurthy, this journal has grown to be an impressive publication.

I would like to congratulate the current and past residents who have been published in the JAOCD. I remember authoring the very first lead article, entitled “Patient Assessment in the Treatment of Premenstrual Acne Flare with Vitamin B6 Therapy: A Two-Year Retrospective Study,” during my second year of residency. It is hard to believe it has been more than 10 years. Many of the resident authors who have published in the JAOCD have now been practicing dermatologists for more than a decade. Some of the residents of yesterday are the program directors of today.

The Journal has provided a publication outlet for the scholastic talent of the College. I remember the residents sometimes feeling overwhelmed by having to comply with the requirements for submission to the JAOCD. However, now the Journal has proven to be the historic record of the AOCD’s scholastic and research activities. The contents and the editorial process are first-rate.

Let us not ever take this precious AOCD publication for granted. I hope to see more attendings and residents contribute manuscripts. In the near future, we will be asking for more support from our members and residents as our dermatology residency moves toward a single accreditation system. The participation of our members will be vital for the survival of the JAOCD.

Fraternally yours,
Rick Lin, DO, MPH, FAOCD
Hello, Everyone,

Here’s to a happy and healthy 2015!

The new year will bring many changes in graduate medical education for osteopathic physicians. Members from the AOA have been nominated to the ACGME Board of Directors; the Osteopathic Principles Committee has been appointed and has begun its work; and each specialty will soon have representatives on the ACGME’s educational Review Committee. Educational forums for Program Directors, Directors of Medical Education and Specialty Colleges will begin in January to assist with the transition. Programs may begin to apply for pre-accreditation status in July 2015.

The AOA and ACGME each have pages on their websites devoted to this transition, and they are regularly updated. Please visit the links below for up-to-date information on the process:

American Osteopathic Association: The Single GME Accreditation System
http://www.osteopathic.org/inside-aoa/single-gme-accreditation-system/Pages/default.aspx

Accreditation Council for Graduate Medical Education: Single Accreditation System for AOA-Approved Programs
http://acgme.org/acgmeweb/tahid/445/GraduateMedicalEducation/SingleAccreditationSystemforAOA-ApprovedPrograms.aspx

The AOCD will also see change. During the General Membership Meeting recently held in Seattle, the membership voted to accept the changes to the by-laws that had been presented last summer. Committees will soon be accepting additional members due to the elimination of required maximum seats allowed. The focus of AOCD CME meetings will also change, which will allow for greater flexibility in scheduling.

Change is never easy, especially after getting comfortable with the routine. Hopefully by July, we will all have a clearer picture of the future and what our roles will be. The AOCD will continue to work to keep the membership informed as new information is released.

We hope you will make plans to attend our Spring 2015 meeting in Charlotte, North Carolina, April 23-26. Lectures will begin at noon on April 23 and will conclude at noon on April 26. The meeting will take place at the Ritz Carlton in Charlotte. More information on the meeting can be found on our website at www.aocd.org and in our weekly Thursday Bulletin email blasts.

Please call or email the AOCD office at dermatology@aocd.org if you need assistance.

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Marsha Wise
Executive Director, American Osteopathic College of Dermatology
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A NEW LEVEL OF DERMATOPATHOLOGY SERVICES
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Osteopathic Manipulative Medicine for Inflammatory Skin Diseases

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****Program Director, Dermatology Residency Program, O’Bleness Memorial Hospital, Athens, OH

Abstract

Osteopathic manipulative medicine (OMM) is a defining feature of osteopathic physician training and can be used in practically all areas of medicine. While the use of OMM by osteopathic-trained physicians continues to decline, its use will be an important feature that distinguishes DOs from their allopathic counterparts as osteopathic and allopathic training programs come to be governed by a unified body. Even in dermatology, OMM can be a useful tool for numerous disorders. We present several different OMM techniques that can be used for inflammatory skin diseases.

Introduction

The planned emergence of the Unified Accreditation System in 2015, a merger between the American Osteopathic Association (AOA) and the Accreditation Council for Graduate Medical Education (ACGME), has created numerous obstacles for virtually the entire medical community. These recent organizational changes to graduate medical education in the United States will undoubtedly affect how osteopathic post-graduate medical training is conducted. Whether in primary care or in specialty medicine such as dermatology, preserving the identity of the osteopathic profession will likely be a challenge as these programs merge. Osteopathic dermatologists are in a special position to promote osteopathic manipulative medicine (OMM) because numerous dermatologic disease processes can be treated with manual therapies. This review focuses on inflammatory skin diseases that can be treated with OMM. Included here is also a brief review of the basic techniques used in OMM.

Background

Also known as osteopathic manipulative treatment (OMT), OMM is based on an understanding of the musculoskeletal system’s role in local and systemic fluid management and tissue mobility, as well as its influence, via the nervous system, on pain, proprioception and autonomic elements. The core techniques of OMM utilize these relationships between the musculoskeletal system and other body systems. The use of OMM, regardless of specialty, has been declining for the past several decades. In dermatology, it is hardly used at all. One survey found that half of all responding osteopathic physicians used OMT on less than 5% of their patients. Spaeth et al., focusing on osteopathic physicians in Ohio, found a negative correlation between osteopathic physicians’ OMM use and their level of post-graduate training.2 In another survey-based study, dermatologists reported zero use of OMM, citing a variety of reasons for not incorporating OMM into their daily practice (Table 1).3 It was found that specialists were most likely to avoid performing OMM due to barriers in use, practice protocols, attitudes toward OMM, and deficiencies in training.

Table 1. Reasons for decreased use of OMM by osteopathic physicians and specialists.3

<table>
<thead>
<tr>
<th>Barriers to OMM Use</th>
<th>Example(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Practice protocols</td>
<td>Exam-room size constraints, lack of administration support</td>
</tr>
<tr>
<td>Lack of emphasis in post-graduate training</td>
<td>Use of video/online tutorials instead of hands-on training</td>
</tr>
<tr>
<td>Time constraints</td>
<td>Some OMM techniques may take 30 minutes or more</td>
</tr>
<tr>
<td>Procedure-based specialties</td>
<td>Mohs, dermatopathology</td>
</tr>
<tr>
<td>Decreased practical exposure</td>
<td>Lack of use reduces comfort with techniques</td>
</tr>
<tr>
<td>Attitudes toward OMT</td>
<td>Belief that technique may not be useful</td>
</tr>
</tbody>
</table>

With the Unified Accreditation System, the instruction in and use of OMM in specialty medicine is in danger of even further decline. However, all osteopathic dermatologists do have the training and potential to perform most of these techniques, especially for reduction of tissue congestion and inflammation due to inflammatory skin diseases.

Despite the decline in use of manipulative medicine, it remains a potential adjunct in treating internal as well as cutaneous disease. Some manual- and physical-medicine techniques, such as compression wrapping for stasis dermatitis and scar massage for scarring, are used widely. Campbell et al. promoted the use of OMT for dysesthesia syndromes, hyperhydrosis and stasis dermatitis using the rationale that alteration of the underlying pathophysiologic mechanisms can alter and possibly prevent the disease processes.4 It is under this same rationale that we propose the use of manipulative medicine in the treatment of inflammatory skin disease.

Discussion

The skin is the primary interface between the environment and the body, making it the initial defense against insults like radiation, heat, microbial invasion and trauma. When these insults occur, cutaneous inflammation arises, a result of an innate and adaptive immune system.5 Table 2 summarizes a variety of cutaneous inflammatory processes by the primary cause of inflammation.

One of the four primary principles of osteopathy states that the body has a propensity for self-healing and is capable of homeostasis and health maintenance.6 While medications such as antibiotics for bacterial infection and steroid-sparing immune-modulating medications for psoriasis remain the mainstay of treatment, manipulative medicine offers a supplementary approach to treatment.7 For example, rib raising is a technique used to normalize or reduce autonomic output to blood and lymphatic vessels. Normalization of this output can enhance blood and lymphatic flow to areas of trauma, infection or stress, supporting the healing process. It may also help with delivery of medication to these areas where tissue congestion is often found.
Osteopathic manipulative medicine has two main branches of techniques: direct and indirect. Direct treatments engage a restrictive barrier, and a final activating force is applied to correct the somatic dysfunction. Types of direct treatments include muscle energy, HVLA, rib raising and myofascial release. Myofascial release can also be accomplished via indirect treatment. Indirect methods disengage the restrictive barrier, placing the dysfunctional body part in a state of ease in all directions until tissue tension is equal, thus potentially taking the tension off the lymphatic vessels in the area of treatment. Indirect treatments also include counterstrain. An example of myofascial release that may aid in inflammatory skin disease is release of the diaphragms, including the abdominal diaphragm and the thoracic inlet. A flattened diaphragm is less effective as a lymphatic pump. Myofascial release of the diaphragm allows the diaphragm to move more efficiently, maximizing its potential as a lymphatic pump through improved intrathoracic pressure changes. The thoracic inlet is considered the endpoint of lymph flow as it reaches the venous system; the lymphatic system is a low-pressure system in which flow can be interrupted or impeded by changes in fascial tension. Congestion in this area will cause end resistance to lymphatic flow even when all other areas of lymph flow are adequate. Myofascial release is often considered the primary step in correcting lymphatic drainage and should be done in conjunction with other lymphatic treatments. Recently, lymphatic-pump techniques have been shown to enhance the lymphatic and immune systems through increase of lymph flow and re-

<table>
<thead>
<tr>
<th>Primary Cause</th>
<th>Condition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infectious</td>
<td>- Bacterial (cellulitis, abscess formation, acne) - Fungal (kerion) - Viral (herpetic lesions, Molluscum contagiosum, Verruca vulgaris)</td>
</tr>
<tr>
<td>Autoimmune</td>
<td>- Psoriasis - Systemic lupus erythematosus</td>
</tr>
<tr>
<td>Idiopathic/Other</td>
<td>- Brachioradial pruritus - Notalgia paresthetica - Raynaud’s phenomenon</td>
</tr>
</tbody>
</table>

**Table 3. OMT techniques and their potential benefits in inflammatory skin disease.**

<table>
<thead>
<tr>
<th>Treatment Type</th>
<th>Mechanism of Action</th>
<th>Therapeutic Benefits</th>
<th>Contraindications</th>
</tr>
</thead>
<tbody>
<tr>
<td>Myofascial Release</td>
<td>Direct or indirect; tissue is guided to a point of maximal restriction with constant force until release is achieved, or is guided along the path of least resistance until release is achieved</td>
<td>Promotion of balanced, homeostatic equilibrium and decreased resistance</td>
<td>Open wounds, recent surgery, deep venous thrombosis, neoplasms or internal injury</td>
</tr>
<tr>
<td>Lymphatic Techniques</td>
<td>Group of techniques employed to encourage movement of lymphatic fluid</td>
<td>Decreased resistance to lymphatic and venous flow; mobilization of local congestion, encouraging re-entry into circulation</td>
<td>Relative: cancer Absolute: coagulopathy (e.g., deep venous thrombosis), chronic infections or infections with risk of reactivation (e.g., tuberculosis)</td>
</tr>
<tr>
<td>- Effleurage</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Pedal pump</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Counterstrain</td>
<td>Indirect; patient is placed in a point of ease that lessens the identified tender point by greater than 70% and is held in that position for 90-120 seconds</td>
<td>Relief of identified tender point, encouraging patient comfort</td>
<td>Ligamentous or tendinous tears, fracture</td>
</tr>
<tr>
<td>Rib Raising</td>
<td>Direct technique; physician applies slow, methodical pressure anteriorly and laterally on the rib angles while encouraging caudal motion</td>
<td>Prolonged reduction in sympathetic tone after initial SNS stimulation, encouraging increased blood and lymphatic flow</td>
<td>Anuria, necrotizing fasciitis</td>
</tr>
<tr>
<td>High Velocity-Low Amplitude</td>
<td>Direct; a rapid force carries a joint through the restrictive barrier within the anatomic range of motion</td>
<td>Increased range of motion, decreased pain</td>
<td>Severe osteoporosis, metastatic or bone cancer, cervical rheumatoid arthritis, fracture, carotid or vertebralbasilar disease</td>
</tr>
<tr>
<td>Muscle Energy</td>
<td>Direct; patient is placed into the restrictive barrier; patient’s muscles are then actively used against a physician’s counterforce for 3-5 seconds</td>
<td>Increased range of motion</td>
<td>Recent surgery, poor vitality of patient, unstable joints</td>
</tr>
</tbody>
</table>

**Table 2: Inflammatory skin conditions by primary cause.**

<table>
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<th>Primary Cause</th>
<th>Condition</th>
</tr>
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<tr>
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</table>
distribution of immune mediators, respectively, further aiding in the body’s ability to heal. The lymphatic pump has been shown to significantly increase total leukocyte count, interleukin-8, keratinocyte-derived chemokine and other immune factors in lymphatic flow following treatment.11,12 Several of these factors have been found to be involved in the pathophysiology of inflammatory skin disease, including IL-8 and keratinocyte-derived chemokine.12,13 Extravasation of these products of inflammation into lymph flow by lymphatic pumps can help promote the immune process involved in inflammatory skin disease.

Table 3 summarizes manual medicine techniques and their advantages in treatment of inflammatory skin conditions.

**Conclusion**

OMM remains a potential adjunct in treatment of disease, internal and cutaneous. At a time of merging osteopathic and allopathic paradigms, manipulative treatment becomes a key to maintaining osteopathic identity and promoting osteopathic principles. Continued emphasis on osteopathic principles in diagnosis and renewed focus on manipulation in post-graduate training may alleviate the decline of manual medicine in osteopathy as well as promote the uniqueness of the profession. Osteopathic manipulation has been shown to aid in normalization of autonomic function and enhance the immune process, thereby promoting the health of the individual. By employing methods of manual medicine, both direct and indirect, osteopathic physicians may enhance the treatment and comfort of the patient as a whole. With few exceptions, employing OMM in the treatment of inflammatory skin conditions can assist in resolving a pathologic state, as manual treatments have been shown to alter the flow of lymph and inflammatory mediators that may be involved in inflammatory skin disease.

Although the dermatology office is a fast-paced environment, we hope to promote the use of OMM, either in-office or by referral to a manipulative-medicine specialist, to encourage the health of patients as well as bolster that which is unique to osteopathic medicine. Continued research into the efficacy of manipulative medicine in dermatologic disease remains necessary as we seek new and innovative treatments for common dermatologic conditions.

**References**


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Lichen Planopilaris: A Case Report and Therapeutic Management Review

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**Traditional Rotating Intern, Nova Southeastern University College of Osteopathic Medicine/Largo Medical Center, Largo, FL
***Clinical Professor, Nova Southeastern University College of Osteopathic Medicine, Largo, FL
****Program Director, Dermatology Residency Program, Nova Southeastern University College of Osteopathic Medicine/Largo Medical Center, Largo, FL

Abstract

Lichen planopilaris is a chronic lymphocytic cicatricial alopecia with an unknown pathophysiology. The therapeutic management of lichen planopilaris is challenging due to the high relapse rate and heavy psychological burden on the patient. Herein, we highlight a case of a 40-year-old female with a 20-year history of biopsy-proven lichen planopilaris, and we discuss her tortuous course of treatment regimens.

Introduction

Lichen planopilaris (LPP) is a chronic, scarring alopecia that predominantly affects females between the ages of 40 and 60 years.1 Classically, the clinical presentation of LPP manifests with atrophic polygonal patches of alopecia with acuminated hyperkeratotic follicular papules and perifollicular erythema.2 Histopathologic diagnosis is confirmed with an interface, lichenoid infiltrate involving the infundibulum and isthmus, in combination with a "squamatized" basal layer, Max Joseph spaces and interfollicular changes of lichen planus.3 Due to the cicatricial and recalcitrant nature of LPP, an extensive therapeutic ladder has evolved in the literature.

Case Report

A 40-year-old female presented to the clinic with a 20-year history of redness and flaking of the scalp. The patient reported previous biopsies, which revealed both lichen planopilaris and folliculitis. She had previously tried numerous topical corticosteroid solutions, suspensions and oils. In addition, her previous dermatologist had utilized intralesional triamcinolone 5 mg/cc injections, systemic corticosteroids, topical tacrolimus, oral plaquenil and oral cyclosporine, with no significant improvement. The patient complained of chronic pruritus despite these numerous treatment regimens.

At the time of initial presentation, physical examination demonstrated diffuse erythema of the scalp with perifollicular scaling (Figure 1). Two 4 mm punch biopsies were obtained from the right vertex of the scalp, and the findings revealed scarring alopecia with mid isthmic fibroplasia consistent with lichen planopilaris (Figure 2). We initially started the patient on a taper of oral methylprednisolone in combination with intralesional triamcinolone 5 mg/cc without improvement. The patient was then started on methotrexate, which was incrementally increased up to 15 mg weekly, in combination with clotetasol scalp solution five days a week. The patient did not respond to a three-month trial of methotrexate 15 mg weekly, at which time we obtained blood work to initiate treatment with 1 gram of mycophenolate mofetil twice daily. After two months of mycophenolate mofetil treatment, she reported symptomatic improvement and cessation of further hair loss. However, after completing four months of mycophenolate mofetil therapy, the patient again started complaining of uncontrollable scalp pruritus. Upon re-biopsy of the mid scalp, the histopathology demonstrated changes consistent with lichen simplex chronicus and resolution of the lichen planopilaris.

Discussion

Though the pathophysiology of LPP is unclear, it appears to be a lymphocyte-predominant inflammatory process. Proposed therapeutic management of LPP utilizes various medications with and without inflammatory targets. Specific therapies aimed at reducing inflammation in the disease include corticosteroids, calcineurin inhibitors, antimalarials, immunosuppressants, antimetabolites, and antibiotics.4 Other proposed therapies targeting non-inflammatory disease components include oral retinoids, peroxisome proliferator activated receptor-gamma (PPAR-gamma) agonists, and minoxidil.4,5

A therapeutic ladder for LPP has evolved within the literature due to the condition’s recalcitrance nature. Opinions regarding the order of stepwise therapeutics vary somewhat from study to study. Similarly, treatment results differ significantly between studies, likely accounting for the variation in opinion regarding treatment order.

First-line Therapy

Mid- to high-potency topical corticosteroids with or without concomitant use of intralesional corticosteroids is generally accepted as first-line therapy for LPP. Reported efficacy of topical corticosteroid treatment, though not statistically significant, varies from disease resolution in 66% of patients and improvement in 70% of patients to a fair-to-good response in 83% of patients.1,6,7 The length of treatment and taper duration of topical corticosteroid ranged from fewer than 90 days to seven months within the various studies.1,6,7 Unfortunately, relapse rates following topical steroid cessation were reported to be as high as 80%.4 Concomitant monthly intralesional corticosteroid injections of triamcinolone acetonide up to 10 mg/mL are recommended to further decrease severe inflammation.4 Even in light of the high relapse rate, topical and intralesional corticosteroids are an ideal first-line treatment because they have few adverse effects when used correctly. There is limited data regarding LPP treatment with other topical therapeutics including calcineurin inhibitors.

Second-line Therapy

Recommended second-line therapy for LPP varies greatly in the literature and primarily includes systemic corticosteroids, immunosuppressants, and antimetabolites. Systemic corticosteroids have been widely recommended and used with good results as acute therapy or as a bridge to other immunosuppressive therapy. Megerhan et
Steroid-sparing immunosuppressants including cyclosporine and hydroxychloroquine have been suggested as second-line options for the treatment of LPP. Cyclosporine therapy is recommended in the literature as a second- or third-line treatment option, with reports of a 77% treatment success rate. Optimal dosing of cyclosporine was reported as 4 mg/kg/day to 5 mg/kg/day for three to six months. The associated side-effect profile may warrant exhaustion of other treatment options prior to initiation of cyclosporine treatment. Hydroxychloroquine 400 mg/day is also often used as a treatment for LPP that does not respond to topical corticosteroids. In the literature, reported results achieved using hydroxychloroquine are inconsistent, varying dramatically between studies. Chieng et al. reported statistically significant (p = 0.001) efficacy of hydroxychloroquine use after six and 12 months of treatment, whereas Assouly et al. reported little success following six months of hydroxychloroquine therapy in 12 patients. 

