Chicago Dermatological Society

Monthly Educational Conference

Program Information
CME Certification
and
Case Presentations

Wednesday, December 4, 2019
Gleacher Center – Chicago, IL

Conference Host:
Section of Dermatology
University of Chicago Hospitals
Chicago, Illinois

Program

Host: University of Chicago
Wednesday, December 4, 2019
Gleacher Center, Chicago

8:00 a.m.	**Registration & Continental Breakfast with Exhibitors** *All conference activities take place on the 6th Floor*
8:30 a.m. - 10:30 a.m.	**Clinical Rounds** Slide viewing and posters
9:00 a.m. - 10:00 a.m.	**Morning Lecture** "Updates in Hair Disorders" *Amy McMichael, MD*
10:00 a.m. - 10:30 a.m.	**Break and Visit with Exhibitors**
10:30 a.m. - 12:15 p.m.	**Resident Case Presentations & Discussion;** **MOC Self-Assessment Questions**
12:15 p.m. - 12:45 p.m.	**Box Lunches & visit with exhibitors**
12:55 p.m. - 1:00 p.m.	**CDS Business Meeting**
1:00 p.m. - 2:00 p.m.	**General Session** LORINCZ LECTURE – "Skin of Color Updates" *Amy McMichael, MD*
2:00 p.m.	**Meeting adjourns**

PLEASE NOTE THE FOLLOWING POLICY ADOPTED BY THE CDS TO COMPLY WITH HIPAA PRIVACY RULES:

Taking personal photos of posters or other displays, of images included in general session lectures or presentations, and of live patients at CDS conferences is strictly prohibited. Making audio recordings of any session at a CDS conference also is prohibited.

Mark the Date!

Next CDS meeting will be on Wednesday, April 15th at the Gleacher Center downtown.

Watch for details on the CDS website: www.ChicagoDerm.org
Save time and money – consider registering online!

Guest Speaker

AMY MCMICHAEL, MD

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

Dr. Amy McMichael is Professor and Chair of Dermatology, as well as Dermatology Residency Director at the Wake Forest University School of Medicine. She earned her medical degree in 1990 at the University of Pennsylvania School of Medicine, and she completed her dermatology residency at the University of Michigan in 1994. She also completed advanced training in epidemiology at the Wake Forest School of Medicine Department of Public Health Sciences. Dr. McMichael is a diplomat of the American Board of Dermatology. Her research focuses on hair and scalp disorders and skin disease of deeply pigmented skin. She has many peer-reviewed articles, chapters, and invited articles on these topics to her credit, and is the the co-editor of the text Hair and Scalp Diseases: Medical, Surgical, and Cosmetic Treatments.

Dr. McMichael has served on the Editorial Board of Cosmetic Dermatology and as a member of the Scientific Advisory Council to the National Alopecia Areata Foundation, President of the Skin of Color Society, and Chair, Career Advancement Committee of Women's Dermatologic Society, among other roles in various professional organizations.

CME Information

December 4, 2019

Overview

The Chicago Dermatological Society was established in 1901 and has strived to provide meaningful educational opportunities to dermatologists in the Chicago area for more than a century. Guest speakers from across the country share their expertise with CDS members, as well as residents in training medical students doing their dermatology rotation. CDS schedules six day-long meetings each year which are "hosted" by one of the dermatology residency programs in the city. Two lectures are given by the guest speaker, and the residents of the host institution present cases which are offered for audience discussion. In addition, posters, microscopic slides and occasionally live patients prepared by the residents are made available during the "clinical rounds" portion of the meeting. CDS also offers a session that qualifies for "Maintenance of Certification" self-assessment questions under the auspices of the American Board of Dermatology.

Target Audience

This activity has been designed to meet the educational needs of dermatologists. CDS members, residents in training and medical students engaged in their dermatology rotation are invited to attend.

Learning Objectives

At the conclusion of the 2019/20 series of meetings, the participant should be able to:

1. Discuss key factors in the diagnosis and treatment for various diseases and conditions of the skin, including use of new or emerging medication options.
2. Describe the surgical techniques for treatment of skin cancers, as well as for cosmetic and other purposes.
3. List the therapeutic options available to the dermatologist for a variety of skin diseases, both medical and surgical, and discuss how new emerging treatments can be successfully incorporated into a dermatology practice.

Physician Accreditation Statement

This activity is planned and implemented by Indiana Academy of Ophthalmology (IAO) and the Chicago Dermatological Society. IAO is accredited by the Indiana State Medical Association to provide continuing education for physicians.

Credit Designation for Physicians – IAO designates this live activity for a maximum of 4.75 *AMA PRA Category 1 Credit(s)*™. Physicians should claim only the credit commensurate with the extent of their participation in the activity.

Attendees are required to submit a CME claim form upon departure from the conference. Please leave your form, along with the evaluation form, at the registration table when you leave the meeting. Thank you for your attention to this important item.

Disclosure of Conflicts of Interest

The IAO and CDS require instructors, planners, managers and other individuals and their spouse/life partner who are in a position to control the content of this activity to disclose any real or apparent conflict of interest they may have as related to the content of this activity. All identified conflicts of interest are thoroughly vetted by IAO and CDS for fair balance, scientific objectivity of studies mentioned in the materials or used as the basis for content, and appropriateness of patient care recommendations. All speakers are asked to follow the "first slide" rule to repeat their conflict of interest disclosures during their talk. The guest speaker for this conference, Amy McMichael, MD, has disclosed the following potential conflicts of interest: Consultant - Aclaris, Allergan, Almirall, Bioniz, Cassiopea, Covance, eResearch Technology, Galderma, Incyte, Johnson & Johnson, Keranetics, Merck & Co., Pfizer, Proctor & Gamble, Samumed; Research - Aclaris, Cassiopea, Concert Pharmaceuticals, Incyte, Proctor & Gamble, Samumed; Grants - Allergan, Concert Pharmaceuticals, Proctor & Gamble; Royalties - Informa Healthcare, UpToDate.

None of the program committee members have disclosed any relevant potential conflicts of interest.

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Contact Information

For information about the physician accreditation of this program please contact the CDS administrative office at: 847-680-1666; email: Rich@RichardPaulAssociates.com

Americans with Disabilities Act

In compliance with the Americans with Disabilities Act, we will make every reasonable effort to accommodate your request. For any special requests, contact CDS at: Rich@RichardPaulAssociates.com

Disclaimer

Participants have an implied responsibility to use the newly acquired information to enhance patient outcomes and their own professional development. The information presented in this activity is not meant to serve as a guideline for patient management. Any procedures, medications, or other courses of diagnosis or treatment discussed in this activity should not be used by clinicians without evaluation of patient conditions and possible contraindications on dangers in use, review of any applicable manufacturer's product information, and comparison with recommendations of other authorities.

Dislosure of Unlabeled Use

This educational activity may contain discussion of published and/or investigational uses of agents that are not indicated by the FDA. The planners of this activity do not recommend the use of any agent outside of the labeled indications. The opinions expressed in the educational activity are those of the faculty and do not necessarily represent the views of the planners. Please refer to the official prescribing information for each product for discussion of approved indications, contraindications, and warnings.

University of Chicago
Section of Dermatology

Dermatology Residents

Third Year
Clifford Hsieh, MD
Emily Lund, MD
Jared Wishik, MD

Second Year
Julia Dai, MD
Arjun Dayal, MD
Esther Kim, MD

First Year
Margaret Boyle, MD
Margaret Bruns, MD
Erin Dodd, MD
Erin Ibler, MD

AT THE FOREFRONT
UChicago Medicine

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CASE 1

PRESENTERS
Margaret Bruns MD; Oluwakemi Onajin MD; Victoria Barbosa MD, MPH, MBA

HISTORY OF PRESENT ILLNESS
A 69-year-old African-American female presented to dermatology for evaluation of hair loss that began three years prior and had progressed to involve most of her scalp. The affected areas on her scalp were pruritic.

PAST MEDICAL HISTORY
Hypertension, Osteoarthritis

FAMILY HISTORY
Negative for autoimmune conditions or hair loss
Daughter died from unknown cause (seizures and respiratory disease)

SOCIAL HISTORY
Denies alcohol and tobacco use

MEDICATIONS
Hydrochlorothiazide
Metoprolol

ALLERGIES
No known drug allergies

REVIEW OF SYSTEMS
Positive for knee pain, leg swelling, and dry cough
Negative for fever, weight loss, dyspnea, sinus issues, visual disturbance, headaches, seizures, chest pain, and palpitations

PHYSICAL EXAMINATION
Well-demarcated pink smooth indurated plaques with significantly decreased hair density, loss of follicular ostia, and focal perifollicular scaling on the vertex and mid-scalp, extending onto the parietal and frontal scalp. Eyebrows and eyelashes appeared normal.

LABORATORY TESTS
Complete Blood Count, Comprehensive Metabolic Panel, Calcium, 25-Hydroxy Vitamin D, Thyrotropin, Antinuclear Antibody, Angiotensin Converting Enzyme, and Quantiferon Gold were within normal limits.

IMAGING/PROCEDURES
Chest X-Ray
Mild nonspecific bronchial wall thickening without significant lymphadenopathy and right upper lobe pulmonary nodule.

Computed Tomography (CT) Chest
Spiculated right upper lobe nodule, scattered nodules, and mediastinal lymphadenopathy consistent with sarcoidosis.

Pulmonary Function Test
Patient could not complete due to claustrophobia

Electrocardiogram
New left anterior fascicular block

DERMATOPATHOLOGY
Punch biopsies from the left vertex scalp (vertical section) and right frontal scalp (horizontal section) showed decreased follicular density and superficial to deep granulomatous inflammation composed of well-formed epithelioid granulomas with a sparse lymphocytic infiltrate. Negative for birefringent foreign material. GMS and AFB stains were negative for infectious organisms.

