San Diego Dermatological Society Annual Meeting at UCSD

October 15, 2015

Hosted by UCSD Medical Center Department of Dermatology
Dedicated to the memory and enduring legacy of
Dr. Terry O’Grady

Oceans

by Edward Louis Severson III

hold on to the thread
the currents will shift
guide me towards you
know something’s left
and we’re all allowed to dream
of the next time we touch...

you don't have to stray
two oceans away
waves roll in my thoughts
hold tight the ring...
the sea will rise...
please stand by the shore...
I will be...
I will be...
there once more.
ORDER OF EVENTS

5:45 – 6:15 PM  Patient Viewing

3rd Floor Medical Offices South (Ambulatory Care Center)
UCSD Hillcrest Hospital

6:15 – 7:00 PM  Buffet Dinner followed by San Diego Dermatological Society Business Meeting

1st Floor Main Auditorium
UCSD Hillcrest Hospital

7:00 – 8:00 PM  Speaker Introduction: Richard Gallo, MD, PhD

Annual Dr. Terry O’Grady Lectureship in Dermatopathology

“Recent Advances in Dermatopathology with Relevance to Clinical Dermatology”
Clay Cockerell, MD
Professor, Departments of Dermatology and Pathology,
University of Texas Southwestern Medical Center

8:00 – 9:00 PM  Patient Case Presentations: led by Taraneh Paravar, MD
CASE #1

NOTE: TRUNK, EXTREMITIES


PRESENTED BY: Robert Dorschner, MD, Laura Romero, MD

HISTORY: MR is a 31-year-old otherwise healthy male who presented with an eleven-year history of a rash. It started on the trunk and proximal extremities in 2004 while in Afghanistan. Since, it has slowly spread to involve the distal extremities and feet. He noted that it was mildly pruritic in hot, dry weather, but is otherwise asymptomatic. He denied any involvement of the palms, soles, oral mucosa or genitals. He also denied any gastrointestinal symptoms, including diarrhea, history of anaphylaxis, bone pain or weight loss. He did endorse chronic joint pains, for which he used meloxicam. Biopsies demonstrated a dermal infiltrate consisting of mast cells, confirming the clinical diagnosis of mastocytosis. Due to the extent of disease, as well as CD25 positive staining on biopsy (which correlates with increased risk of systemic disease), he was worked up by Hematology-Oncology for systemic involvement, which has been negative.

PAST MEDICAL HISTORY: Post-traumatic stress syndrome, back pain, knee pain, alcohol abuse (sober over 1 year)

MEDICATIONS: Epi-Pen PRN, montelukast 10mg daily, cetirizine 10mg daily, ranitidine 150 mg nightly, multivitamin daily

ALLERGIES: NKDA

FAMILY HISTORY: No history of skin disease

PHYSICAL EXAMINATION:
  · Red-brown macules and papules on trunk and extremities.
  · Positive Darier’s sign.

LABORATORY DATA: CBC and CMP unremarkable; Tryptase 17.6 (ULN 11); CT chest/abdomen/pelvis unremarkable; bone marrow biopsy normal; C-Kit mutation not detected

PATHOLOGY:
Right superior and right posterior shoulder punch biopsies:
  · Both specimens demonstrate an upper dermal infiltrate of mononuclear cells, consistent with mast cells.
  · Staining for tryptase highlights these cells and CD25 staining is positive.
DIAGNOSIS: Urticaria pigmentosa

TREATMENT:
- Antihistamines and anti-leukotriene
- Epi-Pen
- Extensive discussion of mast cell degranulation triggers for him to avoid
- Monitoring

DISCUSSION: Presented at the end of Case 2.
CASE #2

NOTE: TRUNK, EXTREMITIES

PATIENT INITIALS: SL   AGE: 36   SEX: F   RACE: HISPANIC

PRESENTED BY: Robert Dorschner, MD, Robert Lee, MD, PhD, Laura Romero, MD

HISTORY: SL is a 36-year-old otherwise healthy female who presented with a one-year history of a rash. It began on the trunk and spread to her arms and legs. She was concerned it was related to tanning bed use. The lesions were asymptomatic and her concerns were cosmetic. She endorsed mild diarrhea, but was on antibiotics for H. Pylori eradication at the time. She denied other gastrointestinal symptoms, including nausea/vomiting, history of anaphylaxis, bone pain or weight loss. Biopsies demonstrated a dermal infiltrate consisting of mast cells, confirming the clinical diagnosis of mastocytosis. Due to the extent of disease, diarrhea and elevated tryptase, she was evaluated by Hematology-Oncology for systemic involvement: a diagnosis of systemic mastocytosis with C-Kit D816V mutation was made.

PAST MEDICAL HISTORY: Dyspepsia s/p H. Pylori eradication

MEDICATIONS: Epi-Pen PRN, cetirizine 10mg daily, ranitidine 150 mg nightly

ALLERGIES: NKDA

FAMILY HISTORY: No history of skin disease

PHYSICAL EXAMINATION:
- Red-brown macules and papules on trunk and extremities.
- Positive Darier’s sign.

LABORATORY DATA: CBC with eosinophils of 12; CMP with total bilirubin 1.81 (ULN 1.2); Tryptase 65.5 (ULN 11); C-Kit mutation positive for D816V; bone marrow biopsy with numerous mast cells, consistent with systemic mastocytosis, but no other hematologic disease; cytogenetics with normal karyotype and FISH.

