PROTOCOL BOOK • NOVEMBER 1, 2023

CHICAGO DERMATOLOGICAL SOCIETY 2023

Monthly Meeting

Co-hosted by Northwestern University Feinberg School of Medicine Department of Dermatology

Chicago Dermatological Society

PROTOCOL BOOK
November 1, 2023

Co-hosted by
Northwestern University Feinberg School of Medicine
Department of Dermatology

Guest Speaker: **Robert S. Kirsner, MD, PhD**
Dr. Phillip Frost Department of Dermatology and Cutaneous Surgery
Department of Public Health Sciences
University of Miami Miller School of Medicine

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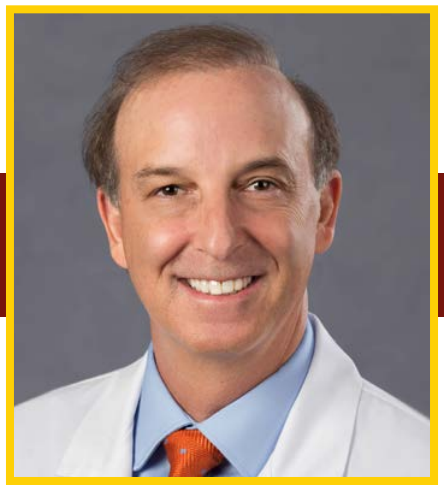
INVITED GUEST LECTURER

Robert S. Kirsner, MD, PhD



Dr. Kirsner is Chairman and the endowed Harvey Blank Professor in the Dr. Phillip Frost Dermatology in the Department of Dermatology and Cutaneous Surgery and Professor of Public Health Sciences at the University of Miami Miller School of Medicine. He is Chief of Dermatology at the University of Miami Hospital and Clinics and Jackson Memorial Hospital and directs the University of Miami Hospital Wound Center. Dr. Kirsner received his undergraduate degree from Texas A&M University, his medical degree from the University of Miami and a PhD in epidemiology from the University of Miami, after he completed his clinical training. His clinical training included internal medicine, a clinical and research fellowship in wound healing and dermatology at the University of Miami. His research interests include Wound Healing and Skin Cancer Epidemiology. Dr. Kirsner serves as one of 3 academic editors for the journal Wound Repair and Regeneration and on the editorial boards for a number of other journals in dermatology and wound healing. Dr. Kirsner serves in national leadership positions in both Wound Healing and Dermatology, including being Vice President of the American Academy of Dermatology and serving on the Wound Healing Society Board of Directors. In addition to career development awards, foundation, industry sponsored funding and CDC funding, he currently leads or is part of a number of NIH funded grants. Independent of books, book chapters and abstracts, he has published over 550 articles.

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PROGRAM

Co-hosted by
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Department of Dermatology

November 1, 2023
University of Chicago Gleacher Center

8:00 a.m.	**Registration & Continental Breakfast with Exhibitors**
8:30 a.m. - 10:15 a.m.	**Clinical Rounds** Slide viewing/posters – ongoing through the early morning
9:00 a.m.	**Welcome and Opening Comments** *Morayo Adisa, MD - CDS President*
9:00 a.m. - 10:00 a.m.	**Morning Lecture** What's New in Wound Healing for the Dermatologist *Robert Kirsner, MD, PhD*
10:00 a.m. - 10:30 a.m.	**Break and Visit with Exhibitors**
10:30 a.m. - 12:00 p.m.	**Resident Case Presentations & Discussion**
12:00 p.m. - 12:30 p.m.	**Box Lunches & Visit with Exhibitors**
12:30 p.m. - 1:00 p.m.	**CDS Business Meeting**
1:00 p.m. - 2:00 p.m.	**Afternoon Lecture** Healing and the Perfect Scar *Robert Kirsner, MD, PhD*
2:00 p.m.	*Program adjourns*

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Chicago Dermatological Society Meeting
November 1, 2023

Dermatology Residents

Fifth Year
Samantha Venkatesh, MD (Med-Derm)

Fourth Year
Taylor Erickson, MD
Joshua Prenner, MD (Med-Derm)
Edward Li, MD, PhD
Yoo Jung Kim, MD
Molly Hales, MD, PhD

Third Year
Simran Chadha, MD
Alecia Blaszczak, MD, PhD
Stephen Li, MD, PhD
Celestina Okoye, MD
Samantha Guhan, MD (Med-Derm)

Second Year
Nathaniel Campbell, MD, PhD
Ellen Wu, MD
Christopher Yang, MD
Anjani Sheth, MD
Prachi Aggarwal, MD
Jaimie Lin, MD (Med-Derm)

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Resident Case Presentations & Discussion

CHICAGO DERMATOLOGICAL SOCIETY **Case #1**

Presented by Ellen Wu, MD, Cuong Nguyen, MD
Department of Dermatology, Feinberg School of Medicine, Northwestern University

HISTORY OF PRESENT ILLNESS

A 30-year-old Senegalese man presented to Northwestern Memorial Hospital with a three-month history of hand contractures with progressive numbness and weakness in both hands and feet. During this time, he sustained multiple injuries to the digits, including burns due to sensory deficits. The patient was born and raised in Senegal but had also recently traveled extensively in Central and South America prior to moving to the United States. He reported difficulty extending his bilateral fingers, limiting his daily activities.

PAST MEDICAL AND SURGICAL HISTORY

The patient had no past medical or surgical history.

FAMILY AND SOCIAL HISTORY

The patient was born and raised in urban Senegal. He traveled through Brazil and Chile to reach the US. During this journey, he had no animal exposures. He has no known family members or contacts with similar findings. He worked as a line cook in a restaurant.

MEDICATIONS

Acetaminophen PRN

PHYSICAL EXAM

The patient was well-appearing. Severe bilateral claw hand deformity was noted with decreased sensation. Skin-colored soft nodules were seen along the dorsal wrists with crusted erosions on the fingers.

LABS/IMAGING

X-ray of bilateral wrists and hands:
Bilateral hand contractures, soft tissue swelling of the wrists, and no acute osseous processes.

Normal labs:
Syphilis Antibody Nonreactive, HIV Antigen/Antibody Nonreactive, TSH 1.06 (0.40-4.00 μIU/mL), B12 398 (180-933 pg/mL), folate 9.1 (>=5.9), hemoglobin A1c 4.6 (4.0-5.6%).

DERMATOPATHOLOGY

Histopathology of a skin-colored nodule on the left hand revealed granulomatous dermatitis with perineural involvement. A potential acid-fast organism was identified on Fite-Faraco staining.

DIAGNOSIS

Leprosy with claw hand deformity

TREATMENT AND COURSE

In the week prior to presentation, the patient had a telehealth visit with a physician in Senegal who had started multi-drug therapy (MDT) for presumed leprosy. During the patient's hospitalization, he was started on prednisone 20mg daily and was continued on rifampin 600mg PO daily, clofazimine 50mg PO daily and dapsone 100mg PO daily. Physical therapy and occupational Therapy recommended functional position orthoses to be worn nocturnally and simple hand orthotics during the day. After discharge, he followed up in infectious disease clinic, where he was continued on MDT and transitioned to prednisone 10mg daily and methotrexate 15mg weekly. He continues to follow with the Illinois Department of Public Health for Directly Observed Therapy (DOT).