DIAGNOSIS
Sarcoidosis-induced alopecia

TREATMENT AND COURSE
Our patient was initially treated with betamethasone augmented 0.05% ointment BID with minimal symptomatic improvement. Therapy was escalated to hydroxychloroquine 200 mg BID with a short course of prednisone 20 mg daily. Prednisone and hydroxychloroquine were subsequently discontinued due to intolerance. She experienced flattening of her scalp plaques and improvement in the pruritus with consistent topical betamethasone monotherapy.

She was evaluated by rheumatology and ophthalmology. Chronic knee pain was attributed to osteoarthritis, and she did not have any evidence of ocular involvement. Transesophageal echocardiogram is pending. Patient has upcoming appointments with pulmonary medicine and cardiology.

DISCUSSION
Cicatricial, or scarring, alopecia is divided into primary and secondary forms. In primary scarring alopecias, the hair follicles are the specific target of inflammation. Primary scarring alopecias are subdivided based on the predominant inflammatory infiltrate (lymphocytic, neutrophilic, or mixed). Lymphocytic primary scarring alopecias include discoid lupus erythematosus, lichen planopilaris, and central centrifugal cicatricial alopecia. Neutrophilic primary scaring alopecia includes dissecting cellulitis. Mixed lymphocytic and neutrophilic primary scaring alopecia includes acne keloidalis. In secondary scarring alopecias, the hair follicles are destroyed randomly with surrounding structures. Cutaneous diseases causing secondary scarring alopecia include deep burns, radiation dermatitis, cutaneous malignancies, cutaneous sarcoidosis, morphea, necrobiosis lipoidica, and tuberculosis.[1]

Sarcoidosis is a multisystem granulomatous disorder that that most commonly affects the lungs, lymph nodes, eyes, and skin. It is characterized by a bimodal age distribution, with peaks between 25 and 35 years and again between 45 and 65 years. There is an increased incidence in

African-Americans and women. Approximately one third of patients with systemic sarcoidosis develop skin lesions and skin lesions may be the only manifestation of sarcoidosis. Cutaneous sarcoidosis most frequently presents as red-brown to violaceous papules and plaques. Lesions most commonly affect the nose, periocular and perioral regions, followed by the neck, upper trunk and extremities. Diagnosis of sarcoidosis is made primarily by histopathology showing superficial and deep dermal epithelioid cell granulomas devoid of prominent infiltrate of lymphocytes or plasma cells.[2]

Among the many presentations of sarcoidosis, scalp involvement is considered to be less common but increasingly recognized. Sarcoidosis of the scalp can have a wide variety of presentations, including scarring and non-scarring alopecia, indurated plaques, and nodules. Approximately 50 cases of sarcoidosis-induced alopecia have been described in patients ranging from 20-87 years old. The majority of cases present in females (39 of 47 cases with sex reported) and approximately one-half of cases occur in African-Americans (22 of 42 cases with race reported). Sarcoidosis-induced alopecia is frequently associated with cutaneous sarcoidosis at sites beyond the scalp, most commonly on the head and neck.[3] It is estimated that 63% of patients presenting with sarcoidosis specific skin lesions at any site on the skin will have systemic involvement.[4] In contrast, in cases of sarcoidosis associated with alopecia, 85% of cases reported systemic involvement, most often pulmonary and lymph node involvement.[3,5–12]

Sarcoidosis of the scalp most commonly presents as scarring alopecia, but non-scarring alopecia has been reported.[13] Alopecia is thought to be due to the effect of the granuloma on the follicle or follicular replacement by the granuloma. Lesions of sarcoidosis-induced scarring alopecia can clinically resemble discoid lupus erythematosus, lichen planopilaris, central centrifugal cicatricial alopecia, and necrobiosis lipoidica.[9] Non-scarring alopecia associated with sarcoidosis can mimic alopecia areata, mucinosis follicularis, and lupus erythematosus.[7] Localized scalp involvement is most common but rarely diffuse alopecia can occur. Indurated plaques and papules, nodules, as well as erythema with scale may be present.[14] The dermatoscopic pattern associated with sarcoidosis has been described as follicular or perifollicular orange spots.[5,12]

The histopathologic findings of scarring alopecia related to sarcoidosis include prototypical "naked" granulomas. These histopathologic findings help distinguish sarcoidosis from other scarring alopecias. Lichen planopilaris typically shows a perifollicular lichenoid infiltrate and hypergranulosis within affected infundibula. Discoid lupus erythematosus demonstrates vacuolar interface alteration of the epidermis and follicular epithelium, follicular plugging, peri-eccrine inflammation and increased dermal mucin. Central centrifugal cicatricial alopecia shows premature desquamation of the inner root sheath, eccentric epithelial atrophy, concentric lamellar fibroplasia of follicles, and a variably dense lymphocytic perifollicular inflammation. In advanced lesions, foreign body granulomatous inflammation may be present in association with total destruction of the follicular epithelium. Dissecting cellulitis shows perifollicular inflammation in the lower half of the dermis, initially dominated by lymphocytes but later by neutrophils. In longstanding disease, chronic abscesses develop into sinus tracts.[1]

Interestingly, one recent case reported coexisting sarcoidosis and frontal fibrosing alopecia based on histopathologic findings showing both naked granulomas and perifollicular lymphocytic infiltrate with occasional dyskeratotic keratinocytes. The authors highlight that while

lymphocytic and granulomatous perifolliculitis with fibrosis can be seen in late-stage FFA, the granulomas in FFA tend to border the hair follicle and develop later into disease secondary to chronic inflammation. This is in contrast to the granulomas in sarcoidosis that infiltrate the dermis independent of the hair follicles.[11]

Patients presenting with alopecia related to sarcoidosis should have a full skin examination and a complete workup for systemic sarcoidosis. The full workup includes Complete Blood Count, Comprehensive Metabolic Panel, Urinalysis, Thyroid testing, 25-hydroxyvitamin D and 1,25-dihydroxyvitamin D_3, testing for TB, Chest X-Rays (posterior-anterior and lateral), Pulmonary Function Tests, Electrocardiogram, and Ophthalmology exam.[2]

A stepwise approach for treatment of cutaneous sarcoidosis is recommended. Treatment options include local therapies, systemic immunomodulatory agents, systemic immunosuppressive agents, and biologics. Local therapies include topical high-potency corticosteroids, intralesional corticosteroids, and topical tacrolimus. When topical or intralesional therapy is not effective for mild disease, or when there is more extensive disease, systemic immunomodulators may be considered, including tetracycline antibiotics, antimalarials, and other anti-inflammatory agents, such as pentoxifylline and apremilast. First-line systemic agents include antimalarials and minocycline, alone or in combination. Systemic immunosuppressive medications are used for severe or recalcitrant disease and include prednisone, methotrexate, thalidomide, TNF inhibitors, and less commonly, mycophenolate mofetil and azathioprine.[15]

As demonstrated by this case, sarcoidosis-induced alopecia may mimic more commonly observed forms of scarring alopecia. This case highlights the importance of obtaining a scalp biopsy in patients who present with symptomatic scarring alopecia. Given the progressive and systemic nature of sarcoidosis, recognizing the cutaneous lesions is important as histopathologic diagnosis by a skin biopsy can prompt further workup and treatment.

We present this case to raise awareness that alopecia of the scalp may be a presenting sign of sarcoidosis.

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CASE 2

PRESENTERS
Erin Dodd MD; Oluwakemi Onajin MD; Adena Rosenblatt MD, PhD

HISTORY OF PRESENT ILLNESS
An otherwise healthy 16-year-old female presented to the emergency room with facial swelling and an acute skin eruption. She initially developed an itchy plaque on the left arm approximately two weeks prior to presentation. She was evaluated by an outside provider who diagnosed her with tinea corporis and prescribed topical clotrimazole 1% cream. After applying clotrimazole for about four days, the patient developed erythematous papules and pustules around the lesion for which she was prescribed cephalexin 250 mg every six hours. Over the following day, the papulopustular eruption rapidly spread to her face, trunk, and extremities. She also developed significant facial and periorbital edema which prompted her to seek care in the emergency room. The patient otherwise felt well and denied shortness of breath or swelling of the tongue or throat. She was febrile to 38.3°C but vital signs were otherwise within normal limits. Dermatology was consulted to assist with diagnosis and management.

PAST MEDICAL HISTORY
No significant past medical history

MEDICATIONS
Clotrimazole 1% cream
Cephalexin 250 mg every 6 hours

ALLERGIES
No known allergies

FAMILY HISTORY
Sister with eczema
Maternal uncles with psoriasis

SOCIAL HISTORY
Lives at home with mother and sister
No pets at home

PHYSICAL EXAM
Physical exam revealed significant facial and periorbital edema. On the left forearm was a well-circumscribed round slightly indurated scaly, crusted pink-to-hyperpigmented plaque. She also had numerous monomorphic erythematous papules and a few pustules scattered diffusely on the face, trunk, and upper and lower extremities. There was no palmoplantar or genital involvement.

DERMATOPATHOLOGY
Histopathology from punch biopsy of a plaque on the left arm showed ulceration, epidermal necrosis and superficial-to-deep perivascular inflammation with eosinophils consistent with possible arthropod assault versus contact dermatitis. Histopathology from punch biopsy of a pustule on the left arm demonstrated suppurative and eosinophilic folliculitis with interstitial

eosinophils. GMS and PAS were negative for fungal organisms in both specimens.