PATHOLOGY:
Left medial thigh punch biopsy:
- Mild superficial perivascular infiltrate composed of lymphocytes and mast cells.
- Staining for CD117 highlights mast cells in the superficial dermis. CD25 staining is essentially negative.
**DIAGNOSIS: Systemic mastocytosis**

**TREATMENT:**
- Antihistamines
- Epi-Pen
- Consultation with Gastroenterology for endoscopy (pending)
- Extensive discussion of mast cell degranulation triggers for her to avoid

**DISCUSSION:** Mastocytosis is a spectrum of disorders characterized by the accumulation of abnormal mast cells in various tissues, including the skin. The majority of patients (55%) present before age 2 and later onset is correlated with an increased risk of systemic involvement (reported at 41-97% of adult-onset cases). In pediatric cases, it is often limited to the skin and resolves in adolescence. In the adult population, patients tend to have systemic disease, which most frequently runs an indolent course. Those with indolent systemic mastocytosis tend to be younger and present with urticaria pigmentosa-like lesions. Many patients are asymptomatic or have minor symptoms related to histamine release, which can be triggered by NSAIDs, exercise, heat, alcohol, salicylates, polymyxin B or other medications or anesthetics. About 1-3% of indolent systemic mastocytosis patients may progress to more aggressive forms and in adults presenting with systemic mastocytosis, up to 40% may have associated clonal non-mast cell hematologic disorder. For this reason, follow up is important.

The diagnosis of cutaneous mastocytosis is typically accomplished with clinical history and biopsy demonstrating a mast cell infiltrate. Serum tryptase levels and C-Kit mutational analysis, as well as a thorough review of systems, can help identify those at risk of systemic mastocytosis. To diagnose systemic mastocytosis, patients must meet either one major and one minor criterion, or 3 minor criteria. The major criterion is the presence of mast cell infiltrates in an extracutaneous tissue – usually bone marrow. Minor criteria include: atypical mast cell morphology (spindled cells); aberrant immunophenotype (eg. CD25 expression); activating mutations at codon 816 of the Kit gene; and persistent serum tryptase over 20ng/ml. 60-70% of adults have a mutation in C-Kit, most frequently D816V, however C-Kit mutations are uncommon in children.

Treatment is typically symptomatic, whether in disease limited to the skin or indolent systemic disease. The mainstays are avoidance of triggers, antihistamines or anti-leukotrienes and an Epi-Pen in case of anaphylaxis. Steroids (topical and intralesional), as well as PUVA, can also be used to treat skin lesions. Cromolyn can treat GI symptoms. In more aggressive systemic disease, or mast cell leukemia, various chemotherapy regimens, interferon therapy or bone marrow transplantation may be utilized, although most therapies are palliative.
REFERENCES:

- Bologna, Dermatology. 3rd edition.
CASE #3

NOTE: PALMS, SOLES


PRESENTED BY: Keith Roby, MD, Corey Frucht, MD, PhD, Taraneh Paravar, MD

HISTORY: MJ is a 32-year-old healthy woman with a past medical history significant for Gilbert's Disease and a left upper lobe bronchial carcinoid tumor at age 27, status post lobectomy, who presented for evaluation of a cyst on her back and was incidentally found to have scattered, non-painful papules on her hands as well as thickening of the soles of her feet. Review of systems was unremarkable. She denied deafness. The patient only noted mild discomfort of her feet with exercise.

PAST MEDICAL HISTORY:
- Bronchial carcinoid tumor (stage T2b) at age 27, status post lobectomy. Recent CT chest negative for recurrence
- Gilbert’s Disease
- Anxiety
- History of bulimia

MEDICATIONS: alprazolam, levonorgestrel IUD, valacyclovir

ALLERGIES: oxycodone, erythromycin

SOCIAL HISTORY: No tobacco use. Occasional alcohol intake.

FAMILY HISTORY: The patient’s mother has similar findings on palms, soles.

PHYSICAL EXAMINATION:
- On the bilateral palmar surfaces are multiple punctate <2mm hyperkeratotic papules.
- On the bilateral plantar surfaces are small firm papules coalescing into plaques at pressure points.

DIAGNOSIS: Punctate palmoplantar keratoderma

DISCUSSION: Palmoplantar keratodermas (PPK) are a diverse group of inherited and acquired disorders characterized by hyperkeratosis of the palmar and plantar surfaces. Punctate PPK is an autosomal dominant genodermatosis characterized by multiple circumscribed small hyperkeratotic firm papules on the palms and hyperkeratotic papules coalescing into plaques at pressure points on the soles. Histopathology often shows a central epidermal depression, prominent orthokeratosis and hypergranulosis.

Until recently, the molecular pathogenesis of punctate PPK was unknown. Several studies within the last 3 years have identified at least 22 separate loss of function mutations in a single gene, AAGAB, located on chromosome 15g.22. AAGAB encodes the α/γ- adaptin
binding protein p34, which is involved in membrane trafficking. It has been proposed that deficiency in this protein leads to impaired recycling of EGFR proteins, subsequently leading to epidermal hyperproliferation.

Associations of punctate PPK with malignancy have been reported in the literature, which includes GI, renal, brain and hematologic neoplasms. Thus, an age-appropriate cancer screening and symptom-directed work up are recommended. Treatment is symptomatic and no standardized approach exists. Systemic retinoids have been used with varying success.

REFERENCES:

CASE #4

NOTE: FACE, TRUNK, HANDS

PATIENT INITIALS: RM  AGE: 56  SEX: M  RACE: CAUCASIAN

PRESENTED BY: Zhe Jessie Hou, MD, PhD, Wiggin Wu Lee, MD, Taneheh Paravar, MD

HISTORY: RM is a 56-year-old male with a history of acute myeloid leukemia status post allogeneic bone marrow transplantation in May 2010, who presented for evaluation of a scaly rash on his face, trunk and extremities 8 days after the transplant. He also presented with abdominal pain and diarrhea. Biopsies of the skin and gut were performed and showed acute skin and gut graft-versus-host disease (GVHD). The patient was on tacrolimus at the time and was then treated with high-dose corticosteroids; the skin lesions resolved over the next month.

In March 2011, he developed a scaly eruption and was diagnosed with chronic GVHD of the skin. He was treated with extracorporeal photopheresis (ECP) from November 2011 to May 2012 with no good effect. In mid-May 2012, he had a dramatic flare of his skin GVHD with sclerotic changes, primarily on his face, neck, hands and upper trunk. He was treated with prednisone 1 mg/kg/day with moderate improvement.

He had another flare of his cutaneous chronic GVHD later in 2012. He restarted ECP briefly in October 2012, and his prednisone was tapered off in February 2013 due to the development of mood disturbances and osteoporosis. In late 2012, he also developed ocular GVHD and a cataract in the right eye. In May 2013, he was diagnosed with restrictive lung disease based on pulmonary function tests.