Adjuvantive Therapy

Supplemental topical corticosteroids in conjunction with systemic therapies may help to reduce the symptoms of LPP. Addition of minoxidil to first- and second-line therapies may be beneficial to regrow hair in telogen arrest and improve overall hair growth. Also, an oral peroxisome proliferator-activated receptor γ (PPARγ) agonist, specifically pioglitazone hydrochloride (15 mg/day), may be considered for some refractory cases of LPP, as the inflammation associated with LPP has been postulated to be due in part to abnormal PPARγ activity. Randomized, controlled prospective studies for the treatment of LPP are needed to further streamline clinical data for accurate classification of this disease entity and its optimal treatment recommendations. Additionally, the need for streamlining data between studies is imperative for better comparability. Use of a standardized grading system, like the Lichen Planopilaris Activity Index scoring system (LPPAI), among studies will, ideally, remove some degree of subjectivity from grading results. Though not purely objective, the LPPAI will provide for some level of continuity between LPP studies. 

Conclusion

Treatment of LPP remains a challenge due to its recalcitrant nature, unclear pathophysiology, and lack of prospective double-blinded studies. The clinical data regarding medication efficacy in LPP is inconsistent and difficult to compare between studies. Ideally, the most effective therapies with the safest side-effect profiles will be utilized as early treatment options in the LPP therapeutic ladder. Mycophenolate mofetil is a well-tolerated and generally safe medication that should be utilized as second-line therapy for the treatment of LPP following the failure of topical and intralesional corticosteroids. Ultimately, randomized and controlled prospective studies with streamlined data reporting are necessary to further the literature in regard to treatment of LPP.

References


Livedoid vasculopathy (LV) is an extremely rare and distinct hyalinizing vascular disease affecting only one in 100,000 individuals per year.1,2 Formerly described by Feldaker in 1955 as livedo reticularis with summer ulcerations, LV is a unique non-inflammatory condition that manifests with thrombi formation and painful ulceration of the lower extremities.3 Clinically, the disease often displays a triad of livedo racemosa, slow-healing ulcerations, and atrophie blanche scarring.4 Although still not fully understood, the primary pathogenic mechanism is related to intraluminal thrombosis of the dermal microvessels causing occlusion and tissue hypoxia.4 We review a case in which the patient had LV undiagnosed and therefore inappropriately treated for more than 20 years. To reduce the current average five-year period from presentation to diagnosis, and to improve management options, we review the typical presentation, pathogenesis, histology, and treatment of LV.4

Case Report
A 62-year-old Caucasian male presented in an assisted living facility setting with chronic, right-lower-extremity ulcers present for more than 20 years. The patient had a past medical history of chronic osteomyelitis, hypertension, and a below-the-knee amputation of the left lower extremity secondary to a motorcycle accident. He denied having seen a primary care physician for more than 15 years as well as any medications, vitamins or supplements. Social history was significant for “many years” of tobacco use, heavy alcohol use, inconsistent housing with reoccurring assisted-living-facility admissions, low economic status, and medical non-adherence. The patient reported that throughout the last 20 years his wound-care management for these lesions was limited to the periods of time in which he was living in assisted-living facilities.

Upon physical exam, the patient was found to have a wound on the right medial malleolus measuring 6.4 cm x 4.0 cm x 0.7 cm with moderate serous exudate, approximately 30% yellow necrosis and 70% granulation, with macerated wound margins (Figure 1), and a second wound on the right lateral malleolus measuring 6.0 cm x 5.5 cm x 0.4 cm with moderate serous exudate, approximately 20% sloughing tissue and 80% granulation (Figure 2). The patient was treated for one year, although inconsistently due to housing circumstances, with a series of necrotic-tissue debridements and a variety of topical antibiotics; however, despite therapy, the wounds failed to close. Throughout the duration of management, the patient repeatedly refused biopsy and hyperbaric oxygen therapy. Following one year of multiple topical antibiotics and debridement treatment resulting in minimal improvement, the patient finally consented to biopsy. The pathology report identified ulceration with fibrin in vessel walls associated with stasis dermatitis characterized by thick-walled capillaries and hemosiderin deposition consistent with livedoid vasculopathy (Figures 3). The patient refused any further treatment and was lost to follow-up.

Discussion
Livedoid vasculopathy affects women three times more than men, with a median age of 45 years, though it can vary from ages 10 to 85.1,2 Likely secondary to the rarity of the condition, there is much discussion regarding the name of the condition, as authors have written about LV under a wide array of monikers. Common names used synonymously with livedoid vasculopathy include: livedoid vasculitis, segmental hyalinizing vasculitis, livedo reticularis with summer ulcerations, and atrophie blanche en plaque.1,4 Although commonly used, the denotation of “vasculitis” is a bit misleading, since the primary mechanism of action is not actually inflammation.4 Due to the bilateral and symmetrical lower-extremity distribution of the eruptions, LV has also been nicknamed “PURPLE syndrome” (Painful Purpuric Ulcers with Reticular Pattern of the Lower Extremities).4

The pathogenesis of LV is not yet fully understood, but there is a consensus that it consists of dermal blood-vessel thrombosis leading to superficial tissue ischemia and necrosis, thus propagating pain and ulceration.1 According to the Virchow triad theory, the three factors that contribute to the development of thrombi, and therefore theoretically LV, include endothelial damage, inadequate blood flow, and hypercoagulability.2,5 It has been demonstrated that patients with LV exhibit decreased flow-mediated vasodilation of the brachial artery, signifying endothelial dysfunction.5 A decreased production or activity of nitrous oxide in endothelial cells has been detected in some cases, supporting the contribution of endothelial damage to LV.6 Additionally, the fact that fibrinolitics, antiplatelets and thrombolytic
Agents have shown to have a positive effect on LV patients demonstrates the contribution of hypercoagulability and decreased blood flow to its pathogenesis.

In fact, several conditions may lead to the creation of these three contributing factors. Patients with LV may be categorized as having primary (idiopathic) LV or secondary LV, in which a known underlying condition is the root of the disease. A thorough investigation must be performed in any patient suspected to have LV to rule out conditions such as systemic lupus erythematosus, scleroderma, protein C or S deficiency, factor V Leiden, homocysteinemia, sickle-cell anemia, cryoglobulinemia, cryofibrinogenemia, increased antiphospholipid, underlying malignancy, altered fibrinolysis, or platelet activation that may be the underlying cause of the hypercoagulability or occlusion. However, unknown individual factors must exist for the development of LV given that, for instance, few people with protein C deficiency develop LV.

Patients with LV clinically present with bilateral, painful, “punched out” ulcerations that are slow to heal and result in stellate atrophic scar tissue. Affected regions may also demonstrate erythema, telangiectasia, hyperpigmentation, and possibly purpura. The triad of livedo racemosa, ulcerations, and atrophie blanche characterizes the unique clinical presentation of LV. Livedo racemosa, a fixed, irregular, reticular pattern on skin, is secondary to the microcirculation disorder and results in local tissue hypoxia and possible necrosis. Although LV is not the only disorder in which livedo racemosa may be seen, it is commonly clinically regarded as an indicator of impending LV. The cutaneous ischemia leads to painful purpuric and erythematous plaques and papules frequently evolving into punched-out ulcerations. The painful eruptions are typically located bilaterally and symmetrically on the lower extremities, most frequently on the malleoli. As the ulcers begin to heal, at approximately four months, they result in stellate, white, atrophic scars around their borders, known as atrophie blanche, resulting in permanent fibrosclerosis of the skin. Additionally, patients may complain of parenthesis or hyperesthesia, indicating potential mononeuritis multiplex, likely secondary to the deposition of fibrin and thrombin in the vasa nervorum resulting in ischemia.

Lower-extremity, reticulated, ulcerated lesions that closely resemble LV should be considered in the differential diagnosis include: lupus-associated antiphospholipid syndrome, sickle-cell anemia leg ulcers, venous stasis with varicosities, hydroxyurea-related ulcerations, dysproteinemia, vasculitis, microscopic polyarteritis, polyarteritis nodosa, granulomatous vasculitis, and peripheral vascular disease.

The cardinal histologic findings of LV are seen at the dermal-epidermal junction and consist of: deposition of fibrinoid material in the vascular lumen, hyalinization of the vessel wall, tissue infarctions and lack of vasculitis. More specifically, the fibrinoid thrombus is found in the lumen of small vessels of the superficial dermis. This may be accompanied by ulceration or infarction of the overlying epidermis. The fibrinoid material may similarly be found on the vessel walls and in the surrounding stroma, creating fibrinoid rings. Hyalinized walls and endothelial proliferation may also be identified, in addition to extravasated erythrocytes in the stroma that may indicate microhemorrhage. Direct immunofluorescence may show immunoglobulin, fibrin and complement deposition in the superficial vessels; however, these are not specific to LV and must be supported by other findings.

Livedoid vasculopathy is diagnosed based on a combination of clinical and histopathological findings. The first step in the clinical workup should be to rule out venous insufficiency and other common causes of atrophie blanche. A detailed personal and family history of hypercoagulable disorders, fibrinolytic disorders, connective-tissue disorders and inflammatory disease should be performed. Chronic venous insufficiency may be evaluated by the presence of varicose veins, ochre dermatitis, lower-extremity edema and an abnormal venous Doppler ultrasound. Peripheral artery disease may also be associated with LV and may present with claudication, painful ulcers, pale and cold extremities and abnormal arterial Doppler ultrasound. Specific laboratory analysis is dependent on clinical presentation and is targeted towards the exclusion of the conditions that are associated with LV. If a connective-tissue disease is suspected based on family and/or personal history and presentation, consider laboratory analyses for antinuclear antibodies, antiphospholipid antibodies, anti-beta-2 glycoprotein I, antiphospholipid antibodies (IgM and/or IgG) and IgM antiphosphatidylserine. Laboratory analyses for hypercoagulable or fibrinolytic disorders may include factor V Leiden, prothrombin G20210A mutation, elevated factor VIII level, protein C and S deficiency, antithrombin III deficiency, hyperhomocysteinemia, plasminogen-activator inhibitor or reduction in plasminogen-activator activity, monoclonal cryoglobulinemia, and cryofibrinogenemia. For paraproteinemias, laboratory workup may include determination of immunoglobulin, kappa and lambda chain levels, protein electrophoresis and immunofixation. Additionally, polyclonal cryoglobulins may be associated with hepatitis B and C and should also be taken into consideration.

Biopsy of tissue for regular histology and immunofluorescence is required for diagnosis. Deposition of fibrin, immunoglobulin (IgG, IgM) and complement C3 may be detected by immunofluorescence. Biopsies revealing intraluminal thrombosis, endothelial proliferation, and hyalinized degeneration of the dermal vessels provide a definitive diagnosis of LV. However, due to the focal and segmental nature of LV, this “classic” presentation may not be visualized with a single biopsy. It is important to note that biopsies actually complicate the healing of the ulcerations. Therefore, it is debatable whether practitioners should opt to obtain repeated biopsies in order to obtain all three histological patterns. Special attention should be given to the biopsy method in which specimens are obtained. Small, wedge-shaped tissue samples obtained from the periphery of the ulcer and including healthy adjacent tissue are often preferred. This is due to the fact that the base of the ulcer predominantly demonstrates inflammation from tissue repair and granulation.

Figure 3. Biopsy reveals vessel walls thickened with pink fibrin, polymorphous infiltrate and a small amount of hemosiderin deposition.
Antithrombotics, such as recombinant tissue-plasminogen activator, are often effective alternatives; however, the need for inpatient therapy may make it a less practical option.4,7 Low-molecular-weight heparin, heparin, and warfarin may also be used to breakdown or prevent thrombi and have been found to be relatively equivalent in effectiveness.4,8,13 Pentoxifylline may be utilized for its effect on coagulation in order to improve cutaneous oxygenation.9 There is still no agreed-upon dose for anticoagulation in the treatment of LV, though most studies and reports that have achieved wound resolution administered dosages indicated for deep-vein thrombosis prevention.6

A review of the literature yielded a wide assortment of other approaches that have been employed with varying results. Anabolic agents, such as danazol and stanozolol, have been demonstrated as beneficial in many reported cases. In patients with systemic lupus erythematosus, antimalarials should be employed. Systemic phototherapy with PUVA, consisting of oral 8-methoxypsoralen and UVA therapy, as well as cyclosporine and intravenous immunoglobulin are being explored as possible therapies.9

Incorporation of antibiotics, specifically doxycycline, has been reviewed for its potential therapeutic effects in LV along with its ability to safeguard against infection.13,16 Doxycycline, a second-generation tetracycline, is known to provide anti-inflammatory and anti-microbial protection; however, its use has been reported to show improvement in patients with LV who have failed other treatment. The mechanism for which doxycycline may be beneficial in a thrombotic condition is unknown, and the use of doxycycline is not meant to replace anti-thrombotic agents in patients with known hypercoagulability.10 Also, as a treatment adjunct, hyperbaric oxygen therapy shows promising results, facilitating the body’s innate healing response and relieving pain.15

Proper wound care, such as with zinc oxide, glycerin, gelatin dressings, frequent dressing changes, and debridement of necrotic tissue is paramount.7 Pressure on the ulcer should be relieved with leg elevation utilizing products such as foam wedges, pillows or rotation devices if necessary. Due to the association of LV with venous disease, compression stockings are an important addition to therapy as they have been shown to stimulate fibrinolytic activity.7 However, in patients at high risk for peripheral arterial disease, ankle brachial pressure index must first be completed before safely proceeding with compression.6

Debridement may be achieved through mechanical, autolytic, or enzymatic mechanisms. Ideal wound care strategy is to cleanse with normal saline, in the least traumatic manner possible, and then apply occlusive dressings that provide a moist environment. Silicone adhesives along with room-temperature wet compresses will minimize the trauma associated with dressing changes.8 Patients should be frequently monitored for signs of infection, including leukocytosis, fever, or inflammation, until wound resolution is achieved. Additionally, smoking-cessation education, proper diet, and management of systemic conditions are essential in order to facilitate proper wound healing.

As discussed, LV is characterized clinically by intensely painful, recurring ulcerations. However, pain management in LV has not been thoroughly studied and is, at most, modestly examined in the literature. Pain should be appropriately assessed, and conservative methods, such as gentle handling with appropriately absorbent dressings, ought to be employed first to minimize pain exposure.14 However, pain management may be necessary as part of the treatment protocol for individuals with severe discomfort. Prior reports have found three to six weeks of aspirin (up to 325 mg per day) along with dipyridamole to be an effective treatment combination, providing pain relief while inhibiting thrombus.17 It is important to note that aspirin should be avoided in patients being managed with warfarin. However, it is important to identify the root of the patient’s pain. Pain secondary to the ulcer is typically limited to the margins and intensified during dressing changes and debridement. Pain resulting from vascular occlusion is more complicated, as it is both nociceptive and neuropathic in nature. In these cases, pain control strategies should be obtained using the World Health Organization algiesic ladder.6,18

Conclusion

Livedoid vasculopathy is a painful, chronic, and recurrent condition that may leave the patient severely debilitated if not recognized early and treated properly. With a current five-year average between onset of symptoms and diagnosis, patients are typically left to suffer through painful ulcers with permanent atrophie blanche.4 Although a rare condition, it is for these reasons that it is critical for clinicians to have LV in their differential diagnoses of lower-extremity purpura with reticulated stellate ulcerations that are difficult or slow to heal.13 Once identified, treatment modalities are aimed at improving microcirculation, preventing infection, wound care, and pain control.3,16

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References


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Abstract
The incidence of basal cell carcinoma, squamous cell carcinoma, and melanoma continues to increase. Surgical excision is a common preferred method for achieving cure. However, surgical closure without distorting the surrounding structures can be arduous in certain areas. Further complicating the situation is having two contiguous defects. We hope to provide an option for closing such a defect.

Objective
We present a novel technique for repairing contiguous surgical defects with a double rotation flap called an “8 to Z” yin and yang flap.

Materials
Standard excision tray.

Conclusion
We describe a novel method for repairing two juxtaposed defects with a double rotation flap to not only minimize wound tension but also maintain the cosmesis of the skin. There are many manners in which a lesion can be closed: by altering the defects to do a primary closure, skin grafting, designing a flap, secondary intention healing, or any combination thereof. We believe our method of closure is simple and can retain the undistorted appearance of the skin.

Introduction
Skin cancers including basal cell carcinoma, squamous cell carcinoma, and melanoma are commonly encountered in dermatologic practice. The incidence of these cancers continues to rise. Complete surgical extirpation is curative in the majority of cases. In addition to surgically curing the patient, the challenge for a dermatologic surgeon is to properly close a defect in a functional manner that not only achieves approximation of the wound but also maintains the cosmesis of an area. Additionally, in sun-damaged patients there is often more than one carcinoma present at a given site, which further complicates the closure. We intend to show the closure of two defects that are in close proximity, as well as present a novel technique for repair and closure of two contiguous surgical defects.

The “8 to Z” Yin and Yang Flap
We present our idea for a flap we call an “8 to Z” double rotation yin and yang flap as a surgical option to close two juxtaposed defects, and we contrast it with a similar flap that we used to close two lesions in proximity. We will first discuss the latter, a flap that has been dealt with previously in the literature. We used this flap to address two lesions that were nearby but not contiguous.\(^1\)\(^,\)\(^2\)

Figure 1 demonstrates two 1.5-cm lesions that were 2.5 cm apart. The flap was designed and excised, which resulted in the surgical defect seen in Figure 2. The tissue was then rotated from the two edges to create the final product seen in Figure 3. Of note, similar closures have been described in the literature as a double Burow’s “advancement” flap; however, we feel that this is best depicted as a double rotation flap when additional tissue for Burow’s triangles are not taken.

Our “8 to Z” yin and yang flap utilizes a similar concept of rotating tissue in two directions to close a defect. However, we build upon this concept to close two contiguous defects. Our patient is a 55-year-old man who presented with a melanoma in situ that was adjacent to a basal cell carcinoma. On the first day, the melanoma in situ on the apical scalp was excised without closure, while histopathology confirmed clearance of the lesion. On the second day, Mohs micrographic surgery was performed on the basal cell carcinoma. Eventually, the basal cell carcinoma defect converged with that of the melanoma and created a bilobed defect shaped like a figure 8.

Secondary intention was not considered, as this lesion occurred in a non-concave area and prolonged healing was not attractive to the patient. A primary elliptical closure would have necessitated the removal of additional tissue and resulted in excess skin tension. We designed an “8
to ‘Z’ double rotation “yin and yang” flap for the purpose of closing this defect in the notoriously tight area of the scalp. Wound A had a diameter measuring 4.1 cm, and wound B measured 3.3 cm, as seen in Figure 4. The right inferior border of wound A was undermined and stretched to attach to the left superior edge of the wound A. In doing this, the left superior border of wound B was approximated with the right inferior border of A. Figure 5 demonstrates the vector lines that were designed to do this. 4-0 VICRYL™ was buried to suture these edges together to create a final Z configuration. Interrupted 4-0 PROLENE™ was used to evert the closure. Figure 6 demonstrates the final lazy “Z” closure, or yin and yang configuration.

