Chicago Dermatological Society

October 2019 Educational Conference

Program & Speaker Information
CME Certification
Case Presentations
David Fretzin Lecture

Wednesday, October 23, 2019
Gleacher Center
Chicago, IL

Conference Host
Department of Dermatology
University of Illinois at Chicago
Chicago, Illinois

Program

Host: University of Illinois at Chicago
Wednesday, October 23, 2019
Gleacher Center, Chicago

8:00 a.m.	**Registration & Continental Breakfast with Exhibitors** *All conference activities take place on the 6th Floor*
8:30 a.m. - 10:30 a.m.	**Clinical Rounds** Slide viewing and posters
9:00 a.m. - 10:00 a.m.	**Morning Lecture** "Lasers in Dermatology" *Keyvan Nouri, MD*
10:00 a.m. - 10:30 a.m.	**Break and Visit with Exhibitors**
10:30 a.m. - 12:15 p.m.	**Resident Case Presentations & Discussion;** **MOC Self-Assessment Questions**
12:15 p.m. - 12:45 p.m.	**Box Lunches & visit with exhibitors**
12:55 p.m. - 1:00 p.m.	**CDS Business Meeting**
1:00 p.m. - 2:00 p.m.	**General Session** FRETZIN LECTURE – "Business of Dermatology and Medicine - How a well functioning practice promotes good patient care" *Keyvan Nouri, MD*
2:00 p.m.	**Meeting adjourns**

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

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

Mark the Date!

Next CDS meeting will be on Wednesday, November 13th at the Gleacher Center downtown.

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

Guest Speaker

KEYVAN NOURI, MD

Professor of Dermatology, Ophthalmology and Otolaryngology; Louis C. Skinner Jr. MD Endowed Chair in Dermatology; Dr. Phillip Frost Department of Dermatology and Cutaneous Surgery
University of Miami Health System; Miami, FL

Dr. Nouri completed a combined undergraduate and medical education program at Boston University in 1993, and went on to pursue a dermatology residency at the University of Miami. He completed his procedural dermatology fellowship in Mohs Micrographic Surgery, Dermatologic, Laser, and Cosmetic Surgery at New York University. As an alternative to the executive MBA, he took part in the Program for Leadership Development (PLD) at Harvard Business School. He was one of four in the University of Miami Miller School of Medicine to be selected to complete an eight-month Physician Leadership Academy program in South Florida. The AAD Advanced Leadership Program through the American Academy of Dermatology, which he also completed in 2017, focused on physician leadership and communication. He is currently completing a health MBA program in 2019 at University of Miami School of Business.

Currently, Dr. Nouri serves as the editor-in-chief of the Lasers in Medical Science journal and the editor of ten well-known textbooks. He is the author of more than 300 peer-reviewed scientific articles, more than 130 book chapters, and many other publications. He also serves in editorial roles, including editor of the Cells to Surgery Quiz Section of the Journal Investigative Dermatology, Section Editor for Dermatologic Surgery section of the International Journal of Dermatology, and the surgical advisory board for JAMA Dermatology, among others.

His study regarding behavioral analysis on sun safety practices for infants received national attention from the media. He has completed and performed many clinical research trials in the areas of skin imaging, lasers for treatment of scars, lasers for treatment of skin cancers, attempting to define the peak absorption of basal cell carcinomas, treatment of acute wounds with artificial skins and lights, etc. He has collaborated with basic scientists in the department of dermatology in a number of translational studies looking for markers in non-melanoma skin cancers. As a member of the UM staff, one of his several contributions is being Director of the Graduate Education Specialty Training Program for the Department of Dermatology and Cutaneous Surgery since 2004. Besides his leadership roles within Miami, he has also held various leadership roles for the Florida Society of Dermatologic Surgeons (Board of Director, Secretary-Treasurer, Vice-President, and President), American Society of Dermatologic Surgery (past program Co-Chairman of mastery of lasers course), American College of Mohs Surgery, the American Society of Lasers in Medicine and Surgery, and the International Society of Dermatology (current vice-president and previous co-chairman for continental meetings).

Dr. Nouri has received numerous honors over the course of his career.

CME Information

October 23, 2019

Overview

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

Target Audience

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

Learning Objectives

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

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

Physician Accreditation Statement

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

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

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

Disclosure of Conflicts of Interest

The IAO and CDS require instructors, planners, managers and other individuals and their spouse/life partner who are in a position to control the content of this activity to disclose any real or apparent conflict of interest they may have as related to the content of this activity. All identified conflicts of interest are thoroughly vetted by IAO and CDS for fair balance, scientific objectivity of studies mentioned in the materials or used as the basis for content, and appropriateness of patient care recommendations. All speakers are asked to follow the "first slide" rule to repeat their conflict of interest disclosures during their talk.

Continued next page

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.

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Department of Dermatology

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Owen Kramer, MD
Krishna Patel, MD

First Year

Nathan Jetter, MD
Elizabeth Kream, MD
Taryn Murray, MD
Cameron Trodello, MD

Table of Contents

**Case Presented by Taryn Murray, MD,
John Groth, MD and Kyle Amber, MD**

History of Present Illness:
A 50 year old female presented to otolaryngology for oral erosions, odynophagia, hemoptysis, hoarseness of voice and recent subjective weight loss. She underwent a microdirect laryngoscopy, which showed several ulcerative lesions on the epiglottis and a nodule on the right vocal cord. Four biopsies were performed at the base of the tongue, vallecula, right false vocal cord and right true vocal cord. All four biopsies showed a range of mild to moderate cytological dysplasia with severe chronic inflammation throughout. Her biopsy findings in conjunction with her significant smoking history were concerning for malignancy. Immunohistochemistry for p16 on the tongue biopsy was negative. Focal p53 in the basal layer was positive. Subsequently, the patient underwent a robotic assisted transoral epiglottectomy. Intraoperative findings included multiple friable, shallow, white based ulcers on the tongue and palate. There was also sloughing of the soft palate and a discrete friable, erythematous mass. Operative pathology from the epiglottic excision showed squamous dysplasia, severe chronic inflammation and acantholysis. Post-operatively, the patient developed new erosions of the oral cavity and vulva. Dermatology was consulted for further evaluation.

Past Medical History:
Hypertension and chronic obstructive pulmonary disease

Medications:
Hydrochlorothiazide

Allergies:
No known drug allergies

Social History:
The patient has a history of tobacco use

Review of Systems:
The patient endorsed oral erosions, odynophagia, hemoptysis, hoarseness of voice and weight loss.
The patient denied cough, shortness of breath, dysphagia, nausea or vomiting.

Physical Examination:
The patient has sharply demarcated erosions with moderate peripheral erythema on the ventral tongue as well as on the vaginal mucosa. She also has a few small healing erosions on the back and scalp.

Laboratory Data/Diagnostic Procedures and Tests:
The following were positive or abnormal:
ELISA for desmoglein 3 is 460U/mL (Ref < 9)
Indirect immunofluorescence on monkey esophagus demonstrates intercellular reticular staining with a titer of 1:10,240

The following were negative or within normal limits:

ELISA for desmoglein 1 is 11 U/mL (Ref < 14)
ELISA for BP180 and BP230 are negative
Indirect immunofluorescence on rat bladder is negative
Vulva, skin: PCR testing for herpes simplex virus type I and II are both negative.

