Chicago Dermatological Society

September 2017 Educational Conference

Program & Speaker Information
CME Certification
Case Presentations

Wednesday, September 6, 2017
Stephens Convention Center – Rosemont, IL

Conference Host:
Division of Dermatology
Loyola University Medical Center

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Program

Host: Loyola University
Wednesday, September 6, 2017
Stephens Convention Center, Rosemont

8:00 a.m.	**Registration & Continental Breakfast with Exhibitors** *Foyer outside Ballroom #42 - Level 2*
8:30 a.m. - 10:30 a.m.	**Clinical Rounds** Slide viewing/posters Patient viewing
9:00 a.m. - 10:00 a.m.	**Basic Science Lecture** "An Interesting Case" *Christen M. Mowad, MD*
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. - 12:15 p.m.	**MOC Self-Assessment Questions**
12:15 p.m. - 12:45 p.m.	**Box Lunches & visit with exhibitors**
12:55 p.m. - 1:05 p.m.	**CDS Business Meeting**
1:05 p.m. - 2:05 p.m.	**General Session** “Contact Dermatitis- an Update: Contactants, Controversies and Conundrums” *Christen M. Mowad, MD*
2:05 p.m.	**Meeting adjourns**

Mark the Date!
Next CDS monthly meeting – Hosted by UIC
Wednesday, October 4; Cleacher Center, Chicago

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

Guest Speaker

CHRISTEN M. MOWAD, MD

Director of Contact and Occupational Dermatitis Clinic; Geisinger Medical Center Danville, PA

Dr. Mowad received her medical degree from the University of Pennsylvania School of Medicine in Philadelphia, and completed both her internship in internal medicine and her residency in dermatology at the Hospital of the University of Pennsylvania, where she served as Chief Resident in dermatology. Dr. Mowad is an adjunct clinical professor at Temple University in Philadelphia. Currently, she is Director of Contact and Occupational Dermatitis Clinic at the Geisinger Medical Center.

Dr. Mowad has published widely and has presented extensively on a national level. She is a past president of the American Contact Dermatitis Society and is a member of the American Academy of Dermatology, the Noah Worcester Dermatological Society, and the American Dermatological Society. She serves on the editorial board of Cutis and is a section editor for the American Journal of Contact Dermatitis. Dr. Mowad is a reviewer for the Journal of the American Academy of Dermatology (JAAD), Pediatric Dermatology, Dermatitis, and Cutis.

Dr. Mowad is board certified in dermatology and has been listed in Best Doctors in America every year since 2005.

CME Information

This educational activity is jointly provided by the Chicago Dermatological Society in partnership with the Indiana Academy of Ophthalmology

Overview

The Chicago Dermatological Society was established in 1903 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. In addition to two lectures given by the guest speaker, the residents of the host institution present cases which are offered for audience discussion. In addition, live patients, posters and microscopic slides 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 2017/18 series of meetings, the participant should be able to:

1. Discuss key factors in the diagnosis and treatment for allergic conditions, viral diseases and bacterial infections.
2. Describe the manifestation of skin cancers and the efficacy of treatments available to the dermatologist.
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 4.5 *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. Note - You may complete the paper version of the evaluation form or submit your evaluation online.

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.

Today's guest speaker, Dr. Christen M. Mowad, has no potential conflicts of interest to disclose. None of the planning committee members have any conflicts of interest to disclose.

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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.

Chicago Dermatological Society
Patient Privacy and HIPAA Compliance

APPROVED
June 3, 2015

Purpose

The purpose of this policy is to reaffirm the intent of the Chicago Dermatological Society (CDS) to appropriately safeguard patient privacy with respect to CDS conferences, publications and its website, and also to adhere to HIPAA requirements. All CDS members are expected to be aware of and conform to all regulations concerning patient privacy when attending a conference or utilizing any materials produced by CDS which contains any form of patient information which could be considered to be Protected Health Information.

Background

The Health Insurance Portability and Accountability Act of 1996 (HIPAA) and its implementing regulations restrict health care providers and others to use and disclose protected health information (PHI). Protected health information means information that is created or received by an entity and relates to the past, present, or future physical or mental health condition of a patient; the provision of health care to a patient; or the past, present, or future payment for the provision of health care to a patient; and that identifies the patient or for which there is a reasonable basis to believe the information can be used to identify the patient. Protected health information includes information of persons living or deceased.

Some examples of PHI are:
- Patient's medical record number
- Patient's demographic information (e.g. address, telephone number)
- Information doctors, nurses and other health care providers put in a patient's medical record
- Identifiable images of the patient
- Conversations a provider has about a patient's care or treatment with nurses and others
- Information about a patient in a provider's computer system or a health insurer's computer system
- Billing information about a patient at a clinic
- Any health information that can lead to the identity of an individual or the contents of the information can be used to make a reasonable assumption as to the identity of the individual

Policy

The CDS takes seriously compliance with HIPAA regulations and safeguards concerning protected health information. Accordingly, the Chicago Dermatological Society has adopted the following provisions:

1. Case descriptions included in clinical conference "protocol books" and posters may not include information that could potentially identify a particular patient.

2. Photos of patients will not be published in clinical conference handout materials, including the protocol book.

3. To the extent possible, posters, slide presentations and videos displayed at CDS clinical conferences should avoid using photos that display a patient's full face or other features that could identify a particular patient. When a full-face photo must be used for clinical/educational reasons, the photo must be altered as much as possible to disguise the identity of the patient.

4. At all times, all attendees of CDS clinical conferences must adhere to appropriate behavior that respects the patient's right to privacy. Taking personal photos of posters or other displays, images included in general session lectures/presentations, and live patients at CDS conferences is strictly prohibited. Making audio recordings of any session at a CDS conference also is prohibited.

5. Attendees may not share materials distributed by CDS as part of the clinical conference or on its website with others who are not participating in the conference or who are not members of the CDS.

6. It is the responsibility of the "host" department partnering with CDS for a clinical conference to obtain all appropriate patient waivers and/or informed consent regarding the patient's participation in the CDS conference, including presentation of their case and display of posters or photos.

7. CDS will include a copy of its patient privacy policy in every meeting packet, and it will display a poster reiterating this policy at the entrance to live patient and poster viewing areas.

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NOTES

Presented by K. Carly Webb[1] MD, Ashish Arshanapalli[1] MD, Daniel Opel[1] MD, Reeba Omman[3] MD, Madhu Dahiya[4] MD, James Swan[1] MD, and David Eilers[2] MD
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[4]Pathology Service, Hines VA Hospital

HISTORY OF PRESENT ILLNESS

Dermatology was consulted to evaluate a 53-year-old male for a non-healing lower back wound of one year's duration. The patient reported developing recurrent ulcerating wounds on the bilateral legs and left arm for the past 30 years. Those wounds appeared each summer, lasted about three months, and reliably resolved after treatment with oral antibiotics and topical antifungals, sometimes leaving behind scars. His current back wound started in a similar manner to his prior wounds but was not responding to the usual treatments; instead, it was slowly enlarging and was becoming progressively more tender. The affected area of skin would occasionally break open and drain fluid at several sites.

Above his primary wound, he noted a separate asymptomatic dark and crusted skin lesion, which appeared around the same time as his other wounds. He denied any history of trauma to the affected areas. He also noticed several new brown nodules on his legs, which erupted over the course of about one month. He reported that his fingertips began cracking easily over the past year, despite no changes in his daily routine or occupational duties. Just prior to admission, he states he was bit by a brown recluse spider on his left third finger. At the time of evaluation, the patient was an inpatient admitted for pleuritic chest pain and right-sided lower extremity weakness. His review of systems was also notable for arthralgias, bilateral thigh pain, right-side predominant lower leg paresthesias, and dysgeusia, resulting in a 55-pound weight loss over the past six months.

PAST MEDICAL HISTORY

Automobile accident 10 years prior resulting in cervical spine fracture, status-post laminectomy
Varicella zoster viral infection affecting right T10 dermatome
Traumatic brain injury complicated by seizures
Hypertension
Gastroesophageal reflux disease
No known autoimmune diseases or blood clots
No known malignancies

MEDICATIONS

Hydrochlorothiazide/lisinopril
Omeprazole
Levetiracetam
Phenytoin

ALLERGIES

None

FAMILY HISTORY

No known history of autoimmune disease or blood clots

SOCIAL HISTORY

No recent international or domestic travel
No history of extensive manual labor
Smokes 1-2 cigarettes when in pain; previously smoked 1 pack-per-day for many years

No illicit drug use

PHYSICAL EXAMINATION

The patient was well-appearing but had marked pain with ambulation and basic maneuvering. Cutaneous examination revealed a large, retiform, crusted plaque with a deep red to violaceous border on the left mid thoracic back. Inferior to this lesion was a thick, dusky red, indurated band-like plaque studded with numerous small ulcerations, heme and serous crusts, and atrophic white plaques. The patient was also noted to have ragged cuticles on all 10 fingers, as well as hyperkeratosis and superficial desquamation of the bilateral palms. Deep fissures were present on the bilateral thumbs, and a large serosanguinous crust was present on the left third fingertip. A few firm grey-brown nodules were scattered on the bilateral legs and right buttock. There were no oral or ocular lesions noted. The remainder of the cutaneous examination was unremarkable.

DERMATOPATHOLOGY

Histopathologic analysis of multiple specimens taken from the representative plaques on the left flank and back demonstrated a superficial and deep perivascular and periappendageal lymphohistiocytic and plasma cell inflammatory infiltrate in the dermis extending into the subcutaneous fat. Lymphocytes were noted within the wall of a medium-to-large sized vessel in the subcutaneous fat. Basal vacuolar change and sparse lymphocytic infiltrates were present at the dermal-epidermal junction. Subsequent wedge biopsies revealed a mixed lobular and septal panniculitis with focal fat necrosis. Colloidal iron and PAS stains revealed dermal and subcutaneous mucin and a thickened basement membrane, respectively. Infectious stains and tissue cultures were all negative.

