Chicago Dermatological Society

Monthly Educational Conference

Program Information
CME Certification
and
Case Presentations

Wednesday, May 1, 2019
Gleacher Center – Chicago, IL

Conference Host:
Department of Dermatology
Rush University Medical Center
Chicago, Illinois

Program

Host: Rush University
Wednesday, May 1, 2019
Gleacher Center, Chicago

8:00 a.m.	**Registration & Continental Breakfast with Exhibitors** *All activities will take place on the 6th Floor of the Gleacher Center*
8:30 a.m. - 10:15 a.m.	**Clinical Rounds** Slide viewing/posters
9:00 a.m. - 10:00 a.m.	**Basic Science/Residents Lecture** "Something for Everyone: Present and Future Therapies for Awful Skin Diseases" *Brett King, MD, PhD*
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** MALKINSON LECTURE - "Treating Alopecia Areata and Vitiligo with JAK Inhibitors: A New Frontier in Dermatology" *Brett King, MD, PhD*
2:00 p.m.	**Meeting adjourns**

Mark the Date!

Next conference: CDS/IDS Joint Meeting & Awards Luncheon
Wednesday, June 5th; Stephens Convention Center; Rosemont

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

Guest Speaker

BRETT KING, MD, PHD

Associate Professor of Dermatology
Yale School of Medicine
Middlebury, CT

Dr. Brett King is Associate Professor of Dermatology, specializing in skin diseases recalcitrant to first-line therapies. He has pioneered the use of Janus kinase (JAK) inhibitors in cutaneous diseases, in particular for alopecia areata, vitiligo, and atopic dermatitis, in addition to other disorders. He sees patients at Yale Dermatology-Middlebury.

Dr. King received his B.A. at the University of California at Santa Cruz, his Ph.D. from Stanford University and his M.D. from Yale University School of Medicine. He completed medical internship at Massachusetts General Hospital and dermatology residency at Yale University School of Medicine. His research interests include Alopecia Areata; Eczema; Stevens-Johnson Syndrome; Vitiligo; Scleroderma, Limited. Dr. King has numerous publications to his credit.

CME Information

5.1.2019

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 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. 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 2018/19 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 and for cosmetic 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.

Our guest speaker, Brett King MD, PhD, has disclosed the following potential conflicts of interest: Grants/Research Support - Pfizer; Consulting fees - Pfizer, Eli Lilly, Concert Pharmaceuticals, Aclaris Therapeutics; Speakers bureau - Pfizer, Regeneron, Sanofi Genzyme; Royalty/Patent holder - JAK inhibitors + UVL for vitiligo. None of the members of the planning committee have any relevant 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.

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*Protocol to be posted same-day on the CDS website

CHICAGO DERMATOLOGICAL SOCIETY **CASE 1**

Presented by Meredith Morse, MD, Mark D Hoffman, MD, Warren Piette, MD and Ralph Fiore III, DO
Department of Dermatology, Rush University Medical Center

HISTORY OF PRESENT ILLNESS

The patient is a 45-year old Indian male with a remote personal history of a bifrontal oligoastrocytoma who presented with new-onset bilateral lower leg lesions, increased thirst and urine output. His skin lesions were asymptomatic and had been present for nearly three months. Complete review of systems was otherwise unremarkable. He denied any sensory or motor deficits in his legs.

Laboratory investigation was notable for a non-parathyroid hormone dependent hypercalcemia, elevated vitamin D levels, and an elevated angiotensin-converting enzyme (ACE) level. Chest CT with contrast showed small bilateral pleural effusions with compressive atelectasis. It was negative for enlarged mediastinal lymph nodes.

Histopathology demonstrated well-formed noncaseating granulomas scattered throughout the dermis, some of which were associated with nerve fascicles. The dermis showed marked sclerosis with upward displacement of eccrine glands. Periodic Acid Schiff (PAS), Gomori methenamine silver (GMS), and Fite stains were negative. Taken together, the biopsy was interpreted as morpheaform sarcoidosis. He was started on prednisone 30 mg daily and pamidronate by rheumatology. The lesions started to slowly improve.

Given the close association of granulomas along nerves, there was concern for pauci-bacillary leprosy. A repeat punch biopsy from the lower leg was performed one month after initial presentation. Histology again showed noncaseating granulomas; PAS, GMS, and Fite stains were negative.

PAST MEDICAL HISTORY

Bifrontal anaplastic Grade III oligoastrocytoma (2003) status post resection, procarbazine, lomustine, vincristine, temozolomide, and radiation therapy

MEDICATIONS

Lamotrigine
Vitamin B12

FAMILY HISTORY

Unremarkable

SOCIAL HISTORY

Born in India
Received BCG vaccine as a child
Moved to United States in 1991; returned to India 5-6 times since, most recently in 2012
No tobacco or alcohol use
Employed as a quality improvement analyst in Chicago
No travel to southern United States

PHYSICAL EXAM

Examination revealed scattered light red-tan slightly scaling patches on the bilateral lower extremities, predominantly on the anterior aspects. There was no appreciable temperature deficit and no sensory or motor neuropathy.

There was no palpable lymphadenopathy or enlargement of superficial peripheral nerves.

HISTOPATHOLOGY

Right lower leg: well-formed noncaseating granulomas scattered throughout the dermis, some of which were associated with nerve fascicles. The dermis showed marked sclerosis with upward displacement of eccrine glands. PAS, GMS, and Fite stains were negative.

Left lower leg: noncaseating granulomas. PAS, GMS, and Fite stains were negative.

LABORATORY AND RADIOLOGY RESULTS

Calcium: 15.8 mg/dL [reference range 8.7-10.7 mg/dL])
Total vitamin D: 244 pg/mL [reference range 18-72 pg/mL])
ACE level: 625 µl [reference range 8-53 µl])

QuantiFERON gold: negative
Histoplasmosis urinary antigen: negative
Complete blood count: hemoglobin of 10g/dL [reference range 13.5-17.5 g/dL]
Complete metabolic panel: within normal limits

Chest X-ray: mild pulmonary vascular distention and trace bilateral pleural effusions. It was negative for hilar and paratracheal lymphadenopathy

Chest CT with contrast: small bilateral pleural effusions; mediastinal, axillary, and supraclavicular lymph nodes were not enlarged

DIAGNOSIS

Granulomatous dermatosis with secondary hypercalcemia; differential diagnosis includes sarcoidosis without systemic involvement or paucibacillary leprosy without clinically evident nerve involvement

TREATMENT AND COURSE

Given that no bacilli were seen on pathology and the patient was improving on high dose prednisone, it was decided that he should continue to be managed as skin-limited sarcoidosis. His prednisone was gradually tapered down to 2.5 mg every other day. His skin lesions have cleared and he remains asymptomatic. He continues to have no subjective, ophthalmologic, or radiologic evidence of sarcoidosis affecting any organs other than the skin. His calcium and vitamin D normalized while on treatment. Despite improvement, we wanted to ensure we more effectively rule-out paucibacillary leprosy. The patient's specimen was sent to the National Hansen's Disease Foundation in Baton Rouge, Louisiana for polymerase chain reaction for *Mycobacterium leprae*. These results are pending.