Histopathology:
Epiglottis: There is indefinite dysplasia with acantholysis of the squamous epithelium.

Vulva, skin: The epidermis shows acantholysis.

Ventral tongue: The squamous mucosa shows focal acute inflammation and is negative for dysplasia and for significant acantholysis. Direct immunofluorescence shows an intercellular, reticular staining pattern for immunoglobulin G and complement component 3 throughout the epidermis.

Diagnosis:
Pemphigus Vulgaris

Treatment and Course:
The patient was started on 60 mg of prednisone daily along with doxycycline, niacinamide, mycophenolate mofetil, and intravenous immunoglobulin per previously published treatment protocol. Within 3 weeks of initiating prednisone her oral erosions healed. She still had some persistent vaginal erosions, which resolved upon an increase to 80 mg of prednisone daily. The patient was able to successfully taper off of steroids and is currently stable on doxycycline, niacinamide, mycophenolate mofetil, and intravenous immunoglobulin.

Discussion:
Pemphigus vulgaris (PV) is an autoimmune blistering disease caused by immunoglobulin G (IgG) autoantibodies targeting adhesive proteins in the desmosomal complex, specifically desmogleins 1 (dsg1) and 3 (dsg3). It is characterized by flaccid blisters and painful erosions on the skin or oral mucosa. PV can be divided into two subgroups. The mucosal dominant type is characterized by mucosal erosions with minimal skin involvement. It is caused by anti-dsg3 IgG autoantibodies. The mucocutaneous type is characterized by mucosal erosions and extensive skin involvement. It is caused by anti-dsg3 and anti-dsg1 IgG autoantibodies. The presence of autoantibodies is most commonly associated with the human leukocyte antigen (HLA) alleles DRB1*0402 and DQB1*0503.

Histologically, PV is characterized by suprabasilar acantholysis without keratinocyte necrosis. Direct immunofluorescence shows IgG or complement component 3 deposition at the intercellular space. Indirect immunofluorescence performed on monkey esophagus substrate reveals, anti-dsg3 antibodies. First line treatment is prednisone 1mg/kg daily for 3-6 months. Second line treatment includes azathioprine, mycophenolate mofetil, cyclophosphamide, cyclosporine, pulse methylprednisolone, methotrexate, high-dose intravenous immunoglobulin and rituximab.

In our patient the initial biopsies from the oropharynx showed no acantholytic process, but instead demonstrated a spectrum of cellular dysplasia and chronic inflammation. Findings of cytological dysplasia in the oropharynx in the setting of a significant smoking history are particularly concerning for a premalignant lesion. Pathology of the excised epiglottis, however, revealed suprabasilar acantholysis. To our knowledge, there have only been two prior reports describing findings of severe epithelial dysplasia concurrent with PV. Similar to these cases, our patient's

lesions resolved with therapy targeting PV. Like these cases, our patient's lesions resolved with high dose steroids. Reactive versus neoplastic epithelial dysplasia remains a challenging distinction to make. In the case of multifocal epithelial dysplasia, a diagnosis of PV should be considered, particularly when multiple mucosal sites are involved.

Essential Lesson:

- In the case of multifocal epithelial dysplasia, a diagnosis of pemphigus vulgaris should be considered, particularly when multiple mucosal sites are involved.
- Identifying pemphigus vulgaris can prevent detrimental surgical procedures.

References:

1. Ahmed AR et al. Major histocompatibility complex haplotype studies in Ashkenazi Jewish patients with pemphigus vulgaris. *Proc Natl Acad Sci USA. 1990;* 87:7658-7662
2. Amber KT, et al. Targeted Therapies for Autoimmune Bullous Diseases: Current Status. *Drugs.* 2018;78(15):1527-1548. doi:1007/s40265-018-0976-5.
3. Caltabiano R, et al. Unusual clinical and pathological features in pemphigus vulgaris: a potential diagnostic pitfall. *Case Rep Med*. 2011;2011:518758. doi:10.1155/2011/518758
4. Gissi DB et al. Unusual Histological Evidence of Dysplasia in a Case of Oral Pemphigus Vulgaris: A Potential Diagnostic Challenge. *Int J Surg Pathol*. 2016;24(8):733-737. doi:10.1177/1066896916653674
5. Grando SA. Retrospective analysis of a single-center clinical experience toward development of curative treatment of 123 pemphigus patients with a long-term follow-up: efficacy and safety of the multidrug protocol combining intravenous immunoglobulin with the cytoto. *Int J Dermatol*. 2019;58(1):114-125. doi:10.1111/ijd.14143
6. Holst VA, et al. Squamous cell carcinoma arising in Hailey-Hailey disease. *J Am Acad Dermatol*. 2000;43(2 Pt 2):368-371. doi:10.1067/mjd.2000.100542
7. Mahomed Y, et al. Squamous cell carcinoma arising in pemphigus vulgaris during immunosuppressive therapy. *Cancer*. 1980;46(6):1374-1377. https://www.ncbi.nlm.nih.gov/pubmed/7417938.
8. Vodo D, Sarig O, Sprecher E. The Genetics of Pemphigus Vulgaris. *Front Med (Lausanne)*. 2018;5:226.

Case Presented by Krishna Patel, MD,
Iris Aronson, MD, Marylee Braniecki, MD and Kyle Amber, MD

History of Present Illness:
A 67 year old Hispanic female presented with a three-month history of several small skin colored to slightly yellow papules on the posterior neck. The lesions were largely asymptomatic with only occasional pruritus and therefore only first noticed by her husband.

Past Medical History:
Hypertension, hypothyroidism, and cataracts

Medications:
Aspirin, atorvastatin, levothyroxine, and lisinopril

Allergies:
No known drug allergies

Family History:
No history of skin cancer, skin conditions, or autoimmune disorders

Review of systems:
The patient reported a recent history of palpitations. She denied any visual changes or gastrointestinal bleeding.

Physical Examination:
The patient has several small monomorphic skin colored to yellow papules on the posterior neck along the hairline. On further examination, the patient also has similar papules in the antecubital fossa. No similar lesions were noted elsewhere on the body.

Laboratory Data:
None

Diagnostic Procedures and Tests:
05/2019: Holter Study: sinus bradycardia to sinus tachycardia with sinus arrythmia

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Histopathology:
Left posterior neck, skin: There is mild epidermal atrophy with a few scattered melanophages in the dermis. There is a marked decrease in elastic fibers in the papillary dermis on the Verhoeff-Van Gieson (VVG) stain. No calcification of elastic tissue is seen.

Diagnosis:
Pseudoxanthoma Elasticum-like Papillary Dermal Elastolysis

Treatment and Course:
Since the lesions were predominantly asymptomatic and not aesthetically distressing to the patient, no further treatment was initiated.

Discussion:

Pseudoxanthoma elasticum-like papillary dermal elastolysis (PXE-PDE) is a rare acquired elastolytic disorder. It is characterized by asymptomatic or mildly pruritic multiple yellow or skin-colored non follicular cobblestone-appearing papules. The papules can coalesce into large plaques over the supraclavicular, lateral, and posterior aspects of the neck, flexor aspects of the forearms, axillae, inframammary folds, and lower abdomen. Approximately 50 cases of PXE-PDE have been reported in the literature, with the majority of cases affecting elderly women over the age of 50.