LABORATORY RESULTS

Laboratory Study	Patient Result	Reference Range
WBC (K/uL)	3.45	4.0-11.0
Lymphs # (K/uL)	0.53	1.0-4.0
Hemoglobin (g/dL)	10.0	13-17
Platelet (K/uL)	328	140-400
Creatinine (mg/dL)	0.676	0.67-1.17
Urinalysis	No RBC or protein	
ALT (U/L)	22	10-65
AST (U/L)	35	10-37
PT (seconds)	12.0	12.2-14.4
aPTT (seconds)	34.1	24.0-35.0
INR	0.91	0.9-1.1
SED RATE (mm/hr)	105	0-15
CK/CPK (U/L)	56	39-309
Cryoglobulin (Qual)	Negative	
Complement C3 (mg/dL)	93.2	90-180
Complement C4 (mg/dL)	18.9	10-40
Aldolase (U/L)	5.6	< = 8.1
ANA titer	1:160	
ANTI dsDNA (IU)	231.12	0-24
Anti-Histone Antibody (titer)	<1.0	<20 Negative
ANTI SSA (EU)	0.19	<20 Negative
ANTI SSB (EU)	5.12	<20 Negative
ANTI Sm (EU)	1.26	<20 Negative

ANTI Sm/RNP	1.94	<20 Negative
Lupus Inhibitor (TTI)	Negative	
Circulating Inhibitor Screen	Negative	
DRVVT Screen	Negative	
Cardiolipin IgA, IgG, IgM AB	Negative	
B-2 GP IgA, IgG, IgM	Negative	
Protein C (functional) (%)	180	65-150
Protein S (functional) (%)	67	65-155
MYOSITIS EXTENDED PANEL		
SSA 52 (Ro) (ENA) Antibody, IgG (AU/mL)	10	< or = 29 Negative
SSA 60 (Ro) (ENA) Antibody, IgG (AU/mL)	4	< or = 29 Negative
Ribonucleic Protein (U1) (ENA) Antibody, IgG (AU/mL)	1	< or = 29 Negative
Jo-1 (Histidyl-tRNA Synthetase) Antibody, IgG (AU/mL)	1	< or = 29 Negative
PL-12 (alanyl-tRNA synthetase) Antibody	Negative	
PL-7 (threonyl-tRNA synthetase) Antibody	Negative	
EJ (glycyl-tRNA synthetase) Antibody	Negative	
OJ (isoleucyl-tRNA synthetase) Antibody	Negative	
SRP (Signal Recognition Particle) Antibody	Negative	
Ku Antibody	Negative	
PM/Scl 100 Antibody, IgG	Negative	
U2 sn (small nuclear) RNP Antibody	Negative	
Fibrillarin (U3 RNP) Antibody, IgG	Negative	
Mi-2 (nuclear helicase protein) Antibody	Negative	
P155/140 Antibody	Negative	
TIF-1 gamma (155 kDa) Antibody	Negative	
SAE1 (SUMO activating enzyme) Antibody	Negative	
MDA5 (CADM-140) Antibody	Negative	
NXP-2 (Nuclear matrix protein-2) Antibody	Negative	

ADDITIONAL TESTS

Computed tomography (CT) scans of the chest, abdomen, and pelvis were negative for any masses concerning for malignancy. Thoracic CT Angiogram revealed mild pleural scarring. A small pericardial effusion was noted on Transthoracic Echocardiogram. MRI of the lumbar spine was negative for signs of myositis but did reveal symmetric prevertebral enhancement at the level of L3 medial to the left psoas muscle. Electromyography was notable for a diffuse sensorimotor polyneuropathy.

DIAGNOSIS

Lupus profundus

TREATMENT AND COURSE

The patient was treated with hydroxychloroquine 200mg po bid and prednisone 20mg po daily. His cutaneous lesions have showed gradual improvement. His pain has improved, and his hands now exhibit less hyperkeratosis and fissuring. Pulmonary function tests and MRI of the bilateral lower extremities are pending.

DISCUSSION

Lupus profundus (also known as lupus erythematosus profundus, lupus panniculitis) is a rare manifestation of chronic cutaneous lupus erythematosus, affecting 1-3% of patients with cutaneous lupus. It was initially described by Kaposi in 1883 and was termed “lupus erythematosus profundus of Kaposi-Irgang” by Arnold in 1956. It may present in patients with discoid or systemic lupus erythematosus (SLE), or it may be observed as an isolated phenomenon. While the terms “lupus panniculitis” and “lupus profundus” are often used interchangeably, “lupus profundus” denotes involvement of the dermis and subcutis, while “lupus panniculitis” should be reserved to convey exclusive involvement of the subcutaneous fat. This condition affects women more commonly than men, in a ratio of about 2:1 and typically presents between ages 20 and 60. It is estimated that 5-10% of patients will meet criteria for systemic lupus erythematosus at the time they are diagnosed with lupus profundus, and up to 50% of lupus profundus patients will go on to develop systemic lupus erythematosus during their lifetime; they should thus be followed closely over time for the development of other cutaneous and systemic symptoms. The presence of lupus profundus confers a favorable prognosis to SLE patients, as these patients typically have less severe renal and neurologic symptoms as compared to their SLE counterparts without panniculitis.

The etiology of lupus profundus is still debated and remains incompletely understood. Unlike other forms of cutaneous lupus, ultraviolet exposure does not appear to play a significant role in lupus profundus lesion precipitation. Several reports in the literature detail lupus profundus lesion development at sites of trauma weeks to months after the insult. A commonly proposed theory is that of the “immunocompromised district,” whereby certain sites of the skin become immunocompromised as the result of trauma, radiation exposure, infection, etc., and then subsequently have dysregulated immunity; this then predisposes those cutaneous sites to developing autoimmune or inflammatory conditions in the future.

Lupus profundus lesions classically present as subcutaneous nodules and plaques which have a predilection for the gluteal region, thighs, and upper extremities; lesions less commonly involve the face, scalp, chest, and even the salivary glands. Interestingly, periorbital edema may be the sole presenting sign of this condition, predating the development of any skin lesions. Lesions are typically quite tender and may ulcerate, especially if left untreated. Individual lesions often heal with atrophic plaques, representing underlying lipoatrophy. The lesions of lupus profundus may be difficult to differentiate clinically from other panniculitides, such as erythema nodosum, pancreatic panniculitis, traumatic fat necrosis, or erythema induratum of Bazin. Importantly, lupus profundus lesions almost always spare the distal extremities, which can be a helpful differentiating clinical feature. Lesions may also mimic those of cutaneous lymphomas, such as subcutaneous panniculitis-like T cell lymphoma. Particularly in late stages, lesions may resemble morphea profunda.

A distinct clinical subset of lupus profundus is that of linear lupus profundus. This is a very rarely reported entity which appears to have a predilection for East Asian males. Lesions present earlier in life, tend to affect the scalp, and often follow the lines of Blaschko. A few of these reports detail the development of linear lupus profundus lesions at sites of previous trauma, which has been likened to a sort of "Koebner phenomenon." In patients without a history of local trauma corresponding to the panniculitic site(s), the theory of epidermal mosaicism has been proposed.

The two most classically observed histologic findings in lupus profundus are lymphocytic infiltrates within the fat lobules and hyaline necrosis of the fat lobule. It is a predominantly lobular panniculitis, but septal involvement may be present in up to 82% of cases. Plasma cells are classically present within the inflammatory infiltrates in the subcutis. When present, epidermal changes, including basal vacuolar change, thickening of the basement membrane, and pigment incontinence, may be helpful in differentiating this entity from other panniculitides, as well as from its histologic mimicker, subcutaneous panniculitis-like T cell lymphoma. However, these epidermal changes are quoted as being present in only one-half to two-thirds of cases. When ulcerations are present within lesions clinically, a lymphocytic vasculitis is typically seen on histology.

ANA is only positive in about 70% of lupus profundus patients. Double-stranded DNA (dsDNA) antibodies are present even less commonly. Other laboratory anomalies may include lymphopenia, anemia, hypocomplementemia (C4), and a positive Rheumatoid Factor. Rapid plasma reagin testing may be falsely positive. If histopathologic findings are concerning for lupus profundus, further workup may include a complete medical history and review of systems, a complete blood count, complete metabolic panel, ANA screen, and autoimmune serologic panels.

Lupus profundus is a chronic condition following a relapsing and remitting course. Mild cases may be successfully treated with potent topical steroids, but systemic therapy is usually necessary. First line systemic treatment is hydroxychloroquine 200mg – 400mg po daily or chloroquine 250mg- 500mg po daily. Patients with concomitant SLE may respond more favorably to systemic steroids. Other therapies less commonly used, which have met with variable success, include thalidomide, dapsone, methotrexate, cyclosporine, cyclophosphamide, and intravenous immunoglobulin. Intralesional steroid injections should be avoided, as the trauma from the injections can worsen and precipitate lesions, and the local steroid itself may exacerbate preexisting atrophy.

At the time of diagnosis of lupus profundus, our patient met criteria for systemic lupus erythematosus, as per the American College of Rheumatology criteria. Interestingly, our patient also presented with findings clinically consistent with mechanic's hands in the absence of a history of extensive manual labor. "Mechanic's hands" is a clinical sign most closely associated with anti-synthetase syndrome, especially among those with positive anti-Jo-1 antibodies; however, it has also been reported in patients with dermatomyositis, polymyositis, childhood sclerodermatomyositis, and mixed connective tissue disease. We believe our patient has systemic lupus erythematosus, and, to the best of our knowledge, mechanic's hands has not been reported as a cutaneous finding within this entity. Therefore, we are uncertain if his hand findings represent an unusual cutaneous finding in the setting of SLE or if his presentation is instead better classified as that of an overlap connective tissue disease. The mechanic's hands sign appears to be restricted to connective tissue diseases in which myositis is a component; therefore, our patient is scheduled to undergo MRI of his lower extremities to evaluate for subclinical myositis.

We present this case for clinical interest, to highlight the presentation of the rare cutaneous condition of lupus profundus in a patient with heretofore undiagnosed systemic lupus erythematosus. We also call to attention the concomitant finding in this patient of mechanic's hands, which is, to our knowledge, not described as a typical cutaneous manifestation of systemic lupus erythematosus.