DISCUSSION

Sarcoidosis is a well-known multisystem granulomatous disease which preferentially affects the lungs, lymph nodes, eyes, and skin. Cutaneous lesions can include erythematous papules, hypopigmented patches, and ulcerative plaques. Non-specific disease manifestations, such as

erythema nodosum, may be seen. Asymptomatic hilar and/or paratracheal lymphadenopathy is the most common finding on chest imaging. Lung involvement is seen in approximately 90% of patients, mandating pulmonary function testing and imaging. Chest computed tomography is the most sensitive radiologic modality for these patients. Hypercalcemia, while classically associated with sarcoidosis, is seen in only 10% of patients; this finding is rather non-specific. Pathology demonstrates well-formed epithelioid granulomas with minimal to no inflammatory infiltrate. An ACE level is often obtained but is more useful for monitoring treatment response than diagnosis.

Leprosy is a chronic granulomatous disease caused by *Mycobacterium leprae*, an intracellular bacterium with predilection for the skin and peripheral nerves. Leprosy demonstrates a wide variety of clinical presentations, from scaling hypopigmented plaques to diffuse tissue infiltration. Lesions may be multiple and ill-defined or few in number and sharply circumscribed. Clinical presentation is determined by the type of host immune response. The Ridley-Jopling classification categorizes leprosy into five types based on cell-mediated response: tuberculoid leprosy (TT), borderline tuberculoid (BT), mid-borderline (BB), borderline lepromatous (BL), and lepromatous leprosy (LL). TT is associated with a strong cell-mediated Th1 response and low bacterial burden. Lesions of tuberculoid leprosy are often anhidrotic and insensate. Conversely, LL is associated with a poor cell-mediated, predominantly Th2 response, and a high bacterial burden. Histopathology mirrors this cell-mediated phenomenon. Tuberculoid leprosy shows well-formed granulomas often arranged linearly along nerve bundles with few to no bacilli. Lepromatous leprosy displays foamy histiocytes (Virchow cells), many clumps of bacilli (globi), and few to no granulomas.

Given the varied clinical presentations and striking pathologic similarities of sarcoidosis and leprosy, diagnosis of either entity may not always be straightforward. This is most certainly the case for our patient. While biopsy stains were negative for bacilli, many granulomas were noted to be associated with nerve fascicles, a feature suggestive of tuberculoid leprosy. He had no radiologic or ophthalmologic findings of sarcoidosis, yet he did respond well to systemic corticosteroids.

Very similar diagnostic dilemmas have been repeatedly reported in the literature. Lui et al reported a case of a 40-year old Chinese woman with borderline tuberculoid leprosy originally misdiagnosed as sarcoidosis. Skin biopsies showed epithelioid granulomas, and Ziehl-Neelsen stain and polymerase chain reaction (PCR) were negative. Real-time PCR and enzyme-linked immunosorbent assays against phenolic-glycolipid-1 (PGL-1) and leprosy IDRI diagnostic (LID-1) were required to make the correct diagnosis.

Huma et al noted a nearly identical clinical scenario in a 26-year old Filipino woman initially misdiagnosed as sarcoidosis. The diagnosis of leprosy was not made until a modified Ziehl-Neelsen stain on repeat biopsy revealed acid-fast bacilli. Simeoni et al reported a 20-year old Indian male treated with high-dose corticosteroids for over one year for presumed sarcoidosis; this patient had an elevated ACE level and no evidence of pulmonary disease. Despite rapid clinical improvement, he experienced severe flares when corticosteroids were tapered. Multiple biopsies were necessary to demonstrate the bacilli. Elevated serum ACE levels, as seen in our patient, are often used by clinicians as a clue to suspect a granulomatous process, particularly sarcoidosis. However, high ACE levels can also be present in 40% of leprosy patients, indicating this is not a very specific finding.

This diagnostic conundrum has even been profiled in the lay media. A recent vignette in the New York Times unveiled the story of a 50-year old man from Asheville, North Carolina who

saw three specialists before the correct diagnosis was made. In this case, a skin biopsy showed noncaseating granulomas and chest x-ray was unrevealing. Swelling of his greater auricular nerve prompted a nerve biopsy which showed numerous bacilli.

Monitoring of patients with skin-limited sarcoidosis, which our patient is currently being managed as, for detection of extracutaneous involvement has not been extensively evaluated. A recent retrospective review of patients with isolated cutaneous sarcoidosis found that 50% of patients evolved to systemic sarcoidosis over a mean of 6 years. There were no clinical of histopathological findings that helped differentiate patients with isolated skin disease from those that would go on to develop systemic sarcoidosis. Given that cutaneous sarcoidosis can progress to systemic disease many years after initial diagnosis, long-term follow-up and monitoring is advisable.

Leprosy is a great mimicker, and this is additionally confounded by its very long incubation time, typically ranging from 3 to 10 years. While most individuals exposed to *M. leprae* do not develop disease given the organism's low infectivity rate, family members of a patient with leprosy are at higher risk for disease transmission. A study out of India showed the secondary leprosy attack rate for close household contacts to be 6.8 per 1,000 person-years. This represents a ten times higher rate when compared to the annual incidence rate of 0.8 per 1,000 person years. This risk is even higher for children, particularly those younger than 15.

Novel testing is becoming available to assist in the diagnosis of leprosy. Detection of serum antibodies to LID-1 and LID-NDO as well as real-time PCR are helpful in detecting paucibacillary disease. New associations between variants of the NOD2-mediated signaling pathway, which regulates components of the innate immune response, and the risk of leprosy have been reported. Despite these advanced techniques, delayed diagnosis of leprosy often remains the rule.