LABORATORY DATA

Complete blood count was notable for slight leukocytosis (WBC 13.7 10*3/uL) with elevated absolute neutrophils (9.78 10*3/uL) and absolute eosinophils (0.92 10*3/uL). Comprehensive metabolic panel, Erythrocyte Sedimentation Rate and C-Reactive Protein were unremarkable. Bacterial wound culture of a pustule was negative. Tissue cultures for bacteria and Acid-Fast Bacilli were negative. Fungal tissue culture was positive for *Trichophyton tonsurans*.

DIAGNOSIS

Id reaction (autosensitization dermatitis) secondary to dermatophyte infection

TREATMENT AND COURSE

The patient was prescribed a six-week course of 250 mg terbinafine daily to treat suspected underlying dermatophyte infection. She was also given a four-week prednisone taper for treatment of severe id reaction. At follow up appointment two weeks later, facial edema had resolved and papulopustular lesions were flattening leaving residual post-inflammatory hyperpigmentation. At that time, tissue culture from initial plaque on left arm was reported positive for *Trichophyton tonsurans,* confirming dermatophyte infection.

DISCUSSION

An id reaction, also known as autosensitization dermatitis, is a secondary cutaneous reaction that develops in response to a remote localized inciting dermatosis. It is most commonly associated with stasis dermatitis and allergic contact dermatitis[1] but is also frequently seen in conjunction with infections and infestations.[1,2] Dermatophyte infections are an especially common cause of id reactions. Although superficial fungal infections such as tinea pedis are the most frequent cause, other subcutaneous and deep fungal infections can also trigger this reaction.[2] Studies have shown incidence ranging from 0.7% to 3% of proven id reactions among those with dermatophyte infections.[3]

Whereas the primary inciting lesion is typically localized, id reactions classically present as a diffuse, widespread and symmetric eruption of eczematous lesions.[1,2] However, the clinical manifestations are polymorphic and include pustular, urticarial, lichenoid, morbilliform and erysipeloid rashes as well as erythema nodosum and erythema multiforme.[4,5] While the majority of patients with id reactions are otherwise healthy, systemic manifestations such as fever, anorexia, lymphadenopathy or leukocytosis may be present. Anaphylaxis, though extremely rare, has also been reported.[2]

While the exact mechanism underlying id reactions has not been elucidated, it is generally thought to be an immunological response due to autosensitization to a remote antigen. Host T lymphocytes are activated and mediate hypersensitivity reactions that result in cutaneous manifestations deemed id reactions.[2] Classically, id reactions are considered type IV delayed-type hypersensitivity reactions; however, other types of hypersensitivity reactions can occur and contribute to the many variable manifestations of id reactions.[2,6] Other studies suggest that inflammation from a primary process lowers the irritancy threshold of the skin which promotes development of secondary eczematous reactions.[7]

The diagnosis of an id reaction can be made based on clinical presentation. In the case of dermatophytid reactions, there is typically a localized dermatophyte infection with subsequent acute onset of distant, widespread secondary lesions.[1,2] These distant lesions will be negative for fungal forms and will resolve spontaneously if the inciting infection is adequately treated.[8] While there are no histopathologic features specific for id reaction, KOH preparation or tissue culture from the primary skin lesion can help confirm an underlying dermatophyte infection.[1,2]

Id reactions are managed by identifying and treating the primary inciting dermatosis. In the case of dermatophyte infection, patients should be treated with appropriate antifungal therapy depending on the location and extent of the infection.[2,9] Id reactions can be treated symptomatically with emollients and topical steroids but typically exhibit prompt resolution after the underlying trigger is eradicated.[8] As in our patient, a short course of systemic steroids may be indicated for severe or refractory cases.[1,8]

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CASE 3

PRESENTERS

Clifford Hsieh MD; Dennis Whiting PA-C; Oluwakemi Onajin MD; Christopher R. Shea MD

HISTORY OF PRESENT ILLNESS

The patient is a 23 year old Hispanic male with past medical history of tuberous sclerosis and seizures, presenting to dermatology clinic for a scalp lesion. One week prior to presentation, the patient was seen for routine follow-up in the neurology tuberous sclerosis clinic, was prescribed doxycycline 100 mg twice a day for this lesion, and instructed to see dermatology for evaluation. He reports having this lesion on the posterior scalp since childhood, which had grown slowly in size with time. There was no associated pain, but he has noted occasional purulent drainage and bleeding seen on his pillowcases. He had a history of multiple excisions on the posterior scalp performed by plastic surgery, with histopathology showing subcutaneous abscesses and foreign body reactions suggestive of perforating folliculitis.

PAST MEDICAL HISTORY

Tuberous sclerosis complex: diagnosed in infancy

- Cutaneous manifestations: shagreen patch on left lower back, multiple hypomelanotic macules, and multiple facial angiofibromas previously treated with pulsed dye laser, topical sirolimus, electrosurgery, and punch removals with good response.
- Neurologic manifestations: seizures, subependymal nodules, cortical tubers, and developmental delay
- Renal manifestations: angiomyolipomas

MEDICATIONS

Lacosamide 200 mg twice a day
Phenytoin extended release 300 mg twice a day
Sirolimus 1% cream daily
Topiramate 200 mg in the morning and 300 mg in the evening
Vagal nerve stimulator

ALLERGIES

Lamotrigine- rash

FAMILY HISTORY

No family history of tuberous sclerosis
Five siblings without any medical conditions

SOCIAL HISTORY

Lives at home with parents and five siblings
No tobacco, alcohol, or illicit drug use

PHYSICAL EXAM

A large, firm, non-tender, skin-colored plaque with superimposed comedones, nodules, and cysts with polytrichia, heme crust, and decreased hair density was present on the posterior vertex scalp.

DERMATOPATHOLOGY

A shave biopsy specimen from the posterior vertex scalp showed thickened collagen bundles with stellate fibroblasts and concentric arrangement of collagen around adnexal structures within the dermis. There were comedones and keratin-filled infundibula, with one ruptured cyst demonstrating a dense diffuse inflammatory cell infiltrate composed of neutrophils, lymphocytes, histiocytes, and multinucleated giant cells, naked hair shafts, and fragments of cyst wall.

DIAGNOSIS

Folliculocystic and collagen hamartoma associated with tuberous sclerosis

TREATMENT AND COURSE

The patient was continued on doxycycline 100 mg twice a day for two more weeks, given evidence of ruptured cyst on biopsy. At his two week follow-up visit, purulent drainage and bleeding from the posterior vertex scalp had stopped. Recommendations were made for clinical observation at this time, with consideration for trial of topical sirolimus or surgical excision in the future if the lesion becomes bothersome.

DISCUSSION

Tuberous sclerosis complex is an autosomal dominant disorder caused by mutations in the tumor suppressor genes hamartin (TSC1) or tuberin (TSC2), leading to seizures, intellectual deficits, various cutaneous findings, and hamartomatous systemic involvement. The complex of hamartin and tuberin negatively regulates mammalian target of rapamycin (mTOR) signaling, which is involved in cell growth and proliferation. Mutations in hamartin and tuberin cause abnormal regulation of cellular differentiation and proliferation, leading to formation of hamartomas. The incidence of tuberous sclerosis is ~1 in 10,000 births. Despite the autosomal dominant inheritance, de novo mutations account for up to 75% of those with tuberous sclerosis complex.[1]

There are many cutaneous findings seen in tuberous sclerosis and may be the first presenting sign. The cutaneous manifestations and its prevalence include hypomelanotic macules (90-100%), facial angiofibromas (~80%), shagreen patch (40-50%), ungual fibromas (30-60%), café-au-lait macules (up to 30%), and molluscum pendulum. Fibrous cephalic plaques are a larger variant of angiofibromas most commonly seen on the face or scalp in approximately 20% of patients.[1]

A relatively new type of complex hamartoma in patients with tuberous sclerosis, termed folliculocystic and collagen hamartoma, was first described by Torrelo et al. in 2012.[2] To date, there have been eleven reported cases in the literature.[2-7] Folliculocystic and collagen hamartomas are large, painless, thick plaques with irregular protruding surfaces. Early on, the plaques have numerous follicular comedo-like openings. Later, cysts form with occasional purulent drainage.[2,3] Involved locations include the scalp, abdomen, back, flank, thigh, and chin.[3] Nine of the eleven cases had a diagnosis of tuberous sclerosis in addition to presence of other cutaneous and systemic findings. Eight of the eleven patients were male. The folliculocystic and collagen hamartomas appeared at birth or early infancy in all but two patients.[3]

Torrelo et al. described the main histopathological features of folliculocystic and collagen hamartomas. There is abundant, thick, collagen deposition throughout the dermis and extending as fibrous strands into the underlying fat. Concentric perifollicular fibrosis surrounding most hair follicles is present and can involve eccrine glands and blood vessels as well. Comedones and keratin-containing cysts lined by infundibular epithelium are seen. These cysts can rupture, leading to a foreign body granulomatous reaction.[2] While folliculocystic and collagen hamartomas share similar histopathological features to angiofibromas and fibrous cephalic plaques, the infundibular cysts are a unique feature not typically seen in these entities, collagen nevi, or other hamartomas.[4] Naked hair shafts have also been seen on histopathology.[4]

The best treatment for folliculocystic and collagen hamartomas is unclear at this time. Several patients in the reported cases had their lesions excised with good cosmetic results and without recurrence.[2,4,5] Topical sirolimus, an inhibitor of mTOR, has been used to treat angiofibromas and fibrous cephalic plaques with variable success. Topical sirolimus can be compounded into ointment, cream, or gel forms with concentrations ranging from 0.1-1%. Topical application of sirolimus 0.1% solution has been used as well with more irritation. Within 3 months of daily topical therapy, reduced erythema and flattening of angiofibromas have been reported, though relapses frequently occur upon discontinuation of therapy.[1] Given its similarities to angiofibromas and fibrous cephalic plaques, topical sirolimus may be a potential treatment for folliculocystic and collagen hamartomas, but further studies are needed to determine its efficacy.[7]

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CASE 4

PRESENTERS

Esther Kim MD; Oluwakemi Onajin MD; Mark Hoffman MD

UNKNOWN

A 73-year-old African-American male with a history of recently diagnosed bullous pemphigoid on oral prednisone and mycophenolate mofetil presented to clinic with new onset retiform purpura on the left lower extremity.