His subsequent treatment history includes:
- 9/2013-2/2014: rituximab (x8 doses)
- 5/2015– 8/2015: etanercept

He has had further progression of his sclerosis over the last few months, with further difficulty using his fingers. He reports continued dyspnea and limitation in chest wall expansion. The patient has been getting physical therapy to improve his range of motion.

He is currently on tacrolimus 0.5 mg daily and prednisone 5 mg daily.

His clinical course has been complicated by an episode of voriconazole-induced photosensitivity, hand dermatitis, and multiple non-melanoma skin cancers, most recently a squamous cell carcinoma of the nose.
PAST MEDICAL HISTORY: AML in remission, hypertension, diabetes mellitus, hyperlipidemia, anemia, thrombocytopenia, pleuritic pain, chronic renal insufficiency, restrictive lung disease, bilateral hand pain, edema, dyspnea, bronchitis, RSV infection, sinusitis, osteoporosis, cataract.

MEDICATIONS: Clobetasol 0.05% cream, desonide 0.05% ointment, tacrolimus 0.1% ointment, 5-fluorouracil 5% cream, etanercept 25 mg subQ twice weekly, tacrolimus 0.5 mg PO daily, prednisone 5 mg daily, escitalopram 20 mg PO daily, gabapentin 100 mg PO daily, lansoprazole 30 mg PO daily, acyclovir 400 mg PO daily, trimethoprim sulfamethoxazole 800-1600 mg PO daily, hydromorphone 2 mg PO q4h PRN, lorazepam 1 mg PO daily PRN, multivitamin, omega-3 fatty acid 100 mg PO daily, erythromycin 5 mg/gm ophthalmic ointment

ALLERGIES: Voriconazole - rash

FAMILY HISTORY: None

PHYSICAL EXAMINATION:
- Multiple pink scaly papules and plaques on forehead and posterior neck
- Flexion contractures of palms with indurated taught skin of digits
- Erythema, telangiectasia, and collarettes of scale on bilateral palms
- Right first dorsal digit with scarring at proximal nail fold to nail bed, consistent with dorsal pterygium
- Indurated bound down plaques of arms with dimpling of medial upper arms
- White to yellow indurated bound down plaques with reticulated erythema on back, abdomen and lower extremities
- Positive prayer sign

LABORATORY DATA: CBC w/ diff, CMP, LFTs are grossly WNL with exception for glucose of 133.

PATHOLOGY: N/A

DIAGNOSIS: Scleroderma-like GVHD

DISCUSSION: Scleroderma-like GVHD is a subtype of chronic cutaneous GVHD, a complication of bone marrow transplantation that historically has been noted to develop 100 days or more after transplantation.

Scleroderma-like GVHD is estimated to be present in 12-15% of chronic GVHD patients. It is considered a late subtype of chronic GVHD and can present as widespread indurated bound down skin, morphea-like plaques, lichen sclerosus-like lesions, and with fascial involvement. Nail changes, alopecia (scarring and non-scarring) and mucous membrane changes including dryness, atrophy, hypertrophy, erosions and ulcers can develop. Complications include joint contractures and skin breakdown with infections.
Lichen planus-like GVHD, on the other hand, is considered an early subtype of chronic cutaneous GVHD.

Treatment for limited cutaneous disease includes topical calcineurin inhibitors and topical corticosteroids. More extensive disease is difficult to treat. First-line treatments include systemic calcineurin inhibitors and systemic corticosteroids. Adjunctive therapies include ultraviolet light therapies (e.g. UVA), ECP, mammalian target of rapamycin (mTOR) inhibitors, and imatinib. There is some data supporting the use of anti-TNFα inhibitors (e.g. etanercept, infliximab), rituximab and IL-2. In addition, a recent clinical trial showed that bortezomib resulted in marked clinical improvement in cutaneous GVHD patients.

REFERENCES:
PATIENT #5 INITIALS: MS  AGE: 38  SEX: F  RACE: HISPANIC

PRESENTED BY: Tiffany Link, MD, PhD, Wiggin Lee, MD, Taraneh Paravar, MD

HISTORY: MS is a 38-year-old woman with a history of Down syndrome, who presented with a twelve-year history of “swollen lips”. She denied any pain, difficulty breathing, diarrhea, or abdominal pain. She had been seen by multiple physicians in Mexico over the last 12 years. A biopsy was done and was read as “rhinoscleroma with Mikulicz cells,” but subsequent review was consistent with “cheilitis granulomatosa”. Prior treatments included: minocycline, intralesional betamethasone, thalidomide, chloroquine and dapsone. Her swelling would decrease then recur with each treatment. Her symptoms persisted and she presented to UCSD Dermatology for a consultation.

PAST MEDICAL HISTORY: Down syndrome, Hypothyroidism

MEDICATIONS: Levothyroxine 75 mcg daily

ALLERGIES: NKDA

FAMILY HISTORY: None

PHYSICAL EXAMINATION:
- Firm indurated lips, lower > upper
- All cranial nerves intact
- Normal tongue

IMAGING DATA: chest x-ray normal.

PATHOLOGY:
Punch biopsy, lower lip:
- In the dermis there are nodules of epithelioid appearing histiocytes associated with lymphoplasmacytic inflammation. Multinucleated giant cells can also be seen. These granulomas are seen extending into superficial skeletal muscle. AFB, GMS, and gram staining failed to identify definitive evidence of microorganisms. Polarization revealed no evidence of polarizable material. These findings are most consistent with a diagnosis of cheilitis granulomatosa. These histologic findings may overlap with sarcoidosis and cutaneous Crohn’s disease.
PATIENT #6 INITIALS: CB    AGE: 24    SEX: M    RACE: HISPANIC

PRESENTED BY: Tiffany Link, MD, PhD, Taraneh Paravar, MD

HISTORY: CB is a 24-year-old healthy man with no significant past medical history, who presented for a five-month history of “intermittently swollen lips”. He denied any pain, difficulty breathing, diarrhea, or abdominal pain. He had not been treated for this and his PCP sent him to dermatology for a consultation.