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NOTES

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PATIENT A

HISTORY OF PRESENT ILLNESS

A 30-year-old woman was referred to Dermatology for evaluation and treatment of burn scars. The patient had a history of a flash flame, second-degree burn injury to the arms and legs from a propane tank explosion eight months prior. Her wounds were initially treated in the Burn Unit at Loyola University Medical Center with serial surgical debridement and local wound care. At the time of Dermatology evaluation, she was treating the scars with silicone gel sheeting and compression garments. She complained of burning pain and itching of the scarred skin managed with gabapentin. The patient was followed closely by psychiatry for anxiety and insomnia secondary to significant psychologic trauma experienced after the accident.

PAST MEDICAL HISTORY

None

MEDICATIONS

Gabapentin

ALLERGIES

None

FAMILY HISTORY

Non-contributory

SOCIAL HISTORY

Radiology technician
No tobacco, alcohol, or illicit drug use

PHYSICAL EXAMINATION

Fitzpatrick phototype III
Bilateral lower and upper extremities including dorsal hands and digits with hypertrophic, erythematous, and dyspigmented scars affecting approximately 30% body surface area

DIAGNOSIS

Burn scars in a Fitzpatrick phototype III patient treated with a combination of pulsed dye and nonablative fractional resurfacing lasers with significant clinical improvement

TREATMENT AND COURSE

The patient received monthly laser treatments for 12 months. Three treatments were performed using a 595 nm pulsed dye laser with the following settings: 7 mm spot size/8 J/6 msec. Nine treatments were performed with a nonablative fractional resurfacing combination device with the following settings: 1550 nm erbium:glass laser/30 mJ/14% density/4-8 passes and 1927 nm thulium laser/10 mJ/30% density/4-8 passes. Adjuvant therapy included 1 session of intralesional triamcinolone acetonide injections (concentration 20 mg/mL, volume 1 mL) to a symptomatic hypertrophic scar on the left hand, tacrolimus 0.1% ointment applied twice daily to hyperpigmented scars on the legs, and diligent sun protection. Treated burn scars became softer, thinner and more normal in texture and color with an overall significant cosmetic improvement.

PATIENT B

HISTORY OF PRESENT ILLNESS

A 33-year-old Spanish-speaking man was referred to Dermatology for evaluation and treatment of burn scars. The patient had a history of an occupational, second-degree chemical burn injury to the left neck, torso, and arm after accidentally being splashed with calcium phosphate while emptying a garbage can 4 months prior. His wounds were initially treated in the Burn Unit at Loyola University Medical Center with serial surgical debridement and local wound care. At the time of Dermatology evaluation, he was treating the scars with massage therapy. He complained of intermittent pain and itching of the scarred skin as well as significant emotional distress due to the appearance of his scars. The patient also noted new areas of hair loss on the scalp, which he believed resulted from the chemical splash. He had no personal or family history of autoimmune disease.

PAST MEDICAL HISTORY

None

MEDICATIONS

Ibuprofen as needed

ALLERGIES

None

FAMILY HISTORY

Non-contributory

SOCIAL HISTORY

Sanitation worker
Smoker; no alcohol or illicit drug use

PHYSICAL EXAMINATION

Fitzpatrick phototype III
Left postauricular and vertex of scalp with circular, well-defined, non-scarring patches of alopecia
Left neck, torso, and upper extremity with hypertrophic, erythematous, and dyspigmented scars affecting approximately 7% body surface area

DIAGNOSIS

Burn scars in a Fitzpatrick phototype III patient with subsequent alopecia areata treated with a combination of pulsed dye laser, nonablative fractional resurfacing laser, and intralesional corticosteroid injections with significant clinical improvement

TREATMENT AND COURSE

The patient received monthly laser treatments for six months. Two treatments were performed using a 595 nm pulsed dye laser with the following settings: 5 mm spot size/7.5 J/6 msec. Four treatments were performed with a nonablative fractional resurfacing combination device with the following settings: 1550 nm erbium:glass laser/30 mJ/14% density/4-8 passes and 1927 nm thulium laser/10 mJ/30% density/4-8 passes. Adjuvant therapy included continued scar massage and diligent sun protection. Treated burn scars became softer, thinner and more normal in texture and color with an overall significant cosmetic improvement. Alopecia areata resolved with four monthly sessions of intralesional triamcinolone acetonide injections (concentration 10-20 mg/mL, volume 0.5-2.5 mL).

DISCUSSION

Burn scars cause significant patient morbidity due to cosmetic disfigurement, contractures, impaired quality of life from associated pain and pruritus, and psychosocial distress. Mainstay treatments for burn scars include silicone gel sheeting, scar massage therapy, compression garments, corticosteroid

injections, and surgical interventions. Laser therapy has emerged as a beneficial treatment for targeting burn scar hypertrophy, pigment, erythema, and textural irregularities. Three types of lasers have demonstrated efficacy in improving burn scars: pulsed dye lasers, the Q-switched neodymium-doped yttrium aluminum garnet (Nd:YAG) laser, and fractional ablative and nonablative resurfacing lasers. Our patients achieved significant clinical improvement utilizing a combination of pulsed dye and nonablative fractional resurfacing lasers.

Pulsed dye lasers cause selective photothermolysis of microvasculature resulting in decreased edema and inflammation in scars. Multiple studies have evaluated the effectiveness of pulsed dye lasers in the treatment of burn scars, surgical scars, and skin grafts with the strongest evidence for reducing scar erythema and pruritus. Earlier intervention with the pulsed dye laser (erythematous scars less than one year old) may result in better outcomes. The most common side effect is post-procedural purpura; the frequency of adverse events is overall very low.

Fractional resurfacing lasers insert evenly distributed columns of thermal injury, referred to as microscopic treatment zones (MTZ), into the dermis. The pulse energy and treatment density determine the depth of injury and number of columns per treatment area, respectively. The untreated skin between MTZs promotes rapid post-procedure healing and collagen remodeling. Histopathologic changes of burn scars treated with fractional lasers include increased vascularity, decreased inflammation, and alteration of collagen to appear more like that of normal skin. Fractional resurfacing lasers have shown efficacy in improving thickness, pliability, pigmentary changes, and textural abnormalities in both early and mature scars. Common side effects include post-treatment erythema, swelling, discomfort, and pinpoint bleeding (ablative lasers only). Prolonged erythema, post-inflammatory hyperpigmentation (PIH), infection, and new scar formation occur less frequently.

Fractional lasers exist in ablative (10,600 nm CO_2 laser and 2940 nm erbium:YAG laser) and nonablative (1550 nm erbium:glass laser) forms. Ablative lasers cause injury to the epidermis and dermis, while nonablative lasers produce a more superficial injury in the dermis sparing the overlying epidermis. Ablative lasers are more effective for thicker or contracted scars due to greater depth of injury, while nonablative lasers are beneficial in treating scar dyschromia. A split-scar comparison study showed ablative lasers were better for scar softening, and nonablative lasers were better for improving scar color. As compared to ablative lasers, nonablative lasers require shorter post-procedure downtime and have a significantly lower risk of undesirable side effects.

Our patients' burn scars were treated with a nonablative fractional resurfacing device containing two lasers: the 1550 nm erbium:glass and 1927 nm thulium. The 1550 nm wavelength injures the dermis to stimulate collagen remodeling, while the 1927 nm wavelength targets epidermal processes, particularly hyperpigmentation. This combination of wavelengths addresses scar thickness, texture, and hyperpigmentation with a low side effect profile. This device is especially advantageous in patients with darker skin types who are at a higher risk of developing PIH after resurfacing treatments, a side effect that may last up to several years. Other treatment factors reported to reduce the likelihood of post-treatment adverse events include lower fluences, reduced treatment densities, and few treatment passes. Additionally, strict sun avoidance post-procedure must be emphasized.

To our knowledge, this is the first report of alopecia areata occurring after a burn injury. Though the patient felt his alopecia was caused by the chemical splash, alopecia areata has been associated with stressful events, which may have been the precipitating factor in this patient’s case. His alopecic condition completely resolved with intralesional corticosteroid treatments.

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HISTORY OF PRESENT ILLNESS

A 10-day-old female was evaluated in consultation for pink firm plaques on the right upper back and buttocks that acutely appeared on seventh day of life. She was born at 39 weeks' gestation with a delivery complicated by left shoulder dystocia and hypoxia. At birth, the neonate was floppy without a pulse or respiration and had Apgar scores of 3 and 4 at 10 and 15 minutes, respectively. The neonate required endotracheal intubation, chest compressions, and endotracheal vasopressors in the delivery room. Three hours after birth, a whole-body cooling protocol using cooling blankets for moderate hypoxic-ischemic encephalopathy was initiated. She was rewarmed beginning on day three of life and was extubated to room air four days later.

PAST MEDICAL HISTORY

See history of present illness

PRENATAL HISTORY

The mother's pregnancy was complicated by pre-eclampsia and *in vitro* fertilization.

MEDICATION

None

FAMILY HISTORY

Mother and father with eczema and seasonal allergies

SOCIAL HISTORY

The baby lives with her mother, father, 2-year-old sister, and dogs.

PHYSICAL EXAM

Physical examination revealed firm, indurated pink dusky nodules coalescing into ill-defined plaques on the right upper back and left buttock. The remainder of her skin was uninvolved.

HISTOPATHOLOGY

Microscopy revealed a lobular panniculitis with lymphocytes, histiocytes, eosinophils, and scattered neutrophils with foci of radially arranged crystalline spaces. These histologic findings favored a diagnosis of subcutaneous fat necrosis of the newborn. Given the presence of neutrophils, infectious stains were performed and were negative.

DIAGNOSIS

Subcutaneous fat necrosis of the newborn

TREATMENT AND COURSE

Serum ionized calcium levels were monitored every one to two weeks for the first six months of life, and all were within normal limits. At her eighth month clinic follow-up, the patient exhibited complete resolution of plaques and nodules.

DISCUSSION

Subcutaneous fat necrosis (SCFN) is a self-limiting condition that occurs predominantly in full term or post-term neonates of normal birth weight during the first six weeks of life. The precise etiology is unknown. However, several fetal insults appear to be associated with this condition, including perinatal

asphyxia, hypothermia, meconium aspiration, and obstetric trauma; and maternal conditions, such as gestational diabetes, hypertension, preeclampsia, seizures, thyroid dysfunction, and illicit drug consumption. Transient localized tissue hypoxia and/or tissue hypothermia may be the common link in reported cases.