Leprosy remains rare in the United States, with less than 250 new cases reported annually. Its only known animal reservoir is the nine-banded armadillo, which is most prevalent in the southern United States. Thus, the diagnosis of leprosy, especially in non-endemic areas, requires an astute clinician and high level of clinical suspicion. New clinical findings should be approached thoughtfully, with a very low threshold to re-biopsy lesions and challenge the presumed diagnosis. We anxiously await the PCR results on our patient and hope this will provide some clarification to our diagnosis and future management.

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CHICAGO DERMATOLOGICAL SOCIETY **CASE 2**

Presented by Carrie Stull, MD and Claudia Hernandez, MD
Department of Dermatology, Rush University Medical Center

Unknown

CHICAGO DERMATOLOGICAL SOCIETY **CASE 3**

Presented by Samantha N Barry, MD, MS, Catherine Maloney BS, Marianne O'Donoghue, MD, Warren Piette, MD and Arthur Rhodes, MD, MPH
Department of Dermatology, Rush University Medical Center

HISTORY OF PRESENT ILLNESS

A 37-year old light skin Hispanic male presented for evaluation of dark spots on his palms and soles. He had been undergoing chemotherapy with procarbazine, vincristine, and lomustine for a recurrent Grade II astrocytoma status post resection. After his second cycle of chemotherapy, he noticed new brown spots on his palmar and plantar surfaces. They were asymptomatic. With each successive cycle of chemotherapy, he noticed more spots and darkening of extant spots. After discontinuation of chemotherapy, the lesions stabilized. Two months later, the numbers and color of the lesions persisted, prompting evaluation. No treatment has been attempted.

PAST MEDICAL HISTORY

Seizures, heavy alcohol use
Right diffuse Grade II astrocytoma s/p resection (8/2014), with recurrence and repeat resection (11/2016) followed by 6 cycles of procarbazine, vincristine and lomustine chemotherapy (5/2017 through 2/2018)

MEDICATIONS

Levetiracetam
Ondansetron

ALLERGIES

No known allergies

LABORATORY RESULTS

None

RADIOLOGY

None

TREATMENT AND COURSE

Eight months after completion of chemotherapy, the acral pigmented lesions began to fade slightly, without treatment. One year post chemotherapy, the lesions are still present and asymptomatic but are much lighter in color. The patient's astrocytoma is stable.

DIAGNOSIS

Chemotherapy-induced eruptive acral lentigines

DISCUSSION

Lentigines may occur on acral and mucosal surfaces, regardless of race and unassociated with chemotherapy. The intensity of pigmentation, number, and size of lentigines are greater in darker skin types. Prevalence of lentigines appears to be greater in those younger than 50 years, but is equal according to gender. Acral lentigines may be observed following injury, and hormonal factors may play a role in women. Histologically, acral lentigines unassociated with chemotherapy are characterized by increased numbers of melanocytes and increased basilar melanin production.

Pigmentary changes are common in cancer patients undergoing chemotherapy, up to 17.7% in one study by Dai et al. Common reaction patterns include oral and acral lentigines, cutaneous hyperpigmentation, and cutaneous hypopigmentation. Herein, we present a patient with new onset of multiple acral pigmented macules while receiving chemotherapy with procarbazine, lomustine, and vincristine.

Acral hyperpigmentation, similar to the presentation seen in this case, has been reported in association with numerous anti-neoplastic agents. For instance, 5-fluorouracil has been known to provoke focal acral hyperpigmentation as well as discrete pigmented macules on palms, soles, and oral mucosa. This medication's prodrug, capcetabine, and its structural analog, tegafur, have been reported to produce similar pigmented lesions. Case reports have implicated cisplatin, carboplatin, and pemetrexed in causing diffuse acral hyperpigmentation.

Lentiginosis may appear in multiple hereditary syndromes and sporadic conditions with known and unknown genetic bases including: agminated lentiginosis, nevus spilus, solar lentigines, PUVA lentigines, genital lentiginosis, central-facial lentiginosis, scar lentigines, lentigo simplex, Peutz-Jeghers syndrome, LEOPARD syndrome, and LAMB syndrome (Carney complex). Despite this, no exact mechanism for development of lentigines has been elucidated. One proposed mechanism for the development of lentiginosis during chemotherapy suggests local accumulation of drug causing stimulatory effects on melanocytes, leading to direct stimulation of melanocytosis and melanin production (Villalon et al).

No permanent long-term sequelae or malignant potential have been described in reported cases of chemotherapy-induced acral lentiginosis. Some reports have described resolution of pigmentary changes after discontinuation of the offending agent. The cutaneous melanoma risk does not appear to be increased based on the prevalence of acral pigmented macules.

To our knowledge, eruptive acral lentiginosis has not been reported with procarbazine, lomustine, and vincristine combination chemotherapy. We present this case to educate patients and providers about the occurrence of acral lentiginosis during chemotherapy.

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CHICAGO DERMATOLOGICAL SOCIETY **CASE 4**

Presented by Nour Al-Hadidi, MD, Claudia Hernandez, MD, Mark D Hoffman, MD and Michael Tharp, MD
Department of Dermatology, Rush University Medical Center

HISTORY OF PRESENT ILLNESS

A 58-year old white man presented with a 3 month history of diffuse erythema of the face with fine scaling and confluent red plaques on the chest, back, and bilateral upper extremities with islands of sparing involving 35-40% of his body surface area (BSA). He was also noted to have waxy keratoderma of the bilateral palms, hyperkeratotic plaques on the bilateral knees, and thickened and dystrophic nails. Associated symptoms included pruritus, scaling and hypohidrosis of the skin, and dry eyes. A representative lesion on the patient's left chest was biopsied and revealed prominent follicular plugging with adjacent "scoreboard" parakeratosis. Clinical impression and histopathology suggested type 1, classical adult onset pityriasis rubra pilaris (PRP). He was treated with methotrexate, topical steroids, and briefly placed on isotretinoin without improvement and was subsequently evaluated at Rush University Medical Center.