The pathogenesis of PXE-PDE is still poorly understood and likely multifactorial. Ultraviolet radiation, intrinsic aging, abnormal elastogenesis, and genetics have all been implicated but remain controversial. Involvement of sun protected sites and lack of prolonged sun exposure challenge the role of ultraviolet radiation. Additionally, a female predominance, reports of younger patients, and immunohistochemical studies demonstrating loss of both elastin and fibrillin-1 dispute intrinsic aging. Histopathology of lesions demonstrate an atrophic epidermis and band-like loss of elastic tissue in the papillary dermis. The reticular dermis is usually unaffected but may show a mild reduction in elastic tissue.

The skin lesions of PXE-PDE can clinically resemble those of classic pseudoxanthoma elasticum (PXE) and white fibrous papulosis of the neck (WFPN). Classic PXE, also known as Grönblad-Strandberg syndrome, is an autosomal recessive inherited disorder of abnormal calcification due to a defect in the ABCC6 gene, an ATP-binding cassette transporter protein. Cutaneous manifestations typically present in childhood or early adulthood. Histopathology demonstrates calcified, fragmented elastic fibers on Von Kossa staining. Abnormal calcification can also affect the retina, gastrointestinal tract, and cardiovascular system leading to angioid streaks and retinal hemorrhage, gastrointestinal hemorrhage, and accelerated atherosclerosis.

The term fibroelastolytic papulosis (FEP) is sometimes used to encompass both PXE-PDE and WFPN. They are clinically and histopathologically similar and are thought to be variants on the same disease spectrum. WFPN tends to have a younger age of onset and equal gender distribution in comparison to PXE-PDE. A distinguishing pathologic feature of WFPN is focal fibrosis and thickening of collagen fibers in the papillary dermis.

There are a limited number of case reports regarding the successful treatment of PXE-PDE. Reduction in elevation of papules and relief in pruritus has been reported after 3 sessions of fractionated carbon dioxide laser treatment. Topical tretinoin has also demonstrated long term clinical improvement even after discontinued use.

Herein, we present a patient with PXE-PDE, a rare acquired elastolytic disorder. Clinical and histopathologic correlation is necessary to distinguish PXE-PDE from other fibroelastolytic diseases that can carry systemic complications. There have been no reported extracutaneous associations with PXE-PDE to date.

Essential Lesson:

- Pseudoxanthoma elasticum-like papillary dermal elastolysis is a rare acquired elastolytic disorder characterized by skin colored or yellow papules and plaques typically on the neck.
- Clinical and histopathologic correlation is important to distinguish PXE-PDE from PXE which can be associated with ocular, gastrointestinal, and cardiovascular complications.
- PXE-PDE is typically asymptomatic. Treatment is aimed at reducing the appearance of skin lesions and improving mild pruritus.

References:

1. Balus L, et. al. Fibroelastolytic papulosis of the neck: a report of 20 cases. *Br J Dermatol* 1997; 137(3):461-6.
2. Byun J, et. al. Pseudoxanthoma elasticum-like papillary dermal elastolysis developed in early middle age. *The Journal of Dermatology* 2007; 34:709-711.
3. Chong S, et. al. Treatment of fibroelastolytic papulosis with fractionated carbon dioxide laser. *Journal of Cosmetic and Laser Therapy* 2015; 17(2):90-2.
4. Foering K, et al. Treatment of Pseudoxanthoma elasticum-like papillary dermal elastolysis with non-ablative fractional resurfacing laser resulting in clinical and histologic improvement in Elastin and Collagen. *J Cosmet Laser Ther* 2017; 20:382-4.
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6. Panagou E, et. al. Pseudoxanthoma elasticum-like papillary dermal elastolysis: a case report and review of literature. *Int J Dermatol* 2019*;* 58:93-7.
7. Patterson A, et. al. Fibroelastolytic papulosis: histopathologic confirmation of disease spectrum variants in a single case. *Journal of Cutaneous Pathology* 2016; 43(2):142-7.
8. Rongioletti F, et. al. Pseudoxanthoma elasticum-like papillary dermal elastolysis: a large case series with clinicopathological correlation. *J Am Acad Dermatol* 2012; 67(1):128-135.

Case Presented by Jacob Charny, MD,
Wenhua Liu, MD and Michelle Bain, MD

Patient 1

History of Present Illness:
A six year old African American boy presented for evaluation of a rash that began several weeks prior to presentation with gradual onset of peeling and erythema of the face, ears, and neck and thickened dark bumpy skin lesions on the elbows, knees, hands, and feet. He also reported thickened skin and peeling of his palms and soles. The rash was asymptomatic. His mother had been applying a bland emollient cream to the affected areas daily without improvement. He had a viral upper respiratory infection about one week prior to the onset of the rash.

Past Medical History:
None

Medications:
None

Allergies:
None

Family History:
No history of skin conditions or autoimmune conditions

Review of systems:
The patient denied any fevers, chills, night sweats, weight loss, or joint pains.

Physical Examination:
There are thin, mildly scaly, erythematous plaques with hyperpigmented borders on the lateral neck and in periauricular areas extending into the posterior scalp. The bilateral elbows have hyperpigmented plaques with many perifollicular papules within, resembling a “nutmeg-grater,” that extend distally along the extensor forearms. There are similar hyperpigmented “nutmeg-grater” plaques in the popliteal fossae and overlying the knees with extension distally along the shins. The palmoplantar surfaces are diffusely hyperkeratotic with a waxy orange-red hue. There are sharply defined lichenified and hyperpigmented plaques overlying the dorsal hands and feet. There is no nail dystrophy.

Laboratory Data/Diagnostic Procedures and Tests:
None

Histopathology:
Right popliteal fossa, skin: There is epidermal hyperplasia with alternating areas of orthokeratosis and parakeratosis. There are mild spongiotic changes in the epidermis. There is a superficial perivascular lymphocytic infiltrate. Periodic acid-Schiff stain for fungal organisms is negative.

Diagnosis:
Pityriasis Rubra Pilaris, Type IV

Treatment and Course:
The patient was initially treated with topical triamcinolone 0.1% ointment twice daily to the affected areas on the body and pimecrolimus 1% cream twice daily to the affected areas on the face. It was also recommended that urea 20% cream be applied to the palms and soles daily. At six month follow-up, there was resolution of all active lesions and prominent post-inflammatory hypopigmentation. The patient was then lost to follow-up.

Patient 2

History of Present Illness:
A seven year old Hispanic boy presented with a three week history of a painful peeling rash on the palms and soles. The rash was preceded by a blistering sunburn of the face and shoulders one week prior. As his sunburn healed, his mother noted increased redness, peeling, and tenderness of his hands and feet as well as asymptomatic thickened brown skin overlying both elbows and knees. The patient noted difficulty walking due to foot pain.

Past Medical History:
None

Medications:
None

Allergies:
None

Family History:
No history of skin conditions or autoimmune conditions

Review of systems:
The patient denied any fevers, chills, night sweats, weight loss, or joint pains.