CASE 5

PRESENTERS
Jared Wishik MD; Arlene Ruiz de Luzuriaga MD, MPH, MBA; Mark Hoffman MD

HISTORY OF PRESENT ILLNESS
An 89-year-old African-American woman first presented to University of Chicago dermatology in 2012 with a ten-year history of a "rash" involving the circumferential neck. Per our patient, the "rash" started as a few stable, asymptomatic "bumps" around her neck. She then slowly developed similar, smaller "bumps" to involve a larger proportion of her lateral neck. At that time, a lesional biopsy was obtained but was inconclusive, showing normal skin. Over the course of the next five years or so, she developed similar changes in her bilateral axillae and underneath both breasts. Occasionally, these would get slightly red and irritated when she washed or manipulated her neck, but otherwise, all areas were asymptomatic. She had tried various over-the-counter moisturizers and washes with no improvement. Comprehensive review of systems was negative. She denied any new medications prior to the onset of these skin findings. She has never used D-penicillamine. No history of gastrointestinal bleeding with a normal screening colonoscopy in 2011. Recent ophthalmologic examination in July 2019 was within normal limits. She had no personal or family history of any cutaneous disorders, ocular abnormalities, cardiac diseases, gastrointestinal diseases, or autoimmune conditions.

PAST MEDICAL HISTORY
Hypertension, hyperlipidemia, depression, osteoarthritis, osteoporosis, gastroesophageal reflux disease

FAMILY HISTORY
No family history of any cutaneous diseases, ocular abnormalities, cardiac diseases, gastrointestinal diseases, or autoimmune conditions

SOCIAL HISTORY
Denied use of tobacco, alcohol, or recreational drugs

MEDICATIONS
Bupropion, citalopram, clonazepam, pantoprazole, calcium and vitamin D supplements

ALLERGIES
Codeine (cramps, nausea, vomiting)

PHYSICAL EXAMINATION
Circumferential neck, but most prominent on her bilateral lateral neck, with numerous symmetric, flesh-colored depressions, accentuating nearby skin as flesh colored to slightly yellow-hued soft, round to ovoid papules coalescing into plaques. Similar, more subtle findings were present in her bilateral axillae and inframammary skin as well.

LABORATORY RESULTS
Recent routine bloodwork including comprehensive metabolic panel, complete blood count, lipid panel, and urinalysis were all within normal limits.

IMAGING
All age appropriate cancer screening examinations were negative including normal mammogram in 2017 and normal colonoscopy in 2011.

DERMATOPATHOLOGY
Histopathologic analysis of punch biopsy specimen from the right neck revealed a sparse superficial primarily lymphocytic perivascular dermatitis. Verhoeff-Van Gieson stain demonstrated fragmentation and partial loss of elastic fibers in the superficial dermis. Colloidal iron stain demonstrated a normal amount of mucin. Trichrome stain highlighted normal appearing bundles of collagen and muscle within the dermis.

DIAGNOSIS
Pseudoxanthoma elasticum-like papillary dermal elastolysis (PXE-PDE)

CLINICAL COURSE
When she initially presented in 2012, prior to this diagnosis being made, a course of triamcinolone 0.1% ointment twice daily for roughly 6 weeks had no impact on the appearance of her skin findings. After diagnosing her with PXE-PDE, we discussed that multiple therapies have been attempted for this condition but that majority of interventions have been unsuccessful. We discussed the possibility of a trial of topical retinoids versus non-ablative fractional resurfacing laser; however, patient deferred treatment due to the expense of these therapeutic interventions.

DISCUSSION
Pseudoxanthoma elasticum-like papillary dermal elastolysis (PXE-PDE) is a rare elastic tissue disorder initially described in 1992 that clinically resembles pseudoxanthoma elasticum (PXE) but differs histologically and lacks systemic manifestations.[1] An understanding of hereditary PXE is necessary in order to recognize and differentiate this acquired entity. PXE is a hereditary disorder characterized by autosomal recessive inheritance of a mutation in the ATP-binding cassette, subfamily C, member 6 (ABCC6) gene, which leads to abnormal mineralization of elastic tissue in various organs including skin, eyes, and arteries.[2] This usually manifests in the second or third decade with thin, yellowish papules in flexural areas, including the lateral neck, that coalesce into cobblestone-like plaques resembling "plucked chicken skin." Ophthalmologic manifestations include mottling of retinal pigment epithelium, angioid streaks, macular degeneration, and retinal hemorrhage leading to blindness. Cardiac involvement is also common, which can present with intermittent claudication, loss of peripheral pulses, renovascular hypertension, mitral valve prolapse, myocardial infarction, and stroke. This progressive calcification of elastic media and intima can lead to various gastrointestinal and obstetric complications as well.[2]

PXE-PDE presents with a similar cutaneous phenotype (hence its name); however, it differs from PXE in that it is not associated with any systemic manifestations, has no known associated genetic mutation, presents much later in life, and demonstrates different histological findings. To date, there are approximately 50 cases reported in the literature. Reported cases all describe a very similar picture to our patient's presentation with a long-standing history of largely asymptomatic, yellow-hued to flesh-colored soft, almost waxy papules coalescing into plaques

with predilection for the neck, axillae, inframammary folds, flexor forearms, and lower abdomen.[1] Notably, all cases have occurred in women, with almost all beginning in their 6th through 8th decades and only three reported cases with onset before age 50. These papules and plaques are usually stable and do not spontaneously resolve. Progressive involvement of other areas has not been reported. In most cases, lesions of PXE-PDE are asymptomatic, but mild pruritus has been reported, as seen in our patient.

Pathogenesis of this entity is poorly understood. Authors have postulated that ultraviolet radiation, intrinsic aging, and/or abnormal elastogenesis are implicated. However, the role of ultraviolet radiation is controversial. Although a majority of patients' lesions are located on photo-exposed sites, many patients have involvement of largely sun-protected areas such as the axillae and inframammary folds. Pathology also supports that this is not the sole contributor in that only one case reported histologic evidence of solar elastosis.[1] Intrinsic aging has also been discussed as an alternative explanation in that it affects patients in middle to late age. However, its exclusive female predominance is an argument against this as both genders should then theoretically be affected. There is also one reported case series of two sisters with PXE-PDE, ages 72 and 74, that may suggest a genetic factor for the development of this disorder, but this has not since been documented.[3] No additional definitive associations have been made with this disease although some have recently reported this developing in patients on high dose prolonged systemic steroid therapy.[1] Current consensus is that PXE-PDE seems to be multifactorial with both intrinsic and extrinsic factors.

Histopathology usually demonstrates focal mild chronic perivascular inflammation and dilatation of blood vessels but otherwise looks like normal skin. An elastic stain, such as Verhoeff-Van Gieson, is required to exhibit the characteristic decreased number of elastic fibers in the papillary dermis. Calcification and abnormal fragmentation, both characteristic of hereditary PXE, are not seen.[1,4]

Clinical differential diagnosis of this entity includes other fibroelastolytic diseases such as white fibrous papulosis of the neck, mid-dermal elastolysis, and hereditary PXE. White fibrous papulosis of the neck presents in elderly women or men with papules on the neck, that are usually more discrete, firm, and whitish in appearance than findings seen in PXE-PDE. Histology shows both a slight decrease in elastic fibers and thickened collagen bundles in the papillary dermis. Mid-dermal elastolysis usually occurs in younger women as one of three distinct phenotypic variants, all of which have a different clinical appearance from PXE-PDE. Biopsy shows loss of elastic fibers in the mid-dermis, mild perivascular lymphohistiocytic infiltrate and elastophagocytosis, which has not been described in PXE-PDE.[5] Some authors proposed the use of the term "fibroelastolytic papulosis," to suggest that PXE-PDE, white fibrous papulosis of the neck, and mid-dermal elastolysis are potentially related diseases on a spectrum.[6]

Diagnosis of PXE-PDE is usually made by combining this characteristic clinical presentation and a lack of systemic manifestations with histopathology demonstrating partial or complete loss of elastic fibers in the papillary dermis using elastic stains. Clinicopathologic correlation is needed. Most authors agree that investigations to assess for systemic associations are unnecessary.[7]

Although a benign entity, patients can be bothered by its appearance and seek treatment for aesthetic reasons. Unfortunately, treatment has been widely ineffective. Trials of topical retinoids have been unremarkable, but a recent single case report of success with non-ablative fractional resurfacing laser may be promising.[8]

We present this case to highlight a rare condition that is likely more prevalent than previously reported.

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CASE 6

PRESENTERS
Erin Ibler MD; Oluwakemi Onajin MD; Christopher R. Shea MD; Keyoumars Soltani MD

PATIENT A

HISTORY OF PRESENT ILLNESS
A 46-year-old man with a past medical history of rheumatoid arthritis presented to the emergency room complaining of progressive shortness of breath and worsening skin lesions on his face and trunk. The patient had recently been diagnosed with pancreatic cancer at an outside institution, with plans to begin chemotherapy, but was unable to follow up with oncology due to insurance issues.

The skin lesions developed a few months prior to his diagnosis of pancreatic cancer, and slowly increased in number and size. He denied bleeding, pain, or itching associated with the lesions. He was admitted to the hospital and dermatology was consulted.