**Discussion**

There are myriad options to close a surgical wound. The simplest manner is by secondary intention, which allows the body to close the wound gradually over time. This method is frequently suitable for concave areas like the medial canthus, conchal bowl, and the junction between the nose and cheek. Secondary intention is also considered when closure of a wound would result in too great of tissue tension or if a patient cannot tolerate further surgery. A primary fusiform elliptical closure is another straightforward closure that can lead to a linear scar that is cosmetically elegant. This manner of closing is relatively low risk for complications such as necrosis. However, one drawback of this procedure is that additional tissue is typically spared to create the elliptical configuration. Beyond fusiform closures, there are flaps and grafts. In full-thickness skin grafts, tissue is excised down to subcutis from a donor area and re-implanted in the surgical defect. However, this results in interruption of vascular supply that is not optimal for wound healing. Surgical defects that expose cartilage, bone, tendon, or have other poorly vascularized beds are not good candidates for this treatment modality. Another drawback of this technique is that the use of dissimilar tissue may result in a repair that contrasts with surrounding skin.

Flaps are often preferred to grafts, as they take advantage of the laxity of adjacent tissue to approximate the wound without a complete interruption of vascular supply. An ideal flap is one that is able to close the primary defect, yet minimize the subsequent secondary defect. The primary motion of the donor tissue surrounding a defect distinguishes a flap as either advancement, rotation, or transposition. An advancement flap is one that moves in a linear direction to close a primary defect. These flaps are best used in areas of tissue redundancy and can produce linear closures that may be hidden parallel to linear relaxed skin tension lines. A rotation flap moves nearby tissue around a pivot point to close a defect. Rotation flaps are able to redistribute and redirect tension to close tight areas such as the scalp. A transposition flap is elevated and carried over intervening skin and then sutured into place. Similar to rotation flaps, transposition flaps also redirect and redistribute tension, but instead of directly moving into a site, they have to surpass nearby tissue. One advantage of this technique is that the transposition flap may be smaller and require less tissue. Two classic examples of transposition flaps include rhomboid flaps and bilobed flaps that are frequently used in nasal reconstruction.

We present a unique double rotation flap that we call the “8 to Z yin and yang” flap. In addition to the flap we demonstrated in Figures 1-3, other literature has described flaps that utilize an advancement flap with Burrow’s triangles in order to achieve closure of two defects. Our flap is similar in that we have two lesions; however, our lesions are attached rather than adjacent. While our flap builds upon the same principle as those in the literature, one advantage of the “8 to Z’ yin and yang” flap is that it doesn’t require additional incisions and tissue sacrifice to create a Burrow’s triangle. Instead, it utilizes the borders of the defects to rotate together to close the lesion. We believe this strategy minimizes the number of incisions as well as the overall defect size, which ultimately leads to a better cosmetic result for the patient.

In a society that is increasingly being diagnosed with skin cancers such as basal cell, squamous cell, and melanoma, a dermatologist’s role as surgeon is critical. The challenge of this role is not only to excise the lesion but also to close it in a cosmetic and functional manner. We present the “8 to Z’ yin and yang” flap as a potential treatment modality to close two contiguous defects.

**References**


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Combination of Topical Imiquimod and Oral Acitretin in the Treatment of Multiple Large Basal- and Squamous-Cell Carcinomas of the Face

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Abstract

Historically, both basal- and squamous-cell carcinoma skin cancers have been treated surgically with high cure rates and good cosmetic results. However, patients with multiple large facial tumors may experience significant cosmetic scarring with surgery, and therefore represent a patient population that may benefit from a trial of medical therapy. The following case involves a 65-year-old white male who presented with multiple basal- and squamous-cell carcinomas of the face who refused surgical or radiation treatment. We treated the patient using combination therapy of topical imiquimod and oral acitretin, resulting in remarkable clearance of all cancerous facial lesions.

Introduction

The treatment of basal- and squamous-cell carcinomas generally involves surgical removal and occasionally radiotherapy.1,2 Additionally, medical therapies such as topical imiquimod, topical 5-fluorouracil, oral acitretin, and most recently vismodegib have become a part of the armamentarium in cutaneous tumor therapy.3,4 Despite these medical innovations, the standard of care remains surgical.5 The majority of basal- and squamous-cell carcinomas may be excised, especially with the increasing availability of Mohs surgery.2 In the event that a patient cannot undergo surgery or if the tumor is too large, radiation therapy may also be considered.5 Generally, surgical and/or radiation therapies result in cure of non-melanoma skin cancers without a major adverse effect on cosmesis or quality of life.

The case presented herein represents one of the rare patients with multiple facial basal- and squamous-cell carcinomas who would experience significant surgical scarring with excision. Ultimately, the patient refused surgery and also opted against radiation therapy. We report that the combination therapy of topical imiquimod and oral acitretin resulted in complete resolution of the basal- and squamous-cell tumors after 16 months of follow-up.

Case Report

A 65-year-old man presented with multiple basal- and squamous-cell carcinomas of the face. Physical exam revealed large, erythematous, crusted plaques over the left side of the face (Figure 1) and smaller plaques on the right side of the face. Over a three-month time period, he was diagnosed with the following pathologies and sizes: a large, well-differentiated squamous-cell carcinoma of the left temple (5.5 cm x 6 cm) (Figure 2), a large squamous-cell carcinoma in...
Discussion

To our knowledge, our case is the first to report effective treatment with prolonged success of 16 months of multiple large basal- and squamous-cell carcinomas of the face with the combination of topical imiquimod and oral acitretin without surgical removal. We suggest this combination therapy may be a novel treatment approach for patients who are not surgical or radiation candidates. The combination of topical imiquimod and oral acitretin has been previously reported in preventing the recurrence of a highly aggressive squamous-cell carcinoma after the tumor was initially surgically excised in a patient status post renal transplant. Another case found this combination effective for the treatment of multiple keratoacanthomas. Acitretin as monotherapy for prevention of squamous-cell carcinoma in renal transplant patients has been established. In additional, acitretin therapy alone was effective in case reports for the treatment of multiple squamous-cell carcinomas and keratoacanthomas.

The combination of topical imiquimod and oral acitretin for the treatment of basal-cell carcinomas is limited to a few case reports. A young boy with xeroderma pigmentosum with multiple facial and oral basal-cell carcinomas was treated with topical imiquimod and oral acitretin for four to six weeks. At six-month follow-up, all tumors were clinically clear. In another report, two patients with giant basal-cell carcinomas were treated with topical imiquimod and oral acitretin to promote tumor regression prior to surgical or radiation therapy. Additionally, topical imiquimod and oral acitretin have been successfully combined to treat extensive bowenoid papulosis in a patient with HIV. While the literature contains examples of cases using this combination therapy in basal- and squamous-cell carcinomas, our case is unique given the large sizes of tumors, mixed pathology, and the extraordinary results with extensive follow-up at 16 months.

The rationale behind the combination of imiquimod cream and acitretin for anti-tumor therapy exists if one considers their individual mechanisms. In particular, imiquimod is an immune-response modifier. Imiquimod stimulates cytokine production (interferon-alpha, interferon-gamma, and interleukin-12), thereby activating cell-mediated immunity, specifically anti-tumor activity. The efficacy of imiquimod in treating superficial basal-cell carcinomas has been well-established with 43% to 100% efficacy, while the efficacy in squamous-cell carcinomas ranges from 73% to 88% for squamous-cell carcinoma in situ and 71% for invasive squamous-cell carcinoma. Acitretin is a retinoid and thus mediates its effects via binding to nuclear-receptor genes and controlling cellular differentiation and proliferation and reducing keratinization. The role of acitretin in skin-cancer therapy has emerged in the renal transplant population as a means of non-melanoma skin cancer prophylaxis. Taken together, imiquimod works to activate the immune system to attack the tumor cells, while acitretin works to prevent further production of tumor cells.

Conclusion

Overall, this patient’s case suggests an innovative medical therapy of basal- and squamous-cell carcinomas with topical imiquimod and oral acitretin. For patients who would suffer from significant surgical scarring or radiation side effects, we believe that dermatologists should be aware of the potential prolonged response with this therapy that may result in a more resectable tumor or in a complete tumor response.
References


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Herpes Zoster Ophthalmicus in a Patient with Wegener’s Granulomatosis

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Abstract

Herpes zoster ophthalmicus (HZO) is a serious presentation of varicella-zoster virus infection in the periorcular region that may manifest cutaneously but can progress to have ocular involvement, justifying ophthalmologic consultation. Co-morbid diseases may complicate the diagnosis and management of HZO, requiring thorough monitoring of the patient’s progress and potential drug interactions of patient’s medications. Early oral antiviral treatment decreases the rate of development of ocular complications. Post-herpetic neuralgia is a frequent complication of herpes zoster and is best managed with multi-modal drug regimens that work on different mechanisms of the disease.

Introduction

Herpes zoster ophthalmicus is a reactivation of herpesvirus-3, also known as the varicella-zoster virus, in the distribution of the ophthalmic branch of the trigeminal nerve (CN V). It represents up to 25% of all herpes zoster presentations.1 Risk factors for re-activation of the virus include old age, immunosuppressive drugs and diseases, emotional stress, neoplastic disorders, fatigue, poor nutrition, and recreational drug abuse.2,3 Clinical presentation may be preceded by malaise, fatigue, headache, fever, and/or photophobia.3 Lesions typically follow the phases of non-ophthalmic zoster or “shingles,” beginning with unilateral dermatomal pruritus, pain, and/or tingling that may be present for up to five days before an erythematous vesicular rash appears. The vesicles eventually rupture, form crusts, and then heal without scarring.

Case Presentation

A 44-year-old Puerto Rican female presented to the emergency department for right periorbital erythema and edema for two days’ duration. She reported difficulty opening the right eye, radiating throbbing pain along the right side of her face, and fever. The blistering rash was present in the right periorbital region, on the right anterior scalp and right dorsum of the nose. The patient also complained of tenderness of affected areas along the right hemi-facial region. The patient also stated that over the past year, she’d experienced gradually increasing weakness in the lower extremities, hearing loss, and joint pain. Past medical history included depression, asthma, and Wegener’s granulomatosis, which was diagnosed in 2010 in Puerto Rico based on a skin biopsy of the patient’s thigh, for which she was placed on chronic prednisone therapy by her primary physician. Past surgical history included multiple skin grafts for perforated nasal septum secondary to Wegener’s granulomatosis. The patient’s home medications included: prednisone, gabapentin, fluoxetine, tramadol, trazodone, iron sulfate, and alprazolam. The patient had a family history of diabetes mellitus and stroke.

Physical examination revealed multiple vesicles on an erythematous base in the right periorbital region, forehead, scalp and nasal dorsum (Figure 1). Additionally, white exudative plaques were visible on the anterior tongue. Coalescing yellow exophytic verrucous plaques were present on the soles of her feet. Examination of extremities revealed multiple, bilateral, atrophic hypopigmented plaques on the anterior tibial and thigh regions (Figure 2).

Urinalysis revealed hematuria and proteinuria. A bilateral renal sonogram was unremarkable; however, ultrasound of the bladder displayed focal bladder irregularity. Computed tomography (CT) scan, with and without contrast, of the head and neck indicated right periorbital cellulitis and pansinusitis. The ophthalmologic service was consulted, and they noted no ocular involvement. Laboratory tests revealed elevated p-ANCA (2.7), but negative c-ANCA. The erythrocyte sedimentation rate (ESR) was also elevated. The patient was rapid plasma reagin (RPR) negative and human immunodeficiency virus negative.

The patient was admitted and placed on intravenous acyclovir 200 mg (TID), methylprednisolone 20 mg (BID), terbinafine for her presumed tinea pedis, nystatin mouth wash for oral candidiasis, and pertinent antibiotics for her periorbital cellulitis. Blood cultures showed no growth after five days, and antibiotics were discontinued. A punch biopsy of the thigh lesion revealed dermal fibrosis with mild inflammation (Figure 3). Elastin staining showed fragmented, thin elastic fibers indicative of scar. The scar most likely was a result of healing from a previous active Wegener’s lesion. Subsequent laboratory testing revealed low absolute lymphocyte counts (468), low absolute CD4 counts (147), and low CD8 counts (147). Because the patient was immunosuppressed, she was given prophylactic sulfamethoxazole/trimethoprim. The patient continued to complain of facial pain and was...
treated with nortriptyline. Serial complete blood counts revealed decreasing red blood cell counts, hemoglobin levels, and hematocrit levels. The patient was eventually discharged with residual erythema and pain for which she was prescribed famciclovir PO 500 mg TID for five days, sulfamethoxazole/trimethoprim for three days, gabapentin and amitriptyline. She was instructed to continue her home medications.

Discussion

Wegener’s granulomatosis, also known as granulomatosis with polyangiitis, represents a systemic, anti-neutrophil, cytotoxic-autoantibody vasculitis that affects small and medium vessels, particularly within the kidneys and within the respiratory system. Although upper airway involvement, including pansinusitis and/or gingivitis, is the most common initial presentation of disease, ocular involvement may represent up to 16% of initial presentations of the disease. Our patient’s chronic prednisone therapy, similar to regimens of many other patients with vasculitides, may have played a role in her immunosuppression and concurrent pansinusitis, which ultimately led to the recurrence of varicella-zoster virus manifesting as HZO. It has been identified that regardless of disease status, patients with Wegener’s granulomatosis have been reported to have decreased numbers of total, absolute, and relative CD4+ T cell counts compared to controls. This can be attributed not only to immunosuppressive systemic medications but also to the relocation of CD4+ T cells to diseased organs. In contrast, CD8+ T cell counts tend to be comparatively increased, with reduced CD4:CD8 ratios in all spectrums of disease.

Herpes zoster ophthalmicus typically presents with a vesicular rash along the distribution of the ophthalmic division of the trigeminal nerve and its branches, including the lacrimal, nasociliary, and supraorbital nerves. Lesions are usually focally present on the forehead and periocular region of the affected side, with some involvement of the nose. Nasociliary nerve involvement, identified by lesions on the tip of the nose, also known as Hutchison’s sign, prognosticates ocular involvement due to the nerve’s location. Zoster ophthalmicus may also present as a blepharitis causing difficulty opening the eye with non-neural ptosis. About 66% of patients with HZO have been found to have corneal denervation associated with keratitis and mesencephalic nuclear brainstem injury. Conveal nerve involvement and injury results in neurotrophic keratopathy, which may cause several complications, including blindness; therefore, it is imperative to seek ophthalmologic evaluation to determine the extent of the disease and whether ocular involvement is present. Other ocular presentations of HZO include conjunctivitis, uveitis, episcleritis, acute retinal necrosis, progressive retinal necrosis, optic neuritis, and cranial nerve palsies.

The diagnosis of HZO is clinical; however, some cases of HZO may be difficult to delineate in the presence of other co-morbid diseases such as granulomatosis with polyangiitis or periobortal cellulitis, as was the situation in our patient. Viral cultures may be performed from lesions, but they are less sensitive and more time-consuming than direct immunofluorescence assay. Differential diagnoses include herpes simplex, varicella, trigeminal neuralgia, erysipelas, cellulitis, sarcoidosis, trigeminal trophic syndrome, cutaneous lupus erythematosus, syphils, cutaneous anthrax, luesmanis, leprosy, zygomycosis, and sporotrichosis. Treatment of HZO is important because approximately half of untreated patients suffer from ophthalmologic complications. Acyclovir, valacyclovir, and famciclovir are FDA-approved for the treatment of herpes zoster. Patients with an active rash can be treated with acyclovir 800 mg five times daily for up to 10 days’ duration. Based on numerous studies, this regimen has been shown to prevent the formation of new lesions, decrease pain, reduce viral shedding, and decrease the incidence of certain late ocular complications including anterior uveitis and early-to-late keratitis. Patients with immunosuppressive states should be treated with intravenous acyclovir. Due to our patient’s concurrent vasculitides and low CD4 counts, she was placed on intravenous therapy, but was discharged on oral valacyclovir, 1000 mg twice daily dosing for one week, which has been shown to prevent ocular complications such as keratitis and conjunctivitis. It has also been found to decrease average time of zoster-related pain in comparison to acyclovir.

Post-herpetic neuralgia is a significant complication of herpes zoster, particularly in the elderly population. It occurs in up to 20% of patients with herpes zoster within the same region of the infection and can last anywhere from a few months to a few years, at times being intractable to many medications. In the management of post-herpetic neuralgia, targeting multiple mechanisms of disease with combination therapies is logical, and often gabapentin, tricyclic antidepressants and/or topical lidocaine patches are used as first-line agents, followed by opioids and capsaicin as second-line agents.

References

Introduction

Wide-local excision (WLE) has been recognized and accepted as a standard treatment for non-melanoma skin cancers (NMSCs), specifically those not meeting the criteria for Mohs micrographic surgery. In WLE, the skin cancer and a small margin of healthy tissue around it is cut out, typically using a fusiform-shaped ellipse. The wound edges are closed, and the tissue is sent for processing and margin evaluation by a pathologist. Surgical failure, or incomplete excision, is often defined by pathologists as residual tumor within 1 mm of the lateral or deep margin of the excised specimen. Although clear surgical margins have not been shown to completely eliminate tumor recurrence, most studies advocate re-treatment of incompletely excised NMSCs, especially those that are defined as high-risk (deep-margin-involve tumors, recurrent tumors, aggressive histological subtype tumors, or tumors in critical anatomic sites). This re-treatment can be very costly, time-consuming, and stressful for patients. Thus, eliminating the need for retreatment through complete excision of NMSCs is important.

Since the 1970s, numerous studies have looked at optimal surgical margins for successful NMSC excision. Unlike in melanoma, where guidelines for excisional margins exist based on Breslow depth of the original tumor, NMSCs do not have set guidelines for margins, merely recommendations. The recommendations for NMSC surgical margins have been largely debated in numerous studies and range from 2 mm to 10 mm for basal cell carcinoma (BCC) excision and 4 mm to 15 mm for squamous cell carcinoma (SCC) excision, depending on tumor type, risk, size, location, and a number of other factors. Despite taking into account these recommendations for NMSC surgeries, our clinic has still had instances of incompletely excised NMSC tumors, which have led to additional procedures for the patients in order to completely eradicate their cancer.

Therefore, we performed a retrospective review of our surgical databases to determine whether the margins used during our NMSC surgeries were directly correlated to incomplete excision of NMSC tumors. We also looked at other variables that previous studies had cited as contributors to incomplete excisions, namely patient age, patient gender, tumor location, and tumor type (SCC or BCC). Our purpose was to identify any factors contributing to incomplete NMSC excision so that we could reduce the burden to patients of having multiple procedures performed to eliminate skin cancers.

Methods

We extracted surgical data for non-melanoma skin cancers over a four-year period, from February 2010 to October 2013. This surgical data was archived within our SOAPware™ database (2010-2011) and our EMA Dermatology™ database (2012-2013). We initially searched the pathology records for patients who had WLEs of NMSCs to find all incompletely excised tumors. We then noted, but did not include in our analyses, the date of excision. All patients within our study...
were Caucasian with Fitzpatrick skin type II.

As this is a case control study, we used all non-positive margin patients between February 2010 and October 2013 as controls for our study. Because our study was specifically related to BCC and SCC, exclusion criteria for both controls and positive-margin patients included patients who had melanoma excisions and dysplastic nevi excisions. One cellular blue nevus patient was also excluded. The current study was approved by the local institutional review board.

A random-intercepts multivariable logistic-regression model was used to test for potential risk factors for positive margins after return from surgery. The patient was treated as a random effect to allow for correlation of surgery results within an individual patient. The potential risk factors were age, gender, location of tumor (neck, trunk, upper extremity, lower extremity), tumor type (BCC or SCC), and size of margins used for excisions. Age was categorized into two groups determined by the median age. Size of margins was broadened into two categories: greater than or equal to 3 mm and less than or equal to 3 mm. Tukey-Kramer adjustments were used in pairwise comparisons of location types. Significance was set at .05. Analyses were conducted using SAS 9.3 (SAS Institute Inc, Cary, NC).