PAST MEDICAL HISTORY: None

MEDICATIONS: None

ALLERGIES: NKDA

FAMILY HISTORY: None

PHYSICAL EXAMINATION:
  - Firm indurated lips, lower > upper
  - All cranial nerves in tact
  - Normal tongue

IMAGING DATA: chest x-ray normal

PATHOLOGY:
Punch biopsy, lower lip:
  - Filling the dermis are nodules of epithelioid appearing histiocytes associated with lymphoplasmacytic inflammation and occasional eosinophils. Multinucleated giant cells can also be seen. These granulomas are seen extending into superficial skeletal muscle. AFB, GMS, and gram staining failed to identify definitive evidence of microorganisms. Polarization revealed no evidence of polarizable material. These findings are most consistent with a diagnosis of cheilitis granulomatosa. These histologic findings may overlap with sarcoidosis and cutaneous Crohn’s disease.

DIAGNOSIS: Cheilitis granulomatosa

DISCUSSION: Cheilitis granulomatosa (CG), also known as granulomatous cheilitis or orofacial granulomatosis, is a chronic swelling of the lip due to granulomatous inflammation which can be seen by itself or in Melkersson-Rosenthal syndrome. Melkersson-Rosenthal syndrome is the term used when CG occurs in conjunction with facial palsy and lingua plicata. CG is occasionally a manifestation of Crohn’s disease and can sometimes precede the development of Crohn’s disease by years, so these patients need to be monitored for the development of gastrointestinal symptoms. Other etiologies of CG include sarcoidosis, metal (eg. gold, mercury), benzoate, or cinnamate hypersensitivity. The cause of CG is unknown. Crohn’s disease, sarcoidosis,
and CG may present with identical clinical and histologic findings. CG is often seen as an episodic non-tender swelling and enlargement of one or both lips, and lingua plicata is seen in 20-40% of patients. Swellings can sometimes involve other areas, including the periocular region. Recurrences can range from days to years.

Initial work up includes serum angiotensin-converting enzyme test and chest x-ray to exclude sarcoidosis. Patch tests may be used to help exclude reactions to metals, food additives, or other oral antigens. A thorough review of systems is necessary to screen for inflammatory bowel disease. Dental films may be helpful in excluding the presence of a chronic dental abscess. CG may improve with implementation of a cinnamon- and benzoate-free diet. Intralesional corticosteroids may be helpful in some patients. Success with other treatments has been reported anecdotally, such as tetracycline antibiotics, dapsone, TNFα inhibitors, methotrexate, and mast cell stabilizers.

Patient number 5 has had minimal response to doxycycline 100 mg PO BID and topical clobetasol for 6 months; therefore, most recently, she was treated with intralesional triamcinolone 10 mg/cc and her response will be reassessed.

Patient number 6 responded to doxycycline 200 mg nightly in addition to topical clobetasol nightly for 4 months. His symptoms slightly improved, and eventually agreed to intralesional triamcinolone 20 mg/kg x 0.5 cc. After one intralesional injection, his lips returned to normal.

REFERENCES:
CASE #7

PATIENT INITIALS: VT    AGE: 40    SEX: F    RACE: Hispanic

PRESENTED BY: Megan Brown, MD, Aimee Two, MD, Daniel Synkowski, MD

HISTORY: VT is a pleasant 40-year-old Hispanic woman born with macrocephaly, coarse facies, low set ears, thick lips, short neck, thick loose skin of the hands and feet, deep palmarplantar creases, and bilateral talipes equinovarus [club feet] who presented to our clinic with a several-month history of a painful nodule on the right mid back.

PAST MEDICAL HISTORY: Born at 40 weeks gestation; pregnancy complicated by polyhydramnios, Rathke cleft cyst, hyperprolactinemia (likely medication induced), nasal papillomata, developmental delay, seizure disorder, behavior disorder, mitral valve prolapse, ovarian cyst, pilomatricoma (right mid back)

MEDICATIONS: Vitamin D-3, iron supplement, cod liver oil, lamotrigine, quetiapine, lorazepam, iloperidone, paroxetine, and olopatadine

ALLERGIES: NKDA

FAMILY HISTORY: No relatives with similar findings

PHYSICAL EXAMINATION:
· Macrocephaly, coarse facies, posteriorly set ears, thick lips, short neck, thick, loose skin of the hands and feet, deep palmarplantar creases, bilateral talipes equinovarus
· Painful 2 cm x 1 cm bluish nodule on the right mid back

LABORATORY DATA: Normal urine and organic amino acids at birth, prolactin elevated at 82 ng/mL (normal <23.3 ng/mL)

PATHOLOGY:
· Skin biopsy with electron microscopy (6/29/1975): no evidence of lipid or mucopolysaccharide storage disease
· Skin biopsy of right mid back (7/23/15): pilomatricoma

DIAGNOSIS: Costello syndrome

DISCUSSION: Costello syndrome (CS) is rare genetic disease associated with short stature, redundant skin of the neck, palms, soles, and fingers, curly hair, benign papillomatous lesions around the mouth and nares, mental retardation, and, in some cases, cardiac anomalies. The most commonly associated malignant tumor is rhabdomyosarcoma. The inheritance pattern is autosomal dominant or idiopathic. Two primary genes—HRAS and KRAS—have been associated with CS. The KRAS and HRAS genes encode small GTPase proteins associated with cellular signal transduction.
Treatment is primarily supportive, and CS patients must have close follow up with cancer screening.

As noted above, our patient has undergone genetic and dermatologic evaluation. The patient requires careful follow-up, cancer screening, and active management of her hyperprolactinemia, mitral valve prolapse, developmental delay, seizure disorder, and behavior disorder by neurology, endocrinology, women’s health, and internal medicine. The pilomatricoma was excised without complications.