Lesions of SCFN most commonly present as subcutaneous rubbery nodules unattached to underlying deeper structures. They range from a few millimeters to several centimeters in diameter, with the overlying skin appearing normal or erythematous to violaceous. SCFN has a predilection for bony prominences of the arms, shoulders, buttocks, thighs, and cheeks. Characteristic histologic features of SCFN include swollen adipocytes and histiocytes that contain abundant radially arranged eosinophilic crystalline spaces resulting from dissolved triglyceride crystals. Such findings may be seen on fine-needle aspiration biopsy and imprint cytology, offering alternative methods to confirm the diagnosis. A heavy inflammatory cell infiltrate consisting of lymphocytes, histiocytes, eosinophils, and numerous foreign body giant cells is often noted, appearing largely as lobular panniculitis. In addition, neutrophils may comprise a large proportion of the infiltrate, especially in early lesions. Septal fibrosis and calcification of fat lobules may be observed in older lesions.

Sclerema neonatorum (SN) is the main clinical differential diagnosis of SCFN. SN primarily affects preterm neonates with low birth weight within the first week of life in the setting of sepsis, cyanosis, respiratory and gastrointestinal diseases, or congenital anomalies. It is characterized by hardening of the skin beginning with the buttocks, thighs, or trunk and often becomes more generalized. Lesions spare the palms, soles, and genitalia. The woody indurated skin hinders respiration and feeding, further worsening the prognosis of an already very ill newborn.

Microscopically, the radially arranged needle-shaped crystals seen in SCFN can also be observed in sclerema neonatorum and post-steroid panniculitis. However, there is little to no inflammatory infiltrate in sclerema neonatorum. Special stains for microorganisms, tissue cultures, and observance for systemic signs and symptoms are helpful in differentiating neutrophil-rich variant of SCFN from an infection.

Post-steroid panniculitis may be histologically indistinguishable from SCFN, although the former sometimes exhibits less adipocytes and histiocytes containing needle-shaped clefts. Post-steroid panniculitis is observed, however, in a completely different clinical setting than SCFN, occurring after a sudden decrease or complete withdrawal of high doses of systemic corticosteroids.

Although SCFN has an excellent prognosis and often spontaneously resolves over several weeks, it has been associated with several metabolic complications such as hypoglycemia, thrombocytopenia, anemia, and hypertriglyceridemia. Complications related to hypercalcemia are of most concern clinically, as it is associated with increased morbidity and mortality due to metastatic visceral calcifications as well as cardiac and/or renal failure. SCFN-associated hypercalcemia is believed to be a result of macrophages in the necrotic fat lobules producing 1,25 dihydroxyvitamin D3, thereby increasing intestinal calcium uptake.

SCFN-associated hypercalcemia often has a delayed onset, occurring on average in the fourth to sixth weeks of life, when the skin lesions begin to resolve; it may persist until the sixth month of life. Monitoring total and ionized calcium levels for several months after diagnosis is recommended, with tests at the time of diagnosis, every one to two weeks for one month, then monthly until about six months of age. Hypercalcemia may be co-managed with an endocrinologist and may involve hydration, calcium-wasting diuretics, such as furosemide, and dietary restriction of vitamin D and calcium. Systemic corticosteroids, calcitonin, and bisphosphonates may be necessary for recalcitrant cases.

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NOTES

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HISTORY OF PRESENT ILLNESS

A 56-year-old female presented with a one year history of a pruritic perianal rash. She was treated with preparation H for presumed hemorrhoids and Vaseline with no improvement. She then developed a scaly perianal rash with crusting and was treated topically for a perianal fungal infection without improvement. The patient reported associated itching that was worse at night and after showers and also noted occasional blood on the toilet paper after stools. She reported normal stools and no change in bowel habits. A review of systems was otherwise negative.

PAST MEDICAL HISTORY

Hypertension
Hyperlipidemia
Gastroesophageal reflux disease
Ovarian cyst
Rosacea

MEDICATIONS

Calcium/vitamin D
Esomeprazole
Lisinopril
Simvastatin
Sulfacetamide-sulfur topical wash

ALLERGIES

Cefazolin
Betadine
Codeine

FAMILY HISTORY

No history of cancer

SOCIAL HISTORY

Denies alcohol, tobacco or illicit drug use

PHYSICAL EXAMINATION

The patient was well appearing. On the right perianal buttock extending toward the anal canal, there was a single, well-demarcated, scaly, lichenified pink plaque.

DERMATOPATHOLOGY

Histologic sections showed a proliferation of cells with atypical nuclei and clear cytoplasm located throughout the epidermis. Immunohistochemistry revealed positivity for CK7, CK20, and CDX2. The cells were negative for Melan-A and HMB45.

ADDITIONAL STUDIES

CBC, CMP, CA125, CEA, and celiac panel normal
CT scan abdomen/pelvis and PET scan with no evidence of internal malignancy or metastatic disease

Colonoscopy normal
Cervical cytology, HPV mRNA, and HPV DNA normal or negative
Mammogram normal

DIAGNOSIS

Primary perianal extramammary Paget's disease (EMPD), recurrent after wide local excision and involving the anal canal

TREATMENT AND COURSE

The patient was initially diagnosed with EMPD in July of 2012. She underwent wide local excision with Mohs micrographic tissue processing of the borders (clear margins at stage two) with anorectal advancement flap and partial vaginectomy along with reconstruction of the perianal region with split thickness skin graft.

In November of 2016, the patient presented with new symptoms of bleeding when wiping, pruritus, and rectal urgency for three to four months. On physical exam, the patient had scaly patches on the anus suspicious for recurrence. Biopsies of anal margin and anal canal revealed recurrent EMPD involving the anal canal. Repeat evaluation for internal malignancy including CT abdomen/pelvis, cervical cancer screening, mammogram and colonoscopy was negative.

The patient refused further surgical intervention or radiation, so she was treated with 16 weeks of topical imiquimod 5% cream as well as low-dose oral cimetidine employed for its immunomodulating properties. To address the internal anal aspect of EMPD, the patient was instructed to lubricate glycerin suppositories with imiquimod and insert them into the anus. Initial dosing of imiquimod 5% cream was started at one packet inserted into the anus once weekly and one packet applied around the anus once daily, but the patient reported flu-like symptoms as well as redness and irritation of the skin. Dosing was adjusted based on the patient's inflammatory response and tolerability. She applied one packet around the anus two to three times weekly and inserted one packet into the anal canal once weekly for the majority of the 16-week treatment course. The cimetidine was initially dosed at 800 mg by mouth one to two times daily as tolerated, but due to stomach irritation the patient decreased her dosing to 800 mg two to three times weekly.

Repeat punch biopsies of the anal canal, right lateral anal margin and left lateral anal margin were taken four weeks after discontinuing imiquimod treatment and showed no residual EMPD. The patient was resumed on imiquimod to be applied once weekly into the anal canal and around the anus for a planned prolonged course of at least one year. She was continued on 800 mg oral cimetidine three times weekly to daily as tolerated. We plan to check a yearly serum CEA and perform yearly follow up anoscope or colonoscopy as well as regular clinical monitoring.

DISCUSSION

EMPD is a rare intraepithelial adenocarcinoma. There is a predilection for Caucasian females, and the average age of presentation is 50 to 80 years. The vulva (65%), perianal region (20%), scrotum, penis and perineum are the most commonly affected sites. Incidence of EMPD is unknown, as there are only a few hundred cases reported in the literature.

EMPD can be primary, arising in the epidermis at the sweat gland level or from primitive epidermal basal cells, or secondary, due to Pagetoid spread of malignant cells from an adjacent or contiguous underlying adnexal adenocarcinoma or visceral malignancy. While primary EMPD is not associated with an underlying adenocarcinoma, it may become invasive, infiltrate the dermis or metastasize via the lymphatics. There are several prognostic factors of EMPD that are associated with greater risk of death including the presence of dermal invasion, elevated CEA levels, nodules in the primary lesion, and bilateral lymph node metastasis.

Secondary EMPD is associated with underlying malignancies which often correlate with the affected site. Perianal Paget's, the most common presentation of EMPD in men, is associated with an underlying malignancy in about one third of cases, and it is most often anorectal carcinoma or another gastrointestinal tract malignancy. Vulvar Paget's, the most common presentation of EMPD in women, is most often associated with genitourinary tract malignancies. While underlying malignancies are generally gastrointestinal or urothelial, they can also be of cervical, prostatic, ovarian or endometrial origin.

Clinically EMPD presents as a chronic, well-demarcated, scaly, eczematous, often expanding plaque that may have crusting, discharge, erosions or ulcerations. Patients may report associated pruritus, burning or tenderness, or the lesions can be asymptomatic. EMPD is often misdiagnosed as dermatitis or lichen simplex chronicus, leading to a median delay of two years for diagnosis.

Histologically, vacuolated Paget cells are seen in the epidermis as single cells in a buckshot distribution or in nests. Immunohistological staining is often necessary for diagnosis and can help differentiate between primary and secondary disease. Paget's cells generally stain positive for CK7, which helps differentiate Paget's from Bowen's disease. Paget's cells stain negative for S100, MART-1 and HMB-45 which helps differentiate it from melanoma. Positive staining for CK20 and CDX2, markers for gastrointestinal adenocarcinoma, can favor secondary over primary EMPD. However, these stains are not entirely specific, and positive staining in primary EMPD has been reported.

Once a diagnosis of EMPD is made, it is important to perform a thorough work-up for possible associated internal malignancy. Complete history, skin, and lymph node exam; rectal, pelvic and breast examination; pelvic ultrasound with Pap smear; mammogram; colonoscopy; cystoscopy; serum CEA and serum PSA; and whole-body CT and PET scan should be considered. Internal malignancy is approximately five times more likely when there is involvement of the anal region as compared to the vulva, penis or scrotum.

Currently mainstay treatment is wide local excision with lateral margins 2-3 cm beyond the clinically affected area. However, margins are often positive, and local recurrence rate is high (33-66%). There are a variety of other therapies that have been reported to be effective in the literature. Mohs micrographic surgery, while more time consuming, has shown a decreased recurrence rate (8-27%). Radiation, topical chemotherapeutics (imiquimod, 5-fluorouracil, bleomycin), photodynamic therapy and CO2 laser ablation have been used alone or in combination. There are no randomized controlled trials comparing surgery to other treatment options for EMPD.