**Results**

Surgical data on 473 surgeries from 374 patients was collected. Of the 473 surgeries, 213 surgeries were for female patients. The average age of patients was 71 years (standard deviation, 13.6 years). Demographic information is presented in Table 1.

<table>
<thead>
<tr>
<th>Table 1. Demographics</th>
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<tbody>
<tr>
<td><strong>Variable</strong></td>
</tr>
<tr>
<td>Age</td>
</tr>
<tr>
<td>Sex, Female</td>
</tr>
<tr>
<td>Margin (mm)</td>
</tr>
<tr>
<td>1</td>
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<tr>
<td>2</td>
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<tr>
<td>3</td>
</tr>
<tr>
<td>4</td>
</tr>
<tr>
<td>5</td>
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<td>≥6</td>
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**Tumor**

BCC 226 (48%)

SCC 240 (51%)

Other 7 (1.5%)

**Location**

Neck 55 (12%)

Upper Extremity 220 (47%)

Trunk 129 (27%)

Lower Extremity 69 (15%)

There were 25 cases from 23 patients with positive post-operative margins. The 448 negative post-operative margin controls came from 357 patients. Of these 357 control patients, 296 had 1 surgery, 58 had 2, 17 had 3, 5 had 4, and 1 patient had 5 surgeries. Six of these 357 patients also provided at least 1 case surgery (Table 2). Of the 66 patients who underwent surgery more than once, 38 were treated for the same type of cancer, and 25 were treated at the same location.

Table 2. Patient distribution by number and type of surgery

<table>
<thead>
<tr>
<th># of Surgeries for Controls</th>
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<tbody>
<tr>
<td>Total</td>
</tr>
<tr>
<td>374</td>
</tr>
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</table>

The multivariable logistic-regression model did not show a significant independent effect of potential risk factors (age, gender, tumor location, tumor type, or size of margins) on the probability of returning from surgery with positive margins (all P ≥ .08) (Table 3). The test for location of tumor trended toward significance (P=.09), with the upper extremity having the highest rate of positive margins at 7.5%, the lower extremity at 5.8%, the neck at 1.7%, and the trunk at 0.9%. The primary aim of the current study was to determine whether a correlation existed between surgical margins used and incompletely excised NMSCs. We also wanted to determine whether age, gender, location of tumor, or tumor type contributed to incompletely excised NMSCs, because previous studies of positive-margin NMSC excisions have also evaluated these factors.2,5,9,15,22-24 Our intention was to use any positive correlations found in the current study to appropriately adjust our WLEs and decrease incomplete excision rate for NMSCs was 5.1% in our study (95% confidence interval [3.4%, 7.6%]).

**Discussion**

NMSC is the most common cancer worldwide, with BCCs comprising roughly 80% of all NMSCs.1 Various treatment options exist for NMSC; however, WLE and Mohs micrographic surgery have the highest potential cure rate and are the most widely accepted therapeutic options.4,5,9,16,21,24-28 WLE for NMSCs is commonly used when tumors do not meet the criteria for Mohs.21 Although the method for excising a tumor is well-defined, recommendations of surgical margins for NMSC are often debated and frequently revised.2,4,6,9,15,16,19,20,27-29

The primary aim of the current study was to determine whether a correlation existed between surgical margins used and incompletely excised NMSCs. We also wanted to determine whether age, gender, location of tumor, or tumor type contributed to incompletely excised NMSCs, because previous studies of positive-margin NMSC excisions have also evaluated these factors.2,5,9,15,22-24 Our intention was to use any positive correlations found in the current study to appropriately adjust our WLEs and decrease incomplete excised NMSC rates.

<table>
<thead>
<tr>
<th>Covariable</th>
<th>Rate</th>
<th>Odds Ratio</th>
<th>P Values (95% CI*)</th>
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<tbody>
<tr>
<td><strong>Tumor Type</strong></td>
<td></td>
<td></td>
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<tr>
<td>BCC vs. SCC</td>
<td>4.33% vs. 2.21%</td>
<td>2.01</td>
<td>.15 (0.77, 5.24)</td>
</tr>
<tr>
<td><strong>Surgical Margin</strong></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>≤3mm vs. &gt;3mm</td>
<td>3.22% vs. 2.98%</td>
<td>1.08</td>
<td>.88 (.39, 2.99)</td>
</tr>
<tr>
<td><strong>Location</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Neck</td>
<td>1.70%</td>
<td>0.21</td>
<td>.47 (0.01, 3.50)</td>
</tr>
<tr>
<td>Trunk</td>
<td>1.20%</td>
<td>0.15</td>
<td>.09 (0.02, 1.21)</td>
</tr>
<tr>
<td>Lower Extremity</td>
<td>5.81%</td>
<td>0.76</td>
<td>.98 (0.14, 4.19)</td>
</tr>
<tr>
<td>Upper Extremity</td>
<td>7.48%</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Age</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤73 vs. &gt;73</td>
<td>3.09% vs. 3.11%</td>
<td>1.01</td>
<td>.99 (0.40, 2.55)</td>
</tr>
<tr>
<td><strong>Gender</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female vs. Male</td>
<td>3.13% vs. 3.06%</td>
<td>1.03</td>
<td>.96 (0.39, 2.71)</td>
</tr>
</tbody>
</table>

*Confidence interval

**The category reference is listed last. For example, the odds for positive margins on neck tumors are 0.21 times the odds on upper extremity tumors.
Surgical margins used in our NMSC excisions followed literature recommendations, but given the variability of these recommendations, we hypothesized that surgical margins would be our main contributor to incompletely excised NMSCs. However, surgical margins were not a statistically significant contributor to incompletely excised NMSCs in our study. Similarly, age, gender, and tumor type were not statistically significant contributors. Location of tumor had the closest positive correlation to incompletely excised NMSCs, with the upper extremity having the highest rate of positive margins, but this correlation was not statistically significant.

WLE with adequate surgical margins is one of the most commonly used treatments for all types of skin cancer, including NMSCs that do not meet Mohs criteria as well as melanomas of all subtypes.8,14,16,19,21,24,26 Over the last few decades, considerable research has been performed that has established appropriate and effective margin sizes for melanoma excisions based on the depth of the tumor, defined as the Breslow depth. Currently accepted guidelines for melanoma margins include the following: 5-mm margin for melanoma in situ; 1-cm margin for melanomas less than 1.0 mm Breslow depth; 1-cm to 2-cm margins for melanomas of 1.0 mm to 4.0 mm Breslow depth; and 2-cm margins for melanomas greater than 4.0 mm Breslow depth.13 While surgical margins for melanoma skin cancers have been well-studied and categorized, surgical margins for non-melanoma skin cancers have not. Hence there is a greater discrepancy in margins used for excision of BCCs and SCCs. While some have endeavored to propose guidelines to standardize NMSC margins, variability in the literature has highlighted discrepancies and a lack of consensus.2,4,6,15,17,19,20,26,27

A study by Thomas et al. claimed that advisable surgical margins for BCC excisions ranged from 2 mm to 10 mm, and for SCC excisions from 4 mm to 15 mm.19 Other authors have recommended a 4-mm surgical margin for primary NMSCs less than 2 cm in diameter that can be safely classified as low-risk. Low-risk NMSCs are defined as tumors that are less than 2 cm in diameter; are primary, well-defined, slow growing, and well-differentiated; occur in non-immunocompromised patients; and are without neurological symptoms and without perineural or vascular involvement.2,4,6,15,20,28

This 4-mm margin recommendation has been shown to increase the peripheral clearance rate of NMSC tumors to approximately 95%, compared with an 85% rate using a margin of 3 mm, and has thus decreased the number of incompletely excised NMSCs.9,16,27 In contrast, Gulleth et al. demonstrated that for low-risk BCCs, similar tumor clearance was observed using 3-mm, 4-mm, and 5-mm margins.4 For low-risk SCCs, both Motley et al. and Pua et al. agreed that a 4-mm surgical margin was adequate, but a 6-mm margin was necessary for high-risk SCCs.5,9 Most recently, Weinstein et al. used clinical and histologic correlations to stratify BCCs and SCCs into high- or low-risk groups.20 They suggested 4-mm margins for low-risk BCCs or SCCs and Mohs or complete peripheral deep resection using 10-mm margins for high-risk BCCs or SCCs larger than 2 cm on the trunk or extremities.

In the current study, location of tumor contributed most to incomplete excision, specifically in the upper extremity, although the association was not significant. Other studies have also assessed location of the tumor and incomplete excision.5,15,16 Unlike our results, these studies reported the head and neck as the locations most significantly associated with incompletely excised NMSCs. However, these studies used WLE for both head and neck tumors with smaller than recommended margins, thus increasing their rates of incompletely excised NMSCs.5,15,16,24

Our clinic uses Mohs surgery where appropriate for head and neck tumors, and we excluded Mohs surgeries from our data analyses.5,15,16,24

Previous studies have reported a difference in rates of incomplete excision between BCCs and SCCs. Therefore, we investigated tumor type as a potential risk factor. Pua et al. reported an overall incomplete excision rate of 2.20% for NMSCs, a 1.54% rate for BCCs, and a 3.90% rate for SCCs.9 We had a similar incomplete excision rate of 5.1% for NMSCs but saw a slightly higher rate for BCCs vs. SCCs (4.3% vs. 2.2%). Thomas et al. reported incomplete excision rates for BCCs ranging from 4.5% to 13.7% and for SCCs ranging from 5.2% to 7.0%, slightly higher than previous studies or our current study.5,19 Most studies did find SCCs specifically to have a higher incomplete excision rate than BCCs. We found the reverse, but our difference was not statistically significant. The reported incomplete excision rates in the literature remain low, and our data concurred with this.

A possible association between incomplete excision of NMSCs and gender has not been extensively studied. Tan et al. and Bogdanov-Berezovsky et al. both reported that gender was not a statistically significant factor for incomplete excision of SCCs.12,13 Hansen et al. had similar results, but found that female patients had a 28% increased risk of an incomplete excision for BCCs.13 In contrast, Farhi et al. failed to find gender as a predictor of incomplete excisions for BCCs.24 The results of the current study supported previous findings that suggested gender was not a statistically significant factor for incomplete excision of NMSCs.

In the current study, age contributed least to incomplete NMSC excision. A possible association between age and risk of incomplete excision has been previously studied. As in our study, Tan et al. found that age was related to completeness of excision, specifically in patients older than 70 years of age.12,23 Other studies have found no statistically significant association between incomplete excision of SCCs and age.15

We found a significantly higher risk of incomplete BCC excisions among patients older than 70 years compared with those younger than 50 years.21

The current study had several limitations. Chart records were primarily created for purposes of clinical care, rather than for study objectives, so the data was not always comprehensive. For example, we did not look at start size of NMSCs, because it was not available for all records. This factor has been shown to be important in other studies of incompletely excised NMSCs and perhaps should be taken into account in future analyses.2,4,6,15,17,20,28 A second consequence is the possibility of erroneous data recording for each surgery. For example, the size of margins used for NMSCs was sometimes reported in our database using units of cm and in other instances using units of mm. The patient population used in our study was obtained from one hospital, which not only limited the sample size of data available (N=25 in our case) but also limited generalizability to other hospitals or larger patient populations. The patient data was recorded over a four-year time period for accuracy, which also limited our sample size. The small sample size inevitably decreased the power of the study and contributed to the lack of statistical significance.

Although the study has the aforementioned limitations, the fact that we used a consecutive four-year time period for retrieving surgical data did reduce selection bias. Also, the retrospective analysis prevented physicians' knowledge of the study, eliminating the potential for influencing performance. The retrospective analysis done in the current study has helped us elucidate specific variables and data-collection methods for future prospective studies, thus allowing for more accurate data reporting.

Conclusion

The use of adequate surgical margins for complete excision of NMSCs continues to be controversial in the published literature.4,6,15,16,20,26,27 The most accepted and consistent recommendations suggest 4-mm margins in low-risk NMSCs and 10-mm margins or Mohs micrographic surgery in high-risk NMSCs.4,6,15,20,28 Other factors, such as age, gender, location of tumor, and tumor type show inconsistent relationships to incompletely excised NMSCs, results that were supported by our study findings. The percentage of incompletely excised NMSCs remains low in many studies, including ours. Because recurrence rates of NMSCs also vary, the recommendation is to re-treat these incompletely excised areas.4,6,16 Although re-treatment of an incompletely excised NMSC adds the burden of a second procedure to the patient, it minimizes tumor recurrence, which is better for overall patient well-being. Efforts should continue to determine the most optimal ways to minimize incomplete excision of NMSCs.

References


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Idiopathic Spiny Keratoderma: A Report of Two Cases and Literature Review

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Abstract

Spiny keratoderma is a rare and likely underreported condition that presents with punctate hyperkeratotic growths localized to the palms and soles. We present two cases of clinically diagnosed spiny keratoderma. Although the lesions were asymptomatic, patients are at risk of an underlying internal malignancy with this condition, so diagnosis is crucial. Neither men were seeking treatment for the lesions when they were discovered, suggesting that this condition may be much more common than reported. Patients with histories of manual labor, increased UV exposure, and non-melanoma skin cancer (NMSC) may also be at higher risk for developing spiny keratoderma. The epidemiology, histopathologic features, differential diagnosis, and current treatments for spiny keratoderma are reviewed.

Introduction

Spiny keratoderma is a rare palmar plantar keratoderma that presents with keratotic, pinpoint papules on the palms and soles. There are both hereditary and acquired forms. When found, a thorough history and physical examination are warranted as there are case reports of spiny keratoderma being associated with underlying internal disease and malignancy of the kidney, colon, breast, lung, and skin.† Acquired spiny keratoderma usually manifests after 50 years of age and may be associated with manual labor.‡ We present two cases in older men with spiny keratoderma of one to 20 years’ duration, and with no underlying malignancy or systemic disease to date.

Case Report

Case 1

An 84-year-old male presented for a full-body skin examination. Upon shaking hands with the patient, we noted diffuse, 2 mm to 3 mm spiny papules on both palms (Figures 1-3) without involvement of the soles. The patient stated he slowly developed these lesions in his 60s, and the lesions are and have always been asymptomatic. His past medical history was negative for any internal malignancies, and he was followed regularly with a family practitioner. He was also current with age-appropriate screenings and examinations. His social history was significant for a long career performing outdoor manual labor while working for a phone company. He had no known direct arsenic exposure or prior radiation treatment. Previous dermatologic history included three basal cell carcinomas in his 70s and 80s that were successfully treated with surgical excision. To treat the spiny projections, he had attempted to “sand” them for a period with some success, but they would always return, and eventually he lost the enthusiasm to do so. He also used trials of salicylic acid and urea, which helped to soften the spines but never provided complete resolution. Although he was embarrassed for many years about his condition, it now no longer bothered him.

Case 2

A 67-year-old Caucasian male presented with a one-year history of insidiously growing, pinpoint hyperkeratotic papules projecting from his palms bilaterally (Figures 4-5). He presented to the clinic for skin examination at six-month follow-up for removal of cutaneous squamous cell carcinomas. Upon shaking his hand, the spiny projections were noted. He stated they were present during the last surgery but were less noticeable and not concerning to him at the time. His past medical history included surgical removal of squamous cell carcinomas from his right temple and left forearm. He had been a gun and weapons enthusiast for his entire life, spending significant time using his hands to maintain and fire his weapons and many hours outside without sun protection. The patient was referred back to his primary care physician for internal evaluation. After colonoscopy, chest X-ray and blood work, no internal derangements were noted.

Discussion

Brown reported the first case of spiny keratoderma in 1971 when he described punctate keratotic projections on the palms of a 20-year-old male.† Spiny keratoderma presents with numerous, flesh-colored, well-marginated keratotic papules on

Table 1. Treatment options for spiny keratoderma

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Course</th>
<th>Results</th>
<th>Follow-up</th>
</tr>
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<tbody>
<tr>
<td>Oral acitretin</td>
<td>10 mg start dose; gradually increased to 30 mg for 8 weeks</td>
<td>Improvement over 4 weeks</td>
<td>At 18 months, still clear</td>
</tr>
<tr>
<td>Topical tazarotene gel</td>
<td>0.1% applied once daily for 1 week</td>
<td>Brisk irritant dermatitis with residual improvement of lesions</td>
<td>Not reported</td>
</tr>
<tr>
<td>Topical 5-FU cream</td>
<td>5.0% applied twice daily for 2 weeks (with occlusion for resistant lesions)</td>
<td>Decrease in size and number of lesions</td>
<td>Recurrence within a few weeks of discontinuation</td>
</tr>
<tr>
<td>Topical tacalcitol ointment</td>
<td>0.002% applied once daily</td>
<td>Dramatic improvement over 3 months</td>
<td>Not reported</td>
</tr>
<tr>
<td>Topical ammonium lactate lotion</td>
<td>5% twice a day</td>
<td>Complete resolution in 2 out of 5 patients</td>
<td>Recurrence within a few weeks of discontinuation</td>
</tr>
<tr>
<td>Salicylic acid in petrolatum and curettage</td>
<td>40% applied at night, followed by curettage in the morning</td>
<td>Improvement of lesions (thinner and less painful)</td>
<td>Not reported</td>
</tr>
<tr>
<td>Salicylic acid gel</td>
<td>6% applied under occlusion at night</td>
<td>Resolution after four days</td>
<td>Recurrence with treatment cessation</td>
</tr>
</tbody>
</table>
the palms, fingers, and soles. Spiny keratoderma has recently been classified as one of the digitate keratoses. It has been alternatively referred to as punctate porokeratotic keratoderma, music box spine keratosis, multiple minute palmar-plantar digitate hyperkeratosis, and filiform hyperkeratosis, but spiny keratoderma is now preferred.4

Spiny keratoderma consists of both inherited and acquired forms, with the acquired form more common in males over 50 and possibly associated with internal malignancy.5 Risk factors for the acquired variant, as seen in both of our patients, include a history of manual labor.1 Others include immunosuppression and underlying malignancy of the kidney, colon, breast, lung, and skin.5 Our patients both had a history of significant UV exposure, which could be another risk factor for spiny keratoderma. However, UV exposure may be a confounding variable in patients with histories of manual labor, too, as our patients invariably performed their years of manual labor under UV exposure.

The pathophysiology of spiny keratoderma is unknown but may involve either abnormal or ectopic keratinization. One study reported biopsy results with overexpression of keratins 6 and 16.6 These keratins are responsible for epidermal hyperproliferation, which manifests clinically as keratotic projections.6 The role of ectopic keratinization on the palms and soles was also suggested in a case series involving six other patients.7 AE13, a monoclonal hair-specific antibody expressed in the normal hair cortex, was also expressed in the compact columns of keratoderma in these patients.7 In this particular study, electron microscopy showed features of keratinization of a normal hair cortex, including keratinization but without the production of keratohyalin granules.7 These findings are similar to that of human hair, which suggests that that spiny keratoderma could be representative of ectopic hair formation on the palms and soles. Furthermore, five out of six patients in this study also worked as manual laborers. It has been postulated that repeated trauma through manual labor may explain the hyperproliferation and parakeratosis seen on microscopy, which would support a theory of manual labor causing hand trauma as a risk factor for this condition.7,8 Although repeated trauma may be a risk factor, the authors did not postulate why some patients’ skin is more susceptible than others.