PAST MEDICAL HISTORY
Rheumatoid arthritis

FAMILY HISTORY
Non-contributory

SOCIAL HISTORY
Denied recent travel
Non-smoker, occasional social alcohol use
No recreational drug use

MEDICATIONS
No home medications on admission

ALLERGIES
No known drug allergies

REVIEW OF SYSTEMS
Denied fever, chills, cough, chest pain, nausea, vomiting, diarrhea, or urinary symptoms on admission.

PHYSICAL EXAMINATION
Pink to red smooth discrete papules and nodules ranging from 1 cm to 3 cm scattered on the face (including the forehead, cheeks, upper and lower cutaneous lips), chest, upper back, and bilateral extensor arms.

LABORATORY RESULTS
CBC, CMP, urinalysis- WNL

Respiratory viral panel, HIV, Quantiferon gold TB, Histoplasma Ag/Ab, Blastomyces Ab, Coccidioides Ab- Negative
Blood, pleural fluid and urine cultures- Negative
Tissue culture (punch biopsy of skin lesion)- Negative for bacteria, fungi, and atypical mycobacteria

IMAGING

Chest X-ray

- Large left pleural effusion with left basilar opacity
- Innumerable nodular opacities throughout the lungs

CT Chest

- Widespread metastatic disease involving the chest with numerous pulmonary, pleural and lymphangitic metastases, loculated left pleural effusion, chest wall metastases, and soft tissue masses/lymphadenopathy visualized in the upper abdomen
- Atypical distribution for pancreatic cancer and limited views of the abdomen did not demonstrate biliary ductal dilatation or a focal pancreatic mass
- Findings compatible with osseous metastatic disease, with a lytic lesion involving the right T11 neuroforamen

DERMATOPATHOLOGY

Skin biopsy from the right upper back demonstrated infiltrative cords and nests of pleomorphic epithelioid blue cells encompassing the entire dermis, and numerous atypical mitotic figures. The neoplastic cells were diffusely positive for CK7 and Napsin A, and negative for CK 20, PAX8, synaptophysin, chromogranin, CD45 (LCA), and TTF1.

DIAGNOSIS

Metastatic adenocarcinoma, favor primary lung adenocarcinoma

TREATMENT & COURSE

The patient's hospital course was complicated by multiple febrile episodes, with blood, urine, and thoracentesis cultures unrevealing of an infection source.

Subsequent biopsy of lung lesions was consistent with metastatic adenocarcinoma, favoring lung primary. The patient declined further workup and treatment, and elected to be discharged home with hospice care.

PATIENT B

HISTORY OF PRESENT ILLNESS

A 58-year-old man presented to dermatology clinic for evaluation of a skin-colored papule of the left chin. The lesion had been present for 3-4 months, with minimal change since it first appeared. He denied any bleeding or itching in this lesion.

His history was significant for recurrent left parotid gland adenoid cystic carcinoma. Since

diagnosis, he had undergone several surgical resections, with recurrence and subsequent progression to metastatic disease of the lung as well as locally advanced left neck disease. He had received palliative chemotherapy and radiation (5/5 cycles of paclitaxel, infusional 5-fluorouracil, hydroxyurea, and twice-daily radiation therapy administered every other week) as well as immunotherapy (18 months of Ipilimumab/Nivolumab), with progression of his disease.

PAST MEDICAL HISTORY
Recurrent left parotid gland adenoid cystic carcinoma, hypertension, aortic aneurysm

FAMILY HISTORY
Father with unknown type of head and neck cancer

SOCIAL HISTORY
15 pack-year smoker (quit 2001)

MEDICATIONS
Esomeprazole, hydrocortisone, ibuprofen, levothyroxine

ALLERGIES
No known drug allergies

PHYSICAL EXAMINATION
On the left side of the chin was a pearly, skin-colored to faintly pink, firm papule with overlying telangiectasias. Atrophic, erythematous, scarred plaques were seen extending from the left neck to the jaw line.

LABORATORY RESULTS
N/A

IMAGING
CT Neck
- Extensive sequelae of prior surgery and therapy
- Soft tissue thickening and scattered nodularity through the operative bed of the left neck with no definite measurable tumor or significant lymphadenopathy

CT Chest/Abdomen/Pelvis
- Bilateral numerous pulmonary metastases and diffuse metastatic disease involving left pleura

DERMATOPATHOLOGY
Histopathology of a shave biopsy specimen from the left chin demonstrated a well-circumscribed intradermal neoplasm composed of islands of basaloid aggregates arranged in a tubular and cribriform pattern, within a fibrotic stroma. The cribriform spaces contained myxoid to eosinophilic material, highlighted by PAS and colloidal iron stains, as well as unattached neoplastic cells and necrotic debris focally. True ductal structures were also present within many of the basaloid islands, and contained amorphous eosinophilic material. While basaloid cells

were overall monotonous, nuclei were hyperchromatic and exhibited some nuclear molding. Mitotic figures were readily identified, with the greatest number at the periphery. Perineural invasion was present. Ber-EP4 and CD117 stains were strongly positive in cells lining the ductules; Ber-EP4 also showed diffuse staining throughout the neoplasm. Vimentin, calponin, p63, and SMA stains were strongly positive for the cells lining the periphery of the tumor islands and cribiform spaces. Variable staining was seen for CEA, EMA, and CK7. Variable staining was present for p16, except for a slight increase in staining of the cells lining the ductules and cribriform spaces. CD10, CD43, and GCDFP-15 stains were negative. S100 protein was mostly negative except for a cluster within the tumor. Up to 20% of the neoplastic cells stained positively for Ki-67.

DIAGNOSIS

Adenoid cystic carcinoma, suggestive of cutaneous metastasis or locoregional recurrence

TREATMENT & COURSE

The patient elected to be managed with clinical observation after completion of immunotherapy, given relatively low burden of disease and slow progression. Molecular studies did not reveal targetable mutations. Oncology discussed lenvatinib (a multiple kinase inhibitor against vascular endothelial growth factor receptor 1-3) as the next step should he choose to pursue therapy.

DISCUSSION

Although cutaneous metastasis from visceral malignancy is uncommon, it is increasing in prevalence as oncologic advances increase patient survival. Estimates of the frequency of cutaneous metastases vary, ranging from 5-10% in patients with visceral malignancy and accounting for 2% of all skin tumors. Skin findings can be an early indicator of metastatic disease, a clue to recurrence, or the initial presentation of an internal malignancy.

Cutaneous metastases usually present as flesh-colored or red-pink, single or multiple firm nodules. The morphologic spectrum also includes zosteriform or disseminated papules and nodules, sclerodermoid plaques, ulcerated papules or plaques, and alopecia. Certain types of tumors preferentially metastasize to specific areas of the skin. Although not always predictable, the distribution of metastasis is related to the location of the primary tumor and the mechanism of its metastasis.

Cutaneous metastases are particularly associated with solid malignancies of the breast, lung, oral cavity-pharynx-larynx and colorectum. Statistics can be further broken down into estimates of visceral tumors in decreasing order for men (lung, large intestine, oral cavity, kidney, breast, esophagus, pancreas, stomach, and liver) and women (breast, ovary, oral cavity, lung, and large intestine), respectively. Cutaneous metastases of thyroid, pancreas, adrenal carcinoma, or sarcoma are infrequently described due to the low incidence of their primaries.

Cutaneous metastasis from lung cancer is the most common cutaneous metastasis in men, and clinically presents as red, pink, or violaceous nodules that may be painful or ulcerate. Less common presentations include zosteriform pattern, inflammatory carcinoma, or telangiectasia. Sites commonly affected include the chest, abdomen, back, upper lip, and upper extremities. Metastatic tendencies differ between the different subtypes of lung cancer, with adenocarcinoma

being the most common. Histology of metastatic lung adenocarcinoma may demonstrate malignant cells arranged in solid nests in the dermis. If well differentiated, a glandular pattern resembling the primary may be seen, although features are usually more anaplastic. Immunohistochemistry is also valuable in interpretation of cutaneous metastasis. Adenocarcinoma of the lung is typically positive for CK7, TTF1, BER-EP4, and CEA, and negative for CK 5/6 and CK20.

Salivary gland malignancies with cutaneous metastases are uncommon, and are estimated to represent about 2% of all cutaneous metastases in men and 1% in women. The clinical presentation often mimics benign lesions, appearing as facial or scalp nodules, although inflammatory metastatic carcinoma of the neck is also described. Of metastatic salivary gland carcinoma, adenoid cystic and mucoepidermoid carcinoma of the parotid are the most common subtypes. Adenoid cystic carcinomas are distinctive tumors that can be found in many organs but have a strong predilection for the salivary glands and rarely arise in the skin. It is important to differentiate metastatic from primary cutaneous adenoid cystic carcinoma because they differ in behavior and outcome. Due to their identical histologic and immunohistochemical features, distinction is dependent on clinical correlation. Histology of these tumors demonstrates islands and cords of basaloid cells with cribiform pattern, mucin-filled pseudocysts, and tubule and/or duct formation. Perineural invasion is almost always present. Tumor cells express cytokeratins, vimentin, as well as SMA and S100 protein focally. CD117 is usually diffusely positive. EMA and sometimes CEA highlight duct differentiation.

Across all studies, the presence of cutaneous metastases is generally a poor prognostic sign. Average survival estimates after developing skin metastases range from 3 to 7.9 months. More recent literature provides slightly higher estimates due to recent advances in cancer therapies. Certain types of cancer (breast, in particular) may have better prognosis despite metastatic disease, based on subtype and therapies available.

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CASE 7

PRESENTERS
Arjun Dayal MD; Caroline Sheppard PA-C; Oluwakemi Onajin MD

HISTORY OF PRESENT ILLNESS
A 59-year-old African American female presented to the dermatology clinic with a four-month history of an asymptomatic facial rash. Previous biopsies demonstrated granulomatous dermatitis suggestive of granulomatous rosacea. She tried several treatments including metronidazole gel, ivermectin cream, and oral doxycycline without any improvement.