DISCUSSION

Leprosy (or Hansen's disease) is caused primarily by infection with the organism, *Mycobacterium leprae* (M. leprae), a weakly acid-fast bacterium that can be cultivated in mouse footpads and armadillos. *Mycobacterium lepromatosis* is a second, more recently identified causal agent. Though declared "eliminated" by the WHO in 2000, the global incidence of leprosy has remained stable across the last decade, with most new cases arising from Brazil, India, and Indonesia, though autochthonous cases have also reported in the US. Clinically, leprosy predominantly affects the skin and nerves, often presenting as hypopigmented or erythematous patches with associated sensory loss. Leprosy presents on a wide spectrum of disease, ranging from isolated skin lesions and mild anesthesia (Tuberculoid Leprosy) to diffuse infiltrative skin disease with multi-organ involvement (Lepromatous Leprosy). Claw hand deformity (CHD) results from severe peripheral neuropathy, most often of the ulnar and median nerves. It is caused by weakened intrinsic muscles of the hand, including the interossei and lumbricals, resulting in hyperextension at the metacarpophalangeal joints and flexion at the proximal and distal interphalangeal joints. CHD can be functionally debilitating, as it impairs grasp and key pinch functions, weakens grip strength, and contributes to overall instability.

Leprosy is most reliably diagnosed with identification of the causative organism on skin biopsy. Punch biopsies should be performed from the active border of typical lesions and should extend into the subcutaneous tissue. Staining for the bacillus with the Fite-Faraco stain is then used to identify M. leprae. Marked neural involvement and nerve enlargement, which are less frequently observed in other disease processes, are also common findings in leprosy.

Long-term MDT with rifampin, clofazimine and dapsone is the standard of treatment for leprosy and consists of an intensive 5-12 month regimen followed by another continuous phase. Exact drug regimens depend on the severity of disease as classified by the WHO, and in the US, treatment is continued until all skin lesions clear. Unfortunately, patients do not usually regain their neurologic deficits after treatment. Management of CHD is therefore multidisciplinary and often requires occupational therapy, with include orthoses, stretching, or strengthening exercises. In cases of severe paralysis and disability, reconstructive surgery may be pursued, with the most common procedure being motor tendon transfer to correct ulnar claw hand. Early recognition and timely treatment remains critical in preventing permanent disability.

KEY POINTS

1. Leprosy predominantly affects the skin and nerves, and it presents on a wide spectrum of clinical manifestations, ranging from isolated hypopigmented patches and mild anesthesia, to diffuse infiltrative skin lesions with progressive neuropathy resulting in claw hand deformity.
2. Diagnosis should be considered in patients who have emigrated from or traveled through endemic areas, although cases of autochthonous leprosy are increasing. Treatment requires long-term MDT and often requires a multidisciplinary team including occupational therapy.

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CHICAGO DERMATOLOGICAL SOCIETY **Case #2**

Presented by Christopher Yang, MD, Lida Zheng, MD
Department of Dermatology, Feinberg School of Medicine, Northwestern University

HISTORY OF PRESENT ILLNESS

A 54-year-old Caucasian woman was referred to Northwestern Dermatology clinic for a diffuse eruption of firm papules present for several months. She reported that these lesions were asymptomatic, and involved the chest, abdomen, back, and extremities. She denied any oral involvement. She also denied any fevers, chills, night sweats, weight loss, easy bruising, bleeding, or changes in appetite.

PAST MEDICAL AND SURGICAL HISTORY

Hypothyroidism

FAMILY AND SOCIAL HISTORY

The patient had an unremarkable family and social history.

MEDICATIONS

Levothyroxine 88mcg daily

PHYSICAL EXAM

The patient was well-appearing. On the chest, abdomen, back, arms, and legs, there were scattered, firm 5-10 mm ill-defined pink papules.

DERMATOPATHOLOGY

Histopathology revealed a monomorphous infiltrate of intermediate size mononuclear cells with fairly abundant cytoplasm and oval nuclei. The cells were scattered throughout the reticular dermis. The cells were somewhat hyperchromatic with fragile nuclear detail. Some mitotic figures were noted. Tumor cells were positive for CD45 (LCA), CD4, CD163, CD68 (weak), and CD7 (partial), and negative for CD10, CD56, CD123, TCL1, lysozyme, myeloperoxidase, SOX10, CD117, S100, CD2, CD3, CD30, CD43, TdT, and PAX5. Next-generation sequencing showed NPM1, TET2, and DNMT3A mutations.

LABS/WORKUP

ABNORMAL

Bone marrow biopsy: Hypercellular bone marrow (~70% cellular) with trilineage hematopoiesis. Flow cytometry revealed no evidence of increased blasts or monocytes. Next-generation sequencing showed TET2 and DNMT3A mutations. Droplet digital PCR detected NPM1 mutation.

Peripheral blood: Flow cytometry revealed no evidence of increased blasts or monocytes.

NORMAL

CBC, CMP, uric acid, LDH, PT/INR, PTT, D-dimer, fibrinogen, peripheral blood smear, serum FLT3-ITD mutation assay

IMAGING

PET/CT: Multiple foci of prominent, but normal-sized lymph nodes in the neck, chest, abdomen, and pelvis.

DIAGNOSIS

Aleukemic leukemia cutis (NPM1-mutated acute myeloid leukemia)

TREATMENT AND COURSE

The patient was treated with FLAG-IDA induction therapy (fludarabine, cytarabine, G-CSF, idarubicin), with complete response and rapid resolution of all skin lesions. This was followed by 2 cycles of FLAG consolidation therapy with intrathecal methotrexate for CNS prophylaxis. Finally, the patient received an allogeneic hematopoietic stem cell transplant and is currently one year post-transplant with no evidence of recurrent disease.

DISCUSSION

Leukemia cutis (LC) is cutaneous infiltration by neoplastic leukocytes and can occur in both myeloid/monocytic disorders and lymphoproliferative disorders. The clinical presentation of LC most commonly involves papulonodules favoring the head, neck, trunk, extremities, and sites of prior trauma. These nodules can become hemorrhagic, ulcerative, and (rarely) bullous.

Aleukemic leukemia cutis (ALC) is a rare condition in which leukemic cells invade the skin before there is evidence of bone marrow or peripheral blood involvement. Interestingly, in our patient, flow cytometry of the bone marrow detected no leukemic cells, but PCR/next-generation sequencing (NGS) of the bone marrow detected the same mutations identified from the skin biopsy. The mechanism by which ALC occurs is unknown; two popular theories include: origination of a leukemic clone in the bone marrow with early seeding to extramedullary sites or origination of a leukemic clone in an extramedullary site (namely, the skin) with subsequent seeding of the bone marrow.