Physical Examination:
There are erythematous, lichenified, scaly plaques overlying both elbows and knees with many perifollicular papules within. There are well-circumscribed orange-red plaques overlying the entire palmar and plantar surfaces bilaterally with transgradiens and superficial desquamation. The palms and soles are tender to palpation.

Laboratory Data/Diagnostic Procedures and Tests:
None

Histopathology:
Left medial palm, skin: Sections of acral skin show marked hyperkeratosis with focal parakeratosis and a small collection of serum. The epidermis exhibits acanthosis and thickening of the granular layer. There is no significant spongiosis or psoriasiform change. A Periodic acid-Schiff stain is negative for fungi. The findings are consistent with a palmoplantar keratoderma.

Diagnosis:
Pityriasis Rubra Pilaris, Type IV

Treatment and Course:
The patient was started on fluocinonide 0.05% ointment twice daily to all affected areas and urea 40% cream daily to the palms and soles. At 3 month follow-up, the patient was improving and tretinoin 0.05% cream was added to his regimen.

Discussion:
Pityriasis rubra pilaris (PRP) is an uncommon papulosquamous disease that affects about 1 in 3,500 to 5,000 people in the United States annually. PRP affects males and females equally and has a bimodal age distribution with peaks in the first to second and sixth decades of life. Currently, there are six recognized types of PRP. Type IV, also known as circumscribed juvenile, is the most common pediatric type of PRP and makes up about 25% of all cases of PRP. The exact incidence and prevalence of Type IV PRP remains unknown.

The pathophysiology and etiology of PRP is unknown. One case of Type IV PRP illustrated normal peripheral B and T lymphocyte counts with increased T suppressor activity and reduced T helper activity. There are several reports of Type IV PRP, including among siblings, associated with recent *Streptococcus pyogenes* or other infections, possibly highlighting the interplay of genetic susceptibility and infectious antigens in disease pathogenesis. Perhaps microbial antigens played a role in the pathogenesis of PRP in Patient 1, who reported a recent upper respiratory infection. There are also reports of exacerbation of PRP with exposure to ultraviolet B radiation and, rarely, a photodistributed presentation. Patient 2 did experience a blistering sunburn of the face, neck, and upper back prior to presentation; however the PRP eruption did not affect these sites.

While the majority of PRP cases are acquired, there is an autosomal dominant familial form associated with a gain-of-function mutation in CARD14. Patient's with this mutation tend to have a generalized or classic clinical appearance and may have overlapping features with psoriasis. There have also been a few reports of PRP linked to current active malignancy; however this was only seen among adults with Type I, classic generalized, PRP. These patients tended to be refractory to conventional treatment modalities, prompting further evaluation.

Type IV PRP is primarily a clinical diagnosis, however, skin biopsy may help rule out psoriasis or other dermatoses. Clinical presentation consists of well-circumscribed, pruritic, perifollicular hyperkeratotic papules coalescent into salmon colored plaques with varying degrees of lichenification on the elbows, knees, dorsal hands and feet. Dermoscopy may show multiple whitish follicular keratotic plugs with a yellow peripheral keratotic ring and linear vessels. Most patients also have a tender edematous and sharply defined waxy red-orange palmoplantar keratoderma with transgradiens to dorsal phalanges, ventral wrist, and Achilles tendon. About 40% of patients, including Patient 1, have a scaly seborrheic dermatitis-like eruption on the scalp, face, and neck.

Histologically, PRP shows psoriasiform epidermal acanthosis with hyperkeratosis marked by alternating vertical and horizontal areas of orthokeratosis and parakeratosis, follicular keratin plugging with perifollicular parakeratosis. Acral samples are less specific, but will show a keratoderma with foci of parakeratosis.

PRP is classically regarded as a self-limited disease. Initial papers estimated about one third of Type IV PRP patients achieve full clearance after three years; however more recent studies have

shown a more variable prognosis with about 60% achieving full clearance at one year and about 17% with persistent disease.

Given the unknown etiology and pathogenesis of PRP, there are many accepted treatments with inability to prove efficacy due to the unpredictable disease course. The pillars of treatment include topical medications, systemic retinoids, and biologic therapy. Phototherapy remains controversial due to the possible role of UVB in pathogenesis. While systemic retinoids are typically first-line treatment for classic generalized PRP, medication side effects may outweigh benefits in juvenile circumscribed disease. There are multiple reports of improvement and clearance of Type IV PRP with topical therapies including corticosteroids, calcineurin inhibitors, retinoids, and keratolytics. Both patients presented here have improved on topical therapy alone. New treatment algorithms advocate for the use of step-wise therapy beginning with topical treatment modalities. Ustekinumab has been shown to be effective for PRP associated with a gain-of-function CARD14 mutation. Evidence for the use of other biologic medications are limited to case reports only.

While Type IV PRP is uncommon and usually self-limited, there remains significant uncertainly as to its etiology, pathogenesis, and most effective treatments. We present these two cases to illustrate the typical clinical presentation and utility of topical therapy as the first line treatment in a step-wise approach to management.

Essential Lesson:

- Type IV pityriasis rubra pilaris (PRP), is a rare pediatric papulosquamous dermatosis that may be triggered by recent infection, sun exposure, and/or genetic susceptibility.
- Topical therapies including mid to super potent corticosteroids, calcineurin inhibitors, retinoids, and keratolytics are the first-line treatment for focal disease.
- Children with generalized PRP should be screened for CARD14 gain-of-function mutations and, if positive, may benefit from ustekinumab therapy.

References:

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Case 4

Case Presented by Cameron Trodello, MD,
and Kyle Amber, MD

History of Present Illness:
This 81 year old Hispanic male presented with a three month history of blisters. These pruritic lesions started on the bilateral hands and arms, and later spread to the neck, scalp, and bilateral legs. He recently had a biopsy for hematoxylin and eosin at an outside facility suspicious for bullous pemphigoid. Aside from a ten day course of doxycycline, he had received no other treatment.

Past Medical History:
Hypertension, diabetes mellitus, hyperlipidemia, five strokes

Medications:
Lisinopril, amlodipine, ranitidine, metformin, atorvastatin, clopidogrel, tamsulosin, insulin degludec, linagliptin, docusate, nortriptyline, and metoprolol

Allergies:
No known drug allergies

Family History:
No history of skin cancer or other skin conditions

Review of systems:
The patient endorsed decreased appetite and weight loss. He denied any fevers, chills, night sweats, nausea, vomiting, diarrhea, or dysphagia.

Physical Examination:
The patient's bilateral upper arms, dorsal hands, palmar hands, and medial thighs are covered with several erythematous erosions with some peripheral desquamation and overlying hemorrhagic crusting. The right anterior shoulder and left palm each have one intact tense bulla with clear fluid. The occipital scalp and suprapubic area each have one erythematous healing erosion. There is no regional lymphadenopathy.

Laboratory Data:
The following were positive or abnormal:
Indirect immunofluorescence IgG to basement membrane zone titer 1:1,2560 (<1:10)
Epidermal pattern on human basement membrane zone split skin titer 1:1,280 (no reference range)
Bullous pemphigoid IgG BP 180 antibodies 105 units (<9 units)

The following were negative or within normal limits:
Pemphigus panel negative. IgA pemphigoid panel negative. Antibody to collagen VII negative.