Given our patient's involvement of the anal canal, repeat wide local excision or Mohs micrographic surgery would require anal resection and would be functionally impairing. The patient refused further surgical intervention as well as radiation. She was treated with a novel combination regimen consisting of 16 weeks of topical imiquimod concurrently with low-dose oral cimetidine and showed clinical and histologic clearance.

Previous literature has shown a good response with imiquimod 5% cream in patients with vulvar and periscrotal EMPD including a large systematic review which analyzed 63 cases of vulvar EMPD, nearly half of which were recurrent, and reported a response rate to imiquimod of 52-80%. Almost 70% achieved complete clearance on a regimen of three to four times weekly for a median of four months of treatment. However, there is minimal literature on the effectiveness of topical imiquimod in primary perianal disease. One case report of a 40-year old female treated with a three-times-per-week regimen for 16 weeks demonstrated complete clearance clinically and histologically on random biopsies of the perianal skin post-treatment. However, this patient developed metastatic lymph node recurrence 18 months after stopping imiquimod treatment.

Given the growing evidence suggesting disease control with imiquimod, we elected for this regimen for our patient, but we opted for the addition of concurrent oral cimetidine for its anti-cancer properties. The anti-cancer action of cimetidine, an H_2 receptor antagonist, has been shown in a broad range of pre-

clinical and clinical studies for a number of different cancer types. Four distinct mechanisms of action have been shown. Cimetidine has an anti-proliferative action on cancer cells by blocking histamine which has been shown to have a direct effect on cancer cell proliferation. It has immunomodulatory effects by reversing the immunosuppressive tumor microenvironment that is associated with histamine. An inhibitory effect on cancer cell adhesion to endothelial cells has been shown independent of it's histamine blocking activity. Lastly, an anti-angiogenic action has been shown by blocking the up-regulation of VEGF that is normally induced by histamine. It has also been postulated in the literature that there may be a synergistic effect of cimetidine with a range of other drugs including chemotherapeutics.

We were interested in cimetidine's anti-cancer properties specifically in the setting of colorectal cancer given the patient's involvement of the anal canal. The most impressive clinical trial data showed a dramatically increased survival for colorectal cancer patients treated with oral cimetidine (800 mg daily) and oral 5-fluorouracil (200 mg daily) for one year following curative resection. The cimetidine-treated group had a 10-year survival of 84.6% versus 49.8% for the 5-fluorouracil-only group.

We present this case of recurrent extramammary Paget's disease to highlight the clinical presentation, disease course and a novel alternative combination treatment regimen for this rare type of malignancy.

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HISTORY OF PRESENT ILLNESS

A 67-year-old Caucasian man with a past medical history of immune thrombocytopenia presented to the emergency department with a 12 hour history of blue-black blisters in the mouth and facial swelling. He awakened in the middle of the night due to oral pain, at which time he noticed blisters on the bilateral buccal mucosa. The pain progressively worsened throughout the day and prompted him to seek care at the emergency department. He had not tried to treat the blisters at home. He had bruising on the abdomen from his insulin injections but otherwise reported no rashes on the skin. He had no history of dermatologic disease. He had never had similar symptoms in the past. He denied new medications and use of dental appliances. Review of systems was positive for minor gum bleeding and dark tarry stool for 12 hours. Due to pain, he had decreased oral intake but felt otherwise well. His platelet count was normal at 230 K/uL seven months prior to presentation.

PAST MEDICAL HISTORY

History of immune thrombocytopenia
Poorly-controlled type II diabetes mellitus complicated by diabetic retinopathy
Hashimoto thyroiditis
Chronic kidney disease stage 3
Gastroesophageal reflux disease

MEDICATIONS

Amlodipine
Atorvastatin
Carvedilol
Codeine/Acetaminophen
Escitalopram
Insulin
Levothyroxine
Lisinopril
Magnesium
Omeprazole
Trazodone

ALLERGIES

No known drug allergies

FAMILY HISTORY

No family history of autoimmune, bleeding, or clotting disorders

SOCIAL HISTORY

45 pack year smoking history; quit in 1992
History of marijuana use; quit in 2002
No alcohol or illicit drug use

PHYSICAL EXAMINATION

Well-appearing elderly male with facial plethora and neck swelling.
Cutaneous examination was notable for a large ecchymosis on the right lateral chin and inferior cheek and two red ecchymotic plaques on the bilateral lower abdominal quadrants. Mucosal examination was notable for multiple soft, black-blue, well-demarcated, tender, non-blanching nodules of varying size with

red crusted centers on the bilateral buccal cheeks in some areas coalescing into large necrotic plaques. Numerous petechiae were noted on the dorsal surface of the tongue with a few tense violaceous bullae on the lateral edges.

DERMATOPATHOLOGY

Biopsy not obtained due to extreme thrombocytopenia

LABORATORY RESULTS

Laboratory Study	Patient Result	Reference Range
WBC	13.78	3.5 - 10.5 K/UL
HGB	14.0	13.0 - 17.5 GM/DL
HCT	40	38.0 - 54.0 %
PLT CNT	2.0	150 - 400 K/UL
INR	1.03	0.0 - 1.1
PT	13.8	12.2 - 14.4 seconds
aPTT	29.3	24 - 35 seconds

DIAGNOSIS

Wet purpura in the setting of relapsed immune thrombocytopenia

TREATMENT AND COURSE

In addition to dermatology, otolaryngology was consulted and performed a nasopharyngolaryngoscopy to rule out possible airway obstruction due to edema and bleeding, which revealed no other lesions aside from the oral mucosa. Initially, he was treated with methylprednisolone 80 mg IV and was transfused 2 units of platelets. The next morning his platelets had increased to 5 K/uL. He was transfused another unit of platelets, maintained on high dose steroids with oral prednisone 100 mg daily (1 mg/kg/day) and received IVIG. His platelet count increased to 20 K/uL the next day. The purpura on his oral mucosa improved, and he was discharged home on high dose prednisone with hematology-oncology follow-up. He recovered without incident. His platelet count obtained one month after discharge was normal.

DISCUSSION

Wet purpura are often diagnosed by clinical appearance alone. They have a wide variety of causes and necessitate a broad differential diagnosis on initial presentation. While wet purpura are sometimes associated with an underlying disease, they can also be an isolated finding in cases of trauma or angina bullosa hemorrhagica (ABH). ABH is an acute, benign condition characterized by painful subepithelial blood-filled blisters of the oral mucosa in an otherwise asymptomatic patient without a hematologic defect. In the absence of a history of trauma, their presence warrants an investigation into potential underlying causes such as hematologic disorders. These include hematologic malignancies as well as any causes of platelet dysfunction or coagulopathies (disseminated intravascular coagulation, heparin-induced thrombocytopenia, von Willebrand disease, bone marrow disorders, liver disease, medications, etc) may cause wet purpura, as evidenced by our patient with immune thrombocytopenia (ITP). Local or systemic infections and a wide variety of systemic diseases may also cause wet purpura, including neoplastic, inflammatory, and autoimmune processes.

Immune thrombocytopenia, previously known as idiopathic thrombocytopenic purpura, is an immune mediated, hematologic disorder which presents as an isolated low platelet count (<100 K/uL). Thrombocytopenia results from IgG autoantibodies directed at glycoproteins on platelets and megakaryocytes. These antibodies result in a reduced lifespan of platelets in the peripheral circulation and suppression of platelet production within the bone marrow due to damage of the megakaryocytes. Immune thrombocytopenia has an incidence rate of approximately 3.3 per 100,000 person years and affects children and adults at similar rates. It can be classified as primary, when no cause can be identified, or secondary, when a probable cause is identified such as a separate autoimmune disease, medication, immunodeficiency, chronic infection, or hematologic malignancy. In adults, ITP often does not have an identifiable trigger and is chronic in 80% of cases. Children with ITP often have an identifiable trigger such as infection 3-4 weeks prior and 80% of cases resolve within 1 year.

History, physical exam, complete blood count, and peripheral smear are essential to diagnosing ITP, which is a diagnosis of exclusion. Platelet counts are less than 100 K/uL and the peripheral smear is normal in cases of ITP, but it must be performed to exclude other causes of thrombocytopenia. HIV and hepatitis C serology should be obtained, as these diseases can frequently present with thrombocytopenia. Antiplatelet antibody testing given the heterogeneity of possible implicated antibodies.

While many patients with ITP are asymptomatic, bleeding is the most common manifestation and is present in two-thirds of patients, often presenting as purpura or petechiae on the extremities or occasionally, ecchymoses. These mucocutaneous findings may be seen on the nasal mucosa, oral cavity, GI tract, uterine lining, or any skin surface. Involvement of the oral mucosa with “wet purpura” usually indicates a more severe case of thrombocytopenia, often less than 10 K/uL. Intracranial bleeding is the most feared complication, but it occurs in less than 0.2% of children and 2% of adults. Children with ITP generally feel well and do not look ill but tend to have lower platelet counts, commonly less than 20 K/uL.

The goal of treatment is to minimize bleeding. Adults presenting with platelet counts greater than 30 K/uL usually do not have significant bleeding, and therefore rarely require treatment. First line therapies for cases that do require treatment include high-dose corticosteroids at one milligram per kilogram per day and intravenous immunoglobulin (IVIG). In the presence of life-threatening bleeds, large transfusions of platelets may be administered to help with clotting.

We present this case to highlight an unusual mucocutaneous finding that should prompt a workup for an underlying hematologic abnormality or alternate probable cause.

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HISTORY OF PRESENT ILLNESS

A 65-year-old male presented to the Dermatology clinic after developing an asymptomatic, rapidly enlarging, 1.5 centimeter pigmented lesion on his right shoulder. By the time of his appointment, several additional lesions had arisen on his trunk. The lesions were not pruritic but were enlarging at a rate of 1 mm per week, with about five new lesions forming every week over a period of one month. They were non-tender to palpation. The patient denied any recent travel or any affected close contacts. He denied having fevers, chills, respiratory symptoms, or other cutaneous complaints. His review of systems was otherwise unremarkable.