Diagnosis of LC and ALC is dependent on skin biopsy. Histologic findings may include perivascular, interstitial, nodular, diffuse, and/or periadnexal infiltrates. Immunohistochemistry (IHC) and molecular studies are often necessary to confirm the diagnosis, discriminate between different leukemia subtypes, and possibly identify molecular targets for targeted therapies. In our case, NGS of the skin specimen identified a mutation in the NPM1 gene, which encodes for nucleophosmin (a nuclear-cytoplasmic transport protein). NPM1 mutation is the most common genetic mutation found in AML, and NPM1-mutated AML was recently established as a distinct genetic entity in the World Health Organization classification of hematopoietic malignancies. It is currently being studied in several large trials of new targeted therapies, thus demonstrating that skin biopsy may be useful for both diagnosis and treatment selection in ALC.

There is little consensus data on the natural history of ALC, but prognosis is thought to be poor. Management is generally directed at the underlying leukemia, and may include chemotherapy, radiation, and/or hematopoietic stem cell transplantation.

KEY POINTS

1. LC is cutaneous infiltration by neoplastic leukocytes. The clinical presentation is characterized by papulonodules involving the head, neck, trunk, and extremities.
2. ALC is a rare condition in which leukemic cells appear in the skin before the bone marrow or peripheral blood.
3. Skin biopsy and IHC are essential for diagnosis of LC/ALC. Furthermore, molecular studies of skin specimens play an important role in diagnosis, classification, and treatment selection.

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CHICAGO DERMATOLOGICAL SOCIETY **Case #3**

Presented by Stephen Li, MD, PhD, Paras Vakharia, MD, PharmD
Department of Dermatology, Feinberg School of Medicine, Northwestern University

HISTORY OF PRESENT ILLNESS
A 70-year-old female presented for evaluation of a large birthmark on her left thigh.

PAST MEDICAL AND SURGICAL HISTORY
Hyperlipidemia

FAMILY AND SOCIAL HISTORY
Family and social history were non-contributory.

MEDICATIONS
Vitamin D

PHYSICAL EXAM
The patient was well-appearing. On the left thigh, there was a large faint tan hyperpigmented patch, within which were numerous light brown and darker brown hyperpigmented macules. Distally, there was a 2 cm asymmetric variegated brown hyperpigmented patch with irregular borders and faint peripheral erythema. Centrally, there was a pink papule with peripheral erythema. In between these two lesions, there was a faint hyperpigmented light brown variegated patch of greater size than the surrounding individual macules.

LABS/IMAGING
No relevant labs or imaging.

DERMATOPATHOLOGY
Histopathology of the distal atypical appearing patch revealed a melanocytic proliferation consisting of atypical epithelioid shaped single melanocytes along the dermal-epidermal junction with marked pagetoid changes. Rare nests of melanocytes were identified. The process was poorly circumscribed. Dermal invasion was not identified. There was no evidence of ulceration or significant regression in the sections examined. Immunohistochemistry was performed with adequate controls. SOX-10 highlighted the melanocytic proliferation and the melanoma marker PRAME was positive. These findings were consistent with melanoma in situ, superficial spreading type.

DIAGNOSIS
Melanoma in situ arising within a nevus spilus

TREATMENT AND COURSE
Additional biopsies of atypical-appearing lesions within the nevus spilus were performed. A deeper shave of the initial lesion confirmed a diagnosis of melanoma in situ, and the two additional biopsies demonstrated atypical melanocytic proliferations concerning for evolving melanoma in situ. TERT promoter mutation analysis identified a C250T missense mutation in the melanoma in situ, while Oncomine testing identified KRAS amplification in one of the evolving melanoma in situ lesions. The patient then underwent scouting biopsies of three non-atypical areas of the nevus spilus, which were benign. The patient subsequently underwent slow Mohs Micrographic Surgery (MMS) for the three atypical lesions with clearance.

DISCUSSION
A nevus spilus (also known as speckled lentiginous nevus) typically presents as an ovoid uniform tan-colored patch. They subsequently develop darker macules and papules that can range from lentiginous, junctional, compound, spitz, and blue nevi. Nevus spilus are found in up to 2% of the population without any sex predilection. They are associated with activating HRAS mutations, with the most common being G13R. The pathogenesis is hypothesized to occur through a “field defect” whereby activating HRAS mutations result in a background tan patch, with subsequent somatic mutations in HRAS or other genes resulting in formation of nevi that give the typical speckled appearance. Another similar entity, a nevus spilus-like congenital melanocytic nevus, is thought to occur due to NRAS mutations (Q61H, Q61L, and

G13R). In addition to isolated occurrences, a nevus spilus can also occur with other findings in phakomatosis pigmentovascularis III (formerly phakomatosis spilorosea), phakomatosis pigmentokeratotica, and speckled lentiginous nevus syndrome.

Nevus spilus has traditionally been viewed as a benign lesion. In 1957, the first melanoma arising from a nevus spilus was reported. Since then, less than 50 cases have been published. It is thought that the malignant potential of nevus spilus is around 0.13 - 0.2%. When melanoma does arise within a nevus spilus, it is most commonly superficial spreading type (68%), followed by nodular (16%). It is not uncommon for multiple synchronous melanomas to develop. The genetics of melanomas arising from a nevus spilus have largely been unexplored. In our case, the prevalence of KRAS amplification and TERT promoter mutations suggest that mutations in typical melanoma pathways may result in malignant transformation of a nevus spilus. A recent publication identified mosaic MAP2K1 variants in melanoma arising from a giant nevus spilus-like congenital melanocytic nevus. Whether MAPK pathway mutations or fusion proteins play a role in malignant transformation of nevus spilus will be an interesting area of further exploration.

KEY POINTS

1. Nevus spilus are melanocytic lesions composed of darker melanocytic nevi on a tan-brown background, such as a cafe-au-lait macule/patch.
2. Nevus spilus can be found as part of phakomatosis pigmentovascularis III, phakomatosis pigmentokeratotica, and speckled lentiginous nevus syndrome.
3. Nevus spilus are associated with activating HRAS mutations.
4. Melanoma arising from nevus spilus is a rare event that may be a due to further mutations in the MAPK pathway.

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CHICAGO DERMATOLOGICAL SOCIETY **Case #4**

Presented by Anjani Sheth, MD, MPH, Anthony J. Mancini, MD
Department of Dermatology, Feinberg School of Medicine, Northwestern University
Division of Dermatology, Ann & Robert H. Lurie Children's Hospital of Chicago

HISTORY OF PRESENT ILLNESS

An 11-year-old male with immunomapping-confirmed dominant dystrophic epidermolysis bullosa (DDEB), subtype EB pruriginosa, was being followed at Lurie Children's and presented for annual follow-up complaining of persistent, severe pruritus in association with his skin lesions. This resulted in propagation of blistering, secondary infections, sleep and school disruption, and severe impact on his quality of life.

