Interesting Cases from the Big Apple

Serge Petrosian D.O., PGY-4
St. John’s Episcopal Hospital
Department of Dermatology
Program Director: Dr. Suzanne-Sirota-Rozenberg
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HPI: 22 y/o Caucasian Female presented to our clinic complaining of an enlarging non-healing ulcer on the left wrist for about 5 months. She stated that the lesion initially started as a bump. She denied any previous trauma to the area.

ROS: Negative

PMHx: ADHD

Meds: Concerta

Allergies: NKDA

SocialHx: denied illicit drug use, tobacco use and sexual activity.
- 3.7cm ulcer with a rolled telangiectatic border and central crust/eschar
The patient had been seen by a PA at another dermatology clinic for a month. She was treated with intralesional kenalog, cryotherapy and topical sylvadene cream. The patient reported no improvement in the lesion.
An astute co-resident, who had coincidentally heard a lecture by an infectious disease specialist 1 week prior suggested asking a thorough travel history.
Travel history was investigated… AND the patient reported traveling to Israel 7 months prior.

A shave biopsy was done to rule out Cutaneous Leishmaniasis or other possible infectious etiologies.
Biopsy results:

“Pseudoepitheliomatous hyperplasia and granulomatous dermatitis with neutrophils, plasma cells and parasitized histiocytes consistent with Leishmaniasis”.
According to the CDC:

Leishmaniasis should have a specimen sent to Atlanta, Georgia for additional testing and culture in special media (if possible) that can be sent out to the clinician prior to biopsy if requested.

Additional Information can be found on the CDC website.
Luckily for us, the infectious disease specialist who gave the lecture was a resident of NYC who practiced close by.

The patient was sent to the ID specialist, a second biopsy was sent to the CDC in Atlanta, Georgia; confirming the diagnosis as well as the species as *Leishmania infantum*. 
Due to the localized nature and lack of systemic symptoms, the decision was made to treat the patient with topical preparation of paromomycin 15% and gentamicin 0.5% cream BID.

Over the span of 3 months, the lesion slowly resolved.
4 weeks of treatment
8 weeks of treatment
12 weeks of treatment
Leishmaniasis

- Chronic infection due to an obligate intracellular protozoan, Leishmania spp.
- Vector – Sandfly – *Phlebotomus or Lutzomyia*

- Classified by geographic region (Old world vs. New World) or clinical presentation (cutaneous, diffuse cutaneous, mucocutaneous or visceral)
- Old World - Eastern Hemisphere – *L. major, L. tropica*
- New World - Western Hemisphere – *L. mexicana, L. braziliensis, L. amazonensis*
Cutaneous Leishmaniasis

Begins as a small papule at the site of inoculation that slowly enlarges over the span of a few weeks to months into a nodule or plaque. The lesions can ulcerate and form a rolled border or become verrucous.

Exposed sites such as arms, legs, neck and face are the most commonly involved.

Lesions are usually solitary, but maybe multiple with satellite or sporotrichoid spread.
Cutaneous Leishmaniasis

Differential Diagnosis includes:

- BCC/SCC
- Arterial, Venous, Diabetic, Pressure ulcers
- Pyoderma Gangerosum
- Vasculitis
- NLD
- Other infectious causes
Cutaneous Leishmaniasis

Treatment of cutaneous Leishmaniasis depends on severity. Some lesions may spontaneously resolve with scarring.

- Oral medications include: Sodium stibogluconate, Pentamidine, Fluconazole, Liposomal amphotericin B
- Topical therapies include: Paromomycin and MBCL ointment, Paromomycin and Gentamicin cream
- Other: Cryotherapy, Heat therapy, PDT
This case teaches us…

- To keep a wide differential diagnosis for a non healing ulcer.
- Not every ulcer with a rolled border is a BCC.
- Yet again proves the most cliché lesson we have all heard since medical school: An extensive history is VERY IMPORTANT!
Case #2
HPI: A 32 y/o Caucasian male presented to clinic complaining of a 3 month history of new onset “red itchy spots”. He stated that they were increasing in number and occasionally had a burning sensation to them.

ROS: Negative for systemic symptoms. Positive pruritus.

PMHx: Negative

Meds: Negative

Allergies: NKDA

SocialHx: Denied illicit drug, tobacco use
Multiple scattered blanchable red to pink telangiectatic macules of varying sizes on the trunk. The remainder of the skin exam was normal.
Two 4mm punch biopsies were taken from the right scapula and lower back.

The patient was recommended zyrtec, allegra and a topical steroid to alleviate symptoms until follow up.
Dilated capillaries within the superficial dermis and sparse perivascular lymphocytic infiltrate with scattered mast cells.
- Leder Stain utilizing chloroacetate esterase. Mast cells stain red
Leder Stain showing approximately 18 mast cells per high power field in the superficial dermis. Highly suggestive of TMEP
After the biopsy results, the patient was sent for additional testing. CBC, CMP, TFTs, and Total tryptase levels. All results returned within normal limits.

Genetic testing was discussed, but the patient refused due to lack of systemic symptoms.

The constellation of symptoms, signs and testing suggested a diagnosis of Telangiectasia Macularis Eruptiva Persitans (TMEP).
- The patient was counseled on avoiding triggers and continued on antihistamines with topical steroids on an as needed bases.

- The lesions persisted but the pruritus subsided.