PAST MEDICAL HISTORY

No history of skin disease
Hypertension
Atrial fibrillation
Diabetes mellitus type 2
Hypercholesterolemia
Benign lung nodules

MEDICATIONS

Aspirin
Amlodipine
Bisoprolol
Enalapril
Glipizide
Hydrochlorothiazide
Metformin

ALLERGIES

Iodine/IV contrast

FAMILY HISTORY

Significant for a maternal grandmother with leukemia, unknown type

SOCIAL HISTORY

Retired, previously employed as a firefighter. No tobacco or illicit drug use. Moderate alcohol use.

PHYSICAL EXAMINATION

On his right posterior shoulder is a hyperpigmented nodule with mild hyperkeratosis, with scattered erythematous-to-brown plaques on the trunk and back.

DERMATOPATHOLOGY

Histopathological analysis of a characteristic lesion from the trunk demonstrated a dense dermal adnexocentric infiltrate of medium to large cells with irregular angulated nuclei and scant cytoplasm, which spared the epidermis. Additionally, there was an associated inflammatory infiltrate with scattered B and T-cells. On immunohistochemistry, the tumor cells were positive for CD4, CD56, CD123 and leukocyte common antigen (LCA) and were negative for CD3, myeloperoxidase (MPO), and *in-situ* hybridization for Ebstein-Barr virus (Table 1).

Positive Markers	Negative Markers	
CD4	CD3	CD67
CD56	CD5	CD79A
CD123	CD7	CD117
LCA	CD8	Bcl-2
	CD30	MPO
	CD34	TCL-1

Table 1: Immunohistochemical markers present in first skin biopsy

Positive Markers	Negative Markers	
CD4	CD3	CD20
CD56	CD5	CD23
Bcl-2	CD8	Bcl-6
		MUM-1

Table 2: Immunohistochemical markers present in second skin biopsy

ADDITIONAL STUDIES

Routine laboratory tests including complete blood count with differential, lactate dehydrogenase, renal and liver function were within normal limits. A bone marrow biopsy and whole body PET-CT scan were performed and demonstrated no evidence of extracutaneous involvement.

DIAGNOSIS

Blastic plasmacytoid dendritic cell neoplasm (BPDCN), which has previously been termed "blastic natural killer (NK) cell lymphoma" or "$CD4^+/CD56^+$ hematodermic neoplasm."

TREATMENT AND COURSE

The patient was treated systemically with two rounds of chemotherapy with cyclophosphamide/doxorubicin/vincristine/prednisone (CHOP) in July and August of 2015 and achieved complete remission and resolution of his skin lesions. With the exception of mild hyperglycemia, toxicity was low. He underwent autologous stem cell transplant in September 2015. One year post-transplant, he returned to clinic with numerous scattered urticarial brownish-red plaques on his chest, back, and bilateral shoulders with extension to his neck. Skin biopsy was again obtained (Table 2). In contrast to the first biopsy, the tumor cells were now positive for Bcl-2, and treatment was initiated with venetoclax, a Bcl-2 inhibitor commonly employed to treat chronic lymphocytic leukemia (CLL). Eleven months later, he remains in clinical remission, without any clinical recurrence of lesions.

DISCUSSION

Blastic plasmacytoid dendritic cell neoplasm is a rare hematodermic malignancy that has been renamed several times since it was first reported in 1994. Initially, cutaneous BPDCN was classified as a T-cell lymphoma based on its $CD4^+$ and $CD56^+$ expression, two prominent markers expressed by cells of T-cell derivation. Subsequently, the lack of other conventional T-cell antigens, such as CD3, precipitated reclassification of this neoplasm as a primary cutaneous NK/T-cell lymphoma. In 2008, researchers discovered a strong presence of interleukin-3 receptor alpha chain (CD123) in this neoplasm. Since CD123 is commonly expressed in plasmacytoid dendritic cells (PDCs), BPDCN was reclassified as a unique myeloid derived PDC neoplasm. Plasmacytoid dendritic cells are mononuclear cells that are produced in the bone marrow, accumulate in lymph nodes when the immune system is activated, and secrete type-1 interferon in response to nucleic acids. These unusual cells, which account for less than 1% of mononuclear cells, also present antigens to T-cells, bridging the innate and adaptive immune systems.

BPDCN typically affects elderly adult males, with the reported mean age at diagnosis ranging from 60 to 67 years. There are two main patterns of evolution of BPDCN. The majority of cases (90%) are characterized by the early presence of multiple skin nodules, followed by rapid tumor dissemination. The second pattern is much less common (~10%) and may initially present as a leukemic phase without any skin involvement. Skin lesions most commonly involve the trunk and extremities, often sparing the maxillofacial region. The lesions can appear as patches, plaques, or nodules and are typically brown to violet in color, resembling ecchymoses.

Histologically, BPDCN is characterized by diffuse, monomorphic infiltrate of medium-sized immature blastoid cells with round nuclei, finely dispersed chromatin, and absent or indistinct nucleoli. Typically, these cells infiltrate the dermis and the subcutaneous tissue, and spare the epidermis. Immunohistochemical analysis is the most reliable method to confirm diagnosis and guide treatment. Typically, a diagnosis of BDPCN requires positivity for CD4, CD56, CD123, and T-cell lymphoma-1 (TCL-1) without any lineage-specific markers of T cells or B cells. Although one or two of the markers may not stain positive in certain cases, it is uncommon for all four to be negative.

Although over 90% of patients diagnosed with BPDCN present with cutaneous lesions, this malignancy tends to spread quickly throughout the peripheral blood and bone marrow. From the time of diagnosis, patients typically have a median survival of 9-13 months. Patients with BPDCN have an extremely poor prognosis, as most patients are older and there are no effective targeted therapies.

Currently, there is no standardized treatment for this neoplasm. Initially, cutaneous lesions can be treated with focal radiation, oral glucocorticoids, or chemotherapy. Although skin-limited disease has been reported to have a better prognosis than extracutaneous disease, it should be treated aggressively, since leukemic dissemination is inevitable. Patients with BPDCN are usually treated with regimens used for other hematopoietic malignancies such as non-Hodgkin's lymphoma (CHOP) and acute myeloid leukemia and lymphoma (CHOP alternating with methotrexate and cytarabine [hyper-CVAD]). Typically, patients initially respond well to chemotherapy with complete resolution of skin lesions, but frequently relapse due to development of chemotherapeutic drug resistance.

Research into alternative targeted therapies to treat BPDCN is currently underway. Although some cases of BPDCN have been reported with positivity for Bcl-2, only one study has reported the effect of targeted therapy aimed at this protein. A study by Montero et al. demonstrated that BPDCN was dependent on the anti-apoptotic gene Bcl-2 and was significantly sensitive to Bcl-2 inhibition with venetoclax. They reported two patients with chemotherapy-refractory disease who experienced decreased cutaneous involvement and decreased lymphadenopathy following treatment with venetoclax. In fact, they found the BPDCN response to venetoclax to be similar to that of CLL.

We present a case of BPDCN that was treated with two rounds of CHOP chemotherapy, autologous stem cell transplant, and an anti-Bcl2 agent, venetoclax. At eleven months post-treatment with targeted therapy, the patient exhibits complete resolution of previous skin findings and remains free of new cutaneous lesions. The patient responded extremely well to treatment with venetoclax, and we hope to continue to see a positive response. Though few reports have described the off-label use of venetoclax for the treatment for BPDCN, this case supports novel therapeutic possibilities for BPDCN patients unresponsive to conventional treatment modalities.

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HISTORY OF PRESENT ILLNESS

A 67-year-old Caucasian woman presented with an eight-month history of three pruritic, pink papules on her right upper chest, right flank, and right waistline. There was initially concern for possible arthropod bites; however, the lesions persisted and slowly grew in size, becoming more nodular in nature. The patient was ultimately referred to our clinic, at which point the lesions had a scar-like nature to them.

PAST MEDICAL HISTORY

Eczema
Hypothyroidism

MEDICATIONS

Levothyroxine
Simvastatin
Naproxen sodium
Probiotics
Multivitamin

ALLERGIES

No known drug allergies

FAMILY HISTORY

No significant family history

SOCIAL HISTORY

The patient lives at home with her husband who is otherwise healthy. No tobacco, alcohol, or illicit drug use. No other significant social history.

PHYSICAL EXAMINATION

Well-appearing 67-year-old Caucasian woman with three pink nodules located on her chest, right flank, and right waistline.

LABORATORY RESULTS

CBC with differential and CMP were unremarkable. ANA was negative.

DERMATOPATHOLOGY

Initial punch biopsy of the right flank was performed. Histopathologic examination revealed superficial and deep perivascular and interstitial inflammation with lymphoid follicle formation and numerous eosinophils. In addition, the dermis showed a diffuse proliferation of vessels in the dermis lined by plump endothelial cells demonstrating cytoplasmic vacuolization. Immunohistochemical stains showed that the CD20+ B cells were predominantly confined to the lymphoid follicles. The reactive germinal centers were positive for CD10 and BCL-6 and were negative for BCL-2. The inter-follicular lymphocytic infiltrate was predominantly composed of T-cells positive for CD3, CD5, and CD7 with a CD4:CD8 ratio of 3:1.

DIAGNOSIS

Angiolymphoid hyperplasia with eosinophilia (ALHE)

TREATMENT AND COURSE

The three lesions were surgically excised and sent for histopathological review, confirming the diagnosis of ALHE for all three lesions. The areas were subsequently treated with three sessions of pulsed dye laser (PDL) therapy (Candela VBeam 595 nm). The first two treatments utilized 7.5J of energy and the last treatment used 7J of energy. The patient had a satisfactory cosmetic outcome, and there has been no evidence of recurrence at sixteen months follow-up.

DISCUSSION

Angiolymphoid hyperplasia with eosinophilia (ALHE) is an uncommon benign vascular proliferation characterized by isolated or grouped red-brown papules or nodules, most often located on the head or neck. Lesions are frequently asymptomatic but may be pruritic or painful. While the incidence and prevalence of ALHE is unknown, ALHE is more common in Asian populations. It is a condition predominantly found in 20- to 50-year-old adults. Many sources cite a sex predilection for females; however, a recent systemic review of the literature revealed no gender bias.