PAST MEDICAL AND SURGICAL HISTORY

The patient was born at 30 weeks gestation, and he had a history of plagiocephaly and dermoid cyst of the midline frontal scalp. He had skin blistering since early infancy, most notably in response to cutaneous trauma or friction, along with hypopigmentation, linear bands of lichenification, scarring, milia, and albupapuloid lesions most prominent over his shins, ankles and dorsal feet. He started to note pruritus at the age of four which was persistent and escalating, eventually leading to a modification of his diagnosis from DDEB to EB pruriginosa. His pruritus had been previously unresponsive to numerous topical and oral therapies.

FAMILY AND SOCIAL HISTORY

The patient's parents are from Yemen and are Arabic-speaking. The patient has six siblings, all born to the same non-consanguineous parents. His parents and siblings are otherwise healthy.

MEDICATIONS

The patient was applying mupirocin 2% ointment and Vaseline gauze to open wounds, along with puncture and drainage of larger bullae as needed. He had failed a number of other medications (see below).

PHYSICAL EXAM

The patient was well-appearing. He had several erythematous erosions and pink atrophic scars with superimposed milia and milia en plaque on his dorsal hands and feet, fingers, extensor elbows and knees, and pretibial legs. There were scaly erythematous and lichenified plaques on the pretibial legs, some of which were in linear configurations (especially over the ankles and dorsal feet). His lower anterior legs had several scattered intact bullae, excoriations, and erosions with serosanguinous and hemorrhagic drainage. There were numerous, linearly-arranged albopapuloid lesions on the dorsal shins, ankles and feet. There were a few erythematous atrophic patches and milia on the forehead, chin, and helix. There were no signs of infection. The oral mucosa was clear. He had anonychia of the right and left middle fingers, and several toenails revealed hyponychia, thickening and/or dystrophy.

DERMATOPATHOLOGY

Histopathology from his first visit on 8/25/2011 revealed normal skin on H&E staining but diminished staining for collagen type VII on immunomapping, confirming the clinical diagnosis of DDEB.

DIAGNOSIS

Dominant dystrophic epidermolysis bullosa (DDEB), pruriginosa subtype, with recalcitrant and life-altering pruritus

TREATMENT AND COURSE

Until the onset of pruritus at four years of age, the patient was managed with supportive care for blisters and erosions, trauma-minimizing preventative strategies, occasional bleach baths, and oral antibiotics (cephalexin) for superinfections. With the onset of pruritus, the patient trialed numerous topical therapies including mometasone ointment with wet wraps, triamcinolone ointment alone, crisaborole ointment, and Sarna lotion without success. He was also treated with several oral therapies to reduce itching including diphenhydramine, cyproheptadine, hydroxyzine, and doxepin, none of which were significantly effective. Additionally, his parents had concerns about mood alterations that he was experiencing with some of these oral agents.

Given these treatment failures, the impact on his quality of life, and some reports in the literature of the potential utility of dupilumab for the pruritus of EB pruriginosa, he was started on dupilumab after a lengthy insurance approval process. At age 11 years, he was loaded with 600 mg of subcutaneously-injected dupilumab followed by 300 mg every four weeks. This led to marked improvement in his pruritus, scratching-induced blisters, and sleep. Skin examinations revealed not only decreased blistering and erosions, but improvement in his pigmentary alteration and albopapuloid lesions. His mental affect improved at subsequent visits, with improved eye contact, smiling and verbal interactions. Though the patient's expected physiologic weight gain made him eligible for the 200 mg every two-week dosing category, he has continued on 300 mg every four weeks given his satisfactory results and tolerance with this regimen.

DISCUSSION

The term epidermolysis bullosa represents a group of blistering disorders that result from genetic mutations in structural proteins within the epidermis or dermis. Dystrophic EB results from autosomal dominant or autosomal recessive mutations in the COL7A1 gene on chromosome three. This mutation leads to dysfunctional type VII collagen which results in defective anchoring fibrils in the papillary dermis just below the basal lamina. In addition to blistering, DDEB is often characterized by scarring, milia, and nail dystrophy. EB pruriginosa is a subtype of DDEB in which patients experience significant pruritus leading to increased scratching, increased blister formation, and decreased quality of life. Clinical findings may also involve pruritic and lichenified papules coalescing in linear arrangements at sites of trauma, particularly the distal extremities. Albopapuloid lesions are often white in color and may be elongated and coalescent into linear streaks, and they are characteristic of this subtype of EB. Treatment for this subtype of EB is generally supportive and aimed at relieving blistering and pruritus. Reported therapies have included topical and systemic steroids, topical calcineurin inhibitors, H1 antagonists, tricyclic antidepressants, cyclosporine, and thalidomide. However, these treatments have not resulted in significant or sustainable effects.

The pathophysiology of EB pruriginosa is not clear but likely involves dysregulated itch mediators and cytokines as well as dysregulated activation of epidermal sensory nerve endings. One case series of seven patients with EB pruriginosa suggests the presence of mast cell infiltration, elevated IgE levels (despite no history of atopy), and increased Th2 subsets with reduced Th1 and Th17 subpopulations may drive pruritus in these patients. This suggests a possible role for dupilumab in the treatment of EB pruriginosa-related pruritus.

Dupilumab is a monoclonal antibody that targets the IL-4 and IL-13 receptor alpha subunit inhibiting the resultant Th2-mediated inflammatory cascade. In recent years, there have been several case reports demonstrating dupilumab's successful use in treating EB pruriginosa-associated pruritus. One case series of three patients demonstrated an improvement in clinical symptoms, skin lesions, and biomarkers including a decreased EBDASI (EB Disease Activity and Scarring Index) score, decreased VAS pruritus score, and decreased percentage of Th2 cells after 20 weeks of dupilumab usage.

At the patient's last visit, the possibility of Vyjuvek (B-VEC), a recently FDA-approved topical gene replacement therapy for dystrophic EB, was also discussed. This herpes-simplex virus type 1 (HSV-1) vector-based gene therapy is for treatment of wounds in DEB patients aged 6 months and older. This gel needs to be applied by a healthcare professional in droplets to skin wounds once weekly; however, this may not be accessible to all patients due to cost. Given our patient's excellent response to dupilumab, he will continue with this therapy for the time being.

KEY POINTS

1. EB pruriginosa is a genetic blistering disorder characterized by lichenified and albopapuloid nodules, scarring, milia, nail dystrophy, and intense pruritus. It is caused by mutations in the COL7A1 gene.
2. Subcutaneous dupilumab injections markedly reduced blistering and pruritus in our patient with EB pruriginosa, as well as several others reported in the literature, and has been extremely well tolerated. This is a prime example of "drug repurposing" of a therapy for conditions that may be off-label.