REFERENCES:
HISTORY: AL is a 38-year-old male with a 15 year history of a rash on the face and scalp associated with regional alopecia. A biopsy obtained approximately 10 years ago at the Balboa Naval Medical center was consistent with discoid lupus erythematosus (DLE). His treatment options have been limited secondary to chronic transaminitis, which hepatology favors is due to fatty liver disease. The patient has intermittently been on hydroxychloroquine, which he thinks brings him modest improvement. He works outside as a construction worker, so sun protection has been a challenge. He has been getting intralesional triamcinolone injections, 5-10 mg/cc into affected areas on face and scalp every 6 weeks with moderate success. Oral prednisone 60 mg/d significantly reduced induration and depth of depression of lesions. Topical cyclosporine solution and clobetasol ointment have not resulted in significant improvement. Ustekinumab was ordered given case reports that this has been of benefit, but it has not yet been approved by the VA.

The patient was seen by rheumatology who had a low suspicion for systemic lupus erythematosus (SLE) given his negative ANA and lack of other clinical criteria.

PAST MEDICAL HISTORY: Likely fatty liver disease, currently smokes, ~15 pack-year history, h/o ethanol abuse, h/o dermatofibrosarcoma protuberans of right chest s/p wide local excision 2008.

MEDICATIONS: Hydroxychloroquine 200 mg BID, clobetasol 0.05% ointment BID, amlodipine 10 mg QD

ALLERGIES: NKDA

FAMILY HISTORY: None

PHYSICAL EXAMINATION:
- Face and scalp with oval to round pink hyperkeratotic, thick, centrally atrophic plaques with central hypopigmentation and peripheral hyperpigmentation
- Affected areas on scalp with alopecia and scarring
- No lesions on the neck or below
- No cuticular dystrophy or dilated periungual capillaries
- Normal proximal muscle strength, grossly
- No oral ulcers

LABORATORY DATA: CBC, electrolytes WNL, AST 110, ALT 183, ESR 15. ANA negative.

PATHOLOGY: Not available
**DIAGNOSIS:** Hypertrophic discoid lupus erythematosus

**DISCUSSION:** Discoid lupus erythematosus (DLE) is an autoimmune disease that is generally limited to the skin, but can progress to systemic lupus erythematosus (SLE) in 5-10% of affected adults. DLE is clinically characterized by scaly or atrophic plaques with follicular plugging, central hypopigmentation and peripheral hyperpigmentation. DLE lesions are most commonly located on the head and neck area, and may be exacerbated or elicited by sun exposure. Patients with lesions on extremities and trunk are more likely to progress to SLE. Hypertrophic DLE is a relatively rare clinical variant in which patients have thicker hyperkeratotic plaques that can mimic psoriasis. Interestingly, some studies suggest a higher likelihood of developing squamous cell carcinoma within lesions of DLE.

Mainstays of therapy include topical and intralesional corticosteroids, topical calcineurin inhibitors, sun protection, and oral antimalarials. Smoking cessation has also proven beneficial.

This patient is presented out of interest given his striking clinical exam. He has also been challenging to treat, as he has not responded well to any of the therapies discussed above. The current plan is to continue hydroxychloroquine, try to improve sun protection, smoking cessation and attempt to get ustekinumab approved.

**REFERENCES:**
- Milam EC, Ramachandran S, Franks AG Jr. Treatment of Scarring Alopecia in Discoid Variant of Chronic Cutaneous Lupus Erythematosus With Tacrolimus Lotion, 0.3. JAMA Dermatol. 2015 Jun 3.
PATIENT INITIALS: RW  AGE: 58  SEX: M  RACE: CAUCASIAN

PRESENTED BY: Natasha Carter, MD, PhD, Wiggin Lee, MD, Richard L. Gallo, MD, PhD

HISTORY: RW is a 58-year-old male with a history of melanoma in situ and non-melanoma skin cancer who presented for total body skin exam and was found to have total body hair loss and nail changes. His hair loss occurred after an episode of rheumatic fever at the age of 5. All 20 nails have been cracking and splitting since childhood. He has had no prior treatments and has no family history of alopecia. His review of systems was negative for fevers, chills, night sweats, unintentional weight loss, malaise, nausea, and vomiting.

PAST MEDICAL HISTORY: Basal cell carcinoma, melanoma in situ, benign prostatic hypertrophy, essential hypertension, major depression, obstructive sleep apnea

MEDICATIONS: atorvastatin 20mg daily, lisinopril 20mg daily, morphine 30mg prn, pregabalin 75mg BID, vitamin D3 daily, venlafaxine 150mg daily

ALLERGIES: simvastatin

FAMILY HISTORY: Non-contributory

PHYSICAL EXAMINATION: Diffuse non-scarring absence of hair on scalp, face including eyebrows and eyelashes, and entire body surface area.

LABORATORY DATA: CBC WNL, CMP WNL, TSH 2.19 (WNL), Vitamin D 22 mildly low

PATHOLOGY: Not applicable

DIAGNOSIS: Alopecia universalis

DISCUSSION:
Alopecia areata is a non-scarring alopecia, which affects approximately 2% of the population, affecting both children and adults. To date there is no cure for alopecia areata. Although there are some effective treatment options, such as corticosteroids, minoxidil, anthralin, and diphencyprone (DPCP), these treatments do not work in all patients and are less reliable in the most severely affected patients. Here we present a case of alopecia universalis which is the most severe form of alopecia areata. Recent breakthroughs have led to a better understanding of the pathophysiology of alopecia areata. New data has shown that NKG2D expressing cytotoxic T cells are both necessary and sufficient to induce alopecia areata in mice by acting through INF-gamma, IL-2, and IL-15Rbeta. Notably all of these cytokines signal through the JAK STAT pathway and furthermore inhibition of JAK signaling can not only prevent the development of alopecia areata but reverse established disease. Many ongoing clinic trials with JAK inhibitors have shown...
promising early results but much work is still needed to determine if these new medications will be effective for a greater population.

REFERENCES:

HISTORY: MR is a 61-year-old male with depigmented patches on his neck, chest and mid-extremities, stable since birth, who presented for evaluation of red, scaly plaques on his bilateral elbows. The elbow plaques first appeared over 10 years ago. He was first seen in dermatology clinic for this issue eight years ago, and they were diagnosed as actinic keratoses at that time. He has since treated them with liquid nitrogen, topical 5-fluorouracil cream, imiquimod, and blue light, each with good resolution; however, the plaques continue to recur within a few months of each treatment. The patient notes that he applies sunscreen to his face and arms, including his elbows, daily, and also wears a hat when he is outdoors.