- The patient was lost to follow up.
DIFFERENCES IN CLINICAL PRESENTATIONS OF CHILDHOOD AND ADULT-ONSET MASTOCYTOSIS

Age at onset

Childhood
- Diffuse cutaneous mastocytosis (rare)
- Mastocytoma (common)
- Urticaria pigmentosa/maculopapular (most common)
- Red to tan macules and papules* (most common)

Adulthood
- Telangiectasia macularis eruptiva perstans (rare)
- Nodular mastocytosis (rare)
- No skin lesions

Involvement of: Bone marrow, Bone, Liver, Gastrointestinal tract, Spleen, Lymph nodes

*Also referred to as urticaria pigmentosa

less likely → systemic disease → more likely
Mastocytosis

Mast cells are derived from pluripotent CD34+ precursors in the bone marrow. They also express the tyrosine kinase receptor KIT (CD 117). Alteration in KIT structure and activity are central to the pathogenesis of Mastocytosis.

Somatic mutations in KIT involving codon 816 represent the most common abnormality, seen in about 40% of cases. The result is a substitution of Aspartic acid with Valine, leading to constitutive activation.
Mastocytosis

The group disorders encompassing Mastocytosis can be as systemic or cutaneous.

Cutaneous variants include – Urticaria Pigmentosa, Nodular Mastocytoma, Diffuse cutaneous mastocytosis, Mastocytoma, and TMEM.

Onset can range from birth to adulthood. Childhood onset typically has cutaneous manifestations that resolve spontaneously, whereas adult onset disease is systemic and has a chronic course.
Urticaria Pigmentosa in a child can present as scattered, clustered, or confluent macules. There are also papular and papulonodular variants.
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Diffuse Mastocytosis can present with blistering and erosions, especially in infants.
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• Darier sign seen after rubbing a lesion.
MAST CELL MEDIATORS AND ASSOCIATED SYMPTOMS OF MASTOCYTOSIS

**Preformed mediators**
- Histamine
- Heparin
- Neutrophil chemotactic factors
- Eosinophil chemotactic factors
- Tryptase/chymase

**Newly formed mediators**
- PGD$_2$
- LTB$_4$, LTC$_4$, LTD$_4$, LTE$_4$
- Platelet activating factor

**Cytokines**
- TNF-α
- IL-6
- IL-4
- IL-8
- IL-5
- SCF
- GM-CSF, IL-13

- **Headaches**
- Cognitive disorganization
- Fatigue

- **Bullae**
- Flushing
- Pruritus
- Urticaria

- **Cramping**
- Diarrhea
- Epigastric pain
- Nausea
- Vomiting
- Weight loss

- **Chest pain**
- Dizziness
- Dyspnea
- Palpitations
- Syncope

- **Bone pain**
  - (Osteoporosis/osteosclerosis)

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Dermatology. 4th edition, Bologna
Telangiectasis Macularis Eruptiva Persitans

TMEP is a very rare cutaneous variant of Mastocytosis.

Most commonly presents in adulthood as symmetric red to brown telangectatic macules between 2-6mm in diameter on the trunk and proximal extremities.

Palms and soles are spared. Lesions are pruritic. Darier’s sign is commonly absent in this form.

Tryptase levels are usually normal, however if elevated can be a sign of possible systemic disease.

Systemic symptoms are rare, although a few cases have been reported.
DDx of TMEP

- Nevus telangiectaticus
- CREST Syndrome
- Telangiectasia secondary to another cause (liver disease or hyperestrogen states)
- Freckles
- Nevi
- Rosacea
- Generalized essential telangiectasias
- Bullous impetigo
Evaluation and Management

Ask and check for constitutional and systemic symptoms

Check for lymphadenopathy and hepatosplenomegaly

Additional testing (age dependent) – CBC, CMP, Tryptase, KIT gene analysis.

If any of the above are positive, consider additional testing.
INITIAL EVALUATION OF THE PATIENT WITH CUTANEOUS MASTOCYTOSIS

History
Inquire about constitutional (e.g. fever, malaise, weight loss) and other systemic symptoms (see Fig. 118.3)

Examination
Examine for lymphadenopathy and hepatosplenomegaly

Laboratory studies*
- CBC with manual differential
- Serum tryptase level
- Liver function tests (LFTs)
- Consider KIT gene analysis

Gastrointestinal symptoms
Further evaluation as indicated (e.g. barium study or endoscopy)

Bone pain or history of fracture
Radiographic skeletal survey or bone scan

Ultrasonography or CT scan; consider liver biopsy
Abnormal

Abnormal LFTs
Consider bone marrow biopsy**

Abnormal CBC or tryptase level
Screen peripheral blood or bone marrow sample for the FIP1L1-PDGFRα fusion gene

Eosinophilia
Evaluation and Management

There is no cure for mastocytosis, management is based on alleviating cutaneous and systemic symptoms. If there are no symptoms, no treatment is needed.

Avoidance of potential mast cell stimuli is key:

- Physical triggers such as friction, exercise, heat or cold
- Dietary triggers such as hot beverages, spicy foods, alcohol
- Medications: Aspirin, NSAIDs, Narcotics/Pain Killers, Anticholinergics, Polymixin B etc.
Evaluation and Management

Localized Therapy:

- Topical steroids, Topical Calcineurin inhibitors, Intralesional Steroids

Systemic Therapy

- Antihistamines, Cromolyn, Omalizumab, PUVA, NBUVB, Steroids,
- Patient’s with systemic symptoms should be given EPI-PEN in case of anaphylaxis
THANK YOU FOR YOUR TIME!