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CHICAGO DERMATOLOGICAL SOCIETY **Case #5**

Presented by Jaimie Lin, MD, Joan Guitart, MD, Xiaolong Zhou, MD
Department of Dermatology, Feinberg School of Medicine, Northwestern University

HISTORY OF PRESENT ILLNESS

A 46-year-old female presented to Northwestern Memorial Hospital with a 2.5 year history of multiple firm, skin-colored facial papules and plaques. The lesions were tender to palpation and intermittently pruritic. She had trialed topical tretinoin and clindamycin 0.1% lotion without any improvement. After her initial visit, the patient was lost to follow up. One year later, she returned with similar facial lesions and reported that the eruption had remained stable over this time.

PAST MEDICAL AND SURGICAL HISTORY

The patient had a history of worsening chronic polyarthralgias since her teenage years. She had a recent episode of pancreatitis which was then complicated by diabetes. During endocrinology work up, she was additionally found to have 1.2 cm incidental thyroid nodule, mild hypercalcemia and hyperparathyroidism.

FAMILY AND SOCIAL HISTORY

Noncontributory

MEDICATIONS

Alprazolam 2 mg daily PRN, Fluoxetine 40 mg daily, Gabapentin 800 mg TID, Ibuprofen 800 mg TID, Lisinopril-hydrochlorothiazide 20-12.5 mg daily, Oxycodone-acetaminophen 10-325 mg QID PRN

PHYSICAL EXAM

The patient was well appearing. On the forehead, cheeks and chin, there were many skin-colored to erythematous, firm papules with bland dermoscopic findings. There was fullness of the neck and palpable submandibular glands.

DERMATOPATHOLOGY

Histopathology revealed a dense superficial and deep lymphoid infiltrate with scattered irregular germinal centers. The infiltrate was composed of centrocytes and centroblasts with rare tingible body macrophages and variable mitotic activity. An interstitial lymphoplasmacytic infiltrate with numerous histiocytes was also noted. Immunohistochemistry was performed on deparaffinized sections. The infiltrate was CD20 positive. Kappa and lambda in situ hybridization demonstrated a ratio of light chains within the normal limits. Light chain restriction was not demonstrated. IgG highlighted scattered cells while many of them (50-70%) expressed IgG4.

LABS

NORMAL

BMP, TSH, Albumin/Protein, Autoimmune panel/ANCA screening, CCP

ABNORMAL

Calcium (8.3-10.5): 11.1	PTH (12.0-88.0): 102.1
ANA positive with (1:160 titer)	Complement C3 (81-157): 227
Platelets (140-390): 413	Anti-smooth muscle Ab positive with (1:40 titer)
Eosinophils (0.0-8.0): 8.8	IgE (0.0-100): 796.0
Hgb A1c (4.0-5.6%): 7.3%	IgG4 (4-86): 97.8

> Accentuated beta band and hypergammaglobulinemia observed on protein electrophoresis without bands seen on immunofixation.

IMAGING

CT Head and Neck:

Several mildly enlarged lymph nodes were visualized in the neck, involving the bilateral parotid. The thyroid gland was enlarged and contained a 12 mm nodule in the left thyroid lobe.

CT Chest, Abdomen, Pelvis: No lymphadenopathy in the chest, abdomen or pelvis. Normal spleen size. Mild mid esophageal wall thickening

DIAGNOSIS

Cutaneous IgG4-Related Disease

TREATMENT AND COURSE

The patient was started on topical clobetasol ointment to the face and prednisone 40 mg daily. At one month follow-up after this treatment course was initiated, she was noted to have significant improvement. Her steroids were tapered with a plan to initiate rituximab therapy.

DISCUSSION

IgG4 related disease (IgG4-RD) is a fibro-inflammatory disease of unknown etiology that can affect multiple organs. While the pancreas, retroperitoneum, salivary glands, parotid glands and kidneys are most often involved, IgG4-RD can affect any organ including the skin. Although there are reports of them occurring concurrently, cutaneous IgG4-RD and systemic IgG4-RD have been proposed as two distinct processes, as the cutaneous form is rarely associated with significant systemic features. Cutaneous IgG4-RD most commonly presents on the head and neck, and glandular involvement may be noted. Interestingly, patients with IgG4-RD may have diffuse polyarthralgias, which may explain our patient's history of chronic pain of unknown etiology. Case reports have also described IgG4 cells in parathyroid and thyroid tumors, which may be relevant to our patient's newly diagnosed thyroid nodule. On pathology, IgG4-RD demonstrates a dense lymphoplasmacytic infiltrate, storiform fibrosis and obliterative phlebitis with a high density of IgG4 positive plasma cells (IgG4/IgG >40%). While elevated serum IgG4 levels can be seen in 70-80% of patients, an elevated serum IgG4 level is not required for diagnosis. Elevated IgE and eosinophilia are common findings, as seen in our patient. Existing theories postulate that elevated IgG4 in IgG4-RD may actually represent a bystander phenomenon that reflects an anti-inflammatory response to a primary pathogenic immune process. The mainstay of treatment in IgG4-RD is corticosteroids, and improvement is often so rapid and profound that steroid response has been proposed as a potential diagnostic criterion. Other treatment options include rituxumab, mycophenolate, azathioprine and methotrexate.

KEY POINTS

1. Cutaneous IgG4-RD is a multi-system fibroinflammatory disorder presenting as papulonodules primarily on the head and neck characterized histologically by the presence of dense lymphoplasmacytic infiltrates, storiform fibrosis, and obliterative phlebitis.
2. IgG4 may represent a bystander phenomenon in IgG4-RD that reflects an anti-inflammatory response to a primary pathogenic immune process.
3. Steroids are highly effective and are the mainstay of treatment

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CHICAGO DERMATOLOGICAL SOCIETY **Case #6**

Presented by Celestina Okoye, MD, Lida Zheng, MD
Department of Dermatology, Feinberg School of Medicine, Northwestern University

UNKNOWN

A 30-year-old female with a history of bipolar disorder presented to dermatology clinic with a lesion of the left upper eyelid present for one year.

CHICAGO DERMATOLOGICAL SOCIETY **Case #7**

Presented by Samantha Guhan, MD, Joaquin Brieva, MD
Department of Dermatology, Feinberg School of Medicine, Northwestern University

HISTORY OF PRESENT ILLNESS

A 57-year-old man presented with eye pain and a cutaneous eruption on his bilateral thighs. The patient had been in his usual state of health until he developed a pulmonary embolism 6 weeks prior to presentation. He subsequently was found to have a renal infarct. During this time, he developed bilateral conjunctivitis and multiple erythematous, edematous nodules on his thighs. He characterized this eruption as painful and pruritic. The patient was readmitted with fevers up to 103F and weight loss.

PAST MEDICAL AND SURGICAL HISTORY

Asthma, eczema, and benign prostate hyperplasia

FAMILY AND SOCIAL HISTORY

The patient's family history was notable for breast cancer (mother), COPD and heart failure (father), lupus (cousin, unknown side. Patient worked at a desk job and lived with his wife at home. He consumed 4-8 drinks/week and did not have any history of smoking or recreational drug use.