PAST MEDICAL AND SURGICAL HISTORY

Hypertension, tonsillectomy, carpal tunnel release, hernia repair, inner ear surgery

FAMILY AND SOCIAL HISTORY

Mother, sister: Crohn's disease
Non-smoker
Employed by a metal and glass packaging company

MEDICATIONS

Rosuvastatin
Amlodipine
Doxepin
Folic acid
Methotrexate
Erythromycin ophthalmic ointment

PHYSICAL EXAM

Examination revealed diffuse erythema and fine scaling on the face. Confluent red plaques with islands of sparing involved the chest, back, and bilateral upper extremities. Waxy keratoderma of the bilateral palms, thickened and dystrophic nails were seen.
Total BSA 35-40%.

PERTINENT LABS/IMAGING

Comprehensive metabolic panel, complete blood count, ANA and autoimmune work-up, C3/C4, TSH, CK, aldolase, ESR, CRP were all normal or within normal limits

HISTOPATHOLOGY

Left chest: alternating orthokeratosis and parakeratosis in a horizontal and vertical pattern, prominent follicular plugging, mild epidermal hyperplasia and a superficial perivascular lymphohistiocytic infiltrate. Periodic acid–Schiff (PAS) stain was negative for fungal forms.

DIAGNOSIS
Pityriasis rubra pilaris (PRP), type 1 classical adult onset

TREATMENT AND COURSE:
The patient was treated with methotrexate 25 mg weekly and prednisone 60 mg daily with partial improvement. However, upon tapering of prednisone, patchy erythema recurred. Given inadequate control, ustekinumab (90 mg subcutaneous at week 0, week 4 and then every 12 weeks) was initiated and his methotrexate was discontinued. Following two injections of ustekinumab, the patient's back, abdomen, and palms were clear. Shortly after initiating ustekinumab, the patient began to develop arthralgias and myalgias in the back, hips and ankles. He was referred to rheumatology where clinical exam, serologic workup, and radiographic findings led to a diagnosis of seronegative spondyloarthropathy. Given inadequate control of musculoskeletal symptoms, transition from ustekinumab to adalimumab was recommended. One year following transition to adalimumab, the patient's arthralgias had resolved and his skin remained clear.

DISCUSSION
Pityriasis rubra pilaris (PRP) is a rare hyperproliferative papulosquamous disorder. The etiology of PRP is unknown, however one suggested etiology thought to play a role is T-cell-mediated immunity. PRP is characterized by follicular hyperkeratosis on an erythematous base and coalescence of papules forming large orange-red plaques with classic islands of spared skin with caudal spread. Palmoplantar orange-red waxy keratoderma may also be observed. The major clinical differential diagnosis is psoriasis.

PRP is typically acquired sporadically, however autosomal dominant cases associated with mutations in the CARD14 gene have been found to cause the familial form. Six subtypes have been described based on age of onset, lesion characteristics, disease course and association with HIV. Type 1, classical adult onset, is the most common type. Up to 80% of type 1 PRP resolves without treatment within 3 years. No specific guidelines or controlled trials for treatment are available, thus therapy is based on the results of small case series and reports. Given its resemblance to psoriasis, classic treatments for psoriasis are often used including: topical corticosteroids, vitamin D analogs, retinoids, methotrexate, cyclosporine, and azathioprine. Tumor necrosis factor- α antagonists have been successful in more severe cases.

Unfortunately when these medications are ineffective, treatment options for patients are limited. Ustekinumab is a human monoclonal antibody directed against the p40 subunit of IL-12 and IL-23. It has been effective at treating psoriasis, a condition with similar clinical and histological features to PRP. While it has been shown to be successful in treating several cases of PRP, its use is limited in the literature. Although IL-12 and IL-23 have not been implicated in the pathogenesis of PRP, ustekinumab's efficacy may suggest commonalities in the inflammatory cytokine profiles in psoriasis and PRP. Moreover, since PRP is thought to be a T cell-mediated disorder, blocking IL-12 and IL-23 and thus preventing the activation of T cells may account for its efficacy in PRP.

A recent study found an increased Th17 expression profile in skin lesions of 3 patients with PRP. In these patients, the levels of Th17 cytokines, but neither of TNF-α nor the Th1 cytokine IFN-γ, paralleled clinical improvement during anti-IL-12/IL-23 treatment of 1 patient. This may provide a rationale for targeting the IL-23-Th17 axis as a treatment option for refractory PRP.

PRP has been considered a skin-limited disorder, however several cases of associated arthritis have been reported. The reported presentations of PRP-associated arthritis are variable and

include asymmetric and symmetric peripheral polyarthritis, axial disease and enthesitis. Optimal treatment of the arthritis remains unclear. One case reported improvement of arthritis with TNF-α inhibition, but no improvement in the skin. This demonstrates that the joints and skin may respond independently or incongruently to treatment.

Ustekinumab likely played a predominant role in the rapid recovery of our patient given near complete resolution after its initiation following failure to respond to methotrexate and systemic steroids. Based on several case reports, ustekinumab is deemed a promising therapeutic choice for PRP due to its rapid efficacy, ease of administration, prolonged time-gap between ensuing administrations, and favorable side effect profile, notably in cases refractory to conventional therapy.

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CHICAGO DERMATOLOGICAL SOCIETY **CASE 5**

Presented by Stacie Clark, MD and Arthur Rhodes, MD, MPH
Department of Dermatology, Rush University Medical Center

Unknown

CHICAGO DERMATOLOGICAL SOCIETY **CASE 6**

Presented by Nick Blickenstaff MD, MS, Vijaya Reddy MD, MBA and Peter Revenaugh MD
Department of Dermatology, Rush University Medical Center

HISTORY OF PRESENT ILLNESS

This patient is a 4-year old white male who presented with his parents to Rush University Medical Center for evaluation of a lesion on the right upper eyelid margin. The lesion had been present for 6 months and had enlarged slightly according to his parents. The child denied any pain, pruritus, or visual complaints. Comprehensive review of systems was negative.

PAST MEDICAL HISTORY

Adenoid hypertrophy
Recurrent sinusitis

PAST SURGICAL HISTORY

None

MEDICATIONS

None

ALLERGIES

No known drug allergies

FAMILY HISTORY

No history of skin cancer, skin conditions, or autoimmune conditions.

SOCIAL HISTORY

Non-smoker

PHYSICAL EXAM

Examination revealed a 3 mm x 4 mm subcutaneous nodule on the right lateral upper eyelid margin. There was no overlying surface change and the lesion was non-tender to palpation. No palpable cervical or axillary lymphadenopathy was appreciated.