The differential diagnosis includes arsenical keratosis and multiple filiform verrucae, both of which can present in a similar localized fashion on the palmar-plantar surfaces. Patients with Cowden’s syndrome can also present with palmar-plantar keratosis, and therefore a physical exam should be performed to rule out mucocutaneous abnormalities and other manifestations of this syndrome. Hereditary keratoses, including Buschke-Fisher-Brauer disease, hereditary spiny keratoderma, and acrokeratoelastoidosis lichenoides, should be considered in a younger patient.9 It should be noted that hereditary spiny...
keratoderma usually manifests between the ages of 12 and 50 years; however, age is not always a reliable distinguishing factor between the acquired and hereditary subtypes, as there are reports of acquired spiny keratoderma in patients as young as 35 years old.² ⁴

Although biopsy is not essential to establish a diagnosis in all cases, it will reveal a compact column of hyperparakeratosis originating from the stratum corneum, and a hypogranular epidermis directly beneath it. The column is sharply demarcated from adjacent skin that consists of an orthokeratotic stratum corneum. The pathologic differential includes porokeratosis, as the hyperparakeratosis observed can resemble the cornoid lamella present in porokeratosis. These two entities can be distinguished by the presence of dyskeratosis, vacuolated cells, or inflammatory infiltrate seen in porokeratosis, features that are absent in spiny keratoderma. Distinction between spiny keratoderma and porokeratosis should be made either clinically or histologically, as porokeratosis can evolve into SCC or BCC at the clinical site.

Acquired or idiopathic spiny keratoderma has been associated with an underlying neoplasm in up to 50% of cases.² ³ The paraneoplastic phenomena include malignancies of the kidney, rectum/colon, breast, and lung. Squamous cell carcinoma, melanoma and chronic lymphocytic leukemia have also been associated with the acquired form.⁶ Despite many associations of spiny keratoderma with these underlying malignancies, there is only one case of clearing of the keratoderma after successful cancer treatment.⁶ Acquired spiny keratoderma has also been associated with underlying disease, including autosomal-dominant polycystic kidney disease with liver cysts, chronic renal failure, Darier’s disease, type IV hyperlipoproteinemia, and pulmonary tuberculosis.⁴ ⁵ As such, a complete physical exam should be performed along with implementation of screening guidelines for colonoscopy and/or mammogram in any patient presenting with spiny keratoderma.

There is reported variability in treatments for this stubborn and persistent condition, outlined in Table 1. Treatments with topical emollients and keratolytics such as salicylic acid and urea cream have resulted in little improvement.¹⁰ However, combination therapy with salicylic acid 40% ointment overnight followed by curettage in the morning has proven more effective.¹⁰ Other options include mechanical debridement with dermabrasion and paring. Recent reports of topical tazarotene or acitretin for four weeks have shown more long-standing success.¹⁰ ¹¹ Of note, patients on oral acitretin should be followed with routine blood tests that include lipid panels, especially because spiny keratoderma already has an association with hyperlipidemia. In one patient, 5% 5-FU procured successful results, and topical tacalcitol achieved success in another.¹² ¹³ 5-FU and tacalcitol have shown marked improvement in the spiny projections in treated patients, but recurrences have occurred upon discontinuation.¹² ¹³ For those wishing to be treated, newer medications show some promise in eradicating the lesions; however, treatment must be continued to prevent recurrence.

Conclusion
Acquired or idiopathic spiny keratoderma is a rare condition that can present exclusively on the palms and fingers, as seen in our patients. Other common presentations involve the soles as well. A thorough intake of family and personal history, appropriate cancer screenings, and regular medical examinations should be performed to rule out underlying disease and malignancy in patients presenting with acquired spiny keratoderma. Furthermore, questioning about risk factors, such as manual labor, UV exposure, and immunosuppression, can help to solidify a diagnosis. Providers must consider the psychological impact and social embarrassment this condition can precipitate and educate patients that, if successful, continued treatment will likely be necessary to prevent recurrence.

References
Allergic Contact Dermatitis Secondary to Latex Headset in Popular Bluetooth Device

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Abstract

We offer a case of latex-induced allergic contact dermatitis caused by a popular Bluetooth headset device and discuss salient features of patient history, physical exam, and treatment. After diagnosis is made, we provide commentary on the condition and elaborate on its diagnosis through patch testing, treatment protocols, and relevance to today's tech-savvy society.

Introduction

Joseph Jadassohn first described allergic contact dermatitis in 1895. Since then, it has become one of the most commonly seen and costly medical conditions. In 2005, treating contact dermatitis cost approximately $1.4 billion annually and resulted in a loss of around $500 million due to missed workdays and low productivity. For many years, specific allergens known to cause allergic contact dermatitis have been described in detail in numerous journals and texts. Furthermore, allergic contact dermatitis related to modern technology devices like cell phones and computers has been discussed in medical literature and case reports. Our case report reveals a patient with allergic contact dermatitis secondary to latex in a popular Bluetooth headset. Our patient is unique because literature searches failed to reveal any prior cases of allergic contact dermatitis specific to Bluetooth headsets. Furthermore, our case is relevant because the Bluetooth industry is growing rapidly, and similar cases will likely become more common in the near future.

Case Report

A 44-year-old African American female presented with a pruritic rash on her neck for two months. She reported no prior treatment of the rash. The patient denied photosensitivity, insulin resistance, or use of perfumes. However, the patient admitted to a recent habit of wearing a Bluetooth device around her neck. The neck strap of the device was made with rubber material. Past medical and surgical history was unremarkable.

Physical exam revealed a well-nourished African American female with a hyperpigmented, lichenified patch bilaterally on the posterior neck (Figure 1). The plaque’s morphology mirrored the shape of the Bluetooth device the patient frequently wore around her neck (Figure 2).

A diagnosis of allergic contact dermatitis secondary to latex in the Bluetooth headset was made. The patient was treated successfully with triamcinolone acetonide 0.1% cream and told to abstain from use of the Bluetooth device. No biopsy or patch testing was necessary.

Background

Allergic contact dermatitis (ACD) makes up at least 20% of new-incident contact dermatitides. Allergic contact dermatitis can affect individuals from all backgrounds. The National Ambulatory Medical Care Survey conducted in 1995 estimated 8.4 million outpatient visits to American physicians for contact dermatitis; this was the second most frequent dermatologic diagnosis. There are approximately 3,000 different chemicals that have been documented as specific causes of ACD. However, about 25 chemicals appear to be responsible for as many as half the cases of ACD.

Allergic contact dermatitis is a pruritic, cutaneous inflammatory reaction caused by contact with a specific exogenous antigen to which the person has developed sensitization. ACD is a type 4 hypersensitivity reaction made up of two phases: sensitization and elicitation. Sensitization is the process by which the immune system is primed to react against the allergen on the next exposure. The sensitization phase of ACD can last from 10 to 15 days. The elicitation phase follows and describes the proinflammatory state that results from re-exposure to the sensitized allergen.

The classic histological finding for acute ACD is spongiosis, intraepidermal vesicles, and superficial perivascular infiltrate. The pathology of acute lesions is extremely valuable since subacute and chronic lesions can produce non-diagnostic patterns that are often confusing. Acanthosis, hyperkeratosis, and mild superficial infiltrate are features in the sub-acute and chronic setting. Pathologic diagnosis of ACD should correlate with clinical findings.

The physical expression of ACD will differ depending on what stage of the disease is present. Acute-phase ACD is identified by lesions marked with edema, erythema, and vesicle formation. Acute dermatitides usually subside within three to four weeks. However, if a patient has repeated exposure to the allergen, chronic ACD will develop. Chronic ACD presents with scaling, fissuring, and lichenification.

When trying to discover the causative allergen of ACD, recognizing the anatomic distribution of dermatitis has proven valuable. The neck region is a very common site for ACD. Cosmetics, nail polish ingredients, perfumes, and metal allergens in jewelry have all been implicated as common causes of ACD in the cervical region. If the diagnosis of ACD is questionable, or the specific causative agent is unknown, patch testing should be considered.

Patch Testing

Patch testing is an underutilized diagnostic tool in the field of dermatology. When patch testing is indicated, it should be performed with a large number of common allergens as well as occupational and personal-care products relevant to the patient.

Proper patch testing requires three visits: one to apply the allergens; another to remove the tests, read, and grade the results after 48 hours; and the last for a final, delayed reading around...
72 hours to one week after the application of initial patch.4 The second reading is important to catch the delayed reactions common in elderly patients. The Finn method and TRUE are the two most common methods in use today. The Finn Chamber method is set up by placing a small amount of allergen into individual aluminum wells affixed to a strip of paper tape. The Finn Method allows screening for hundreds of allergens and is usually performed after the TRUE method. The TRUE test method requires no advanced preparation because the allergens have already been incorporated into the back of the paper tape strips. The TRUE test is limited because there are only 28 screening allergens available.5 For both tests, the strips are applied to the patient’s upper back. Topical steroids and systemic steroids should both be avoided for at least one week before beginning a patch test.5 Antihistamines do not affect the outcome of the test.5 The classic positive patch test reaction shows spreading erythema, edema, and closely set vesicles that persist after the removal of the patch after two to seven days. False negative tests can occur when there is not a sufficient amount of the allergen to elicit a reaction.

Therapy
The definitive treatment for controlling ACD is avoidance of the allergen implicated. If the allergen is unknown, the provider should begin treatment and further evaluate with patch testing. Topical treatment should be the initial treatment, while all moisturizers, lotions, and topical medications except plain petroleum for dryness should be discontinued. The topical corticosteroid should be used twice a day for two to three weeks.5 Unfortunately, topical corticosteroids have been increasingly recognized as allergens themselves. An allergy to topical corticosteroids should be considered when one has persistent eruption of worsening lesions. The strength of topical steroid should be tailored to anatomic treatment area. For example, high-potency steroids should be used on hands and feet; medium potency for the arms, legs, and trunk; and low potency for the face.

Also, corticosteroid ointments are preferred over cream form due to additives in creams that may be allergenic. Second-line treatments for ACD are topical immune modulators like tacrolimus and pimecrolimus.3 The immunomodulators are especially effective for ACD in areas of the face and eyelids. If the ACD is severe or generalized throughout the body, a three-week tapering course of oral corticosteroids is necessary. A more rapid taper can result in rapid rebound dermatitis. Another effective treatment option for refractory ACD is phototherapy. Numerous studies have shown the effectiveness of oral psoralen photochemotherapy (PUVA) and shortwave ultraviolet (UVB) in the treatment of chronic ACD. Systemic antihistamines such as hydroxyzine or diphenhydramine are useful for pruritus.5

Discussion
With almost universal availability of technology devices, ACD to modern electronic devices has become increasingly common. Modern devices such as personal laptop computers, cellular phones, and video consoles have been linked to many different dermatologic conditions. There have been numerous case reports verifying ACD to nickel and chromium in cell phones and other modern devices.10 Interestingly, our case report demonstrating ACD to latex in a popular Bluetooth headset is a newly documented finding according to literature resources. A literature search on PubMed, MEDLINE, EMBASE, and Ovid MEDLINE failed to demonstrate any literature connecting Bluetooth devices to latex-induced ACD. However, it is likely that this specific case of ACD will become a more frequent finding as the use of modern technology devices rapidly increases. In 2010, the Strategy Analytics North American Automatic Market forecasted that 85% of all mobile phones would be Bluetooth enabled by 2015, with that number growing to 90% by 2016.6 Furthermore, ABI Technology Research Company predicts over 3 billion Bluetooth-enabled devices will ship in 2014, and in 2018 there will be over 10 billion enabled devices in the market.7

While the risk of latex allergy in the general population is low at 1% to 2%, the risk of developing an allergy to latex is higher in people with increased latex exposure, such as health-care workers. Health-care workers have a three times higher risk of developing latex allergy than the general population. Also, patients with spina bifida have a 20% to 67% chance of latex allergy. Research has shown that latex-glove ACD is caused by a delayed-type hypersensitivity reaction to rubber accelerators (e.g., thiurams, carbamates, mercapto compounds) and antioxidants (not latex proteins). More specifically, the latex allergy to gloves was caused by thiurams in 72% of cases, carbamates in 25% of cases, and mercapto compounds in 3% of cases.4

In the future, we will likely see Bluetooth devices being used for many different applications, including sensors that monitor activity levels and medical wellness devices that monitor health-care statistics.7 It is essential that physicians investigate the possibility of ACD related to Bluetooth devices and ask patients about possible usage of Bluetooth devices. As a preventative measure, companies are developing protective coverings that can be attached to the latex area of the Bluetooth headset strap to protect patients from this allergen.9 Awareness of this diagnosis is essential, because the longer the individual has dermatitis the longer it is believed it will take the dermatitis to resolve once the causative agent is identified. Knowledge of potential latex allergy to Bluetooth neck straps and familiarity with prophylactic and effective treatments can help diagnose and treat patients with ACD to latex in Bluetooth devices.

References

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A Case Report of Extragenital Lichen Sclerosus with Anogenital Sparing

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Abstract
Lichen sclerosus is an uncommon, chronic inflammatory condition primarily affecting the anogenital region; however, it can have concurrent or sole extragenital involvement. The etiology is controversial, and lichen sclerosus, specifically the anogenital type, has been linked to future development of squamous cell carcinoma. We present a case of extragenital lichen sclerosus, along with a review of the literature to discuss presentation, etiology, diagnosis, management, and risk of future squamous cell carcinoma.

Introduction
In most cases, lichen sclerosus is identified in the anogenital region, but solely extragenital presentations are not unheard of. When present, most extragenital lesions are visualized on the superior trunk, axillae, buttocks, and extremities, often in conjunction with anogenital lesions. This patient presents with a case of classical-appearing lichen sclerosus on the inferior, posterior aspect of the trunk with anogenital sparing.

Review of the literature revealed other reported cases of lichen sclerosus devoid of anogenital involvement, including those with bullous presentations and those following the lines of Blaschko on the face.1,2 In addition, a rare case of extragenital lichen sclerosus involving the oral mucosa has previously been documented.3 Lichen sclerosus, like many dermatologic diseases, has multiple proposed etiologies, including those related to genetics, infection, and autoimmune disease. The patient presented in this case lacked any of the above predispositions and was placed on topical corticosteroids, which are the mainstay of therapy and are generally known to be effective. However, regardless of the simplicity or complexity of the patient’s medical history, choosing effective therapy can prove to be quite challenging when patients do not respond to topical corticosteroids. Recalcitrant lichen sclerosus may require additional therapies including trials of calcineurin inhibitors, methotrexate, cyclosporine, and phototherapy.

Case Presentation
An 83-year-old Caucasian female presented to the clinic complaining of an “itchy discomfort” on her lower back that had previously bled. She denied discomfort elsewhere. She reported a history of hypertension, thyroid disease, and arthritis but denied any history of skin cancer or other dermatologic issues. On physical exam, she was found to have large, hypopigmented, atrophic plaques extending over the central lower thoracic and lumbar areas of the back with a cigarette-paper-like, wrinkled texture (Figure 1). The area was devoid of blisters, erosions, and excoriations. Concomitant vulvar disease was not present.

A 4-mm punch biopsy was taken and revealed subepidermal clefting with homogenization and edema of the papillary dermis with expansion, as well as mild superficial lymphocytic and eosinophilic infiltrate in the superficial dermis (4x).

Conclusion
Lichen sclerosus is a chronic, relapsing,
inflammatory condition affecting mucocutaneous junctions and cutaneous surfaces, leading to epidermal atrophy.\textsuperscript{4,5} This lymphocyte-driven condition has a predilection for the anogenital area; however, extragenital lichen sclerosis has been reported to occur in 15\% to 20\% of patients with lichen sclerosis.\textsuperscript{4,6} Of note, this condition is commonly referred to as lichen sclerosis without the ‘atrophicus’ portion.\textsuperscript{6} This is attributed to findings that lichen sclerosus can result in hypertrophic rather than atrophic epithelium.\textsuperscript{6}

The etiology of lichen sclerosus is unknown. Studies have determined that there is a change in the expression of certain proteins, specifically extracellular matrix protein-1 (ECM-1), and connective-tissue growth factor in patients with lichen sclerosus.\textsuperscript{7} Some studies have proposed autoimmune, endocrine, and even an infectious etiology. To elaborate, studies have located tissue-specific antibodies, and clinicians have persistently recognized its association with other autoimmune conditions such as vitiligo, thyroid disease, and pernicious anemia in genetically predisposed individuals.\textsuperscript{1,5,8} With prepubescent children and postmenopausal women being affected, many have also attributed the onset to decreased estrogen levels.\textsuperscript{1,5,8} Although controversial, several reports suggest the disease may be triggered by an infectious agent, specifically Borrelia burgdorferi.\textsuperscript{5,8,9} In addition, koebnerization has been described in the development of extragenital lesions.\textsuperscript{6}

Lichen sclerosus can affect individuals across all age groups.\textsuperscript{5} However, the condition typically demonstrates a bimodal onset among prepubertal children and postmenopausal women, with the latter being the most commonly affected group.\textsuperscript{5,7} The incidence of lichen sclerosus is difficult to assess because of the large number of asymptomatic individuals and the multi-specialty patient coverage.\textsuperscript{6}

Lesion distribution is most commonly in the vulvar, perianal, and groin regions.\textsuperscript{9} Extragenital lesions are usually visualized on the upper trunk, axillae, buttoks, extremities or lateral thighs.\textsuperscript{5,6} The most commonly reported presenting symptoms are pruritus and irritation, especially at night, though many individuals are asymptomatic.\textsuperscript{5} Symptoms can also be location-dependent. For example, patients with vulvar lichen sclerosus often experience dyspareunia, dysuria, or bleeding secondary to irritation and introital narrowing, whereas those with perianal lichen sclerosus may experience dyschezia due to similar mechanisms.\textsuperscript{5,7} The predominance of chronic pruritus inevitably leads to lichenification, fissures, and future atrophy, scarring, and potential malignancy.\textsuperscript{5,8}

In lichen sclerosus, lesions evolve with time. Classically, preliminary lesions appear as small, minimally raised, pink- or ivory-colored papules.\textsuperscript{9} These early lesions are usually flat-topped with white or brown follicular plugs referred to as “delling.” Over time, these papules become confluent, forming white, porcelain-like plaques with a characteristic atrophic and wrinkled appearance.\textsuperscript{9} Dermoscopy of extragenital lesions often reveals scaling and keratotic plugs.\textsuperscript{4} Interestingly, an erythematous halo visible on dermoscopy is indicative of an active lesion.\textsuperscript{10}

On histology, lichen sclerosus usually reveals an edematous papillary dermis, effaced epidermis, and blurred border of separation between the two layers.\textsuperscript{6,9} The damage and subsequent atrophy of the epidermis results in contraction of the skin and therefore the characteristic wrinkled appearance of the skin lesions. Additional histopathological features consistent with both genital and extragenital lesions include hyalinosis in the upper dermis, vascular ectasia, and basal vacuolization.\textsuperscript{5,7}

The use of biopsy to establish a diagnosis for lichen sclerosus has been controversial for some time. Many clinicians discourage biopsy, arguing that lichen sclerosus is more of a clinical diagnosis. However, should biopsy be pursued in questionable cases, it is important to be aware that biopsies of lichen sclerosus are not always straightforward and that an inconclusive biopsy does not necessarily rule out the diagnosis of lichen sclerosus.\textsuperscript{5,9} Cases where biopsy is warranted include those that have signs of neoplasia such as chronic ulceration, fissuring, or hyperplasia.\textsuperscript{9} Biopsy is also recommended in lesions unresponsive to treatment, lesions with pigmentation, and in lesions that must be differentiated from other conditions that present similarly to lichen sclerosus, including lichen planus, lichen simplex chronicus, guttate anetoderma, cutaneous T-cell lymphoma, chronic graft-versus-host disease and extramammary Paget’s disease.\textsuperscript{6,9,11} In addition, it is important to consider the social history, especially in children with anogenital lesions, as sexual abuse must be ruled out.