MEDICATIONS

Fluticasone-salmeterol inhaler, warfarin

PHYSICAL EXAM

The patient was febrile. Edematous, erythematous, purpuric patches with some erosions were noted on the thighs. Numerous palpable purpura and petechiae were seen on the legs with significant pitting edema. His face, axillae, and palms/soles were clear. Ocular exam was notable for bilateral conjunctivitis.

LABS

ABNORMAL

Absolute lymphocyte count: 0.7. ALT 68 IU/L. ESR 106 mm/hr (3-10 mm/hr). Ferritin 1521.7 ng/ml (24-336 ng/ml). ANA: + 1:320. dsDNA of 6 IU/mL. C3 246 mg/dL (90-180 mg/dL). C4 70 mg/dL (16-47 mg/dL)

NORMAL

RNP, SSA/SSB, anti-histone, anti-Smith, Scl-70, Jo-1, anti-cardiolipin, B2-glycoprotein, HIV, CMV, EBV, Hepatitis B/C, Syphilis RPR. SPEP/immunofixation with normal kappa/lambda ratio and no definitive monoclonal bands

IMAGING

PET/CT: Prominent skeletal uptake, splenomegaly and pathologic adenopathy in chest, abdomen, pelvis

Bone marrow biopsy: Slightly hypercellular bone marrow (65%) with slightly increased granulopoiesis and megakaryocytes, a moderate number of myeloid and erythroid precursors with distinct cytoplasmic vacuoles, and normal flow cytometric results.

DERMATOPATHOLOGY:

Histopathology of the thigh showed marked papillary edema with abundant diffusely scattered neutrophils with some karyorrhexis, consistent with Sweet syndrome. Subsequent biopsies revealed leukocytoclastic vasculitis.

TREATMENT AND COURSE

Patient was subsequently admitted to the hospital several times in the following years with fevers of unknown origin, complicated by severe pneumonias and numerous abscesses. The patient also developed relapsing polychondritis. Extensive rheumatologic, infectious, hematologic, pulmonary, and dermatologic work-up was largely unrevealing. It was initially determined that patient had an undefined hyper-IL6-autoinflammatory syndrome and was trialed on a variety of therapies by rheumatology, all with limited success. Treatments included IVIG, Anakinra, Methotrexate, Tocilizumab, Tofacitinib,

Canakinumab, Rituximab, and varying courses of high-dose steroids. The patient ultimately developed myelodysplastic syndrome and was treated with lenalidomide and Azacytidine. Eventually, the patient underwent genetic screening by the NIH and was found to have a somatic mutation in UBA1. He ultimately passed away from complications of MDS.

DIAGNOSIS
VEXAS Syndrome

DISCUSSION
VEXAS (vacuoles, E1-ubiquitin-activating enzyme, X-linked, autoinflammatory, somatic) syndrome is an autoinflammatory disorder first described in 2020 by the NIH. The initial study characterized 25 men with myeloid-restricted somatic missense mutations in the UBA1 gene located on chromosome Xp11.23, which is the master enzyme for ubiquitylation. A recent study found the prevalence to be higher than initially thought, about 1 in 40,000 men about the age of 50. Common clinical features include recurrent fevers, pulmonary infiltrates, neutrophilic dermatoses, cutaneous vasculitis, relapsing polychondritis, ocular inflammation, progressive myeloid hematologic disease, and bone marrow vacuolization in erythroid/myeloid precursor cells. Relapsing polychondritis, male sex, macrocytosis and thrombocytopenia have been found to be sensitive and specific for this condition. The official diagnosis relies on identification of the pathologic mutation.

There is significant variability in reports of treatment efficacy. Most patients improve with courses of systemic corticosteroids but tend to relapse with tapering. Case reports support the use of the IL-1 receptor antagonist anakinra or the IL-6 inhibitor tocilizumab, sometimes in combination with steroids or methotrexate. Given that the mutation is myeloid-restricted, hematopoietic stem cell transplant (HSCT) is gaining favor as a curative treatment.

KEY POINTS:
1. VEXAS syndrome is an autoinflammatory disease caused by mutations in the UBA-1 gene, with key symptoms including high fevers, neutrophilic dermatoses, cutaneous vasculitis, relapsing polychondritis, ocular inflammation and myeloid hematologic disease.
2. VEXAS syndrome is likely more common than initially thought and should be considered in the differential for a man with an unexplained autoinflammatory syndrome.
3. Hematopoietic stem cell transplant is gaining favor as a treatment for VEXAS syndrome.

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CHICAGO DERMATOLOGICAL SOCIETY **Case #8**

Presented by Alecia Blaszczak, MD, PhD, Paras Vakharia, MD, PharmD
Department of Dermatology, Feinberg School of Medicine, Northwestern University

HISTORY OF PRESENT ILLNESS

A 19-year-old male presented to Northwestern Dermatology with a progressive eruption on the L knee. Approximately four months prior to presentation, the patient scraped his knee while hiking in Israel. After he scraped his knee, he also went swimming in the sea. He denied any associated joint pain, was able to ambulate without issue and denied any other systemic symptoms. Prior to presentation at Northwestern, the patient was treated with many topical and oral medications including Neosporin, triamcinolone 0.1% ointment, gentamicin 0.1% cream, mupirocin 2% cream, oral doxycycline and oral TMP-SMX. The patient was also evaluated by orthopedic surgery after undergoing an MRI of the L knee which demonstrated a possible underlying joint effusion. Patient was referred from orthopedics to dermatology for further evaluation.

PAST MEDICAL AND SURGICAL HISTORY

The patient had a past medical history significant for eczema managed with topical steroids, treatment-refractory cystic acne managed with adalimumab, and anxiety managed with escitalopram.

FAMILY AND SOCIAL HISTORY

The patient is a student in Chicago. He denied any family history of recurrent infections.

MEDICATIONS

Adalimumab, escitalopram, hydrocortisone 2.5% ointment

PHYSICAL EXAM

The patient was well-appearing. On the L knee, there was a large, erythematous, verrucous, ulcerated plaque. Remainder of skin exam was unremarkable. Joint exam of L knee demonstrated full range of motion and no joint effusion. Neurologic exam revealed 5/5 strength in hip, knee and ankle flexion and extension with intact sensation.

DERMATOPATHOLOGY

Histopathology revealed mixed inflammation including granulomatous inflammation with multinucleated giant cells and plasma cells. Special stains (DPAS, Gram and acid fast bacilli) were negative for microorganisms.

LABS

Tissue Culture: bacterial culture grew rare *Staphylococcus epidermidis* and rare *Propionibacterium acnes*; fungal and AFB tissue cultures had no growth

Serologies: HIV Ag/Ab nonreactive, urine *Histoplasma Galactomannan* Ag < 0.2 ng/ml, urine *Blastomyces* quantitative Ag negative, fungal blood culture with no growth at 4 weeks, AFB blood culture with no growth at 8 weeks

Because suspicion for infection was high, and workup was negative, 28S rDNA Broad-range PCR and next-generation sequencing from formalin-fixed paraffin embedded tissue was sent to the University of Washington. This was positive for *Neosartorya hiratsukae*

DIAGNOSIS

Neosartorya hiratsukae cutaneous infection

TREATMENT AND COURSE

Initially, the patient was instructed to hold adalimumab his antimicrobials. After *Neosartorya hiratsukae* was identified via rDNA sequencing, the patient was started on voriconazole 200mg BID which was up titrated to 300mg BID based on blood voriconazole levels by infectious disease. The patient was treated for a total of 16 weeks with significant improvement.