HISTOPATHOLOGY

Right lateral upper eyelid: effacement of the epidermal rete and a poorly circumscribed neoplasm characterized by storiform arrangement of spindle-shaped cells in short interlacing fascicles.The infiltrate focally extends to the base and lateral edges of the excision, enveloping the subcutaneous tissue and muscle. Lesional cells stain strongly positive for CD34 and negative for S-100, Factor XIIIa and smooth muscle actin. Fluorescent in-situ hybridization testing positive for the fusion of collagen type I, α1 (COL1A1) (17q21) and platelet derived growth factor-β (PDGFB) (22q13) loci.

LABORATORY RESULTS

None

DIAGNOSIS

Dermatofibrosarcoma protuberans (DFSP)

TREATMENT AND COURSE

The patient was scheduled to undergo adenoidectomy due to a history of adenoid hypertrophy and recurrent sinusitis. Since the right-sided periorbital lesion had been slowly growing in size, the parents elected to coordinate removal of the lesion with the patient's adenoidectomy. Following lesion excision the diagnosis of DFSP was confirmed by histopathology, immunostaining and molecular analysis. The patient was presented at the Rush Cutaneous Tumor Board which prompted referral to ophthalmology at Lurie Children's Hospital (LCH) for a second opinion. Mohs micrographic surgery was ultimately performed at LCH. There was no evidence of residual spindle cell neoplasm after 1 stage. The patient now follows with pediatric dermatology every 6 months for total body skin exams and has done well postoperatively without recurrence.

DISCUSSION

Dermatofibrosarcoma protuberans (DFSP) is a rare soft tissue sarcoma that accounts for approximately 0.1% of all malignancies. Most cases are seen in early to middle adult life, with only 5.9% of DFSPs occurring in infancy or childhood. Early diagnosis of pediatric DFSP is critical to minimize surgical disfiguration and can be challenging due to its diverse presentations in childhood. The tumor may clinically mimic a vascular birthmark, vascular tumor, morphea, a hamartoma, cyst, lipoma or other entities in its early stages. Although DFSP frequently occurs on the trunk and extremities, only 10-15% of cases occur on the head and neck.

The diagnosis of DFSP is classically based on histologic findings: spindle cells with a storiform growth pattern invading the subcutaneous tissue forming projections into the fat lobules. The central areas of the lesion have greater cellularity, whereas the periphery is more diffuse with a honeycomb pattern. Immunohistochemical analysis is typically positive for CD34 (although 10%–20% may be negative), vimentin, and CD99 but negative for factor XIIIa, S-100, actin, and desmin. Greater than 90% DFSPs have the chromosomal translocation involving 17q22;22q13, with fusion of the genes encoding COL1A1 and PDGFB (COL1A1-PDGFB). The tumor's growth can be attributed to the constitutively expressed PDGF receptor that acts as an autocrine factor stimulating the growth of DFSP cells. There are several variants of DFSP. Included in these variants are pigmented DFSP (Bednar tumor) with melanin-containing dendritic cells and fibrosarcomatous DFSP, the variant most at risk for recurrence and metastasis (18% vs 1% for conventional DFSP). Rapid change in a lesion is suggestive of a fibrosarcomatous transformation due to TP53 missense and silent mutations, as well as high microsatellite instability.

The treatment of choice for DFSP is complete surgical resection. Recurrence rates depend on the type of surgery performed including: conservative surgical resection (26-60%), wide local excision with 2 cm margins including the fascia of underlying muscles (0-30%), and Mohs (1%). Because of the high recurrence rate of these lesions, Mohs is preferred over wide local excision for definitive treatment. Since Mohs was performed on our patient, he did not require the use of radiation therapy or imatinib mesylate (PDGF-β inhibitor), which have been used as adjuvant therapy after surgery, primary therapy for unresectable lesions, and treatment for metastatic disease.

We present this case to highlight a rare presentation of periorbital DFSP in a child masquerading as a benign cyst. It is important that physicians consider the diagnosis of DFSP in the pediatric population because it is a malignant neoplasm that requires surgical excision. Clinical follow-up is required every six months for five years, then every year for ten years, and should include palpation of the surgical scar and regional lymph nodes.

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CHICAGO DERMATOLOGICAL SOCIETY **CASE 7**

Presented by Carolyn Stull, MD, Meredith Morse, MD and Warren Piette, MD
Department of Dermatology, Rush University Medical Center

HISTORY OF PRESENT ILLNESS

A 66-year old white man presented to clinic with a three month history of a rash on his bilateral lower extremities. He reported progressively worsening swelling, pain and numbness. One month prior to his first visit to Rush, the patient underwent a punch biopsy of the left anterior ankle by an outside dermatologist. Histopathology was remarkable for livedo reticularis with thrombotic vasculopathy. He was being treated for this presumed diagnosis with pentoxifylline, aspirin, and gabapentin without improvement. A review of systems was negative for fevers, chills, night sweats and abdominal pain.

PAST MEDICAL HISTORY

Prostate cancer

MEDICATIONS

Pentoxifylline
Aspirin
Gabapentin

ALLERGIES

Levocetirizine
Ciprofloxacin

FAMILY HISTORY

None

SOCIAL HISTORY

Non-smoker

PHYSICAL EXAM

Examination revealed tender, retiform, partially blanching erythematous to violaceous patches, some with central duskiness and slight induration on the bilateral lower extremities. There was 2+ pitting edema of both lower legs.

HISTOPATHOLOGY

Left anterior ankle, punch (outside dermatologist): livedo reticularis with thrombotic vasculopathy.

Left anterior leg, incisional biopsy (Rush): deep dermal medium vessel lymphocytic vasculitis

LABORATORY RESULTS

CBC, CMP, UA, total serum protein, SPEP and immunofixation, cyroglobulin quantitative screen, cardiolipin IgG and IgM, lupus anticoagulant, beta-2 glycoprotein I IgG antibody and IgM antibody, Hepatitis B surface antigen and core antibody, Hepatitis C antibody, ANA screen, ANCA panel, Lyme antibody all within normal limits/negative.