REVIEW OF SYSTEMS
Notable for right earache, right sided headache, pain of the right side of the neck that extends to the right arm, numbness and tingling of bilateral hands, mild left sided weakness (residual from prior stroke).
Pertinent negatives include fevers, night sweats, chills, weight loss, lymphadenopathy, vision changes, shortness of breath, cough, or any gastrointestinal symptoms.

PAST MEDICAL HISTORY
Diabetes, hypercholesterolemia, hypertension, coronary artery disease, stroke, cervical cancer

MEDICATIONS
Amlodipine, aspirin, atorvastatin, empagliflozin, enalapril, glipizide, loperamide, metformin, metoprolol succinate, ascorbic acid, vitamin D3, vitamin B12, iron, vitamin E

ALLERGIES
No known drug allergies

FAMILY HISTORY
Mother with breast cancer
Brother with prostate cancer
No known personal or family history of skin or autoimmune disease

PHYSICAL EXAM
Numerous smooth pink, firm and round papules and nodules scattered on cheeks and forehead.
No lymphadenopathy.

LABORATORY AND IMAGING DATA
ANA 1:320 with a speckled pattern
CRP 14 (<5 mg/L)
ESR 58 (1-44 mm/Hr)

Normal CBC, CMP, rheumatoid factor, HIV, PT, PTT, immunoglobulin levels, Quantiferon Gold, Hepatitis C and Hepatitis B serologies

DERMATOPATHOLOGY

Fibrotic upper to mid dermis with dense and diffuse sheets of large foamy histiocytes admixed with lymphocytes and plasma cells. The histiocytes demonstrate emperipolesis. There are nodular lymphoid aggregated interspersed throughout the dermis. Rare neutrophils are present.

The histiocytes within the dermis stain positive for S100, CD68, and factor XIIIa and negative for langerin (CD207) and CD1a.

DIAGNOSIS

Cutaneous Rosai-Dorfman disease

TREATMENT AND COURSE

CT scans of head, neck, chest, abdomen and pelvis were performed without evidence of orbital mass, malignancy or lymphadenopathy. The patient had an elevated ANA but she did not meet criteria for systemic lupus erythematosus. Evaluation by ophthalomology was without evidence of ocular involvement.

The patient was prescribed methotrexate 10 mg weekly with folic acid 1 mg daily. She reports that her skin lesions are clearing after being on therapy for 8 weeks.

DISCUSSION

Rosai-Dorfman Disease (RDD), also known as sinus histiocytosis with massive lymphadenopathy, is a rare non-Langerhans cell histiocytosis with heterogenous clinical manifestations.[1] In this condition, activated histiocytes accumulate in affected organs, including the skin.[2] The pathogenesis is unknown, but leading hypotheses suggest immune dysregulation or a reactive process to an infectious trigger as the etiology of the disease. RDD can occur in isolation or in association with hereditary, malignant or autoimmune diseases such as systemic lupus erythematosus and idiopathic juvenille arthritis.[1,3] Germ line mutations in *SLC29A3* have been reported in patients with familial RDD and certain forms of extranodal RDD have been associated with an increased number of IgG4 positive plasma cells.[1]

RDD is rare with a prevalance of 1 in 200,000 and approximately 100 new cases are reported per year in the United States. It is most often seen in children and young adults with a mean age of 20.6 years. RDD tends to be more common in men and in people of African descent, although a skin limited form of the disease tends to favor adult women.[1]

The clinical features of RDD can be further classified into classic (nodal) disease and extranodal disease. Most patients with classic (nodal) disease present with painless, massive, bilateral, cervical lymphadenopathy. Axillary, mediastinal, and inguinal lymphadenopathy may be present as well.[4] Many patients also present with systemic symptoms including fevers, weight loss, and night sweats. Extranodal involvement occurs in 43% of RDD cases and 10% of extranodal RDD cases have skin findings.[1,3] Skin lesions typically present as slow growing, asymptomatic yellow to red–brown papules, nodules or plaques on the eyelids or malar regions. The clinical differential diagnosis usually includes acne vulgaris, sarcoidosis, rosacea, cutaneous lymphoma and metastasis. Ophthalmologic involvement is seen in 11% of RDD cases and may present as a mass in the orbital soft tissues or with compressive optic neuropathy.[1] Less commonly, the histiocytes may infiltrate the bones, central nervous system, and other organs.

Histopathology of cutaneous lesions shows fibrosis and a dense, dermal infiltrate of large histiocytes with abundant pale cytoplasm and scattered lymphocytes, plasma cells, and neutrophils.[5] The histiocytes stain positively for S100, CD68, and CD163, variably positive for Factor XIIIA, and negative for CD1a and CD207 (langerin).[5] Emperipolesis, which is the uptake of intact inflammatory cells by histiocytes, is a helpful finding, but not required for diagnosis as it can also be seen in other histiocytoses.[1]

It is important to thoroughly screen for extranodal involvement in a patient with a new diagnosis of RDD. Prognosis is variable and depends on the number of nodal groups involved by RDD and by the organs affected by extranodal disease. Recent multidisciplinary consensus recommendations for evaluation include: thorough history and physical examination, CT imaging of the neck, chest, abdomen, and pelvis for adults, and whole body MR imaging for children to avoid excessive radiation exposure. Laboratory evaluation includes CBC with differential, CMP, ESR, CRP, quantitative immunoglobulin levels, serologies for HIV, hepatitis B and hepatitis C, antinuclear antibodies, and rheumatoid factor. In patients with cytopenias or abnormal peripheral blood smear, bone marrow biopsy is required.[1]

No uniform treatment approach has been proposed due to the heterogeneous nature of this disease. For the purposes of this case, only treatment of cutaneous RDD will be discussed. Cutaneous RDD is often self-limited but can have a long course with exacerbations and remissions. Observation is a reasonable option for patients with asymptomatic cutaneous and lymph node involvement as 20-50% with nodal and cutanetous RDD will experience spontaneous remission. Surgical excision is the most effective treatment for unifocal cutaneous disease. Multifocal cutaneous disease can be treated with low dose methotrexate (alone or with 6-mercaptopurine).[1,6] Systemic and intralesional corticosteroids have shown mixed results in the literature.[1,7,8] Thalidomide or lenalidomide may be used for recalcitrant disease.[9-11] Recently, there have been reports of successful treatment with ALA-PDT, dapsone and topical imiquimod.[12-14]

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CASE 8

PRESENTERS
Emily Lund MD; Sarah Stein MD

HISTORY OF PRESENT ILLNESS
A 14-year-old girl with a history of mild atopic dermatitis presented to dermatology for evaluation of chronic lower extremity wounds. The patient and family reported non-healing ulcerations on the lateral thighs, calves, lower shins, and heels for the past three years. The patient described noticing pain focally at a site which would be followed by "cracking" of the skin and then formation of an ulcer. She denied any contributing trauma in these areas. The ulcers themselves were not particularly painful. At the time of presentation, the patient had been receiving wound care at a local wound clinic. She was applying triamcinolone cream to the ulcer bed with twice daily dressing changes, and she noted gradual decrease in the size of the ulcers on this regimen.

She was hospitalized two years ago for pseudomonal osteomyelitis associated with a non-healing wound on her left heel. She was hospitalized again last year for new onset progressing ulcerations on her bilateral lower legs, which were ultimately managed with debridement and split thickness skin grafts.

She had been evaluated by pediatric immunology, rheumatology, and hematology without a unifying diagnosis. Prior skin biopsies were nonspecific, with pathologic findings consistent with scar and mixed granulomatous inflammation.

PAST MEDICAL HISTORY
Born full term
Hospitalized as an infant for pneumonia
Mild atopic dermatitis

MEDICATIONS
Mometasone 0.1% ointment BID as needed for flares of atopic dermatitis

ALLERGIES
No known drug allergies

FAMILY HISTORY
No family history of skin conditions or immunodeficiency

SOCIAL HISTORY
Born and raised in Illinois. Parents are from Mexico.
Lives with mother, father, and older sister
Parents are nonconsanguineous
No recent travel
Patient not formally diagnosed with intellectual or learning disability, but failing multiple classes in school

PHYSICAL EXAM

The patient had a low anterior hairline, hypertelorism, flattened nasal bridge, thin upper lip, down-turned oral commissure, and malocclusion of teeth. Her thumbs were short.
There were deep ragged ulcerations with fibrinous base and surrounding erythema affecting the bilateral heels and the R lower leg. Smaller erosions with surrounding pink erythema and hyperpigmentation, as well as stellate scarring, affected the lateral thighs. On the bilateral posterior calves, there were irregularly shaped, intact, and well-healed split thickness skin grafts with overlying scale and xerosis.

LABORATORY DATA

Abnormal
ANA 1:80 (<1:40)
IgE elevated 2835 (reference range <100 [iU]/ml)
IgG elevated 2806 (reference range 800-1700 mg/dl)

Homozygous partial deletion of the peptidase D (*PEPD)* gene

Normal
Complete blood count, complete metabolic panel, dsDNA antibody, cANCA, pANCA, Sm antibody, RNP antibody, total complement, C3, C4, antiphospholipid antibody syndrome screen, IgA, IgM, IgD

IMAGING

Chest X-ray normal
Abdominal ultrasound with no hepatosplenomegaly

DIAGNOSIS

Prolidase deficiency due to a homozygous partial deletion of the *PEPD* gene

TREATMENT AND COURSE

The patient and her family were referred to genetics for genetic counseling. Wound care is being coordinated with a wound care clinic closer to her home to allow for regular biweekly visits. Collagenase ointment is intermittently applied to the wound bases for gentle debridement as needed. Occasional antibiotic courses are required when the ulcers develop signs of secondary infection. A trial of proline 5% ointment in plasticized base applied to both ulcerated and intact skin for several weeks did not accelerate healing of established ulcers or prevent breakdown of previously healed sites.