DISCUSSION

Neosartorya hiratsukae is a species in the genus *Aspergillus* and in the section *Fumigati*. This species was first identified in 1991 and has been isolated from air and aloe juice. The first published case of human infection was in 2002. It was isolated from a patient in Brazil with cerebral aspergillosis. The patient was treated with itraconazole based on susceptibility testing with initial improvement but ultimately died from multiorgan failure. Additional cases of human infection have been reported including fungal rhinosinusitis and fungal peritonitis. MIC testing has been completed on the aforementioned isolates which have demonstrated variable resistance patterns. In all cases, isolates have been sensitive to voriconazole. In most cases, the patients were immunocompromised or immunosuppressed suggesting that this species is more likely to cause an opportunistic infection. The only reported cutaneous infection to date is in a hedgehog that presented with an alopecic patch with underlying scale and pinpoint hemorrhages. There is likely underreporting of this infectious agent as it forms slow growing white colonies that may be discarded as contaminants.

Our case is the first-reported cutaneous infection in humans with *Neosartorya hiratsukae.* Our patient was immunosuppressed in the setting of adalimumab therapy for management of treatment refractory cystic acne. He was likelyl inoculated during his trip while hiking or swimming. Holding his immunosuppression and treatment with oral voriconazole allowed for clinical improvement of this cutaneous infection.

KEY POINTS

1. *Neosartorya hiratsukae* is a rare cause of infections mainly in immunocompromised or immunosuppressed hosts.
2. Systemic treatment is often driven by MIC testing which demonstrates variable resistance patterns, but there appears to be consistent sensivity to voriconazole.

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CHICAGO DERMATOLOGICAL SOCIETY **Case #9**

Presented by Nathaniel Campbell, MD, PhD., Walter Liszewski, MD
Department of Dermatology, Feinberg School of Medicine, Northwestern University

UNKNOWN

A 64-year-old female with a history of nasopharyngeal SCC, NSCLC, and metastatic breast cancer presented to dermatology clinic with several months of “stiff skin” on the bilateral arms.

CHICAGO DERMATOLOGICAL SOCIETY **Case #10**

Presented by Prachi Aggarwal, MD, Annette M. Wagner, MD and Amy S. Paller, MD
Department of Dermatology, Feinberg School of Medicine, Northwestern University
Division of Dermatology, Ann & Robert H. Lurie Children's Hospital of Chicago

HISTORY OF PRESENT ILLNESS

An 11-year-old girl first presented at 4 years of age with multiple curvilinear, verrucous plaques that had progressively extended since birth to encompass a large portion of the left side of her body. Several areas were pruritic, and intertriginous areas intermittently bled. Two years prior to her presentation, she was given a diagnosis of systematized inflammatory linear verrucous epidermal nevi (ILVEN) based on lesional biopsy. She had been treated with topical steroids and keratolytics without benefit. The patient was otherwise healthy and met her developmental milestones.

Tazarotene cream 0.1% was prescribed and was more effective than previous keratolytics at reducing hyperkeratosis but was still suboptimal. Isotretinoin 10 mg (0.5mg/kg) was started at 4.5 years of age, which flattened many of her plaques; however, efficacy waned after 6 months of use.

PAST MEDICAL AND SURGICAL HISTORY

The patient was born full-term with no known pregnancy complications. She had well-controlled asthma.

FAMILY AND SOCIAL HISTORY

The patient lives with her biological mother, father, and younger sibling who are otherwise healthy.

PHYSICAL EXAM

The patient was well-appearing. There were multiple curvilinear, brightly erythematous verrucous plaques that involved the left side of the body following lines of Blaschko. Lesions were present on the face, arm, trunk and legs, encompassing nearly 50% of her left side.

GENETIC TESTING

Genetic testing using whole-exome capture was performed (IDT xGen Exome Research Panel V1.0) and identified germline heterozygous *PMVK* c.79G>T p.E27X and somatic *PMVK* c.379C>T, p.Q127X mutations which result in a defect in the mevalonate pathway.

DERMATOPATHOLOGY

Histopatology revealed an acanthotic and corrugated epidermis. There were numerous cornoid lamella noted and dilatation of acrosyringial structures.

DIAGNOSIS

Linear porokeratosis

TREATMENT AND COURSE

Two variants were found in PMVK (see above), one shared with the patient's father (who did not have a history of skin disease) and the other *de novo*, suggesting a diagnosis of porokeratosis with type 2 mosaicism. Given the role of phosphomevalonate kinase in cholesterol biosynthesis and previous experience with blockade of this pathway in CHILD syndrome, the patient started treatment with topical 2% lovastatin/2% cholesterol every other day with 3% diclofenac gel (anecdotally found useful for porokeratosis) mixed with tacrolimus 0.03% ointment on alternate days. She was continued on isotretinoin 0.5mg/kg daily. Within a few months, her plaques had become much thinner and less erythematous, with nearly 70% improvement. She was eventually weaned off isotretinoin by 7.5 years of age. She has continued her topicals, although she increased to 4% lovastatin/4% cholesterol due to some thickening of plaques noted at 9.5 years of age.

DISCUSSION

Linear porokeratosis presents in infancy or childhood as one or many plaques that follow the lines of Blaschko as a form of somatic mosaicism of keratinocytes and may resemble ILVEN. In recent reports, heterozygous germline mutations of the mevalonate pathway genes MVK, PMVK, MVD, and FDPS have

been identified in sporadic and familial forms of porokeratosis. The mevalonate pathway is an essential pathway in the creation of many biomolecules, including cholesterol synthesis. Deficiency of cholesterol has been found to sensitize keratinocytes to apoptotic signals, and it has been postulated that cholesterol deficiency along with the accumulation of toxic proximal metabolites may contribute to the disease phenotype.

Current treatment for linear porokeratosis mainly focuses on managing symptoms and improving the appearance of the skin. However, given the marked improvement in cutaneous disease in this case and reports of improvement in other forms of porokeratosis with topical statins, there appears to be great potential for further pathogenesis-directed therapy for this debilitating disorder, especially in pediatric populations.

KEY POINTS

1. Linear porokeratosis is a disorder of keratinization that often presents with papules and plaques following the lines of Blaschko and may resemble ILVEN.
2. Topical statins have emerged as a first-line treatment for linear porokeratosis.

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CHICAGO DERMATOLOGICAL SOCIETY **Case #11**

Presented by Simran Chadha, MD, Paras Vakharia, MD, PharmD
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HISTORY OF PRESENT ILLNESS

A 31-year-old female with a history of systemic lupus erythematosus (SLE) presented with two months of pruritic erythematous subcutaneous nodules on the legs. Lesions would develop and resolve over the course of one to two weeks and improved with use of over-the-counter topical steroid creams. The patient endorsed a concurrent flare of her SLE and was experiencing polyarthritis.