CRP: 3.17 [ref <1 mg/dl]
ESR: 27 [ref 0-10 mm/hr]

DIAGNOSIS
Cutaneous polyarteritis nodosa with nerve involvement

TREATMENT AND COURSE
One week after initial presentation, the patient developed severe pain and retiform purpura of the left leg and was started on prednisone 30 mg daily. He subsequently developed new left hand and right leg pain as well as numbness and was referred to neurology for evaluation. Neurological assessment was remarkable for left ulnar and bilateral peroneal neuropathies thought to be consistent with mononeuritis multiplex in the setting of vasculitis. His prednisone was increased to 60 mg daily. Despite the increased dose of prednisone, he developed bilateral hand numbness and began dragging his right foot which prompted hospitalization. Methylprednisolone and cyclophosphamide were administered intravenously with subsequent improvement of cutaneous and neurologic symptoms. He has since received a second cyclophosphamide infusion and is currently maintained on high dose gabapentin (2400mg) daily, prednisone (60mg), and aspirin (325mg).

DISCUSSION
Polyarteritis nodosa (PAN) is a segmental necrotizing vasculitis that predominantly affects medium-sized arteries. Focal areas of involvement create vessel wall weakening and necrosis that result in aneurysmal dilation or stenosis. PAN may affect several organ systems including the skin, peripheral nerves, joints, kidneys and gastrointestinal tract. Its underlying etiology is unknown.

Cutaneous polyarteritis nodosa (cPAN) denotes a “skin-predominant” variant that often follows a chronic yet benign course. This form comprises approximately 10% of all cases of PAN, and is the most common form in children. cPAN classically presents with livedo racemosa and tender subcutaneous nodules that may progress to “punched out” ulcerations. The lower extremities are the most common site of involvement. Fever, arthralgias, myalgias and neuropathies often occur in conjunction with skin findings. Neuropathy is typically confined to areas of cutaneous involvement but may also occur at distant sites.

Cutaneous PAN may occur in association with conditions such as inflammatory bowel disease, and streptococcal upper respiratory tract infections. Medications such as minocycline have also been implicated in cPAN induction. This form is uniquely associated with p-ANCA positivity and typically resolves with drug cessation.

Histopathologic findings in cPAN include segmental necrotizing vasculitis involving arteries in the deep dermis or subcutaneous tissue. Vessels within the upper dermis may only demonstrate nonspecific perivascular inflammation. Direct immunofluorescence may demonstrate deposits of C3, IgM or fibrin within or around vessel walls. Deep incisional biopsy of the border of a nodule or ulcer should be performed, as superficial biopsies may not capture adequate depth or tissue quantity. Adequate tissue sampling is particularly important in distinguishing cPAN from livedoid vasculopathy, which is a common clinical and histopathologic mimicker. Further work-up including nerve conduction studies, electromyography, electrocardiogram and angiography should be performed on a case-by-case basis in accordance with presenting symptoms.

Progression of cPAN to systemic PAN has been reported, albeit rarely. The vast majority of cases follow a chronic, relapsing course without visceral involvement. A recent case series by

Alibaz-Oner et al of 41 cPAN patients found that only one progressed to develop systemic involvement. Riku et al reported progression of cutaneous to systemic PAN in 2 of 20 patients. Documented cases of progression have occurred one to two decades after initial cutaneous presentation. Given the potential for organ damage, long-term follow-up is advised.

Treatment varies according to severity of presentation. Initial treatment for systemic PAN consists of systemic corticosteroids tapered over a 6-month period. Patients with severe disease may require pulsed methylprednisolone with the addition of cyclophosphamide. In contrast, patients with cPAN may not require aggressive therapy. Topical or intralesional corticosteroids can be used for local areas of cutaneous involvement, and NSAIDs may provide sufficient symptomatic relief. However, even in cPAN, systemic corticosteroids may be required in extensive cases. Escalation to treatments such as methylprednisolone or cyclophosphamide should be reserved for refractory and progressive cases with prominent symptoms.

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CHICAGO DERMATOLOGICAL SOCIETY **CASE 8**

Presented by Meredith Morse, MD and Kevin Cavanaugh, MD
Department of Dermatology, Rush University Medical Center

HISTORY OF PRESENT ILLNESS

The patient is an 83-year old white male with a past medical history significant for myelodysplastic syndrome who presented for a rash on his bilateral hands of one month duration. He endorsed pruritus and pain. There were no new medications or exposures prior to onset. The patient did admit to dealing with a great deal of emotional stress as his wife was struggling with a terminal illness. He felt otherwise well and complete review of systems was unremarkable. He was given triamcinolone ointment to use twice daily for two weeks. During his follow-up, the patient noted new blisters and his current lesions were worsening. He was then started on clobetasol ointment twice daily. Given very minimal clinical improvement at his next follow-up, a biopsy for hematoxylin and eosin as well as for direct immunofluorescence was performed.

PAST MEDICAL HISTORY

Myelodysplastic syndrome with refractory anemia
Hypertension
Hyperlipidemia
Diabetes mellitus
Asthma

MEDICATIONS

Darbepoetin alfa subcutaneous injection
Danazol
Testosterone gel
Flomax
Hydrochlorothiazide
Insulin
Atorvastatin
Vitamin B12
Vitamin B6
Aspirin
Albuterol
Acetaminophen

ALLERGIES

Sulfonamides

FAMILY HISTORY

Father: colon cancer

SOCIAL HISTORY

Former smoker

PHYSICAL EXAM

Examination revealed erythematous indurated plaques with crusting and collarettes of scale on the palms, extending to the dorsum of the hands. The dorsal hands also showed annular plaques with central clearing, raised erythematous edges, and trailing scale.

HISTOPATHOLOGY

Left palm, lesional (H&E): eosinophilic spongiosis and a superficial perivascular lympho-eosinophilic infiltrate

Left palm, peri-lesional (DIF): linear staining of the basement membrane zone with C3 and faint IgG

LABORATORY RESULTS

Complete metabolic panel: within normal limits
Complete blood count: hemoglobin 8.8 g/dL [reference range 13.5-17.5 g/dL] (patient's baseline)
Potassium hydroxide preparation: negative

Bullous pemphigoid antigen 2 (BP180) serology: elevated (17)
Bullous pemphigoid antigen 1 (BP230) serology: within normal limits

DIAGNOSIS

Bullous pemphigoid, dyshidrotic variant (dyshidrosiform bullous pemphigoid)

TREATMENT AND COURSE

The patient was continued on clobetasol ointment twice daily and started on doxycycline 100 mg twice daily with niacinamide 500 mg three times daily. He had an excellent response with clearance of his bullae and pruritus within 6 weeks.