Diagnostic Procedures and Tests:
None

Histopathology:
Right wrist, skin: Sections of this skin fragment demonstrate superficial epidermal-dermal necrosis and subepidermal vesicular alteration with many eosinophils and fibrin within the blister cavity. A brisk superficial infiltrate composed of many eosinophils, lymphocytes and a few neutrophils is present in the upper dermis. A few scattered intra-epidermal eosinophils are seen.

Diagnosis:
Drug-induced Bullous Pemphigoid

Treatment and Course:
At the initial visit, the patient was given an intramuscular injection of 80 mg triamcinolone acetonide, and he was started on doxycycline 100 mg BID, niacinamide 500 mg TID, and triamcinolone 0.1% ointment BID to affected areas. The patient's primary care physician was encouraged to discontinue linagliptin due to suspicion that it may have precipitated the bullous pemphigoid, as it was started shortly before the onset of the bullae. One month later, the patient was still taking linagliptin, and the patient experienced only moderate improvement. At this time, he began a three-month prednisone taper starting at 60 mg. One week later, linagliptin had been discontinued. At the next visit, patient did not have any new skin lesions, and he was continued on the prednisone taper. At the most recent visit, seven months after discontinuing linagliptin and four months after finishing the prednisone taper, the patient had no residual dermatitis, bullae, or pruritus.

Discussion:
Bullous pemphigoid (BP) is the most common autoimmune blistering disease, characterized by deposition of immunoglobulin G (IgG) autoantibodies to the hemidesmosomal proteins BP180 and BP230 in the basement membrane. The condition typically affects the trunk and extremity flexures, and manifests as several tense, pruritic, fluid-filled vesicles and bullae on an erythematous base. Histologically, BP is characterized by a subepidermal blister with numerous eosinophils in the blister cavity, as well as dense lymphoeosinophilic inflammation in the dermis. This inflammation leads to a distinctive histologic pattern of eosinophilic spongiosis, which is most prominent in early lesions of the disease. In addition to these typical biopsy features from a sample lesion, diagnosis is also made by direct immunofluorescence of a perilesional sample, showing linear IgG along the basement membrane, as well as indirect immunofluorescence of a serum sample, showing epidermal IgG staining of salt-split skin.

To date, several classes of medications have been shown to either trigger or induce BP. These include various antibiotics, anti-hypertensives, diuretics, and neuroleptics, among others. First described in 2012 by Skandalis et al., prior use of dipeptidylpeptidase-4 inhibitors (DPP-4i) has been suggested to induce BP. Out of six diabetic patients they were treating with BP, five of them were on a DPP-4i for several months prior to BP onset. After withdrawal of the DPP-4i, all five patients achieved great control of their eruption within one week of discontinuation. To further support this association, the disease was well-controlled after withdrawal in two of the patients who had severe treatment-refractory disease for several months.

Since this initial study, there has a been a growing body of evidence supporting the link between DPP-4i and BP induction. Recently, one case-control study in Israel of 82 patients with BP and diabetes and 328 controls with diabetes without BP demonstrated an overall threefold increased risk for BP with DPP-4i exposure (adjusted odds ratio [OR], 3.2; 95% CI, 1.9-5.4). This association was strongest with vildagliptin and linagliptin, which had ORs of 10.7 (95% CI, 5.1-22.4) and 6.7 (95% CI, 2.2-19.7), respectively. The median time of onset between drug exposure and disease onset was 10.4 months (range, 1.0-26.5 months). Of the 19 patients who had their culprit

medication withheld after development of BP, 6 (32%) experienced complete remission off therapy, and 9 (47%) experienced complete remission on minimal therapy. Of the thirteen patients who continued DPP-4i therapy, eight deaths (62%) occurred between 2 months and 4.9 years from the initial diagnosis in this subgroup. Large case-control studies with similar outcomes have been reported in France, Finland, Japan, and Korea.

The exact mechanism underlying the association between BP and DPP4-1 therapy is not yet fully understood. One hypothesis involves the action of DPP-4 as a cell-surface plasminogen receptor. When it is stimulated to activate plasminogen to form plasmin under normal conditions, plasmin cleaves BP180 into two smaller fragments. With the inhibitor, therefore, it is postulated that the lack of BP180 cleavage leads to altered antigenicity and the subsequent development of new epitopes for antibodies to DPP-4i. Other models have also demonstrated that inhibition of DPP-4 stimulates eosinophil migration to the skin, which is one of the histologic features of BP further supporting its association with this class of drugs.

Essential Lesson:

- BP is one of the most common autoimmune blistering diseases and is characterized by autoantibodies to basement membrane proteins BP180 and BP230.
- Prior use of DPP-4i has been shown to be associated with inducing the subsequent development of BP.
- DPP-4i should be switched to alternative diabetic medications in patients with BP.

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Case Presented by Regina O'Brien, MD,
Marylee Braniecki, MD, Paul Storrs, MD and Michelle Bain, MD

FAST BREAK

Case 6

Case Presented by Elizabeth Kream, MD,
Wenhua Liu, MD and Michelle Bain, MD

History of Present Illness:
A 58 year old Caucasian female presented with a one year history of a dry pruritic rash on the chest, abdomen, arms, and legs. The patient used African black soap and Eucerin cream with only minimal relief of the itching. Her primary doctor prescribed her triamcinolone 0.1% cream, which provided some relief. Around onset, the patient started taking hydrochlorothiazide and was concerned that the medication caused her rash.

Past Medical History:
Hypertension, chronic obstructive pulmonary disease, seasonal allergies

Medications:
Aspirin, hydrochlorothiazide, loratadine, losartan, mometasone furoate inhaler, sertraline, triamcinolone 0.1% cream

Allergies:
Codeine

Family History:
No history of skin cancer, skin conditions, or autoimmune conditions

Social History:
Patient endorsed smoking a few cigarettes daily, drinking 1-2 alcoholic beverages per week, and occasionally smoking marijuana. She denied any other recreational drug use.

Review of Systems:
The patient denied any fevers, chills, night sweats, weight loss, joint pain, genital rash, genital pruritus, or pain with intercourse.

Physical Examination:
There are hypopigmented to erythematous atrophic papules and plaques, some with overlying excoriations, on the chest, abdomen, and bilateral upper and lower extremities. The abdominal plaque has follicular keratotic plugging. Examination of the genitalia shows a five by two centimeter light pink atrophic plaque on the right labia majora.

Laboratory Data/Diagnostic Procedures and Tests:
None

Histopathology:
Left thigh, skin: Atrophic epidermis with variably compact hyperkeratosis. The superficial dermis exhibits homogenization of collagen and pallor. There is a patchy interstitial lymphocytic infiltrate. Periodic acid–Schiff stain is negative for fungus.