DISCUSSION

The first case of prolidase deficiency was likely described in 1968 by Goodman et al, who reported a patient with dysmorphic features, intellectual disability, lower extremity skin breakdown, imidodipeptiduria, and abnormal dermal collagen crosslinking, in a syndrome they compared to lathyrism.[1] In 1972 Buist et al. hypothesized that the syndrome reported by Goodman et al. was caused by a defect in tissue prolidase activity.[2] Two years later, Powell et al. confirmed prolidase deficiency in a patient using an enzyme assay.[3] Since then, fewer than 100 cases of prolidase deficiency have been reported in the literature, with an estimated incidence of

1 in 1-2 million births. There seems to be a higher incidence in areas of northern Israel and the Geauga settlement of Ohio, although the condition has been reported in individuals with a variety of ethnic backgrounds.[4,5]

Prolidase deficiency is an autosomal recessive condition caused by mutations in the peptidase D (*PEPD*) gene, located on chromosome 19. The *PEPD* gene encodes the prolidase enzyme, a ubiquitous metalloenzyme that functions in collagen metabolism.[6,7] Specifically, prolidase is the only enzyme that hydrolyzes imidodipeptides, which contain C-terminal hydroxyproline or proline. This hydrolysis is the final step in collagen catabolism. Under normal circumstances, the proline residues are then recycled for use in collagen synthesis, while hydroxyproline residues are excreted in the urine. Proline constitutes approximately 30 percent of the amino acids in collagen, and almost all of it is recycled via this pathway.[7]

In prolidase deficiency, there are high levels of circulating imidodipeptides. Biochemically, this manifests as increased urinary excretion of imidodipeptides (imidodipeptiduria) and deficiency of proline in the tissues. While the exact pathophysiologic mechanism for the clinical consequences of this deficiency are unclear, it is hypothesized that impaired collagen synthesis leads to the poor wound healing seen clinically.[8] Additionally, it may be that the accumulation of imidodipeptides results in cellular necrosis, leading to ulceration and predisposing to infection. The high proportion of proline in neuropeptides makes them susceptible to proline deficiency as well, which may explain the intellectual disability of these individuals.[6]

The clinical presentation of prolidase deficiency is heterogeneous, and expressivity varies. Most individuals present in infancy or early childhood, although delayed presentations have also been described. Dermatologic manifestations include, most prominently, recalcitrant skin ulcerations that most often affect the lower extremities. Additionally, patients develop eczematous eruptions and telangiectasias on the face and hands. Distinctive facial features are notable, particularly a low anterior hair line, facial hirsutism, hypertelorism, a saddle nose, a thin upper lip, and mandibular protrusion. Recurrent infections, particularly of the skin and respiratory tract, are common. Other features described in these patients include intellectual disability, chronic lung disease, hepatosplenomegaly, cytopenias, hypergammaglobulinemia, hypocomplementemia, and skeletal anomalies. An association with systemic lupus erythematosus also seems to exist, although the pathologic mechanism for this association is unclear. Diagnosis requires clinical suspicion based on the presenting features and documentation of either massive imidodipeptiduria or a homozygous mutation in the *PEPD* gene.[4,6]

There is no definitive treatment for prolidase deficiency. A number of topical, systemic, and surgical therapies have been described to address the recalcitrant lower extremity ulcerations, most of which have been ineffective or inconsistent. Topical formulations of proline and combined proline and glycine have been used with some success, although these are not universally reliable, as seen in our case.[7,9,10]

Therefore, management of this condition is primarily supportive. Due to its multisystem involvement, individuals with prolidase deficiency require multidisciplinary care. Rigorous and consistent wound care is important to promote healing of the chronic ulcerations and prevent infection. Referrals to the appropriate developmental therapists should be made promptly to

address any detected delays in mental development and any physical limitations that develop as a result of the long-standing lower extremity ulcerations. Regular dermatologic examination to monitor for the development of squamous cell carcinoma in the chronic wounds is also critical. Individuals should have annual laboratory testing to monitor their blood counts and liver function, and an abdominal ultrasound to assess for hepatosplenomegaly. Patients with splenomegaly must be cautioned against participating in contact sports due to the risk for splenic rupture. Regular chest imaging and consultation with pulmonary medicine as needed can also be considered to monitor for the development of lung disease. Finally, follow-up with a rheumatologist should be established to ensure regular clinical and laboratory screening for systemic lupus erythematosus.

In this case, the patient is homozygous for a partial deletion of the *PEPD* gene, specifically affecting exon 7. This mutation is previously unreported, and it is hypothesized to be pathogenic. Our patient did not respond to application of proline ointment to her ulcers, and continues to require diligent wound care. A recent case report published by Good et al. in *Pediatric Dermatology* reports a marked improvement in the ulcers of a patient with prolidase deficiency after application of tacrolimus 0.03% ointment applied twice daily to the ulcer edges for three months, which may represent a novel treatment strategy for our patient.[11]

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PRESENTERS

Julia Dai MD; Mark Hoffman MD; Oluwakemi Onajin MD

CASE 1

A 61-year-old female with metastatic uterine leiomyosarcoma who underwent treatment radiotherapy to lung and pelvic metastases followed by ongoing treatment with nivolumab and cabiralizumab presented with numerous 2-8 mm well-demarcated, atrophic depressions admixed with few erythematous papules on the neck, chest, back, and proximal extremities. Skin lesions developed during the third month of therapy. She denied associated symptoms, history of similar lesions, and preceding dermatitis or trauma.

Therapy was discontinued after 8 months due to treatment-associated pneumonitis. Skin lesions resolved with virtually no trace of the antecedent dermopathy within 3 months after discontinuation of therapy.

CASE 2

A 32-year-old female with metastatic breast cancer who underwent treatment with radiotherapy RT to lung metastases followed by ongoing treatment with nivolumab and cabiralizumab presented with an eruption of numerous 2-8 mm well-demarcated, atrophic depressions on the face, neck, chest, abdomen, back, arms, and legs. No inflammatory lesions were identified. Skin lesions developed during the second month of therapy. She denied associated symptoms, history of similar lesions, and preceding dermatitis or trauma.

She demonstrated a partial response to therapy and discontinued treatment after 12 months per clinical trial protocol. Skin lesions continue to be persistent at her most recent evaluation one month after discontinuation of therapy.

CASE 3

A 53-year-old female with metastatic breast cancer who underwent treatment with radiotherapy to liver metastases in combination with nivolumab and cabiralizumab developed an eruption of innumerable 2-8 mm well-demarcated, atrophic depressions on the face, neck, chest, abdomen, and back 3 months after initiating treatment. She denied associated symptoms, history of similar lesions, and preceding dermatitis or trauma.

CASE 4

A 32-year-old female with metastatic papillary urothelial carcinoma who underwent treatment with radiotherapy to lung metastases in combination with nivolumab and cabiralizumab developed an eruption of multiple 2-8 mm well-demarcated, atrophic depressions on the chest 3 months after initiating treatment. She denied associated symptoms, history of similar lesions, and preceding trauma. One month prior, she had discontinued nivolumab and cabiralizumab due to a widespread, pruritic maculopapular rash refractory to topical steroid therapy. Atrophic skin lesions resolved within 3 months after discontinuation of therapy.

CASE 5

A 31-year-old female with metastatic cholangiocarcinoma who underwent treatment with radiotherapy to liver metastases followed by ongoing nivolumab and cabiralizumab developed an eruption of numerous 2-8 mm well-demarcated, atrophic depressions on the neck and chest. Skin lesions developed during the second month of therapy. Treatment was discontinued at 3 months due to progressive disease, and the patient was lost to follow-up.

DERMATOPATHOLOGY

Case 1: A punch biopsy of a light pink papule suspected to represent a primary lesion was compared to an adjacent punch biopsy of clinically normal skin. Biopsy of the primary lesion demonstrated a diffuse dermal infiltrate composed of foamy histiocytes with engulfed elastic fibers within the cytoplasm. The histiocytic infiltrate was positive for CD68. An elastic stain demonstrated significant reduction of elastic fibers in the superficial to mid dermis. The second biopsy from adjacent normal skin demonstrated sparse perivascular and interstitial lymphocytic inflammation without loss of elastic fibers.

Case 2: A punch biopsy of an atrophic lesion was compared to an adjacent punch biopsy of clinically normal skin. Biopsy of the atrophic lesion revealed a sparse interstitial granulomatous infiltrate within the superficial dermis. The interstitial infiltrate was positive for CD68. An elastic stain demonstrated mildly decreased and altered elastic fibers in the superficial and mid dermis of the atrophic lesion. The second biopsy from adjacent normal skin demonstrated sparse perivascular and interstitial lymphocytic inflammation. An elastic stain demonstrated mildly decreased and altered elastic fibers in the superficial and mid dermis.

DIAGNOSIS

Immunotherapy-related punctate anetoderma

DISCUSSION

The advent of targeted immunotherapies has led to an emergence of unique toxicity profiles, of which cutaneous toxicities represent a significant proportion. Cutaneous adverse effects may have a profound impact on patients' quality of life, and improved characterization of these toxicities and their potential prognostic significance may better guide practitioners in avoiding unnecessary treatment interruption or discontinuation.

In a phase I study investigating radiotherapy with combination nivolumab and cabiralizumab in patients with metastatic solid tumors, we observed five cutaneous eruptions characterized by widespread, punctate, atrophic depressions. Histopathology obtained in two cases demonstrated shared findings of granulomatous inflammation with elastophagocytosis. We speculate that skewing of the immune response towards an antitumorigenic, pro-inflammatory propensity promotes hyperactivation of macrophages with increased phagocytic activity resulting in a unique immunotherapy-related punctate anetoderma.