DISCUSSION

Bullous pemphigoid is the most common autoimmune blistering disorder. Its pathogenesis is related to auto-IgG antibodies (primarily IgG4 and IgG1) that target hemidesmosomal proteins, resulting in subepidermal bullae. Target antigens include bullous pemphigoid antigen 2 (BPAg2, BP180, collagen XVII) and bullous pemphigoid antigen 1 (BPAg1, BP230). The BPAg2 NC16A ectodomain is thought to be the primary disease mediator, with attack on BPAg1 a result of epitope spreading.

Pathology can vary but classically demonstrates a subepidermal blister cavity with eosinophils. In early lesions, eosinophilic spongiosis or eosinophils lining up at the dermo-epidermal junction may be all that is seen. Direct immunofluorescence typically shows linear C3 and IgG along the basement membrane zone. Salt-split skin localizes antibodies to the epidermal side (blister "roof"). ELISA can be used to detect circulating BPAg2 and BPAg1 antibodies; these levels correlate with disease activity and can be useful for monitoring.

Dyshidrosiform bullous pemphigoid is a rare localized variant of bullous pemphigoid in which vesicles and bullae are localized to the palms and/or soles. The mechanism of localization to palmoplantar skin is unclear. It has been suggested that normally hidden antigens are uncovered by an inflammatory process such as tinea pedis or manuum, but this remains to be proven. The histopathology and direct immunofluorescence findings are identical to classic bullous pemphigoid.

The prevalence of this rare variant is not fully known. The first case was reported in 1979 (Levine et al), but fewer than 40 cases have been described in the literature. In several of the reported cases, patients progressed to generalized bullous pemphigoid, with the interval between localized and generalized disease varying from 1 week to 5 years. There are, however, few reports of palmoplantar involvement without further spread. Barth et al showed that palmoplantar lesions were observed in 28% (20/71) of patients with bullous pemphigoid. In four of these patients, palmoplantar lesions were the presenting features, and all of these patients went on to develop generalized bullous pemphigoid. In another study, 9 out of 20 patients presented with palmoplantar vesicles as prodromal symptoms of bullous pemphigoid. Two of these patients had a vesicular eruption that remained exclusively on the palms and the soles.

Most cases of dyshidrosiform bullous pemphigoid resolve with potent topical corticosteroids or low-dose prednisone. Given the localized nature of this variant, less aggressive treatment including oral tetracyclines with niacinamide is often sufficient to achieve disease control. For rapid control or more severe palmoplantar disease, a combination of higher dose systemic corticosteroids and/or dapsone may be necessary. Very seldom are mycophenolate mofetil, azathioprine, or rituximab required; use of such agents in this localized variant to our knowledge has yet to be reported.

The manifestation of dyshidrosiform bullous pemphigoid can be quite similar to pompholyx. Both entities may present as a persistent dermatitis on the palms or soles. A key clinical finding suggestive of dyshidrosiform pemphigoid is the presence of hemorrhagic blisters. If noted, histopathology and immunofluorescence should be performed in these patients to elucidate the correct diagnosis.

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CHICAGO DERMATOLOGICAL SOCIETY **CASE 9**

Presented by Nour Al-Hadidi, MD, Faiyaaz Kalimullah, MD and Mark D Hoffman, MD
Department of Dermatology, Rush University Medical Center

HISTORY OF PRESENT ILLNESS

A 38-year old black man presented with a 1 month history of erythematous patches on bilateral lower extremities. The patches had progressed to swelling, ulceration, and drainage associated with severe pain. He reported a similar presentation 8 years ago with ulcerations of the lower extremities and lesions involving the upper extremities. At that time, a skin biopsy of a lesion on his left arm demonstrated noncaseating granulomas and a chest x-ray demonstrated hilar adenopathy with pulmonary nodules. This led to a diagnosis of pulmonary and cutaneous sarcoidosis. Treatment with hydroxychloroquine and prednisone yielded no improvement, therefore infliximab was started. The patient's ulcerations rapidly resolved. He was maintained on infliximab until June 2018 at which time he lost his insurance. The ulcerations returned within 3 months prompting him to reestablish care at Rush University Medical Center. On initial evaluation, a superficial wound swab was obtained for culture given concern for superinfection and cultures grew *Staphylococcus aureus, Pseudomonas aeruginosa, and Streptococcus agalactiae* (Group B). He was treated with oral antibiotics (trimethoprim-sulfamethoxazole and levofloxacin) based on susceptibilities with minimal improvement and subsequently returned for skin biopsy.

PAST MEDICAL AND SURGICAL HISTORY

Pulmonary and cutaneous sarcoidosis

MEDICATIONS

Naproxen

PHYSICAL EXAM

Examination of the lower extremities revealed several irregularly shaped ulcerations overlying erythematous and violaceus papules (some with vaguely retiform appearance). Ichthyosiform scale was also noted. There were several hypopigmented patches (some with overlying smooth pink papules) predominantly involving the upper extremities with less involvement of the lower extremities and trunk.

PERTINENT LABS/IMAGING

Chest x-ray (2018): stable bilateral hilar fullness and linear infrahilar opacities

CT chest (2018): multiple enlarged mediastinal and hilar lymph nodes with multiple micronodules along the perilymphatic and bronchovascular distribution. Enlarged heterogeneous spleen with multiple micronodular densities suggestive of noncalcified splenic granulomas. Enlarged abdominal lymph nodes.

Bilateral lower leg x-ray: no evidence of osteomyelitis.

Comprehensive metabolic panel:
AST 49 U/L [ref: 3-44 U/L], ALT 50 U/L [ref: 0-40 U/L], AP 194 U/L [ref: 30-125 U/L]
Angiotensin converting enzyme: 71 U/L [ref: 9-67 U/L]
CRP: 9.1 mg/L [ref: 0-8 U/L]
ANA: positive (1: 640)
Rheumatoid factor: 38 IU/mL [ref: 0-29 IU/L].

CBC, ESR, C3/C4, Urinalysis, Hepatitis C Ab and Hepatitis B surface Ag, cryoglobulins, ANCA, and QuantiFERON-TB Gold were all negative/within normal limits.

HISTOPATHOLOGY

Right proximal leg: noncaseating granulomas consistent with sarcoidosis.
Right distal leg, ulcer edge: ulceration, granulation tissue and adjacent granulomas consistent with sarcoidosis. No necrosis was appreciated.
PAS, GMS and Fite stains were negative for microorganisms. No polarizable foreign body material was identified.