Preliminary management of lichen sclerosus is with high-potency topical steroids.\textsuperscript{4} Clobetasol propionate ointment 0.05\% has been found to be effective for symptomatic relief across all age groups and has been shown to induce recovery of skin changes such as atrophy and even reverse the histological changes.\textsuperscript{11} It is unclear as to how topical steroids recover skin atrophy, but it can be assumed that this reversal is a product of steroid action on reducing inflammation, edema, and subsequent tissue damage that would lead to skin atrophy. This high-potency topical steroid is commonly used twice daily for one month, followed by once daily for another month, followed by tapering until a three-month follow-up is scheduled with the dermatologist.\textsuperscript{9} A majority of patients do benefit from therapy with topical steroids.\textsuperscript{5} Moisturizing agents aid in symptomatic relief, are often used in conjunction with topical steroids, and are a mainstay of long-term supportive therapy.

In patients who have failed therapy with or those with contraindications to topical steroids, a trial of a topical calcineurin inhibitor such as tacrolimus ointment 0.1\% or pimecrolimus cream 1\% is reasonable.\textsuperscript{9} Calcineurin inhibitors are appropriate for management of genital or extragenital lichen sclerosus and have been shown to decrease exacerbations.\textsuperscript{5,8} Other considerations include methotrexate for cases of widespread disease and cyclosporine for refractory cases.\textsuperscript{5} Narrow-band UVB phototherapy and low-dose psoralen–UV A has also been shown to be effective for widespread extragenital lichen sclerosus.\textsuperscript{12}

In consideration of the possibility of infection by Borrelia burgdorferi as a cause of lichen sclerosus, some patients have benefited from treatment of intramuscular penicillin G following failed attempts of management with topical steroids.\textsuperscript{9} Finally, surgery is a last resort and is generally limited to patients with severe cases of genital lichen sclerosus who have failed medical therapy.\textsuperscript{9}

The development of squamous cell cancer is a feared complication seen in 4.5\% of individuals affected by lichen sclerosus.\textsuperscript{9} These neoplastic changes are most commonly seen with female genital lichen sclerosus and are not a part of the natural history of extragenital lesions.\textsuperscript{11} This oncologic manifestation is seen an average of 10 years following diagnosis of lichen sclerosus.\textsuperscript{9}

Management and follow-up is fairly individualized due to the variability of the course of lichen sclerosus. Interestingly, most cases seen in children usually improve.\textsuperscript{9} However, it is imperative that patients with anogenital involvement be evaluated every six months to monitor for progression of disease.\textsuperscript{13}

**Conclusion**

Lichen sclerosus is a chronic inflammatory disorder that presents with genital involvement, extragenital involvement, or both. ECM-1 has been linked to lichen sclerosus; however, other autoimmune and endocrine etiologies, as well as infection by Borrelia burgdorferi, are still being considered. Lesions have a predisposition for the anogenital region, are pruritic, and most commonly affect postmenopausal women. Biopsy is generally unnecessary but may be required to differentiate lichen sclerosus from other pathologies, including squamous cell carcinoma. There is generally a good response to high-potency topical steroids combined with emollients, but other options are available for resistant cases.

**References**

4. Larre Borges A, Tiodorovic-Zivkovic D, Lallas
Pseudoepitheliomatous Hyperplasia Resembling Multiple Keratoacanthomas Arising in a Tattoo

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Abstract

Tattoo-associated reactions are well-recognized in the literature, including granulomatous, lichenoid, pseudolymphomatous, sarcoidal, and eczematous. There are rare reports of pseudoepitheliomatous hyperplasia and keratoacanthoma arising in tattoos. We report a case of a 28-year-old woman who presented with three growths confined to a tattoo placed one year prior. Clinical and histologic features were suggestive of a differential diagnosis that would include keratoacanthoma, pseudoepitheliomatous hyperplasia secondary to chronic wound healing or trauma, and, less likely, infection. Distinguishing between these entities can be a subject of histopathologic debate. Overlap of histologic features requires excisional biopsy with culture for comprehensive analysis and diagnosis, and close follow-up is necessary.

Introduction

Dermatologic conditions associated with tattoo placement are a well-recognized complication seen in dermatology practices. They have been reported to occur within hours to over 45 years after tattoo placement.5,8 Within the last decade, there have been rare reports of eruptive keratoacanthomas presenting in tattoos as well as pseudoepitheliomatous hyperplasia, particularly in the setting of red tattoo pigment or infection.8 Distinguishing between these entities requires careful clinicopathologic correlation, often necessitating surgical excision.4 Herein, we describe a case that demonstrates histologic features suggestive of pseudoepitheliomatous hyperplasia (PEH) or squamous cell carcinoma of the keratoacanthoma (KA) type.

Case Report

A 28-year-old female presented to the...
dermatology clinic for evaluation of three growths on her left foot. The patient reported getting a tattoo of three stars on her left foot one year prior to presentation and stated that the tattoo never healed well. Over the course of six months she noticed development of the aforementioned growths confined to the tattoo. A thorough review of systems was performed and was negative except for localized tenderness over the growths. Past medical history was noncontributory, and medications consisted of ibuprofen as needed. She denied tobacco, alcohol, or illicit drug use.

Physical exam was exceptional for three 2.4 cm round verrucous plaques, two with an erythematous halo, on the dorsolateral aspect of the left foot contained within the boundaries of the tattoo (Figure 1). Of note, the tattoo did not contain any red pigment. Differential diagnosis included keratoacanthoma, foreign-body reaction, or infection, such as coccidioidomycosis or mycobacteria. Two 4-mm punch biopsies were obtained; one specimen was submitted for hematoxylin-eosin (H&E) analysis and the other for fungal, bacterial, and atypical mycobacterial culture. The patient was also given a course of doxycycline on initial presentation for signs of secondary impetiginization.

Histologic examination of the biopsy disclosed a central, keratin-filled crater surrounded by marked epidermal hyperplasia with irregular, epidermal tongues extending deep into the reticular dermis (Figures 2 and 3). A brisk and diffuse inflammatory infiltrate occupied most of the dermis, which had histiocytic, lymphocytic, and neutrophilic components, and displayed marked, focal exocytosis into the epidermis (Figure 4). Occasional deposits of black and green pigment corresponding to tattoo ink were noted in the dermis as well as degeneration of collagen bundles (Figure 5). Higher magnification of the epidermis revealed very focal cytologic atypia of the keratinocytes in the follicular infundibulum (Figure 6), whereas the majority of the remaining keratinocytes were eosinophilic, contained glassy cytoplasm, and lacked atypia (Figure 3). In addition, viral cytopathic effects were absent.

Possible fungal or mycobacterial cutaneous infection. Given the widespread inflammation and the presence of a few ill-defined granulomas, the possibility of an atypical mycobacterial infection arising in a tattoo and resulting in extensive pseudoepitheliomatous hyperplasia was a diagnostic consideration; however, a biopsy sent for bacterial and fungal cultures showed no growth.

The clinical and histopathologic exam as well as negative cultures in this case favored a diagnosis of tattoo-associated pseudoepitheliomatous hyperplasia. The lesions were treated by electrodessication and curettage, with no evidence of recurrence.

Discussion

Tattoos are widely popular, both in the United States and internationally, for decorative, religious, cosmetic, or cultural purposes. Some tattoos are accidental, such as occurs from deposition of exogenous pigment substances in puncture wounds; or iatrogenic, such as occurs from Monsel’s solution when used for hemostasis. Commonly reported tattoo reactions include allergic and hypersensitivity reactions. Reports of pseudoepitheliomatous hyperplasia or keratoacanthoma-like eruptions are rare. Distinguishing between these reactions is difficult due to similar histologic features and often requires complete excision for diagnosis.

Pseudoepitheliomatous hyperplasia is a reactive pattern showing benign, irregular, epidermal hyperplasia characterized by prominent acanthotic downgrowths and keratinocytes with abundant cellular cytoplasm. It can be seen in chronic healing wounds, chronic irritation, trauma, and infection. Histologically, it can mimic keratoacanthoma or squamous cell carcinoma. Fraga et al. detail a series of 11 tattoo-associated keratoacanthomas arising in eight patients, the majority of which were initially diagnosed as invasive squamous cell carcinoma or pseudoepitheliomatous hyperplasia. They note that 82% of the keratoacanthomas occurred in areas of red tattoo pigment, with half of these showing displacement of red tattoo ink into the overlying keratin through transepidermal elimination, suggesting a foreign-body reaction to the tattoo pigment. They acknowledge that there is considerable overlap of histologic...
features seen in pseudoepitheliomatous hyperplasia and keratoacanthomas, but conclude that the features noted are likely describing a single reactive pattern better grouped under the classification of keratoacanthoma.2 Kluger et al. and Balfour et al. collectively describe four similar presentations, and describe histologic findings of pseudoepitheliomatous hyperplasia, the majority seen in areas of red tattoo pigment.8,9 They note the lack of abundant mitosis, major architectural disruption and cytologic atypia in pseudoepitheliomatous hyperplasia, distinguishing it from keratoacanthoma. Balfour et al. also note that a regressing keratoacanthoma could not be excluded in their particular case.9 These reports underscore the challenging distinction between keratoacanthoma and pseudoepitheliomatous hyperplasia, and the need for full-thickness biopsies or excision to rule out a neoplastic process.

Pseudoepitheliomatous hyperplasia can be a reactive process seen in the setting of infection as well, and such etiologies must not be overlooked.7 Of note, the Centers for Disease Control reported an outbreak of 22 cases of tattoo-associated non-tuberculous mycobacterial skin infections in 2011-2012 from gray tattoo ink.3 There are no explicit regulations by the Food and Drug Administration requiring sterility of tattoo inks; contamination can occur through use of nonsterile water, contaminated ink products or poor manufacturing processes. Therefore it is essential that cultures and tissue stains are performed for tattoo-associated reactions suspicious for infection.

Conclusion

Pseudoepitheliomatous hyperplasia in a tattoo is rarely reported, and it has marked histologic similarity to keratoacanthoma. It can be distinguished from keratoacanthoma by lack of abundant cellular atypia, frequent mitoses, and abnormal architecture. Still, distinguishing between pseudoepitheliomatous hyperplasia and keratoacanthoma is a challenge and likely requires a complete excision to rule out a neoplastic process.

References


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Case Report
A patient presented to our office with a circumscribed, pink nodule localized to left angle of the mouth (Figure 1). Upon our initial evaluation of the patient, we considered angular cheilitis or basal cell carcinoma, and a shave biopsy was subsequently performed. The biopsy results revealed an amorphous, dull, pink material extending through the thickness of the reticular dermis with many associated plasma cells arranged in a perivascular and interstitial distribution (Figure 2). Additionally, the dermal material was positive on Congo red staining, and immunoperoxidase-stained sections revealed a marked predominance of Lambda over Kappa light chains (Figures 3, 4).

Discussion
The term “amyloid” was first introduced into medicine by Virchow in 1853. In general, amyloidosis refers to the abnormal tissue deposition of misfolded β-sheet fibrillar protein known as amyloid. However, amyloid is not a single protein, but rather a broad term used to describe one of the many types of amyloid proteins that may become abnormally deposited in tissues (Table 1). Amyloid deposits display a characteristic apple-green birefringence after being stained with Congo red and viewed under polarized light microscopy. The misfolded proteins arise from specific precursor proteins, which help us to classify amyloidosis based on the individual protein chemical compositions (Table 1).

Amyloidosis itself is not necessarily a disease, but rather a manifestation of several underlying disease processes. There are numerous forms of amyloidosis, which consist of various primary and secondary manifestations. Likewise, amyloidosis may present in a wide variety of clinical settings, and it is important for any practitioner to be able to identify this disease process and its appropriate management.

Localized cutaneous amyloidosis may be further classified as either systemic or localized deposition. Systemic amyloidosis can be further classified as primary systemic amyloidosis, which is associated with plasma-cell dyscrasias such as multiple myeloma, and secondary systemic amyloidosis, which is associated with chronic inflammatory and infectious states such as rheumatoid arthritis and tuberculosis, respectively. Localized amyloidosis is limited to one organ, which may be the skin, endocrine organs, or the brain, for which Alzheimer’s disease is the classic example. Amyloidosis is thus a highly variable disease with a wide variety of clinical presentations. Nevertheless, cutaneous manifestations are often the initial presentation in systemic disease.

Localized cutaneous amyloidosis is of particular importance to dermatologists and may be further sub-classified as either primary cutaneous amyloidosis or secondary cutaneous amyloidosis. Primary cutaneous amyloidosis may present as one of three types: macular amyloidosis, papular/lichenoid amyloidosis, or nodular amyloidosis. However, macular...
and papular amyloidosis may also be present simultaneously in what is referred to as biphasic amyloidosis. Secondary cutaneous amyloidosis refers to amyloid deposition seen in association with basal cell carcinomas, Bowen's disease, other cutaneous tumors, and following PUVA therapy. Both macular and lichenoid amyloidosis, in addition to secondary localized cutaneous amyloidosis, result from the abnormal misfolding and deposition of keratin protein. Familial forms of both disorders may be associated with RET oncogene mutations.

Nodular amyloidosis is perhaps one of the rarest forms of amyloidosis. It presents as either single or multiple waxy nodules or plaques that most commonly affect the trunk or extremities. Nodular amyloidosis may present as a primary cutaneous disorder, but it may also present as a cutaneous manifestation of primary systemic amyloidosis associated with plasma-cell dyscrasias, such as multiple myeloma. Nodular amyloidosis is particularly associated with immunoglobulin γ light-chain deposition, which is believed to be secreted by an infiltrate of plasma cells. The presence of nodular amyloidosis confers an approximate 7% risk of progression to systemic involvement. In a study of 16 patients with nodular amyloidosis without systemic involvement, one patient was noted to have a serum monoclonal IgGκ protein upon initial evaluation and subsequently developed symptoms of systemic amyloidosis within one year. Thus, it is important to delineate the etiology in all cases of nodular amyloidosis, as it may be indicative of underlying malignancy. Approximately 25% of patients with primary systemic amyloidosis have cutaneous manifestations, which present as waxy, translucent or purpuric papules, nodules, and plaques localized to the palms and soles that can affect the tips of the fingers. These cutaneous manifestations can be associated with autoimmune connective-tissue disorders, such as systemic lupus erythematosus, scleroderma, and dermatomyositis. Familial amyloidosis confers an approximate 7% risk of progression to systemic involvement. In a study of 16 patients with nodular amyloidosis without systemic involvement, one patient was noted to have a serum monoclonal IgGκ protein upon initial evaluation and subsequently developed symptoms of systemic amyloidosis within one year. Thus, it is important to delineate the etiology in all cases of nodular amyloidosis, as it may be indicative of underlying malignancy. Approximately 25% of patients with primary systemic amyloidosis have cutaneous manifestations, which present as waxy, translucent or purpuric papules, nodules, and plaques localized to the palms and soles that can affect the tips of the fingers. These cutaneous manifestations can be associated with autoimmune connective-tissue disorders, such as systemic lupus erythematosus, scleroderma, and dermatomyositis.

Table 1. Amyloid Proteins and Clinical Syndromes

<table>
<thead>
<tr>
<th>Precursor Protein</th>
<th>Amyloid Protein</th>
<th>Clinical Syndrome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Immunoglobulin light chain</td>
<td>AL</td>
<td>Primary systemic amyloidosis (plasma-cell dyscrasias and multiple myeloma)</td>
</tr>
<tr>
<td>TR</td>
<td>Primary cutaneous nodular amyloidosis</td>
<td></td>
</tr>
<tr>
<td>Cytokeratin (CK5)</td>
<td>AK</td>
<td>Primary cutaneous lichenoid and macular amyloidosis</td>
</tr>
<tr>
<td>β2-microglobulin</td>
<td>Aβ, M</td>
<td>Chronic hemodialysis</td>
</tr>
<tr>
<td>Aβ precursor protein (AβPP)</td>
<td>Aβ</td>
<td>Alzheimer's disease</td>
</tr>
<tr>
<td>Calcitonin</td>
<td>ACAL</td>
<td>Medullary carcinoma of the thyroid</td>
</tr>
</tbody>
</table>

The majority of cases of systemic amyloidosis occur as a result of plasma-cell dyscrasias, including but not limited to multiple myeloma and monoclonal gammapathy of undetermined significance (MGUS), which account for approximately 30% of these cases. The majority of cases of systemic amyloidosis occur as a result of plasma-cell dyscrasias, including but not limited to multiple myeloma and monoclonal gammapathy of undetermined significance (MGUS), which account for approximately 30% of these cases. The majority of cases of systemic amyloidosis occur as a result of plasma-cell dyscrasias, including but not limited to multiple myeloma and monoclonal gammapathy of undetermined significance (MGUS), which account for approximately 30% of these cases. The majority of cases of systemic amyloidosis occur as a result of plasma-cell dyscrasias, including but not limited to multiple myeloma and monoclonal gammapathy of undetermined significance (MGUS), which account for approximately 30% of these cases. The majority of cases of systemic amyloidosis occur as a result of plasma-cell dyscrasias, including but not limited to multiple myeloma and monoclonal gammapathy of undetermined significance (MGUS), which account for approximately 30% of these cases.

Treatment options for cutaneous amyloidosis are limited, and there are few randomized controlled trials involving the treatment of this disease. First-line treatments include topical steroids under occlusive dressings and intralesional steroid injections. However, dermabrasion, shave excision, and curettage with cautery have been used successfully in some cases. Systemic amyloidosis with cutaneous manifestations requires a multidisciplinary approach to treatment, possibly involving systemic chemotherapy with melphalan. Thus, the treatment options will vary depending on the underlying cause.

**Conclusion**

This case highlights the important role that dermatologists play in diagnosis and management of cutaneous manifestations of both localized and systemic disease.

**References**

Systematic Review of Phototherapy in Pruritic Disorders

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**Research Fellow, Department of Dermatology, University of California, San Francisco, CA
***Professor and Vice Chairman, Department of Dermatology; Director, Psoriasis Treatment Center, University of California, San Francisco, CA

Abstract
Phototherapy is a proven method for the management of many pruritic disorders, including atopic dermatitis (AD), prurigo nodularis (PN), and generalized pruritus (GP). Objective: This review aims to give an update on the use of phototherapy for managing pruritus in these disorders to establish it within the spectrum of possible therapeutic options. Methods: A thorough literature search of the PubMed database was conducted to identify studies that examined a variety of phototherapy methods in these disorders. Results: AD is best managed with narrow band (NB)-UVB. NB-UVB and broadband (BB)-UVB are also effective in decreasing pruritus in PN. BB-UVB is the preferred modality to decrease GP caused by uremic pruritus (UP). Conclusion: Phototherapy is a safe and beneficial option when other measures fail to control pruritus in these disorders.

Introduction
Pruritus, or the sensation of itch, is the most common symptom among dermatology patients.1 Both cutaneous and systemic conditions may present with pruritus as the primary symptom. Chronic pruritus is a major cause of distress to patients and has a significant impact on quality of life. All ages are affected by pruritus, ranging from children to seniors, and it is the most common dermatologic complaint in the latter group.2,3 For many sufferers of pruritus, topical therapy is not adequate in controlling their symptom. Therefore, providing additional therapeutic options becomes essential for the successful dermatologist. Phototherapy is a safe and efficacious management modality that decreases pruritus and can be used across age groups.4

Ultraviolet-based therapy (phototherapy and photochemotherapy) can provide relief for pruritic patients without many of the risks and adverse effects of systemic medications. UVB (290-320 nm) and UVA (320-400 nm) are implemented in UV-based therapy. Broadband UVB (BB-UVB) and broadband UVA (BB-UVA) use a light source covering their entire spectrum. Narrowband UVB (NB-UVB) uses 311-313 nm, and UVA1 uses 340-400 nm with a peak at 365 nm. UVA1 can be administered at high-dose (HD-UVA1) (130 J/cm²), medium-dose (MD-UVA1) (50 J/cm²), and low-dose (LD-UVA1) (20 J/cm²). Monochromatic excimer light (308 nm), or MEL, is a more targeted phototherapy device that delivers 308 nm UVB to a localized area and can expand treatment options by sparing unaffected areas. This review article focuses on the efficacy of these forms of phototherapy to treat non-psoriatic, chronic, pruritic disorders triggered by an inflammatory response including atopic dermatitis (AD), prurigo nodularis (PN), lichen simplex chronicus (LSC), and generalized pruritus (GP). To our knowledge, this type of review has not been published before for phototherapy of pruritus.