Tumor-associated macrophages (TAMs) are highly plastic and adaptable to the stromal environment of malignant tumors. Akin to its T-cell counterparts, macrophages are either polarized toward a pro-inflammatory, tumoricidal (so-called "M1") phenotype through activation by granulocyte-macrophage colony-stimulating factor (GM-CSF) or an anti-inflammatory,

tumor-promoting (so-called “M2”) phenotype through activation by colony-stimulating factor-1 (CSF1). TAMs tend to resemble M2-polarized macrophages, thereby promoting angiogenesis, production of immunosuppressive cytokines, inhibition of T-cell effector function, and ultimately facilitating tumor preservation. In solid tumors, TAM infiltration is associated with tumor progression, metastases, and a poor clinical prognosis.

Therapeutic strategies that selectively shift the TAM profile from an M2- to an M1-predominance is thought to render the tumor microenvironment inhospitable and enhance the antitumor T-cell response. Cabiralizumab is a monoclonal antibody that binds to colony stimulating factor 1 receptor (CSF-1R), thereby antagonizing downstream activation of M1 macrophages and shifting the macrophage balance toward an M2 phenotype. This response is enhanced by direct tumor debulking with radiotherapy, which facilitates antigen presentation and the generation of memory T-cells, and with upregulated T-cell checkpoint inhibition through PD-1 blockade, a frequently utilized mechanism of tumor cells to escape immune surveillance. These synergistic mechanisms may, however, tip the immune response toward a hyperactivated autoimmune response.

Dickinson et al. report two patients ongoing treatment with combination nivolumab and cabiralizumab who developed atrophic lesions characterized histologically by papillary dermal elastolysis. We report five cases of immunotherapy-related punctate anetoderma with histopathology in two cases demonstrating granulomatous inflammation with elastophagocytosis, suggesting that hyperactivation of macrophages with increased phagocytic activity toward elastin resulted in this unique clinical phenotype. Through this same mechanism, these cutaneous adverse events may reflect induction of a systemic antitumor response, and further studies are needed to determine whether punctate anetoderma is a positive prognostic factor for patients ongoing therapy. The striking rapid and near-complete normalization of skin lesions upon cessation of therapy in two patients suggests a concomitant compensatory immunologic signaling that facilitated repair. There are currently six active phase I/II clinical trials evaluating nivolumab in combination with cabiralizumab, and we suspect additional cases of this unique immunotherapy-related punctate anetoderma will continue to emerge in the literature.

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CASE 10

PRESENTERS
Margaret Boyle MD; Oluwakemi Onajin MD

HISTORY OF PRESENT ILLNESSS
A 22-year-old female was referred to the dermatology clinic for hair loss, and a widespread rash with associated scarring on the scalp, face, ears, arms, legs, and trunk. Four years prior, she was diagnosed with systemic lupus erythematosus (SLE) with neuropsychiatric features, lupus nephritis, and generalized discoid lupus erythematosus (DLE).

PAST MEDICAL HISTORY
SLE with neuropsychiatric symptoms, lupus nephritis, DLE, hypertension, tobacco use

MEDICATIONS
Alclometasone 0.05% ointment twice a day for face
Fluocinolone 0.01% scalp oil nightly
Betamethasone 0.05% ointment twice a day for body
Hydroxychloroquine 200 mg twice daily
Methotrexate 22.5 mg PO weekly
Folic acid 1 mg daily
Prednisone 10 mg daily
IVIG monthly for hypogammaglobulinemia and recurrent nasal/ear infections
Aspirin 81 mg daily
Mirtazapine 30 mg daily
Ca/vit D supplementation
Etonogestrel 68 mg subdermal implant
Famotidine 20 mg nightly
Ferrous sulfate 325 mg daily
Fluticasone 50 mcg daily intranasal

PHYSICAL EXAMINATION
Widespread well-defined erythematous scaly plaques with central depigmentation and peripheral hyperpigmentation involving the scalp, face, conchal bowls, upper and lower extremities, and trunk. Scalp lesions demonstrate hair loss and absent follicular ostia.

LABORATORY DATA
The following were positive or abnormal:
ANA: 1:640
SS-A AB: >8.0 (normal <1.0)
SMITH AB: >8.0 (normal 1.0)
SMRNP AB: 7.3 (normal <1.0)

The following were negative or within normal limits:
CBC, CMP, CRP, C3, C4, urine protein:Cr, urinalysis
Lupus anticoagulant/anti-phospholipid antibody test-no evidence of antiphospholipid syndrome
Anti-dS DNA <12.3 (normal <30), SS-B AB: <0.2 (normal <1.0), RNP AB: 0.4 (normal <1.0)

DERMATOPATHOLOGY

Skin biopsy of the right arm demonstrated epidermal atrophy, papillary dermal edema, vacuolar interface dermatitis, increased dermal mucin, perivascular and periadnexal inflammation consistent with lupus erythematosus.

DIAGNOSIS

Generalized discoid lupus erythematosus in the setting of SLE

TREATMENT & COURSE

Her SLE was initially managed with cyclophosphamide and methylprednisolone, and subsequently mycophenolate mofetil, with improvement in her systemic symptoms. She also underwent three courses of rituximab with moderate benefit to her skin. However, cutaneous disease persisted despite treatment with prednisone, methotrexate, hydroxychloroquine, IVIG (for hypogammaglobinemia, recurrent sinus and ear infections), high potency topical steroids, and topical calcineurin inhibitors. She was referred to dermatology for management of her skin disease.

She presented to dermatology on prednisone 10mg daily, hydroxychloroquine 200 mg twice a day, monthly IVIG, and methotrexate 22.5 mg weekly which were managed by Rheumatology. Given severe, diffuse cutaneous symptoms refractory to multiple topical and systemic treatments for SLE, treatment with lenalidomide (Revlimid) was considered.

She was enrolled in the REVLIMID Risk Evaluation and Mitigation Strategy (REMS) program, and baseline CBC, CMP, lupus anticoagulant/anti-phospholipid antibody, and urine pregnancy tests were safely within parameters to initiate therapy. She successfully quit smoking and was continued on aspirin 81 mg daily to decrease risk of thromboembolism. Within two months of treatment, the patient reported decreased symptoms, less erythema of pre-existing lesions, no new lesions, and repigmentation of hypopigmented DLE scars. After three months, she no longer required topical therapy and remarkably demonstrated continued repigmentation. She experienced no adverse events and has been on Revlimid 5mg PO QHS for eight months.

DISCUSSION

Systemic lupus erythematosus (SLE) is a multisystem disorder that frequently involves the skin. Cutaneous manifestations can be an indicator of internal disease and a significant source of disability for patients. Cutaneous lupus erythematous (CLE) has roughly the same incidence as SLE, approximately 3-4 per 100,000. Cutaneous lupus lesions are subdivided into acute cutaneous lupus erythematosus (ACLE), subacute cutaneous lupus erythematosus (SCLE), and chronic cutaneous lupus erythematosus (CCLE) including discoid lupus erythematosus (DLE). About 10-20% of patients with DLE may meet classification criteria for SLE, with a slightly higher risk with disseminated DLE.

Sun protection and smoking cessation are essential nonpharmacologic interventions for CLE. First-line treatments for CLE include topical or intralesional corticosteroids, topical calcineurin inhibitors, and antimalarial therapy. Second-line treatments for diffuse CLE include systemic corticosteroids, mycophenolate mofetil, methotrexate, azathioprine, thalidomide, and lenalidomide. Third-line treatments include dapsone, retinoids, biologics and IVIG.

Approximately 10% of patients with cutaneous lupus erythematosus remain refractory to immunosuppressive therapies.

Lenalidomide is currently FDA-approved for adult patients with hematologic malignancies. Lenalidomide is a thalidomide analogue with more potent anti-tumor necrosis factor-α activity, IFN-γ inhibition, and a lower risk of peripheral neuropathy compared to thalidomide. Several case series and small prospective non-randomized studies have reported lenalidomide as a potential therapy for severe DLE refractory to systemic and topical treatments. Lenalidomide (Revlimid) is prescribed through the REVLIMID REMS® program which requires prescribers and pharmacies to be certified, and patients to enroll and comply with program requirements. The primary goal of the program is to prevent risk of embryo-fetal exposure.

Lenalidomide can be initiated at 2.5 mg QHS and titrated up to a total dose 5-10 mg QHS. Baseline CBC and CMP are recommended. Females of reproductive potential require two forms of contraception, one negative pregnancy test 10-14 days prior, and a second negative pregnancy test within 24 hours prior to writing the initial prescription. Monitoring labs include weekly CBC with differential for four weeks, then CBC with differential every one to two months. Females of reproductive potential require weekly pregnancy tests for four weeks, then pregnancy testing monthly. All patients must not donate blood while on treatment and for four weeks after treatment. Contraindications include pregnancy and hypersensitivity to lenalidomide. Caution must be used in patients who smoke, have a history of deep vein thrombosis (DVT)/pulmonary embolism (PE) and cytopenias. Concurrent treatment with antimalarials and aspirin is recommended to decrease risk of thromboembolic events. Reported side effects include teratogenicity, neutropenia, thrombocytopenia, increased risk of thromboembolic events (DVT/PE), nausea, diarrhea, constipation, fatigue, and headache.

Patients frequently relapse after stopping lenalidomide. Lenalidomide can be tapered and patients can remain on doses as low as 5mg every three days.

We present a case of generalized discoid lupus erythematosus in the setting of SLE effectively treated with the addition of lenalidomide, providing additional support for the its use in refractory cases.

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