PAST MEDICAL AND SURGICAL HISTORY

The patient had a longstanding history of SLE with manifestations including discoid lupus erythematosus (DLE), photosensitivity, oral ulcers, arthritis, fatigue, sicca, and cytopenias. She followed closely with rheumatology and her disease was generally well-controlled on methotrexate, hydroxychloroquine, and intermittent prednisone tapers. Her DLE first presented with scarring alopecia and characteristic plaques in the concha of her bilateral ears, but was in remission on her regimen of oral medications.

FAMILY AND SOCIAL HISTORY

The patient's maternal aunt was also diagnosed with SLE. The patient denied tobacco and illicit drug use. She endorsed social alcohol use.

MEDICATIONS

Methotrexate 17.5mg weekly, folic acid, hydroxychloroquine 400mg daily, prednisone 5mg daily, and celecoxib 200mg as needed

PHYSICAL EXAM

The patient was well-appearing. On the bilateral anterior legs were scattered indurated nodules with central hyperpigmentation and surrounding ill-defined erythema. On the vertex scalp were two atrophic plaques with alopecia. On the bilateral auricular concha were thin pink-brown plaques with slight scale. Examination of the oral mucosa, trunk, and arms was unremarkable.

DERMATOPATHOLOGY

Histopathology revealed a medium-sized vessel at the junction of the deep dermis and subcutaneous tissue with fibrinoid necrosis and perivascular lymphohistiocytic infiltrate. The vessel was hyalinized and thrombosed and showed numerous mononuclear cells infiltrating. Elastic Van Gieson stain was performed and showed disruption of the internal elastic lamina.

LABS

ABNORMAL
WBC 3.2 (3.5-10.5 10^3/uL)
ANA 1:1,280 (speckled), anti-dsDNA 212 (0-4 IU/mL), anti-RNP >8.0 (0.0-0.9 AI), anti-Sm >8.0 (0.0-0.9 AI), anti SSA/Ro >8.0 (0.0-0.9 AI), C3 79 (81-157 mg/dL), C4 17 (12-39 mg/dL)

NORMAL
HGB 12.5 (11.6-15.4 g/dL), PLT 243 (140-390 10^3/uL)
Creatinine 0.99 (0.60-1.30 mg/dL)
Hepatitis B Surface Antibody non-reactive, Hepatitis B Surface Antigen non-reactive, Hepatitis B Core Antibody non-reactive, Hepatitis C Antibody non-reactive

IMAGING

CT Angiogram Abdomen and Pelvis with Contrast: Normal caliber aorta. Origins of the celiac axis, superior mesenteric artery, bilateral renal arteries, and inferior mesenteric artery were widely patent. No aneurysm identified.

DIAGNOSIS
Polyarteritis nodosa (PAN)

TREATMENT AND COURSE
Given the patient's involvement was isolated cutaneous and nonsevere, her immunosuppression was slightly uptitrated. Her methotrexate dosage was increased from 17.5 mg weekly to 20 mg weekly. Her celecoxib was increased from as needed to scheduled 200 mg twice daily. On this regimen, her cutaneous PAN significantly improved without further nodules.

DISCUSSION
Polyarteritis nodosa is a necrotizing vasculitis that predominantly affects medium-sized muscular arteries. The disease has both a systemic and cutaneous subtype, the latter being our patient's presumed diagnosis. Cutaneous PAN largely presents with purpura, livedo reticularis, and tender subcutaneous nodules with a predilection to the lower extremities. Risk of progression from cutaneous to systemic PAN is estimated at 10%; thus patients require diligent follow-up and screening with clinical history, physical exam, and imaging. Systemic manifestations of PAN are multifold, but common manifestations include constitutional symptoms, mononeuropathy multiplex, vascular aneurysms (classically involving the renal arteries creating the "rosary sign" on radiography), renal insufficiency, hypertension, gastrointestinal distress ("intestinal angina" due to mesenteric arteritis), and myalgia.

PAN can be primary, idiopathic, or secondary. Classically, systemic PAN can be associated with hepatitis B, hepatitis C, and hairy cell leukemia. Similarly, cutaneous PAN is associated with a variety of infections as well as inflammatory bowel disease and long-term exposure to minocycline. Few case reports have noted PAN-like vasculitis in patients with SLE . One describes a necrotizing medium vessel vasculitis in the musculature of a patient with SLE, and another describes a patient initially diagnosed with PAN-associated mononeuropathy multiplex who later developed classic manifestations of SLE. Apart from isolated reports, however, no direct association between SLE and PAN has been established. Lupus vasculitis is largely a disease of small vessels, with medium vessel disease affecting 1.6-14% of patients with SLE.

Cutaneous lupus vasculitis largely presents with palpable purpura, but nodular, ulcerative, and livedoid lesions have also been described. Thus, the distinction between lupus vasculitis and PAN in the skin is largely histopathologic. Skin biopsy in PAN reveals neutrophilic vasculitis of medium vessels at the dermal-subcutis junction with accentuation at arterial bifurcations. Giant cells and macrophages are found in the arterial lumen and more advanced lesions demonstrate vessel wall hyalinization, fibrinoid necrosis, and adventitial neovascularization. Elastin staining can highlight disruption of the internal elastic lamina. In contrast, the histopathology of lupus vasculitis typically exhibits neutrophil-rich leukocytoclastic vasculitis of small vessels, though lymphocytic vasculitis of any caliber vessel can be seen. The isolated involvement of a medium-sized vessel at the dermal-subcutis junction with hyalinization of the vessel wall, disruption of the internal elastic lamina, and presence of a predominantly lymphohistiocytic infiltrate helped differentiate our patient's pathology from lupus vasculitis.

Treatment for both systemic and cutaneous PAN varies by disease severity. In general, treatment is continued for one year, then patients are monitored for relapse. Cutaneous disease relapses more frequently as compared to systemic disease, and thus, often requires chronic treatment. Limited cutaneous disease can be treated with topical steroids, oral non-steroidal anti-inflammatories (NSAIDs), oral steroids, dapsone, and colchicine. Relapses are managed with immunomodulatory agents including methotrexate and azathioprine. Severe disease may require high doses of oral steroids, cyclophosphamide, and plasma exchange.

KEY POINTS
1. Polyarteritis nodosa is a necrotizing vasculitis affecting medium-sized vessels of multiple organ systems. Cutaneous findings include purpura, livedo reticularis, and tender subcutaneous nodules with a predilection to the lower extremities.
2. Cutaneous polyarteritis nodosa is a vasculitis pathologically distinct from cutaneous small vessel vasculitis. Skin biopsy reveals mixed neutrophilic and lymphocytic vasculitis of medium-sized vessels, hyalinization of vessel walls, fibrinoid necrosis, and disruption of the internal elastic lamina.

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