Methods
For this systematic review, we concentrated on the therapeutic role of phototherapy for AD, PN, LSC, and GP in adults. The computerized bibliographic database PubMed was used to conduct a search for English articles from inception to August 2014. Research articles of randomized controlled trials (RCT), open prospective studies, pilot studies, and retrospective observations on NB-UVB, BB-UVB, UVA, PUVA, and MEL were used. The following key words were used: phototherapy pruritus, phototherapy eczema, phototherapy atopic dermatitis, phototherapy prurigo nodularis, phototherapy lichen simplex chronicus, phototherapy neurodermatitis, and phototherapy pruritic disorders. Based on the keywords chosen, 1,194 articles were revealed. After screening title and abstract, those studies in which phototherapy was not used as a treatment for the chosen disease processes were excluded. Reference lists in review articles were also searched. Abstracts-only and duplicates were excluded. This left 105 articles for the screening phase. These records were then assessed for eligibility, excluding children, hand eczema, nummular eczema, and other modes of treatment as primary analysis, thereby leaving 58 studies. Relevant data including study design, number of participants, duration of treatment, cumulative phototherapy dosing, adverse effects, and clinical outcome were retrieved from the articles and formulated into spreadsheet databases. Thus, the total number of trials included in the final analysis is 58. When specific pruritus assessment scales were mentioned, we cited them in the results. If no particular assessment scale was used, extent of disease, sleep improvement, and remission were evaluated. Because pruritus is the main symptom of these disorders, the above criteria may be considered synonymous with the resolution of pruritus.

Results
We separated our data based on our disease processes of interest, and further viewed each category of phototherapy based on current widespread availability and use. Atopic Dermatitis
AD is a common, chronic inflammatory skin disease characterized by intense pruritus leading to secondary cutaneous findings. It is a genotypic diathesis in which a heightened immune response is triggered once the skin is irritated by an environmental stimulus, subsequently producing the sensation of itch. Genetically predisposed individuals have an imbalance in the T-helper (Th) 2 versus Th1 immune responses. AD develops secondary to this intensified immune response once the patient continuously scratches.4 Hence, AD is colloquially known in dermatology as “the itch that rashes,” because the itch is the chief symptom and the foremost indicator of treatment efficacy.

NB-UVB:
The reduction of pruritus in AD by NB-UVB radiation has been demonstrated in multiple studies (Table 1). A double-blind RCT was conducted by Reynolds et al. to compare the efficacy of NB-UVB to BB-UVA and a placebo of visible fluorescent light.7 The NB-UVB group experienced a 90% reduction in pruritus from baseline, compared to 63% reduction in the BB-UVA group. When compared to placebo, there was a 38% greater reduction in pruritus for NB-UVB versus an 11% reduction for BB-UVA. Seventy-one percent of patients had an improvement in their loss of sleep when on NB-UVB, as opposed to 53% on BB-UVB. NB-UVB also showed an improvement in disease activity in the three-month follow-up period. Although patients in this study were allowed to use moderate-to-potent topical steroids simultaneously, their use was quantified and included in the evaluation of treatment efficacy. This is in line with the real-world usage of phototherapy, as dermatologists rarely use phototherapy-only in practice. Other studies that evaluated the use of NB-UVB support these positive results.8-11 In a nonrandomized, single-blind, half-side comparison study between NB-UVB and the combination treatment of UVA and UVB (UVAB), NB-UVB significantly reduced pruritus (mean visual analogue scores 2.7 and 3.8; p=0.043).12 Legat et al. conducted...
### Table 1: Phototherapy for treatment of pruritus in atopic dermatitis (AD)

<table>
<thead>
<tr>
<th>Study Type</th>
<th>Participants (no.)</th>
<th>Treatment Regimen</th>
<th>Cumulative Dose (J/cm²)</th>
<th>Concomitant TCS allowed</th>
<th>Pruritus Outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>NB-UVB</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>RCT⁷</td>
<td>NB-UVB: 22</td>
<td>2x/week (wk) for 24 weeks (wks)</td>
<td>NB-UVB: 24.8</td>
<td>Yes</td>
<td>NB-UVB &gt; BB-UVB &gt; placebo</td>
</tr>
<tr>
<td></td>
<td>BB-UVB: 19</td>
<td></td>
<td>BB-UVB: 315</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>- Visible light (placebo): 19</td>
<td></td>
<td>Placebo: 320 minutes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>RCT, open⁴</td>
<td>21</td>
<td>3x/wk for 12 wks</td>
<td>NB-UVB: 35.05</td>
<td>Yes</td>
<td>- 68% reduction in AD severity scores</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>- 88% reduction in TCS use</td>
</tr>
<tr>
<td>RCS³</td>
<td>37</td>
<td>2x/wk</td>
<td>NB-UVB: 21.9</td>
<td>Yes</td>
<td>81% improved</td>
</tr>
<tr>
<td>RCS¹⁸</td>
<td>40</td>
<td>3x/wk</td>
<td>NB-UVB: 16.371</td>
<td>Yes</td>
<td>80% improved</td>
</tr>
<tr>
<td>RCT, BCS²¹</td>
<td>10</td>
<td>3x/wk for 6 wks</td>
<td>- NB-UVB: NR</td>
<td>Yes</td>
<td>NB-UVB &gt; UVAB</td>
</tr>
<tr>
<td>RCT, BCS²³</td>
<td>9</td>
<td>3x/wk for 8 wks</td>
<td>- NB-UVB: 26.7</td>
<td>No</td>
<td>NB-UVB = MD-UVAl</td>
</tr>
<tr>
<td>RCT, BCS²⁴</td>
<td>13</td>
<td>3x/wk for 8 wks</td>
<td>- NB-UVB: 10.5</td>
<td>In follow-up period</td>
<td>NB-UVB = MD-UVAl</td>
</tr>
<tr>
<td>RCT, CoS²⁵</td>
<td>47</td>
<td>3x/wk for 6 wks</td>
<td>- NB-UVB: 23.4</td>
<td>No</td>
<td>NB-UVB = MD-UVAl</td>
</tr>
<tr>
<td>RCT¹¹</td>
<td>5</td>
<td>5x/wk for 3 wks</td>
<td>NB-UVB: 9.2</td>
<td>No</td>
<td>100% patients improved</td>
</tr>
<tr>
<td><strong>BB-UVB</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>RCT, BCS²⁶</td>
<td>17</td>
<td>3x/wk for 8 wks</td>
<td>- BB-UVB: NR</td>
<td>Yes</td>
<td>BB-UVB &gt; placebo</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>- Daylight tubes (placebo): NA</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CS⁹⁷</td>
<td>1*</td>
<td>2x/wk for 3 months</td>
<td>- BB-UVB: NR</td>
<td>No</td>
<td>BB-UVB &gt; NB-UVB</td>
</tr>
<tr>
<td>RCT¹⁹</td>
<td>BB-UVB: 52</td>
<td>5x/wk</td>
<td>- BB-UVB: 2.70</td>
<td>No</td>
<td>UVAB &gt; BB-UVB</td>
</tr>
<tr>
<td>RCT²⁸</td>
<td>89</td>
<td></td>
<td>- UVAB: 1.77 (UVB), 104 (⁵)</td>
<td></td>
<td>UVAB &gt; BB-UVB</td>
</tr>
<tr>
<td>RCT²¹</td>
<td>BB-UVB: 33</td>
<td>5x/wk</td>
<td>- BB-UVB: 2.3</td>
<td>Yes</td>
<td>UVAB &gt; BB-UVB</td>
</tr>
<tr>
<td>- UVAB: 23</td>
<td></td>
<td></td>
<td>- UVAB: 1.4 (UVB) 160 (⁵)</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>PUVA</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>RCT, BCS²³</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Whole-body PUVA vs. control: 5</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- PUVA vs. no treatment: 5</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- PUVA vs. BB-UVB: 5</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>RCT²⁴</td>
<td>113</td>
<td>PUVA: 3x/wk for 8 wks</td>
<td>PUVA: 115.3</td>
<td>80% decrease in severity</td>
<td></td>
</tr>
<tr>
<td>RCT, BCS²⁷</td>
<td>12</td>
<td>PUVA: 3x/wk for 6 wks</td>
<td>NB-UVB: 14</td>
<td>No</td>
<td>PUVA = NB-UVB</td>
</tr>
<tr>
<td>CoS²</td>
<td>40</td>
<td>- MOP+UVA: 3x/wk for 5 wks</td>
<td>- PUVA: 48.1</td>
<td>No</td>
<td>PUVA &gt; MD-UVAl</td>
</tr>
<tr>
<td></td>
<td></td>
<td>- MD-UVAl: 5x/wk for 3 wks</td>
<td>- MD-UVAl: 1138.8</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>UVA1</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>RCT, BCS²⁹</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- UVA + UVAB: 28</td>
<td></td>
<td></td>
<td>- UVA + UVAB: 361 (UVB) 109 (⁵)</td>
<td>Yes</td>
<td>- UVA = UVAB</td>
</tr>
<tr>
<td>- BB-UVB + UVAB: 20</td>
<td></td>
<td></td>
<td>- BB-UVB (0.282) + UVAB: 0.558 (UVB) 130 (⁵)</td>
<td></td>
<td>UVAB &gt; BB-UVB</td>
</tr>
<tr>
<td>RCT³⁰</td>
<td>HD-UVAl: 15</td>
<td>Daily for 15 total exposures</td>
<td>HD-UVAl: 1950</td>
<td>No</td>
<td>HD-UVAl &gt; UVAB</td>
</tr>
<tr>
<td></td>
<td>UVAB: 10</td>
<td></td>
<td>UVAB: 1950</td>
<td></td>
<td></td>
</tr>
<tr>
<td>RCT³¹</td>
<td>HD-UVAl: 20</td>
<td>Daily for 10 total exposures</td>
<td>HD-UVAl: 1300</td>
<td>No</td>
<td>HD-UVAl &gt; fluocortolone &gt; UVAB</td>
</tr>
<tr>
<td></td>
<td>UVAB: 16</td>
<td></td>
<td>UVAB: 1300</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>- Topical fluocortolone: 17</td>
<td></td>
<td>UVAB: 0.33</td>
<td></td>
<td></td>
</tr>
<tr>
<td>RCT³²</td>
<td>MD-UVAl: 75</td>
<td>- MD-UVAl: 5x/wk for 3 wks</td>
<td>- MD-UVAl: 750</td>
<td>No</td>
<td>MD-UVAl-cold-light &gt; MD-UVAl</td>
</tr>
<tr>
<td></td>
<td>- MD-UVAl-cold-light: 50</td>
<td>- MD-UVAl-cold-light: 5x/wk for 3 wks</td>
<td>MD-UVAl-cold-light: 750</td>
<td></td>
<td>MD-UVAl-cold-light &gt; MD-UVAl</td>
</tr>
<tr>
<td></td>
<td>- UVAB: 20</td>
<td>- MD-UVAl: 5x/wk for 3 wks</td>
<td>UVAB: 0.29 (UVB) 7.9 (⁵)</td>
<td></td>
<td>MD-UVAl-cold-light &gt; MD-UVAl</td>
</tr>
<tr>
<td></td>
<td></td>
<td>- MD-UVAl-cold-light: 5x/wk for 3 wks</td>
<td>UVAB: 1x/day</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
a randomized, nonblinded comparison of NB-UVB to MD-UV1 and found them equally efficacious in reducing pruritus, a claim supported by other, similar studies.13-15 Taken together, these trials suggest NB-UVB as a preferred treatment for AD.

**BB-UVB:**
BB-UVB has largely been replaced by NB-UVB in today’s dermatology clinics, as more studies have demonstrated the superior efficacy of NB-UVB in treating psoriasis. However, there is a small subset of eczematous patients who are unable to tolerate NB-UVB but can tolerate BB-UVB. Previous studies have demonstrated the superiority of BB-UVB to placebo in treating AD, with a 76% improvement in patients (p < 0.001).16 Pugashetti et al. reported the case of an AD patient in whom NB-UVB caused irritation and was less effective when compared to BB-UVB. The authors hypothesized that the higher doses required by NB-UVB to achieve minimal erythema and induce apoptosis resulted in burning and cutaneous sensitivity, which was not experienced during BB-UVB treatments.17,18 Finally, a few studies found the combination of BB-UVB with UVA superior to BB-UVB alone.19,21 However, BB-UVB was comparable to LD-UV1A in improving the pruritus score.22

**PUVA:**
The use of PUVA in AD treatment dates back to the 1970s, when Morrison et al. demonstrated 8-methoxypsoralen (8-MOP) PUVA as superior to both placebo and BB-UVB.21 8-MOP PUVA has resulted in an 80% decrease in pruritus severity, and 5-MOP PUVA has caused a greater reduction in SCORAD than MD-UV1A (mean +/- SD 54.3 +/- 25.7% vs. 37.7 +/- 22.8%; p = 0.041).24-26 The average length of remission was also longer for PUVA than MD-UV1A (12 weeks vs. 4 weeks; p = 0.012). Bath PUVA was compared with bath NB-UVB in an investigator-blinded half-side study.27 It yielded no significant difference when evaluated using SCORAD (65.7% vs. 64.1%; p = 0.48), even though a faster response to bath PUVA was noted during the first two weeks.

**UVA:**
Older studies have compared the traditional combination UVA and BB-UVB (UVAB) to UVA1 and other types of phototherapy.

---

**Table:**

<table>
<thead>
<tr>
<th>Study</th>
<th>Patients</th>
<th>Treatment</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>RCT35</td>
<td>10</td>
<td>5x/wk for 3 wks</td>
<td>- HD-UV1A: 1710 - MD-UV1A: 855</td>
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<tr>
<td>RCT34</td>
<td>MD-UV1A:</td>
<td>5x/wk for 3 wks</td>
<td>- MD-UV1A: 50 - LD-UV1A: 10</td>
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<tr>
<td>RCT33</td>
<td>32</td>
<td>5x/wk for 3 wks</td>
<td>MD-UV1A: 750</td>
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**UVAB:**

<table>
<thead>
<tr>
<th>Study</th>
<th>Patients</th>
<th>Treatment</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>RCT, BCS26</td>
<td>39</td>
<td>3x/wk for 8 wks</td>
<td>- UVAB: NR - BB-UV: NR</td>
</tr>
</tbody>
</table>

BCS: bilateral comparison study; CR: case report; CS: case series; CoS: crossover study; NA: not applicable; NR: not reported; RCT: randomized controlled trial; RCS: retrospective cohort study; TCS: topical corticosteroid

*The other cases in this case series were excluded because they did not pertain to AD.*
Table 2: Phototherapy for treatment of pruritus in prurigo nodularis (PN)

<table>
<thead>
<tr>
<th>Study Type</th>
<th>Participants (no.)</th>
<th>Treatment Regimen</th>
<th>Cumulative Dose (J/cm²)</th>
<th>Concomitant TCS allowed</th>
<th>Pruritus Outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>NB-UVB</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PCS44</td>
<td>10</td>
<td>NB-UVB: 1x/week for mean 24.3 irradiations</td>
<td>NB-UVB: 23.88</td>
<td>No</td>
<td>Improved, with long remission</td>
</tr>
<tr>
<td>RCT46</td>
<td>4</td>
<td>- NB-UVB: 3x/wk for 32 irradiations - Thalidomide therapy: 100mg/day for 12 wks</td>
<td>- NB-UVB: 40.5 - Thalidomide therapy: NA</td>
<td>NR</td>
<td>Excellent response to thalidomide after 8-10 wks; well-controlled with NB-UVB</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>BB-UVB</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CR50</td>
<td>8</td>
<td></td>
<td>BB-UVB: NR</td>
<td>NR</td>
<td>50% improved</td>
</tr>
<tr>
<td>CS57</td>
<td></td>
<td>- BB-UVB: 8 - Bath PUVA: 4 - Oral PUVA: 7</td>
<td>- BB-UVB: NR - Bath PUVA: 7.5 mL 1.2% 8-MOP bath solution diluted in 70L of water - Oral PUVA: 8-MOP, 25 mg/m2</td>
<td>NR</td>
<td></td>
</tr>
<tr>
<td>CS57</td>
<td>Case 1</td>
<td>- BB-UVB: 3x/wk for 6 wks - 8-MOP Topical PUVA: 3x/wk for 8 wks</td>
<td>- BB-UVB: 6234 - 8-MOP Topical PUVA: 240</td>
<td>Yes</td>
<td>Well-controlled lesions and itch</td>
</tr>
<tr>
<td></td>
<td>Case 2</td>
<td></td>
<td></td>
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<tr>
<td></td>
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</tr>
<tr>
<td>PUVA</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>RCT43</td>
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<tr>
<td>CS57</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PS55</td>
<td>11</td>
<td>once/wk for 8 wks</td>
<td>MEL: 13.5</td>
<td>No</td>
<td>81% had partial or complete remission</td>
</tr>
<tr>
<td>RCS42</td>
<td>17</td>
<td></td>
<td>650</td>
<td>NR</td>
<td>82.4% improved</td>
</tr>
<tr>
<td>RCS42</td>
<td>19</td>
<td>23 median treatments</td>
<td>6.07</td>
<td>No</td>
<td>78.9% improved</td>
</tr>
<tr>
<td>RCS42</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

BCS: bilateral comparison study; CR: case report; CS: case series; CoS: crossover study; NA: not applicable; NR: not reported; PCS: prospective cohort study; PS: pilot study; RCT: randomized controlled trial; RCS: retrospective cohort study; TCS: topical corticosteroid

treated with MD UVA1. While this seems to indicate that PUVA loses its effect quickly, 86% of patients in another study extended into the maintenance phase.54

MEL:
MEL has also been used to target the pruritic nodules.55,56 Nistico et al. observed a decrease in pruritic symptoms in all nine PN patients they studied. MEL provides a more targeted approach and reduces the total number of treatments needed to reach remission. A combination study comparing PUVA + MEL to PUVA alone demonstrated the decreased need for overall treatments in the combination group, although both groups were successful in improving eruptions and achieving complete clearance.57 Long-term benefits of reduced itching were also noted.

UVA:
There are a limited number of studies on the efficacy of UVA1 for PN treatment, with 82.4% improvement in pruritus in one study and 78.9% in another.42,58 The latter group used a UVA lamp with a spike at 390 nm for deeper penetration as the biological effects of UV radiation are directly proportional to its wavelength. Bath PUVA and MD UVA1 have longer wavelengths and therefore are more capable of penetrating the thickened epidermis of PN.39,59
**Lichen Simplex Chronicus**

LSC, also termed neurodermatitis, is a secondary skin disorder that results from excessive scratching. Thus, therapeutic options depend on interrupting the itch-scratch cycle. LSC is often associated with an atopic disorder and is similar to PN in pathogenesis. Lichenification results from thickening of epidermis (acanthosis) and stratum corneum (hyperkeratosis) from the constant trauma of rubbing and scratching for roughly 90 hours, or 140,000 scratches. A case of vulvar LSC was treated with NB-UVB light source, signifying the tolerability of NB-UVB even in sensitive areas.