The pathogenesis of ALHE is largely unknown. Some consider ALHE a benign neoplasm of endothelial cells, while others suggest it is an inflammatory vascular reaction to external trauma. There have also been reports of onset or worsening of ALHE nodules with initiation of oral contraceptives and during pregnancy, implicating hyperestrogenemia in the pathogenesis. T-cell clonality has been demonstrated within a subset of cases, and there are a few published cases of synchronous or metasynchronous T-cell lymphoma arising in ALHE patients, suggesting that ALHE could be a low-grade lymphoproliferative disorder or at least a specific variant of reactive lymphoid hyperplasia. Lastly, tortuous or damaged vessels can be seen at the base of lesions, suggesting a possible role of arteriovenous malformation in ALHE. Ultimately, the uncommon and benign nature of ALHE has contributed to a lack of disease understanding.

Histologically, ALHE is characterized by an expansive proliferation of small, capillary-sized vessels with thickened walls and characteristic plump epithelioid endothelial cells with cytoplasmic vacuolization. Surrounding the small vessels is a variably dense inflammatory infiltrate composed of lymphocytes with numerous eosinophils. Nodular lymphoid aggregates occasionally form reactive germinal centers.

ALHE was once thought to be a variant of Kimura’s disease, or eosinophilic hyperplastic lymphogranuloma. However, ALHE is now accepted as a separate disease entity. Contrasted with ALHE, Kimura’s disease presents as unilateral and painless cervical lymphadenopathy and/or subcutaneous lymphoid masses, usually on the head and neck. Beyond involvement of nodal tissue verses the dermis and subcutis, individuals with Kimura’s disease tend to have elevated IgE levels and almost always have peripheral eosinophilia. Histologic distinction between ALHE and Kimura's disease can be challenging. ALHE more characteristically shows dermal vessels lined by epithelioid endothelial cells with cytoplasmic vacuolation, while the vessels in Kimura's disease typically lack these changes. Histologic features favoring Kimura's disease include eosinophil microabscesses and stromal sclerosis. Both conditions can exhibit lymphoid follicle formation.

Given the uncommon nature of ALHE, there is a lack of evidence to guide therapy. While lesions are completely benign, they do not spontaneously regress, and treatment is often undertaken for symptomatic and/or cosmetic reasons. Surgical excision is the mainstay of treatment, but recurrence is common. A recent review showed recurrence in 40% of cases following simple surgical excision, with a four-year mean time to recurrence. Importantly, this same review found that steroids are an ineffective treatment modality, with a treatment failure rate of 79 to 98%. Numerous other therapeutic approaches have been described. Notably, treatment with vascular-specific pulse-dye lasers has been shown effective, with a recurrence rate only slightly higher than surgical excision.

Our patient’s atypical cutaneous findings of an uncommon entity, ALHE, presented a diagnostic challenge. Given relatively high recurrence rates with surgical excision and pulsed dye laser therapy,

alone, we employed a dual therapy approach combining both of these modalities. Ultimately, our patient was pleased with the cosmetic outcome of her treatment and has had no signs of recurrence at sixteen months follow-up.

We present this case of angiolymphoid hyperplasia with eosinophilia, an uncommon entity, for clinical interest and to highlight treatment options.

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NOTES

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PATIENT A

HISTORY OF PRESENT ILLNESS

A 75-year-old male presented to dermatology for evaluation of multiple skin-colored growths on the face and neck. The lesions first appeared in his twenties and are overall asymptomatic.

PAST MEDICAL HISTORY

Cystic lung disease
Multiple spontaneous pneumothoraces
Hyperlipidemia
Venous thromboembolism
Diabetes Mellitus Type II
Hepatic cysts

MEDICATIONS

Fluocinolone ointment

ALLERGIES

None

FAMILY HISTORY

Father with similar skin findings, cancer of the kidney, spleen and stomach

SOCIAL HISTORY

No tobacco, alcohol, or illicit drug use

PHYSICAL EXAMINATION

Face, neck, and upper back with multiple discrete skin-colored firm papules

PATHOLOGY

Benign cutaneous neoplasm with follicular differentiation. Well circumscribed, non-encapsulated tumor with a well-formed, cystically dilated hair follicle with keratinous debris. There are thin epithelial strands branching from the central portion of the tumor and surrounding fibrotic stroma.

DIAGNOSIS

Birt-Hogg-Dubé syndrome

PATIENT B

HISTORY OF PRESENT ILLNESS

A 55-year-old male presented to dermatology for evaluation and treatment of asymptomatic skin-colored papules on the face. They started appearing about 30 years prior. They were asymptomatic, but the patient requested treatment for cosmesis.

PAST MEDICAL HISTORY

Osteoarthritis
Alcoholic cirrhosis
Deep vein thrombosis

Anxiety
Essential hypertension
Hyperlipidemia

MEDICATIONS
Diclofenac sodium
Enalapril
Hydrocodone/acetaminophen
Pantoprazole
Sertraline
Simvastatin

ALLERGIES
None

FAMILY HISTORY
Father with lung cancer (smoker)

SOCIAL HISTORY
Occasional alcohol use

PHYSICAL EXAMINATION
Fitzpatrick phototype II
Cheeks, chin, temples with skin-colored papules

DIAGNOSIS
Birt-Hogg-Dubé Syndrome

TREATMENT AND COURSE
The patient received laser and spot hyfrecation treatments over a two month period. One treatment was performed using a nonablative fractional resurfacing combination device with the following settings: 1550 nm erbium:glass laser at 40 mJ, treatment level 7 with 8 passes. Three treatments were performed with electrodessication at a low setting. Treated areas had a more normal skin texture and color with an overall significant cosmetic improvement.

DISCUSSION
Birt-Hogg-Dubé Syndrome (BHD) is a rare autosomal dominant genodermatosis affecting approximately 1/200,000 people worldwide. It is caused by a germline mutation in the *FLCN* gene on chromosome 17p11.2, encoding the tumor suppressor folliculin.

Diagnostic criteria according to the European Birt-Hogg-Dubé consortium includes meeting either one major or two minor criteria: Major criteria, 1) At least five fibrofolliculomas or trichodiscomas, at least one histologically confirmed, of adult onset, 2) Pathogenic *FLCN* germline mutation; Minor criteria, 1) Multiple lung cysts: bilateral nasally located lung cysts with no other apparent cause, with or without spontaneous primary pneumothorax, 2) Renal cancer: early onset (<50 years) or multifocal or bilateral renal cancer or renal cancer of mixed chromophobe and oncocytic histology, 3) A first degree relative with BHD.

Cutaneous findings include the characteristic triad of fibrofolliculomas, trichodiscomas, and acrochordons. Fibrofolliculomas and trichodiscomas are benign hamartomas of the hair follicle that are thought to represent the same entity on a histologic spectrum. Clinically, they appear as small skin-colored dome shaped papules most often affecting the face, neck and upper torso in the second or third decade of life. These benign lesions do not require treatment, but patients often seek treatment for

cosmesis. Treatment options include carbon dioxide laser ablation, dermabrasion or superficial electrodessication. Patients often require multiple treatments, as recurrence is common.

Pulmonary involvement is common and usually presents in the fourth to fifth decade of life. Approximately 80% of patients develop pulmonary cysts with multiple basilar cysts and a 50-fold increased risk of spontaneous pneumothorax. The risk of pneumothorax increases with increased number, volume and diameter of the lung cysts. Carriers of mutated *FLCN* gene can develop pneumothoraces much earlier in life, with reports of patients as young as age 7. Baseline high-resolution chest CT is recommended to better characterize the extent of the disease and facilitate patient education. There is no established lung cancer association.

Patients with BHD have a seven-fold increased risk of developing renal tumors, affecting 12%-34% of patients. The mean age of onset is 50 years (range: 30-70 years) with a male predominance. Tumors are slow growing and can be bilateral, unilateral, or multifocal. The most common type of renal tumors are chromophobe tumors; however, hybrid oncocytic tumors, oncocytoma, papillary renal cell carcinoma and clear cell renal cell carcinoma have also been described. Renal tumors associated with BHD usually follow a favorable clinical course. Abdominal CT or MRI with IV contrast is recommended to evaluate for renal masses.

Management of patients with BHD should involve a multidisciplinary approach that includes dermatology, nephrology, pulmonology and genetic counseling. Genetic testing and counseling should be offered to patients with suspected BHD. Surveillance is recommended starting at age 20 in patients with *FLCN* mutations. Renal surveillance with an MRI every 12-36 months beginning at age 20 is recommended. Patients are strongly encouraged not to smoke as this can be a risk factor for pneumothorax. Patients should also be counseled on the risk of pneumothorax development with air travel and scuba diving.

We present this case series of Birt-Hogg-Dubé syndrome for clinical interest and to demonstrate an effective approach to treating cutaneous manifestations of the disease.

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NOTES

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HISTORY OF PRESENT ILLNESS

A 75-year-old Caucasian female with a history of rheumatoid arthritis presented with multiple painful ulcerations. The ulcerations affected her arms, upper back, abdomen, and legs. She had been developing ulcers for the last three years, but they were increasing in number and severity over the last six months. She denied any trauma or medical procedures prior to the onset of the ulcerations. The lesions started as itchy red areas that became swollen, ulcerated, and then painful. They healed slowly and resolved with atrophic scars. At any given time, she had lesions in various stages of development. She had seen multiple dermatologists in the past and had been on various treatments including cephalexin, doxycycline, methotrexate, dapsone, and hydroxychloroquine without any improvement in her lesions. She had a history of rheumatoid arthritis which had been chronically treated with prolonged courses of prednisone, and she was started leflunomide three months prior by her rheumatologist.