PAST MEDICAL HISTORY: Coronary artery disease, hypertension, hyperlipidemia, diabetes, obesity, colon polyp

MEDICATIONS: Amlodipine 2.5 mg PO daily, aspirin 81 mg PO daily, ezetimibe 10 mg PO daily, glipizide 10 mg PO BID, hydrochlorothiazide 25 mg PO daily, metformin 1000 mg PO BID, niacin 1000 mg PO BID

ALLERGIES: NKDA

FAMILY HISTORY: Mother and brother with skin pigment changes similar to those of patient; Brother with history of melanoma

PHYSICAL EXAMINATION:
- Depigmented patches on neck, chest, and central portion of arms and legs bilaterally
- Hyperpigmented macules within the depigmented patches described above
- Scaly erythematous plaques on bilateral elbows

LABORATORY DATA: None

PATHOLOGY: None

DIAGNOSIS: Piebaldism (with recurrent actinic keratoses on bilateral elbows)

DISCUSSION: Piebaldism is a rare genetic condition that affects all ethnicities and both genders equally. It is characterized by the presence of depigmented patches containing hyper- to normo-pigmented macules and patches that are present at birth and remain relatively stable throughout an individual’s lifespan. Areas typically involved include the central face, anterior trunk and mid-extremities, while the hands, feet, shoulders and back are typically spared. Mutations in two different genes have been identified in patients with
piebaldism: the SLUG gene, which plays a role in the development of neural crest derived cells, and the c-kit proto-oncogene, which encodes a tyrosine kinase receptor that controls differentiation and migration of neural crest derived cells.

Treating piebaldism can be challenging, as the condition is not usually responsive to medical therapies or phototherapy. Photoprotection is important given the absence of melanocytes within depigmented patches. Camouflage creams have been used in an attempt to conceal depigmentation; however, the effects of such creams are temporary, lasting for a maximum of six days. Skin grafts are able to restore pigmentation over a longer period of time; however, these are mostly designed for treating small surface areas and can cause significant scarring. A relatively new technique, autologous cell suspension transplantation, may prove to be more useful in treating piebaldism in the future. In a recent study of a device designed for completing these transplants, seven of 10 patients undergoing this treatment had repigmentation in over 75% of the transplanted area six months after the transplant. While more research on such devices is necessary, this tool offers hope that better management techniques for these patients may be available in the future.

REFERENCES:

HISTORY: AR is a 38-year-old man with a history of skin tightening, cutaneous calcinosis and muscle weakness. His symptoms began at age 14 in Iraq, his native country, with recurrent, painful cutaneous calcifications and skin tightening over the distal fingers. His condition progressed over the subsequent years, developing cold-sensitivity in the fingers, weakness of the proximal extremities, and dysphagia; he was re-evaluated at age 18 and was diagnosed with systemic sclerosis-dermatomyositis overlap syndrome (SSc-DM). He established care at UCSD in 2010 after immigrating to the U.S. where his care is coordinated between Rheumatology, Gastroenterology, and Dermatology. The subsequent workup revealed mild restrictive pulmonary disease, myositis, esophageal achalasia, calcinosis universalis, and primary biliary cirrhosis. UCSD Dermatology was initially consulted in 2012 for complications from cutaneous calcinosis, with recurrent draining sinus tracts and wound infections, as well as for a photo-distributed dermatitis. Additionally, he has received care since 2012 for persistent molluscum contagiosum in the groin.

PAST MEDICAL HISTORY: As per HPI

MEDICATIONS: Fluocinonide 0.05% cream BID PRN rash, mupirocin BID to sinus tracts, imiquimod 5% cream for molluscum, cephalaxin 500 mg TID PRN infection, mycophenolate mofetil 1000 mg BID, prednisone alternating 2.5/5 mg daily, diltiazem 60 mg BID, ursodiol 300 mg TID, alendronate 70 mg, calcium-vitamin D 600-400 BID, vitamin D 50,000 U weekly, ferrous sulfate 324 TID, omeprazole 20 mg daily, diclofenac 25 mg BID PRN joint pain, hydrocodone-acetaminophen 5/325mg QID PRN

ALLERGIES: NKDA

FAMILY HISTORY: None

PHYSICAL EXAMINATION:

- Violaceous, poikilodermatous plaques distributed on peri-orbital skin, central upper chest and back
- Ill-defined violaceous papules and plaques overlying metacarpal-phalangeal joints and elbows
- Cuticles: roughened, with dilated capillary loops and areas of dropout
- Distal fingers: taught, shiny skin and tapering of the distal phalanges
- Over the extremities and trunk, scattered draining sinus tracts
LABORATORY DATA: 8/2015: CBC normal, BUN/Cr normal, CK = 198, (nl 0-175). 6/2013: ANA was positive >1:640 (atypical speckled pattern). Anti-mitochondrial antibodies were positive >1:640. 10/2010: Anti-smooth muscle antibodies were positive >1:160 (10/2010). Tests for antibodies against RNP, Scl-70, Jo-1, ANCA and F actin IgG were negative.

IMAGING: MRI with/without contrast of the bilateral LE showed soft tissue signal enhancement (10/2010). Chest CT showed no masses, no fibrosis (12/2010).

STUDIES: Pulmonary function testing showed a restrictive pattern with diminished DLCO (08/2015). Upper and lower endoscopy (12/2013 and 12/2011, respectively) were grossly normal. Esophageal motility studies show atypical achalasia, not consistent with sclerodermatous changes (12/2013). Liver biopsies (last 07/2013) showed mild portal inflammation, consistent with primary biliary cirrhosis.

DIAGNOSIS: Systemic sclerosis-dermatomyositis overlap syndrome

DISCUSSION: Systemic sclerosis-dermatomyositis (SSc-DM) overlap syndrome is an uncommon manifestation of dermatomyositis; of the dermatomyositis-associated overlap syndromes, SSc-DM is the most common presentation, representing approximately half of these cases.