Diagnosis:
Lichen Sclerosus

Treatment and course:
Given multifocal involvement, narrowband ultraviolet B light therapy was offered however the patient opted for only topical therapy due to the inconvenience of frequent office visits. She was started on a combination of triamcinolone 0.1% ointment and calcipotriene 0.005% cream. Additionally the association of genital lichen sclerosus with vulvar squamous cell carcinoma was discussed and the patient was advised to establish care with a gynecologist for regular check-ups. The patient missed two follow-up visits but was reached by phone. On the telephone encounter, the patient endorsed some improvement and we urged her to follow-up with us in clinic.

Discussion:
Once thought of as an atrophic variant of lichen planus, lichen sclerosus (LS) is a distinct inflammatory disease of the superficial dermis or submucosa resulting in scar-like atrophy. Extragenital LS occurs in 15-20% of patients with genital LS, while exclusive extragenital LS accounts for around 2.5% of all cases of LS. Similar to anogenital LS, extragenital LS appears to have a female predilection. The pathogenesis is not well understood and most studies in this area focus solely on anogenital disease. Extragenital LS is also associated with autoimmune conditions such as autoimmune thyroiditis and vitiligo. The disease has been noted more frequently in families, most commonly those with an HLA-DQ7 haplotype. IgG autoantibodies to extracellular matrix protein-1 (ECM-1) are found in 80% of patients with LS and may play a role in pathogenesis. Alternatively autoantibodies to ECM-1 may be an epigenetic result of the disease itself.

Classically, lesions of extragenital LS present as flat-topped, ivory-white, and atrophic appearing papules and plaques. There is sometimes a blue, pink, or violet hue. Longstanding lesions may develop a shiny or wrinkled “parchment paper” appearance or have associated bullae. The most commonly involved areas are the trunk and upper extremities, specifically at areas of trauma or continuous pressure. Rarely oral mucosal involvement is seen, marked by intraoral bluish white papules. There are few case reports describing a linear or Blaschkoid pattern. Extragenital LS is usually asymptomatic, however patients may complain of associated dryness or pruritus. On physical exam, follicular plugging can be a helpful sign that distinguishes LS from morphea. Dermoscopy classically reveals homogeneous white areas with comedo-like openings corresponding to plugged follicles.

Early histopathology of extragenital LS shows superficial dermal edema and a band-like lymphocytic infiltrate with vacuolar degeneration of the basal layer. With time, the epidermis becomes atrophic with orthohyperkeratosis and flattening of the rete ridges. While the superficial dermis is initially pale due to edema, later lesions show homogenized collagen and loss of elastic fibers in this area. The loss of elastic fibers is an important histologic feature in distinguishing LS from morphea. Long-standing lesions may also show subepidermal clefting and displacement of the lymphocytic infiltrate deep to the zone of homogenized collagen. In contrast to the superficial dermis, the deeper dermis may show increased elastic fibers, possibly reflecting a reactive repairing process.

Potent topical corticosteroids are the first line therapy to extragenital LS. Alternative therapies include topical calcineurin inhibitors, intralesional corticosteroid injections, systemic corticosteroids, retinoids, and phototherapy. Extragenital LS is more likely to clear than anogenital LS. Extragenital LS is not believed to predispose to cutaneous malignancy; however, anogenital LS is associated with a 5% risk of progression to squamous cell carcinoma and 50-55% of vulvar and penile squamous cell carcinomas are associated with underlying LS. It is therefore important to examine for anogenital involvement in all cases of extragenital LS. We present this case to

highlight an example of extensive LS with predominant extragenital involvement. Additionally this case underscores the importance of anogenital examination as early detection of subclinical involvement can prevent irreversible scarring, associated morbidity, and possible progression to malignancy.

Essential Lesson:

- The pathophysiology of LS is unknown however autoimmunity may play a role given that 80% of patients with LS have serum IgG auto-antibodies to extracellular matrix protein-1.
- While histopathology is the gold standard for diagnosis, dermoscopy of atrophic plaques showing follicular plugging can be a helpful tool in distinguishing clinically between morphea and extragenital LS.
- There is no apparent increased risk of malignancy in extragenital LS although all patients should be screened for anogenital involvement.

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Case 7

Case Presented by Thomas Klis, MD,
Michelle Bain, MD, Marylee Braniecki, MD and Maria Tsoukas, MD, PhD

History of Present Illness:
An 11 year old African American female presented for evaluation of a cystic lesion located on her left upper back that was first noticed by mom when the patient was 2 years old. The lesion was asymptomatic up until several months ago, at which time it began to become swollen, painful, red, and later had "burst" with some leakage of fluid. She was seen in the emergency department for this skin development, and was treated with a 7 day course of cephalexin which helped with the swelling, but the lesion remained. The patient had no other medical complaints.

Past Medical History:
None

Medications:
None

Allergies:
None

Family History:
No family history of skin conditions, autoimmune diseases, or genetic diseases

Social history:
None

Review of systems:
The patient denied any fevers, chills, nausea, vomiting, abdominal pain, night sweats, weight loss, or joint pains.

Physical Examination:
Examination of the left upper back shows a 2cm x 2cm soft and compressible, relatively mobile subcutaneous nodule. No significant epidermal changes are present apart from subtle pigment changes. A 5 mm linear red scar is evident at the lateral aspect of the nodule. She has no other significant skin findings.

Laboratory Data:
None

Diagnostic Procedures and Tests:
Ultrasound, left upper back: Sonographic images of the site of the patient's palpable lump demonstrate a 2.3 x 0.8 x 1.7 cm well-circumscribed cystic mass with internal septations within the subcutaneous fat. No adjacent lymphatics or vascular flow were evident on Doppler.

Histopathology:
Left upper back, skin: Tissue sections showed a squamous epithelial lined cystic cavity with foci of pseudostratified columnar epithelium and goblet cells which contained mucin, in addition to foci

of pilosebaceous structures communicating with the cyst wall. The periodic acid-Schiff (PAS) and Alcian blue stains highlighted the goblets cells. There was evidence of rupture demonstrated by multinucleated cells containing keratinous and hair shaft debris accompanied by inflamed granulation extruding into the cystic cavity. The lesion was completely excised.

Diagnosis:
Coexisting Dermoid and Bronchogenic Cyst

Treatment and Course:
The patient presented initially with this nodule, and the following month it was completely excised in our clinic. No reoccurrence has been noted as of date.

Discussion:
Dermoid cysts are derived principally from germinal epithelium and can occur throughout the body including the head and neck region, with the most common site being the lateral eyebrow. Bronchogenic cysts, on the other hand, are abnormalities of pulmonary differentiation that are usually detected in children, and are usually found in the mediastinum along the tracheobronchial tree or peripherally in the lung parenchyma. Cutaneous bronchogenic anomalies are very rare. These present as a cyst which originates from the primitive tracheobronchial tree. They are primarily located in the thorax; however, remote locations such as lingual, intra-abdominal and cutaneous regions have also been reported.

The origins of both dermoid and bronchogenic cysts are embryological. It has been suggested that dermoid cysts are derived from epithelial nests that are trapped during the midline closure of the first and second branchial arches. Bronchogenic cysts are thought to arise in developing lung buds during embryogenesis when the tracheobronchial groove separates the primitive foregut into dorsal and ventral structures. The location of extrathoracic cysts occurring at unusual sites such as the back (as seen in our case) has been explained by the migration of these sequestrated structures in the developing embryo.