PAST MEDICAL HISTORY

Coronary artery disease with stent placement
Rheumatoid arthritis
Depression
Cholecystectomy
Knee replacement
L4-L5 spine surgery

MEDICATIONS

Leflunomide
Prednisone
Metoprolol succinate
Sertraline
Tramadol
Rosuvastatin

ALLERGIES

Amlodipine, dapsone, lisinopril, losartan, neomycin, ranitidine

FAMILY HISTORY

No history of skin cancer or autoimmune diseases
Daughter with B cell lymphoma in remission
Father with bladder cancer (passed away at age 85)
Mother with leukemia (passed away at age 95)

SOCIAL HISTORY

No tobacco or use alcohol. No history of intravenous drug use.
Retired registered nurse
Enjoys gardening

REVIEW OF SYSTEMS

No fevers, chills, chest pain, cough, nausea, vomiting, night sweats, or other symptoms

PHYSICAL EXAMINATION
Well-appearing elderly female.
Upper back, abdomen, and bilateral upper extremities and lower extremities with scattered violaceous to erythematous plaques, some with punched out ulcerations with yellow fibrinous bases and scattered pink atrophic scars

DERMATOPATHOLOGY
Initial biopsy showed a superficial perivascular inflammation with primarily lymphocytes and mucin deposition. Repeat biopsy showed a lobular and septal panniculitis with mixed inflammation including neutrophils, with abscess formation and necrosis. Ziehl-Neelsen stained positive for organisms. PCR was positive for *Mycobacterium chelonae.*

ADDITIONAL STUDIES
Complete blood count with differential: unremarkable
Antinuclear antibodies: negative

Tissue culture showed rapidly growing mycobacterium species with final identification as *M. chelonae*

Acid fast bacilli blood culture: negative

DIAGNOSIS
Disseminated cutaneous *Mycobacterium chelonae* infection

TREATMENT AND COURSE
The patient was sent to infectious disease clinic and was started empirically on azithromycin and moxiflocacin, and she was instructed to wean off her prednisone. Her regimen was changed to clarithromycin twice daily after culture susceptibilities were available. She still was getting new lesions, so imipenem was added, but she was unable to tolerate imipenem and discontinued it. Her leflunamide was also discontinued at that time, and she has been on monotherapy with clarithromycin twice daily. Her skin lesions are improving gradually, but she still has flares during which she develops new skin lesions. Overall, she believes the rate she is developing new skin lesions is decreasing.

DISCUSSION
Mycobacterium chelonae is a non-tuberculous mycobacterium species that can manifest with a variety of infections. *M. chelonae* grows quickly in culture and is grouped with other non-tuberculous mycobacterial species such as *M. fortuitum, M. abscessus, M. mucogenicum, M. mageritense,* and *M. wolinskyi* into the group known as rapidly growing mycobacteria (RGM). Of the RGM, the vast majority of infections are caused by *M. chelonae and M. fortuitum.* Initially *M. chelonae* and *M. abscessus* were considered identical, but some genetic and susceptibility profile differences have been identified between the two groups.

M. chelonae is a saprophyte found ubiquitously in the environment in soil, water, dust, and animals. It is most commonly associated with skin and soft tissue infections, but it has also been found to cause pulmonary disease, endocarditis, keratitis, and osteomyelitis. Infection occurs in both immunocompromised and immunocompetent individuals, especially after trauma or medical procedures. Non-tuberculous mycobacterial infections are non-reportable, so true prevalence is unknown, but in some parts of the United States *M. chelonae* infection prevalence is estimated to be between 0.08-.2 cases per 100,000 cases. The incidence and prevalence of infections are increasing over time.

Cutaneous infection manifests as three main subsets: localized, catheter-related, or disseminated. Localized infection is most often associated with immunocompetent hosts after trauma, surgery, or other medical interventions. There have been cases in the literature of infection following procedures such as sclerotherapy, liposuction, filler injections, tattooing, and breast implants. Disseminated infections

primarily occur in immunosuppressed patients, especially patients on corticosteroids. In one study, 92% of patients with disseminated cutaneous *M. chelonae* infections had received corticosteroids in the past. Disseminated cutaneous infection presents in one of two clinical scenarios. Patients who are immunosuppressed with underlying conditions such as renal transplant or acute leukemia often present acutely ill with skin findings, fever and other systemic symptoms, positive blood and bone marrow cultures, and high mortality. The majority of patients, however, present with a more indolent course with chronic skin lesions, few to no systemic symptoms, negative blood cultures, and slow response to therapy.

All forms of cutaneous *M. chelonae* infection can present with a variety of physical exam findings including cellulitis, ulcers, nodules, sporotrichoid lesions, abscesses, papules, and pustules. *M. chelonae* grows optimally slightly lower temperatures than body temperature, so lesions often favor the extremities, but more proximal lesions are found in disseminated disease. Presence of greater than five skin lesions is indicative of disseminated cutaneous disease. Cutaneous lesions are chronic and are often present for months to years before a definitive diagnosis is established.

The histopathology of lesions is highly variable depending on the clinical presentation, but lesions will often show neutrophilic microabscesses and granuloma formation with foreign body cells and necrosis. Organisms may be detected on Fite or Ziehl-Neelson stains and with polymerase chain reaction, but the gold standard for diagnosis involves culture and genetic testing.

Treatment of cutaneous *M. chelonae* consists primarily of extended courses of antimicrobial therapy with some reports in the literature requiring six months or more of therapy before resolution. Antimicrobial therapy should be guided by susceptibilities obtained from laboratory testing. Recommended empiric treatments include multidrug therapy consisting of clarithromycin with the addition of imipenem, tobramycin, or amikacin due to low rates of resistance amongst *M. chelonae* isolates. Monotherapy with clarithromycin can be effective, but a case of acquired resistance with monotherapy has been reported. Other therapeutic considerations include removal of foreign bodies, catheters, and surgical debridement when necessary. Recalcitrant lesions may also be treated with surgery, cryosurgery, or thermal therapy.

We present this case of disseminated cutaneous *Mycobacterium chelonae* infection to highlight a rare infection that presents primarily with cutaneous findings and for clinical interest.

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HISTORY OF PRESENT ILLNESS

A 60-year-old male with a long history of enlarging and multiplying fatty deposits presents for discussion of non-surgical treatment options for his condition. The tumors are growing slowly and seem to be predominantly located on his neck, shoulders, proximal arms, and upper trunk. They are asymptomatic, though he feels they are unsightly and make it hard to wear clothing at times. He has had numerous excisions and at least two liposuction procedures and explains that he is tired and frustrated from all of the cutting. Otherwise, he believes he is healthy. He is not having sensory or motor weakness, difficulty breathing, and is without other cutaneous concerns. Though he does not presently drink alcohol, he reports regular use of an unspecified amount in the distant past.

PAST MEDICAL HISTORY

Approximately twenty lipoma excisions starting in his thirties
Liposuction (’08, ‘90s)
Hypercholesterolemia (currently well managed by diet and exercise)

MEDICATIONS

No current medications

ALLERGIES

No known allergies

FAMILY HISTORY

No confirmed family history of similar condition

SOCIAL HISTORY

The patient worked as an information technology technician but is now retired. He has no recent history of alcohol, tobacco, or illicit drug use.

PHYSICAL EXAMINATION

The patient appears to be in no distress. He has multiple large mobile fatty masses present symmetrically and bilaterally on his shoulders, superior torso, back, and bilateral upper arms. Of note, his lower half is significantly less involved. Additionally, a similar smaller mass is appreciated on the neck with an inferior linear scar. Various surgical scars are observed scattered on the cephalic one-third of his body.

LABORATORY STUDIES

The patient’s complete blood count, complete metabolic panel, hemoglobin A1C, and lipid levels are all within normal limits.

DIAGNOSIS

Benign symmetrical lipomatosis (BSL, e.g. Madelung disease)

TREATMENT AND COURSE

The patient’s diagnosis of BSL was affirmed in our clinic. He has a history of multiple treatment regimens which met with variable success. He did not want additional surgical intervention due to exhaustion from the procedures and their lengthy recovery time. However, he still wanted further management for the most bothersome lesions. We discussed an off-label usage of an injectable treatment, deoxycholic acid. Since then, he has been receiving 3 milliliters (mL) of deoxycholic acid into lipomas in the bilateral upper

arms and right abdomen at an increment of approximately once monthly. At present, he has had four treatments and is pleased with his progress.

DISCUSSION

Benign symmetrical lipomatosis (BSL) is a rare and disfiguring disorder that affects approximately 1 in 25,000. Often beginning in the second to fourth decade of life, BSL has shown a male predominance. While the exact etiopathogenesis has not been elucidated, mutations in mitochondrial tRNA, specifically the lysine gene, as well as dysfunction of signaling in brown adiposities has been suggested. Furthermore, chronic alcohol consumption has been found to be commonly associated and worsens the condition.

BSL is characterized by the growth of lipomas and symmetric fat accumulation around the neck, shoulders, and upper trunk. “Madelung’s collar” is the classic lesion of this condition and represents a slowly progressive asymptomatic unencapsulated lipoma that encircles the neck and nearby anatomic structures. While malignant transformation of these growths is rare, tracheal and vascular compression can be of concern. As such, CT and MRI studies may be warranted in some cases. As an example, a patient with BSL that has daytime sleepiness should be considered for imaging to evaluate for peripharyngeal lipomas. Additionally, BSL can present with concomitant polyneuropathy of a sensory, motor, or autonomic nature. Typically, BSL can be identified clinically and is commonly seen with metabolic conditions including impaired fasting glucose, diabetes, and hyperlipidemia.

The management of BSL has historically relied upon alcohol abstinence to slow progression and surgical methods (either liposuction or excision) for palliation. Liposuction, especially tumescent, may be a safe therapeutic modality for these patients, notably when sculpting large volume areas. However, in many patients, lipomas are fibrous and resilient to liposuction techniques. While surgical excision may be more efficacious in these cases, a high risk for post-operative hematoma has been observed in this cohort. Additionally, metabolic disorders often prohibit anesthesia. The Madelung’s collar often makes intubation technically difficult, as patients frequently have limited head motion, tracheal compression and displacement, or a small mouth opening.

A new substance, deoxycholic acid (Kybella^{TM} or ATX-101), has been FDA-approved for the reduction of submental fat. This compound has been found to act as a detergent which solubilizes fat, causing subcutaneous cell lysis and reabsorption. Mechanistically, this medication can be efficacious for fat sculpting at sites other than the submandibular location. Concerns for nerve damage and skin ulceration secondary to adjacent anatomical location and superficial injection could be minimized based on location. In this case, test sites for this off-label treatment were selected via patient preference and anatomic location that reduced the aforementioned risks. Furthermore, an appropriately sized area was needed to adhere to the recommended maximum of 10 mL of deoxycholic acid per session. We used 0.2 mL of deoxycholic acid spaced 1-cm apart to the left lateral upper arm, right lateral upper arm, and right abdomen. We feel that deoxycholic acid, when chosen in the ideal patient who is adequately counseled on its risks and benefits, may be helpful, chiefly in those cases where treatment options are limited.

We present this case to highlight benign symmetrical lipomatosis, a rare condition.

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