Typical findings in SSc-DM overlap syndrome include sclerodactyly, Raynaud’s phenomenon, restrictive lung disease, mild myositis, dysphagia, and acro-osteolysis of small joints of the hand. Dermatologic findings may also include poikiloderma and Gottron’s sign. Roughly 50% of patients have positive titers of PM-SSc antibodies, a nonspecific but diagnostically helpful marker for disease.

Good treatment response has been reported with systemic corticosteroids, methotrexate, and cyclophosphamide. Efficacy has also been reported with intravenous immunoglobulin and mycophenolate mofetil.

Overall, patients with SSc-DM experience a relatively mild clinical course, with a favorable prognosis compared to patients with classic dermatomyositis. Overall, the myositis tends to be mild, and patients often respond well to systemic treatment. Additionally, the overall risk of malignancy may be lower in SSc-DM overlap patients.

REFERENCES:

CASE #12

NOTE: TRUNK, ARMS, LEGS

PATIENT INITIALS: AL  AGE: 57  SEX: F  RACE: CAUCASIAN

PRESENTED BY: Dawn Eichenfield, PhD, Maryam Afshar, MD, Taraneh Paravar, MD

HISTORY: AL is a 57-year-old healthy woman with no past medical history, who presented for a nine-month history of “red welts” on her back. Ten months prior to presentation, she developed a red rash on her left eyebrow and below her left collarbone, which spread to her face, arms, and forehead. She denied trauma to her back. Her rash worsened with sun exposure. An initial diagnosis of subacute cutaneous lupus erythematosus was made and treatment with hydroxychloroquine (200 mg BID) was begun. Her symptoms persisted and she presented to our clinic for a consultation.

PAST MEDICAL HISTORY: None

MEDICATIONS: Hydroxychloroquine 200mg BID

ALLERGIES: NKDA

FAMILY HISTORY: None

PHYSICAL EXAMINATION:
- Erythematous linear flagellate patches and plaques on the back (but sparing the mid upper region)
- Thin violaceous to pink papules over the metacarpal-phalangeal joints (Gottron’s papules)
- Pink patches at the elbow joints (Gottron’s sign)
- Ragged cuticles, periungual dilated capillaries with areas of dropout
- Fine scalp scale
- Violaceous xerotic patches of the lateral thighs (Holster sign)
- Erythema and poikiloderma on the face, ears, chest, and abdomen
- There was no dermatographism or oral ulceration
- Proximal muscle strength was full

LABORATORY DATA: CBC, CMP, ESR, and CK WNL. ANA was positive (by direct fluorescent antibody) in a speckled pattern at a titer of 1:80. Tests for antibodies against dsDNA, Smith, RNP, Scl-70, Ro, La, Jo-1, Centromere B, and chromatin were negative.
PATHOLOGY:
Upper back biopsy:
- Lymphocytic inflammation along the dermal-epidermal junction associated with focal vacuolar degeneration and necrotic keratinocytes at the basal layer. Pigmented melanophages were seen in the upper portions of the dermis. There was a superficial and deep perivascular lymphoplasmacytic inflammatory infiltrate. These findings were consistent with an interface dermatitis seen in connective tissue diseases.

DIAGNOSIS: Amyopathic dermatomyositis with flagellate erythema

DISCUSSION: Flagellate erythema presents with characteristic linear wheal-like manifestations and has been associated with multiple etiologies, including chemotherapy (e.g., bleomycin, bleomycin-derivatives, docetaxel), toxins (e.g., Shiitake mushrooms, Cnidarians, Rove beetles), and rheumatologic diseases (e.g., dermatomyositis, Adult-onset Still’s disease). Although present in only 5% of patients with dermatomyositis, flagellate erythema has been associated with active disease.

A review of the literature found nineteen articles corresponding to flagellate erythema and dermatomyositis. Only three cases of amyopathic dermatomyositis have been explicitly described in the literature in association with flagellate erythema, although two other cases (including the current case) may represent clinically amyopathic dermatomyositis. Pathology typically shows features consistent with interface dermatitis. The majority of cases showed elevated muscle enzymes or other muscular involvement (12/15 cases, 80%). Twenty percent (3/15) of cases were complicated by lung disease, while 40% (6/15) of cases had concurrent malignancies.

REFERENCES:
HISTORY: SM is a 53-year-old healthy Filipino woman with no significant past medical history, who presented with a large plaque on her left lower abdomen. One year prior to presentation, she developed a “pimple” on the left abdomen. Four months later, it started to grow and became painful; she also developed tender left inguinal lymph nodes. She went to urgent care where they attempted to drain the lesion with no success. Bacterial cultures were negative. Over the next few months, the lesion flattened but continued to spread and she developed satellite lesions that were occasionally pruritic and tender. An initial punch biopsy showed nonspecific findings concerning for an infectious process. She was then seen by the Infectious Disease team who suspected tuberculosis; however, her labs were all negative. She presented to our clinic for a consultation.

PAST MEDICAL HISTORY: History of infertility

MEDICATIONS: Daily multivitamin

ALLERGIES: NKDA

FAMILY HISTORY: Noncontributory

PHYSICAL EXAMINATION:

- Large firm erythematous plaque with satellite papules on the left lower abdomen, tender to palpation.
- Tender left inguinal lymphadenopathy. No other lymphadenopathy.