To date, approximately 60 cases of cutaneous heterotopic bronchogenic cysts have been reported. The most common locations for a cutaneous bronchogenic cyst are the suprasternal notch, followed by the presternal area, paramedian chest, and neck. The back is a rare location for cutaneous bronchogenic cysts. The coexistence of dermoid and bronchogenic cysts has also been reported, but only in the mouth. We present this unique case of a coexistent dermoid and bronchogenic cyst located on the back for clinical interest.

Essential Lesson:

- Dermoid cysts are derived principally from germinal epithelium and can occur throughout the body including the head and neck region, with the most common site being the lateral eyebrow.
- Bronchogenic cysts are abnormalities of pulmonary differentiation that are usually detected in children. The most common site for a cutaneous bronchogenic cyst is in the suprasternal notch.
- Coexistent dermoid and bronchogenic cysts are rare, but have been reported in the mouth. This is the first case of a coexistent dermoid and bronchogenic cyst occurring on the back.

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Case Presented by Kurt Ashack, MD, MHS,
Wenhua Liu, MD and Michelle Bain, MD

FAST BREAK

Case 9

Case Presented by Nathan Jetter, MD,
Iris Aronson, MD, Benjamin Garden, MD, Wenhua Liu, MD and Michelle Bain, MD

History of Present Illness:
An 11 year old African American female presented with five years of an intermittent vesicular eruption on her face. She stated that pruritic lesions appeared singly or in clusters, burst after several hours to one day, crusted, and left dark persistent spots. Outbreaks were more frequent in the summer. She did not have strict adherence to sunscreen use and sun avoidance. However, the family remained unconvinced that sunlight exposure was a trigger because the patient had eruptions year-round. Treatment with hydroxychloroquine did not help. A prednisone taper reduced frequency of outbreaks.

Past Medical History:
None

Medications:
None

Allergies:
No known drug allergies

Family History:
Mother with history of urticaria

Review of systems:
The patient denied any fevers, chills, night sweats, weight loss, joint pains, or eye problems

Physical Examination:
Left nasal ala with a 4mm fluid filled yellow vesicle. Cheeks, forehead, and nose with multiple ~4-5mm hyperpigmented macules and few pox-like scars. Numerous closed comedones on forehead and cheeks.

Laboratory Data:
The following were positive or abnormal:
Epstein-Barr Virus capsid antigen immunoglobulin G >8.0 and Epstein-Barr Virus nuclear antigen 1 immunoglobulin G >8.0

The following were negative or within normal limits:
Herpes Simplex Virus serology and deoxyribonucleic acid, Varicella Zoster Virus deoxyribonucleic acid, Epstein-Barr Virus capsid antigen immunoglobulin M, Epstein-Barr Virus immunoglobulin G, and bacterial culture are negative

Antinuclear, anti-U1 ribonucleoprotein, anti-Ro/SSB and anti-La/SSA antibodies are non-detected or within normal limits. C3, C4, and serum free protoporphyrins are non-detected or within normal limits.

Pemphigus and pemphigoid antibody panels are non-detected or within normal range

Histopathology:
Skin, left forehead: Direct immunofluorescence is negative. Fibrinogen has non-specific, patchy staining in the papillary dermis

Skin, right nasolabial fold: Intraepidermal vesiculation, edematous papillary dermis, superficial and mid-dermal perivascular lymphohistiocytic infiltrate with prominent neutrophils, eosinophils, and extravasated red blood cells.

Diagnosis:
Hydroa Vacciniforme

Treatment and Course:
Following biopsy suggestive of hydroa vacciniforme, the patient was started on treatment with β-carotene 25,000 IU 3-4x/day, fish oil supplementation, Polypodium leucotomos supplementation and strict sun protection. The patient initially experienced reduced frequency of vesicular eruptions. However, adherence to sun avoidance proved challenging, especially during summer months, and the patient continued to have periods of outbreaks several times per year. Though at subsequent follow up visits the patient continued to report occasional eruptions, she did not have active lesions on exam for another two years, when a newly erupted vesicle was biopsied for direct immunofluorescence that was negative. On the next follow up visit the patient again had a newly erupted vesicle on the central face which was scraped for Epstein-Barr Virus DNA probe. The results were inconclusive. Epstein-Barr Virus serologies indicated past infection.

Discussion:
Hydroa vacciniforme (HV) is a rare childhood photodermatitis that presents with vesiculopapules on sun-exposed areas which heal with depressed scars. Originally described by Bazin in 1862, the meaning of the Greek term “hydroa” is debated but generally thought to mean “sweat rash” or “boils,” while “vacciniforme” refers to the pox-like permanent scars which develop. Prevalence has been established in Scotland as 0.34 cases per 100,000; whether this prevalence holds in other geographies is not known. Mean age of onset is six-eight years with a mean duration of nine years, though a few cases of persistence to late adulthood have been reported.

There are two clinically distinct presentations, a typical form and a severe form. In the typical form, pruritus and/or burning sensation develops on sun-exposed areas, most often the face and hands, within hours of exposure. This is followed by the appearance of erythematous macules that progress to tender papules, vesicles and, one to two days later, necrotic crusts. Healing over weeks leaves depressed vacciniform scars. In the severe form, the photodermatitis described above is accompanied by systemic symptoms, laboratory abnormalities including transaminitis, and ocular findings including conjunctivitis and uveitis. Though the pathogenesis is not well understood, the etiology is thought to involve Epstein-Barr Virus (EBV). The vesiculopapular lesions have significantly more EBV-positive cells than adjacent normal skin. Additionally, more EBV DNA has been found in blood samples from HV patients compared with other photosensitivity disorders. Furthermore, patients with the severe form of HV have a higher incidence of EBV-associated NK- and T-cell lymphomas.

On histology, the nearly pathognomonic findings in newly erupted lesions are prominent reticular keratinocyte degeneration, intraepidermal vesicles containing fibrin and inflammatory cells, and confluent epidermal and focal upper dermal necrosis. In situ hybridization for EBV RNA usually shows lymphoid infiltrate positivity. Diagnosis is made on the basis of lesional morphology and

histology as described above, along with evidential support by tests to rule out alternative photodermatoses, in particular antinuclear antibodies (ANA) and direct immunofluorescence (DIF) for bullous lupus erythematosus and erythrocyte protoporphyrin level for erythropoietic protoporphyria. ANA, DIF and erythrocyte protoporphyrin levels were within normal limits for this patient.

Though the typical form of HV as seen in our patient is not life threatening, quality of life for these patients can be highly impaired. There are no controlled trials for treatment, and in many cases only photoprotection provides relief. Physical photoblockers are necessary, including films for car and home windows. As in our patient, the literature indicates that full adherence to photoprotection can prove challenging, and therefore systemic therapies may be necessary. Immunosuppressive options include antimalarials, cyclosporine, azathioprine, and thalidomide, though none has been shown superior or universally effective. There are also several non-pharmaceutical treatments reported, most notably oral β-carotene, as well as fish oil and Polypodium leucotomos (cabbage palm fern) extract.

Essential Lesson:

- Hydroa vacciniforme is a very rare childhood photodermatosis with permanent scarring.
- Strict photoprotection is the most effective treatment, but adherence is a challenge.