**Generalized Pruritus**

GP is chronic itch that occurs without any associated diagnosable skin diseases or primary skin lesions. Although frequently idiopathic, it can be secondary to neurologic disorders, chronic renal failure, cholestasis, systemic infections, malignancies, and endocrine disorders. A judicious history, thorough physical examination, and suitable laboratory investigation must be performed to elucidate the cause. Systemic disease has been implicated in up to 20% of patients with GP.

Special emphasis should be placed on drug exposure, travel history, environmental irritants, lifestyle, extracutaneous symptoms, and prior hospitalizations. Initial laboratory tests may include complete blood count, liver- and renal-function tests, serum glucose, iron, ferritin, thyroid-function tests, erythrocyte sedimentation rate, protein electrophoresis, and urinalysis. Many cases of GP begin in a localized area, and phototherapy can often lead to cessation of generalized itch and reveal a previously localized itch. Generalization can be caused by a lowering of itch threshold on other body parts through a combination of neurologic and/or psychological mechanisms.

Those with a negative workup for GP fall into idiopathic pruritus (IP). In those over the age of 65, this form of idiopathic itch is often dubbed “senile pruritus” or Willan's itch, as it is often associated with dry skin. The stratum corneum thickens with age and has decreased keratohyalin granules. Elderly patients with dry skin have a decreased number of surface lipids, impairing the stratum corneum's ability to hold water. Clearance of debris from the dermis also increases with repeated treatment of itch. Generalization can be caused by a lowering of itch threshold on other body parts through a combination of neurologic and/or psychological mechanisms.

Of all the systemic disorders linked to pruritus,
uremia is the most common.67 Fifteen percent to 49% of those with chronic renal failure (CRF) and 90% of those receiving dialysis have uremic pruritus (UP).68 Up to 50% of UP patients complain about generalized pruritus.57,69 In the remaining, UP predominantly affects the back, face, and shunt-arm.70 The term uremic pruritus is not apt because UP does not result from an increase in serum-urea levels. Clinically, UP skin resembles that of hemodialysis patients without pruritus, dry and scaly. No primary skin lesions are seen; however, chronic excoriations, linear crusts, and ulcerations can evolve into a presentation similar to that of PN. Pruritus of hemodialysis and that of peritoneal dialysis occur with similar frequencies.71,72 Although the incidence of pruritus increases as renal function deteriorates, it does not improve with dialysis and is an independent marker of mortality at three years for those on hemodialysis.73 The severity of UP is associated with the duration of dialysis and xerosis. Unfortunately, the prevalence and burden of pruritus in end-stage renal disease (ESRD) is often underestimated by nephrologists, even though it is perceived by patients as a severe and distressing symptom of renal failure.74,75 Its chronic nature is an independent predictor of poor quality of life with severe sleep disturbances.72,76

**NB-UVB:**

Forty-nine percent of the GP patients treated with NB-UVB resulted in moderate to significant improvement.77 A study conducted by Seckin compared UP to IP.78 Sixty-eight follow-up.5,81 While the NB-UVB group showed control during the course of phototherapy and significant reduction of pruritus intensity within an average of 2.5 months. A more complete remission occurred six months after completing therapy.77,82 Forty-three percent of patients who responded. In addition, the beneficial effects of UV exposure were only experienced after a lag time of two weeks in some patients. In another study, 80% of patients with severe UP had relief at least one month after therapy was discontinued, with 60% maintaining relief for at least six months. Cohen et al. reported that 57% of those claimed relief everywhere except for the palms and soles. All patients in this study had relief at least one month after therapy was discontinued, with 60% maintaining relief for at least six months. Cohen et al. reported that 57% of a series of pruritic patients experienced relief after BB-UVB therapy with a decrease in dermal mast-cell counts accompanying improvement in VAS scores.80 Finally, a case report by Hsu et al. found BB-UVB more effective than NB-UVB in decreasing pruritus in UP.90

**Discussion**

Although pruritus is the most common chief complaint in dermatology, there are still many unknowns regarding its pathophysiology. Bernhard classified itch into dermatologic, systemic, neurogenic, psychogenic, mixed, and other categories.51 While this can help determine the etiology to address management options, the inability to quantify pruritus remains a significant barrier to evolving understanding. Because objective measurements of pruritus are lacking, it is difficult to adequately assess and compare treatments; a uniform, consistent, and reliable scale of evaluating pruritus and scratching is needed. Nonetheless, based on current methodologies, which involve subjective evaluations, we have attempted to compare different forms of phototherapy in treating pruritus.

**Efficacy of Phototherapy in AD**

Morison et al. published the earliest known reports of UV phototherapy for AD.23 This, combined with the general observation that atopic patients improved during summer months, led to the use of phototherapy as a treatment modality for AD. As PUVA became integrated into the dermatologic practice in 1974, its long-term side effects of photo-aging began to limit its use in AD. UVA and UVB monotherapies were introduced in the 1980s, but also had some downsides. UVB at times caused burning, xerosis, and erythema, although it required less time than UVA. UVB had a better therapeutic effect with light reactions, but with the drawback of lengthy procedure times. This led to the use of combination UVA/UVB therapy for AD. This was less time-consuming, decreased the total UV dose, and also minimized the risks of developing both short-term and long-term side effects.

NB-UVB is the modality of choice for AD when choosing phototherapy, as it is easily available in most dermatology clinics and is widely used for other conditions as well. BB-UVB is an alternative for those unable to tolerate the intense dosing of NB-UVB or in combination with UVA to increase efficacy. Despite the different doses, regimens, and clinical scoring systems used in the studies examined, UVA1 is a possible mode of treatment for AD. It is more suited for acute AD flares as it achieves results faster than UVAB and is more efficacious than either UVAB or topical corticosteroids. In addition, cold-light UVA1 is superior to UVA1 in reducing AD severity as it eliminates a potential trigger. Long-term follow-up reports are needed and further investigation is recommended to determine maintenance treatments. PUVA is also an option for AD. However, additional studies are needed to document its efficacy in treating pruritus.

**Efficacy of Phototherapy in PN**

NB-UVB is also the treatment of choice for PN, especially when combined with thalidomide to maximize the therapeutic potential of both treatment forms. BB-UVB is effective in treating PN as well, with a supportive reduction in pruritus. Although patients typically prefer topical PUVA over more painful treatment modalities such as intralesional steroid injections, BB-UVB was found to be more effective in treating cases of generalized PN and itch.58 Due to its more localized approach, MEL eliminates UVB exposure to healthy skin. It is also more powerful than NB-UVB (TL01), thereby reducing the number of treatments required to reach remission. The advantage of weekly treatments as opposed to daily for topical treatments and phototherapy regimens also increases patient compliance in MEL. The use of combined synergistic therapies to reach remission is necessary in a chronic condition like PN, which requires similar UV radiation doses as psoriasis chronically to allow patients to undergo further phototherapy sessions.56,59,60 The use of UVA1 for PN treatment needs further investigation, although the studies we found thus far support its utility in treating PN. PUVA has also been
found beneficial in reducing not only pruritus but also the number of papules. PUVA also has a greater maintenance phase than other forms of phototherapy. Mild erythema is a possible side effect of all forms of phototherapy but quickly subsides. Mild hyperpigmentation at the lesional sites was common to most PN studies. Because of the longer wavelengths of UVA, it is potentially able to penetrate PN lesions better. Finally, the limited number of studies completed for the use of phototherapy in LSC supports the use of UVB to decrease pruritus.

Efficacy of Phototherapy in UP

Even though NB-UVB is beneficial in decreasing GP and UP, is less erythrogenic, has a lower pruritogenic potential, and is less carcinogenic than BB-UVB, BB-UVB is the treatment of choice for UP, while UVA is equal to placebo.94,95 In patients who are not candidates for kidney transplant, BB-UVB is considered the treatment of choice by some.96 While UVB radiation is safe, the risk for skin malignancies and long-term immunosuppression remains controversial in immunocompromised patients due to renal transplant. We did not find any studies on the use of PUVA in UP. Thus, more randomized, placebo-controlled trials are needed to determine the safest and most efficacious form of phototherapy for decreasing pruritus in patients on dialysis.

Safety of Phototherapy

Phototherapy is a safe form of treatment. When given long-term, PUVA has been associated with increased risk of cutaneous squamous cell carcinoma, but even high-dose exposure does not increase basal cell carcinoma risk.59 However, none of the published studies in a comprehensive review of BB-UVB and skin cancer risk demonstrates increased skin cancer risk, with one outlier of genital tumors in men receiving both PUVA and BB-UVB, thus necessitating the contemporary practice of genital shielding.90 A 25-year retrospective study looking at 280 psoriasis patients treated with BB-UVB and coal tar also did not demonstrate an increased skin cancer risk.91,92 A similar study conducted on 426 patients with atopic dermatitis and neurodermatitis treated with coal tar ointments and ultraviolet light (Goeckerman regimen) concluded that the incidence of skin cancer is not significantly increased above the expected incidence for selected populations in the United States.93 NB-UVB also has an excellent safety profile. In a 2008 study of 4,665 patients who received NB-UVB for 17 years, there was no increase in non-melanoma or melanoma skin cancer.94 Finally, in a retrospective study of six years, no evidence for increased skin cancer risk was found for either BB- or NB-UVB phototherapy.95

Limitations

The conclusions that one can draw by systematically analyzing the current medical literature regarding the use of phototherapy in pruritic disorders are limited due to several factors. Publication bias must be considered in any review article, as trials leading to positive results are more likely to be published.102 Poor statistical power resulting from small sample size must also be taken into account. Uncommon adverse effects are often not disclosed or perhaps unrecognized. The variability in parameters of each of the different trials must also be taken into account. Different methods for selecting patients, dosing UV radiation, and assessing response limit the ability to draw detailed conclusions through a comprehensive review of available studies. Despite these drawbacks, the authors found overwhelming evidence after reviewing the data to conclude that phototherapy is helpful for most types of pruritus.

Conclusion

We conclude that phototherapy is a beneficial, efficacious, efficient, and safe method of treatment for AD, PN, LSC, and GP. NB-UVB is a superior form of phototherapy for AD. It is also effective in PN and LSC. However, BB-UVB is the most efficacious for UP. MEL provides targeted therapy with a reduction in the total number of treatments required for PN. PUVA induces a greater maintenance phase for PN and is beneficial for AD. UVA is favorable for AD and PN but equal to placebo for UP. These data conclude the overwhelming evidence of the benefit of phototherapy in decreasing pruritus of multiple causes.

References


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Zosteriform Lichen Planus: An Unusual Clinical Variant

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Abstract
Lichen planus (LP) is a relatively common papulosquamous dermatosis affecting the skin and mucous membranes. It has several morphological variants. Zosteriform LP is a rare form of linear LP. Linear LP accounts for less than 1% of cases and presents in a unilateral, linear distribution.1 The zosteriform type of linear LP is an uncommon variant with dermatomal or zonal distribution. Zosteriform LP is distinguished clinically from linear LP in that it forms a broader band that corresponds to specific dermatomes.1 Zosteriform LP may arise de novo in previously normal skin, at sites of trauma (koebnerization), or as Wolf’s isotopic response at the site of healed herpes zoster.2 We report a rare case of a 52-year-old female diagnosed with zosteriform LP arising de novo in previously normal, non-traumatized skin with no history of herpes zoster.

Case Description
A 52-year-old woman presented with a six-week history of a pruritic eruption on her right leg. The patient had a previous history of discoid lupus erythematosus (DLE) on the scalp, which was previously treated with hydroxychloroquine 200 mg twice daily and clobetasol ointment. The patient at the time of presentation had no DLE lesions. There was no significant family or drug history. The patient had no associated comorbidities. Hepatitis C serology was negative.

On physical examination, numerous purple pruritic papules and plaques with an overlying white scale were present on her right thigh (Figure 1). The lesions were arranged in a linear pattern in the L1, L2, and L3 dermatomal distribution. A linear white patch was seen on her left buccal mucosa (Figure 2), and her genital mucous membranes were normal. There was neither scalp nor nail involvement.

A biopsy was taken from a typical lesion on her right thigh. Histopathology showed wedge-shaped hypergranulosis, acanthosis, saw toothed of the rete ridges, and a lichenoid infiltrate (Figure 3). A diagnosis of zosteriform lichen planus was made based on the clinical and pathological correlation.

The patient was given an intramuscular injection of triamcinolone acetonide 40 mg and started on tacrolimus ointment 0.1%, which was applied to the cutaneous and oral lesions twice daily.

Discussion
Lichen planus is an idiopathic inflammatory disease affecting the skin and mucous membranes. Middle-aged individuals are most commonly affected, with the average age of onset being 50 years. The occurrence is evenly distributed worldwide with no racial predilection. Females are affected more often than males. The mucous membranes are affected in 65% of cases. In cases of oral LP, the buccal mucosa exhibits a lacy white reticulation, known as Wickham’s striae, and may develop into squamous cell carcinoma in 0.2% of cases per year.3 The nails may be affected along with the scalp, causing a scarring alopecia.

Clinically, zosteriform LP is characterized by flat-topped, pruritic, violaceous papules or plaques. The eruption has a predilection for the flexure surfaces of the extremities and is usually symmetric in nature. It may occur in association with certain medications and diseases such as hepatitis C, but the etiology is unknown and is thought to arise from a T cell-mediated immune response.

In addition to the classic appearance, there are more than 20 variants that are categorized based on the morphology and configuration of the lesions. There are many atypical presentations of LP that have been described, such as linear, hypertrophic, acinic, and vesiculobullous.4 Linear LP refers to lichen planus with a unilateral, linear distribution. It can present in a segmental distribution corresponding to a dermatome, referred to as zosteriform lichen planus. Zosteriform LP may arise as Wolf’s isotopic response at areas of healed zoster, secondary to koebnerization from trauma, or in very rare cases as a de novo eruption on previously normal skin.

The zosteriform pattern can occur without evidence of herpes zoster, and the incidence is extremely infrequent. The lesions are arranged in a band several centimeters wide and run along the course of a peripheral cutaneous nerve and its branches. It is thought that the cutaneous manifestation of the zosteriform pattern could possibly be triggered by neural factors.5 It has recently been suggested that the lesions in zosteriform LP actually follow the lines of Blaschko rather than a dermatome.6 Blaschko’s lines are invisible lines in the skin believed to trace the migration of embryonic cells. Still, some believe that true zosteriform LP only occurs if the lesions develop at sites of healed herpes zoster.7 In our patient, there was no history of herpes zoster, and multiple dermatomes were involved. Therefore, a more appropriate term may be dermatomal LP rather than zosteriform LP.

The differential diagnosis of zosteriform lichen planus is vast and includes linear psoriasis, lichen striatus, linear epidermal nevus, linear Darier’s disease, and inflammatory linear verrucous epidermal nevus, to name a few.2 LP can be differentiated based on histopathologic examination, which shows a band-like infiltrate of lymphocytes at the dermal-epidermal junction. Other noticeable features include hyperkeratosis, wedge-shaped hypergranulosis, vacuolar degeneration of the basal layer, and acanthosis with saw-toothed rete ridges. Civatte bodies (colloid or cystoid bodies) are present at the junction of the dermis and epidermis and also in the papillary dermis.4 On direct immunofluorescence (DIF), lichen planus shows shaggy fibrin, cystoid bodies, and deposition of IgM immunoglobulins at the dermoepidermal junction. This can distinguish LP from hypertrophic lupus erythematosus, which would show a continuous granular band of IgG, IgM, IgA, and C3 at the dermoepidermal junction on DIF.8

Figure 1
Figure 2
Treatment and Prognosis

There is no definitive cure for LP, and the disease is self-limiting. There are various treatment modalities available to alleviate the associated pruritus and induce remission. Treatments may consist of topical and systemic therapies. Oral antihistamines such as diphenhydramine and hydroxyzine may be used to relieve pruritus. Topical antipruritic agents such as menthol, camphor, pramoxine or doxepin may also be used. First-line therapy for cutaneous lesions includes high-potency topical steroids applied twice daily. Systemic corticosteroids can be used as a second-line treatment or in those with more extensive disease. Alternative treatments include immunosuppressive agents such as cyclosporine, methotrexate, azathioprine, dapsone, retinoids and topical tacrolimus. Narrow-band ultraviolet-B phototherapy and psoralen plus ultraviolet A (PUVA) can also be used as adjuvant therapy.

In cases of oral LP, corticosteroids are the mainstay of therapy, based on their ability to reduce cell-mediated immune response. They can be given topically, intralesionally or systemically. Systemic and topical steroids, when given together, are extremely effective. A steroid mouth rinse used twice daily can be used to treat generalized oral lesions. Topical ointments can be used to treat localized oral lesions and are applied two to four times daily after meals. Candida albicans superinfection can occur with immunosuppressive therapy and should be managed with topical antifungals.

Lichen planus often resolves over an average period of 18 months, but approximately 20% of patients will have a second occurrence. In a subset of patients, the disease may persist for many years. Oral LP is more therapy-resistant, and close follow-up is advised given the increased risk of developing squamous cell carcinoma.

Conclusion

Zosteriform LP is a rare form of linear LP. It may arise secondary to trauma as Koebner phenomenon, at sites of healed herpes zoster as Wolf’s isotopic response, or very rarely de novo in normal, non-traumatized skin, as in our patient. Given that our patient had no history of herpes zoster and that multiple dermatomes were involved, a more appropriate term may be dermatomal LP rather than zosteriform LP.

Our patient is currently doing well on a treatment regimen of tacrolimus ointment 0.1% applied to her cutaneous and oral lesions. Per the current recommendations, we are closely following the oral lesion for any malignant transformation.

References


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**REFERENCES:**
1. Blecker J. Double-blind comparison between two topical steroids, halcinonide 0.1% and dexamethasone ppropionate cream 0.05%. Cutis Med Res. 1975;21:255-257.

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- Systemic absorption of topical corticosteroids has produced reversible hypothalamic-pituitary-adrenal (HPA) axis suppression, manifestations of Cushing’s syndrome, hyperglycemia, and glucosuria in some patients.
- Conditions which augment systemic absorption include the application of the more potent steroids, use over large surface areas, prolonged use, and the addition of occlusive dressings.
- Children may absorb proportionally larger amounts of topical corticosteroids and thus be more susceptible to systemic toxicity. Parents of pediatric patients should be advised not to use tight-fitting diapers or plastic pants on a child being treated in the diaper area, as these garments may constitute occlusive dressings.
- Administration of topical corticosteroids to children should be limited to the least amount compatible with an effective therapeutic regimen. Chronic corticosteroid therapy may interfere with the growth and development of children.
- This medication is to be used as directed by the physician. It is for dermatologic use only. Avoid contact with the eyes.
- Patients should be advised not to use this medication for any disorder other than for which it was prescribed.
- The treated skin area should not be bandaged or otherwise covered or wrapped as to be occlusive unless directed by the physician.
- Patients should report any signs of local adverse reactions especially under occlusive dressing.
- Pregnancy Category C: Topical corticosteroids should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus. Drugs of this class should not be used extensively on pregnant patients, in large amounts, or for prolonged periods of time.
- Systemically administered corticosteroids are secreted into breast milk in quantities not likely to have a deleterious effect on the infant. Nevertheless, caution should be exercised when topical corticosteroids are administered to a nursing woman.

ADVERSE REACTIONS
The following local adverse reactions are reported infrequently with topical corticosteroids, but may occur more frequently with the use of occlusive dressings (reactions are listed in an approximate decreasing order of occurrence): burning, itching, irritation, dryness, folliculitis, hypertrichosis, acneiform eruptions, hypopigmentation, perioral dermatitis, allergic contact dermatitis, maceration of the skin, secondary infection, skin atrophy, striae, and miliaria.