LABORATORY DATA:

- CBC, CMP within normal limits
- RPR: negative
- Leishmania PCR and DNA sequencing negative
- Stool ova and parasite: none detected
- Quantiferon Gold: negative
- Histoplasma Ag: negative
- Cryptococcal Ag: negative
- Tissues cultures #1&#2:
  - negative for bacteria/fungus
- Tissue culture #3:
  - negative for anaerobic bacteria, aerobic bacteria, fungal, and AFB
  - negative M. Tuberculosis Rifampin Resistance PCR
**PATHOLOGY:**
Punch biopsy of left lower quadrant of abdomen:

- Mild acanthosis and spongiosis of the epidermis. Large polygonal histiocytes with abundant lightly eosinophilic cytoplasm and vesicular nuclei in the superficial to mid-dermis. Several of the histiocytes showed intracellular inflammatory cells, a finding which is known as emperipolesis. There was a dense surrounding inflammatory infiltrate consisting of nodular aggregates of CD20+ B-cells, CD138+ plasma cells and CD3+ T-cells. Focal collections of neutrophils were also appreciated.
- The histiocytes were positive for S100 and CD68 and negative for CD1a. CD56 highlighted rare admixed cells in the nodular aggregates.
- A GMS stain was negative for fungal organisms. An AFB was negative for mycobacteria.
- These findings are consistent with Rosai-Dorfman disease.

**DIAGNOSIS:** Cutaneous Rosai Dorfman

**DISCUSSION:** Rosai Dorfman disease (sinus histiocytosis with massive lymphadenopathy) is a non-langerhans cell histiocytosis usually characterized by massive, bilateral, painless cervical lymphadenopathy. Lymphadenopathy of the neck is the most common location of histiocyte accumulation; however, accumulation outside of lymph nodes may also occur. The most common sites of accumulation outside of the lymph nodes are the skin, upper respiratory tract, and sinuses. Cutaneous Rosai Dorfman (RD) is a distinct form of the disease in which involvement is restricted to the skin. This occurs in approximately 3% of RD cases. Cutaneous RD is more common in older age groups, women, and those with Asian or Caucasian backgrounds. Clinical findings include brown to yellow or erythematous papules, nodules, and plaques that vary between ~1 cm to 30 cm most commonly occurring on the trunk, head, neck, and extremities. It is classified into papulonodular type, indurated plaque type, and tumor type. Lymphadenopathy and systemic symptoms are rare in cutaneous RD.

Pathology typically shows a dense dermal infiltrate with lymphocytes, plasma cells, and numerous histiocytes. Emperipolesis is common. Immunohistochemistry will show S100 positivity, CD68 positivity, and CD1a negativity. Upon review of the literature, in many cases, cutaneous RD is asymptomatic and will resolve spontaneously in 1-3 years and does not need treatment. Treatment is only indicated for symptomatic or systemic cases and includes topical, intralesional, and systemic corticosteroids, cryotherapy, radiotherapy, surgery, high-dose thalidomide, alkylating agents, dapsone, isotretinoin, methotrexate, and acitretin. Response to therapy is variable.

Our patient was started on topical steroids for mild pruritus and the plaque improved over the next few months with no progression or recurrence.
REFERENCES:

HISTORY: CM is a 21-year-old female with no past medical history, who presented for evaluation of red/brown papules on her face, trunk and extremities. One year ago, the patient developed irritation and swelling of her eyelids, shortly after that developed red/brown bumps papules on her eyelids. She shortly thereafter developed more extensive involvement of her face and neck and 6 months later had more diffuse involvement of trunk and proximal extremities. The lesions are pruritic and go through cycles where they flare up and then calm down and become hardly noticeable. She had previously been treated with liquid nitrogen with no significant improvement. Electrocautery lead to resolution of the treated lesions, but with resultant post inflammatory hyperpigmentation.

The patient denied any fevers, chills, weight loss, headaches, and seizures. She noted some increased thirst and urination, but attributed this to the warm weather at the time.

PAST MEDICAL HISTORY: None

MEDICATIONS: None

ALLERGIES: NKDA

FAMILY HISTORY: None

PHYSICAL EXAMINATION:
- Numerous 3-5mm red brown papules on face, neck, trunk, upper extremities and upper thighs, highest density of lesions is in the periorbital area, sparing of the axillae and groin
- Shallow erosion right buccal mucosa
- No lymphadenopathy

LABORATORY DATA: HIV and RPR negative

PATHOLOGY:
Left abdomen and left arm:
- Dermal proliferation of epithelioid histiocytes with abundant cytoplasm, multinucleated cells, and eosinophils.
- Stains were performed to confirm histiocytic lineage of the epithelioid cells, which were CD1a negative, S100 negative and CD68 positive.
- Taken together with the H&E findings, the changes are most c/w a Non-Langerhans Cell Histiocytosis.
DIAGNOSIS: Non-Langerhans cell histiocytosis (favor generalized eruptive histiocytoma)

DISCUSSION: Non-Langerhans cell histiocytoses (Non-LCH), also known as non-x histiocytoses, consist of a group of disorders that can be difficult to classify. They can predominantly affect the skin (e.g., benign cephalic histiocytosis, juvenile xanthogranuloma, generalized eruptive histiocyroma), or they can affect the skin and have a major systemic component (e.g., xanthoma disseminatum, mulicentric reticulohistiocytosis), or they can primarily involve extracutaneous sites (e.g., Erdheim–Chester disease, sinus histiocytosis with massive lymphadenopathy).

Generalized eruptive histiocyroma (GEH) is the favored diagnosis in this case as the patient has disseminated lesions which occur in crops affecting the face, trunk and extremities, sparing the flexures. GEH is a rare histiocytosis with approximately 30 cases reported world-wide. Lesions typically regress on their own, but can take several years. Association with acute leukemia has been reported. The Non-LCHs fall on a continuum and GEH can evolve into xanthoma disseminatum (XD) which can have systemic (including central nervous system) involvement. Although review of systems did not identify any specific concerns, the patient is currently undergoing work-up for internal organ involvement.

REFERENCES:
CASE LIST

Case 1: Urticaria pigmentosa
Case 2: Systemic mastocytosis
Case 3: Punctate palmoplantar keratoderma
Case 4: Scleroderma-like GVHD
Case 5: Cheilitis granulomatosa
Case 6: Cheilitis granulomatosa
Case 7: Costello syndrome
Case 8: Hypertrophic discoid lupus erythematosus
Case 9: Alopecia universalis
Case 10: Piebaldism
Case 11: Systemic sclerosis-dermatomyositis overlap syndrome
Case 12: Amyopathic dermatomyositis with flagellate erythema
Case 13: Cutaneous Rosai Dorfman
Case 14: Non-Langerhans cell histiocytosis