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Case 10

Case Presented by Owen Kramer, MD,
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History of Present Illness:
A 26 year old female was referred to dermatology for evaluation of "lumpy skin" on her arms and legs which had been present for the past 4 months. The lesions, which initially began on her arms and progressed quickly to the legs during the first month, slowly continued to worsen. Her first symptoms were "Achilles tendon pain" and muscle tightness before the lesions presented. She saw a vascular surgeon and rheumatology with work up unrevealing for a specific cause. She also notes a longstanding history of Raynaud's phenomenon. She also notes joint discomfort that began one month before presentation in the hands and ankles, particularly worse with certain movements.

Past Medical History:
"Shoulder surgery" in 2018

Medications:
Oral contraceptive (norethindrone acetate and ethinyl estradiol)

Allergies:
No known drug allergies

Family History:
Paternal aunts and maternal aunt with Raynaud's phenomenon. Mother and maternal aunts with hypothyroidism.

Social History:
She is an avid rugby player and works out often with intense exercises

Review of systems:
The patient denied any fever, chills, shortness of breath, dysphagia, or weight changes.

Physical Examination:
The patient has firm, pseudo-cellulitic appearing skin on upper medial arms and thighs. Skin is somewhat firm to palpation on the upper calves. Few varicose veins are present on the right medial thigh.

Laboratory Data:
The following were positive or abnormal:
C-reactive protein 15.9 mg/L (<8)

The following were negative or within normal limits:
Complete blood count with differential, complete metabolic panel, serum protein electrophoresis, urine protein electrophoresis, creatine kinase, quantiFERON-TB Gold, erythrocyte sedimentation rate, thyroid stimulating hormone, and serum IgG level are within normal limits. Antinuclear, anti-centromere and anti-Scl70 antibodies are negative

Diagnostic Procedures and Tests:
Magnetic Resonance Imaging with/without contrast, lower extremities: Superficial fasciitis along the thigh muscle fascia bilaterally, most pronounced over the right vastus lateralis

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Histopathology:
Right thigh, full-thickness biopsy: Superficial fasciitis with sclerosis. Lymphoplasmacytic infiltrate with eosinophils noted.

Diagnosis:
Eosinophilic Fasciitis

Treatment and Course:
Her biopsy was complicated by post-operative infection requiring prolonged treatment with clindamycin. Prednisone was initiated at 1mg/kg. Four weeks later, the patient noted no further progression and notes reduction in "tightness" in her arms and legs. On exam, the patient's skin is less firm to palpation. Methotrexate was then initiated at 10mg weekly and prednisone reduced to 40mg daily. The patient also agreed to see physical therapy.

Discussion:
Eosinophilic fasciitis (EF), also known as Shulman's syndrome, is a poorly understood fibrosing disease that was first described in 1974. EF usually results in symmetrically appearing pseudo-cellulitic, firm skin on the extremities with sparing of the face, hands, and feet. Pitting edema and erythema may be seen in the acute and subacute stage of the disease. Other areas, such as the trunk, may be uncommonly involved. The "groove sign," which is well described in EF, is represented by a linear depression on the skin along the course of veins which can be accentuated by elevation. 70-83% of patients have involvement of all their extremities, 25% of patients have leg involvement only, and 5-6% have involvement of their arms only. This can be accompanied by weight loss, myalgia and fatigue. Joint contractures may also occur in about 50% of patients. EF has a mean age of onset between 47-57 years of age and gender predominance varies by study.

The gold standard for diagnosis of EF is via full-thickness biopsy that includes the fascia and muscle. On histology, there is a thickened fascia with a lymphocytic infiltrate that may be accompanied by eosinophils and plasma cells. Eosinophils may be absent on biopsy due to protracted disease or the use of immunosuppressants, including corticosteroids. Imaging, especially magnetic resonance imaging (MRI), has an increasing role in EF, and can be helpful in identifying a target biopsy site. Given the invasiveness and complications associated with a full-thickness biopsy, as seen in our patient, some experts suggest the use of MRI without biopsy for clinching the diagnosis of EF. Laboratory findings can also support a diagnosis of EF; peripheral eosinophilia (58-85%), hypergammaglobulinemia (35-46%), elevated inflammatory markers, and monoclonal gammopathy (16%) can all be seen in EF. It is important to note that eosinophilia and elevated inflammatory markers can be present early on but may disappear with treatment as well as time. Eosinophilic fasciitis is also associated with malignancy in about 5-10% of patients. Hematological malignancies are more common than solid tumors. Further studies to screen for malignancy can be utilized on a case by case basis according to risk factors and symptoms.

The pathogenesis of EF is poorly understood, but may be related to a dysfunction in the immune response, which has been supported by findings of serum hypergammaglobulinemia plus occasional IgG and C3 deposition in the fascia. Eosinophils are thought to contribute to the disorder via degranulation and the subsequent release plus accumulation of proteins with toxic

and potentially fibrotic properties. It is also important to recognize that exercise was historically thought to have nearly a 50% association in precipitation of this disease but figures now place it as a possible trigger in only about 28% of cases.

The diagnosis of EF is often delayed by many months. One retrospective study found that up to 79% of patients with EF are initially misdiagnosed, most frequently with systemic sclerosis. A timely, accurate diagnosis is paramount to avoid inappropriate workup and treatment. The differential diagnosis of EF may consist of morphea, systemic sclerosis, nephrogenic systemic fibrosis, as well as some scleroderma-like disorders such as eosinophilia-myalgia syndrome and toxic oil syndrome. Differentiating morphea from EF may be difficult, especially because some argue that EF may be a variant of or exist on the spectrum of morphea. There is also a reported concomitant presence of plaque morphea in up to 41% of patients with EF. However, histological findings of fasciitis with eosinophils may help differentiate EF from morphea.

Distinguishing EF from systemic sclerosis is particularly important since treatment and comorbidities differ. Many factors may support a diagnosis favoring EF over scleroderma including peripheral eosinophilia as well as the lack of acro-facial involvement, autoantibodies, evidence of systemic involvement, Raynaud's phenomenon, and abnormal nail fold capillaries, among others. A lack of distal digit involvement is a useful finding to differentiate EF from systemic sclerosis. Nephrogenic systemic fibrosis can be ruled out based on the lack of renal failure and a history of gadolinium administration. Internal organ involvement and history differentiate EF from eosinophilia-myalgia syndrome caused by ingestion of contaminated L-tryptophan and toxic oil syndrome, which now mostly have only a historical significance.

Early treatment of EF may result in improved outcomes and systemic corticosteroids are often the first treatment employed. However, combination therapy with methotrexate may have higher complete response rates as well as a steroid sparing effect. Significant range of motion deficits that occur with disease activity highlight the importance of early aggressive treatment and utilization of physical therapy. Other treatments for EF may include IV methotrexate, sirolimus, rituximab, azathioprine, infliximab, and mycophenolate mofetil.

Essential Lesson:

- Eosinophilic fasciitis is an uncommon, poorly understood disorder that is often misdiagnosed. Prompt diagnosis and treatment may result in improved outcomes.
- Histological and peripheral eosinophilia may frequently be absent and are not required to make a diagnosis of eosinophilic fasciitis.

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