DIAGNOSIS

Recurrent ulcerative sarcoidosis

TREATMENT AND COURSE:

The patient completed a course of oral antibiotics with minimal improvement. Following biopsy, he was started on prednisone 20 mg daily for 1 month, which was subsequently tapered. He was referred to wound care for additional management, where he underwent debridement of devitalized tissue. The combination of silvadene, nystatin and hydrocortisone alternating with collagenase was recommended for infection control and chemical debridement given extensive fibrin and occasional necrotic tissue. Given excellent clinical response to infliximab with prior treatment, decision was made to resume infliximab once his insurance was reinstated. Infliximab was resumed (5 mg/kg at week 0, 2, 6, and then every 6 weeks). Two months following initiation of infliximab, the patient was noted to have appreciable healing of his wounds. Three ulcerations remained; all had decreased in size and pain. Patient was referred to ophthalmology and pulmonology for evaluation and monitoring of systemic involvement of disease.

DISCUSSION

Sarcoidosis is a multisystem, idiopathic disease, characterized by lymphocyte-poor, noncaseating granulomas. Persistent inflammation driven by poorly degradable antigens such as microorganisms, metals, organic and inorganic dusts, insecticides, and autoantigens, has been proposed in its pathogenesis. Sarcoidosis affects the skin in approximately 20 to 35% of cases. Cutaneous involvement can present as granulomatous infiltration or non-specific reactive eruptions. The presentation of granulomatous infiltration may be variable and includes periorificial papules, discoid lupus erythematosus-like plaques, asymptomatic mobile subcutaneous nodules, lupus pernio, hypopigmented macules and patches, and ulcerative lesions. The most common reactive eruption lacking granulomatous inflammation is erythema nodosum.

Although cutaneous involvement is common, ulcerative sarcoidosis is rare, and in its earliest description by Boeck, was not noted to occur. It is estimated to represent 5% of cutaneous sarcoidosis. It shows a predilection for young adults, women, and patients of African American or Japanese descent. Only 1% of white patients affected by sarcoidosis develop skin ulcers. It can arise within existing papulonodules on the lower extremities or may occur on previously unaffected skin and in a generalized distribution. Patterns include ulceration within necrotic yellow plaques (with substantial overlap in clinical appearance with ulcerative necrobiosis lipoidica) or violaceous nodules arising in an annular confluent pattern that subsequently ulcerate. In some cases it may be the initial presenting sign of this disease.

While the pathogenesis of ulceration is not known, it has been suggested that it may be secondary to dermal proliferation of epithelioid cells causing necrosis of the overlying epidermis,

or secondary to trauma superimposed on atrophic plaques. Healing with scarring tends to occur. Most patients have extracutaneous disease, and 60% are noted to have elevated serum angiotensin-converting enzyme (ACE) levels produced by sarcoid granulomas.

Ulcerative sarcoidosis may mimic other ulcerative conditions such as venous stasis or pyoderma gangrenosum. The diagnosis requires correlating clinical findings, evidence of non-caseating epithelioid granulomas, and exclusion of other diseases. The histopathologic differential includes foreign bodies, metastatic Crohn's disease, granulomatous infections, granulomatous lymphoproliferative diseases, and granulomatous pyoderma gangrenosum.

Ulcerative sarcoidosis can be resistant to treatment with failures observed with antimalarials, topical steroids, intralesional steroids, isotretinoin, antimicrobials and radiation therapy. Methotrexate has been effective in some cases, and combination treatment with systemic corticosteroids, antimalarials, and either mycophenolate mofetil or thalidomide has been used with success.

In patients with sarcoidosis who have been refractory to standard treatment, treatment options include anti-TNF-α agents. In 2001, a few case reports documenting the efficacy of infliximab in treating cutaneous sarcoidosis began to be published. In 2005 a report of ulcerative sarcoidosis responding to adalimumab was published. Release of TNF-α, which plays an important role in the formation and maintenance of granulomas, has been found to be increased in patients with sarcoidosis. Infliximab, a chimeric monoclonal anti-TNF-α antibody, binds to and inactivates this cytokine with resultant break down of pathologic granulomas. In a retrospective study of 10 patients with various manifestations of sarcoidosis, 9 patients demonstrated a dramatic clinical response with use of infliximab.

Although successful use of infliximab is reported in the literature (with some reports of no recurrence following discontinuation), little is known regarding whether there is a long-term sustained response. The risk of relapse tends to be high, and maintenance therapy may be required to attain disease remission. While the side-effect profile of infliximab allows for its use as a long-term therapy, it may be associated with the reactivation of tuberculosis. Therefore, one must be careful to avoid mistaking tuberculosis as sarcoidosis or perceiving active tuberculosis as worsening sarcoidosis. Moreover, it is important to note that there have been reports of paradoxical development or exacerbations of sarcoidosis in patients on TNF-α inhibitor therapy (notably etanercept), which demonstrates the variable effects of this treatment modality.

Our patient's results are in line with the case series reporting efficacy of infliximab in sarcoidosis. The prompt recurrence of his ulcerative sarcoidosis following discontinuation of infliximab demonstrates the likely need for long-term maintenance therapy to control his disease.

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CHICAGO DERMATOLOGICAL SOCIETY **CASE 10**

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HISTORY OF PRESENT ILLNESS

A 63-year old white male developed a deep ache, redness and swelling in the left knee one week after right knee arthroplasty. After physical therapy, the knee blistered and had associated pain. At follow up with orthopedics the patient had an arthrocentesis. Synovial fluid analysis revealed many white blood cells, red blood cells and no organisms. The patient continued to worsen. His blister ulcerated, enlarged and became more painful. He was taken to the operating room for a washout of the artificial joint and a polymer liner exchange. Aerobic, anaerobic, acid-fast bacilli and fungal wound tissue cultures were negative. The patient was started on empiric cefepime and vancomycin. Despite this, the patient continued to have progressive pain, swelling and ulceration with fever and leukocytosis. The patient was taken to the operating room for a repeat washout and polymer liner exchange. Sharp debridement of the wound was performed by plastic surgery and per the operative note "milky fluid" was noted to be "integrated with the skin". A wound culture grew mild *Staphylococcus epidermidis* in one out of four tubes. A tissue sample for histopathologic analysis showed marked neutrophilic exudate. Repeat tissue cultures were positive for one colony *Staphylococcus haemolyticus*, otherwise negative for anaerobic, acid-fast bacilli and fungus. Continued wound enlargement prompted a Dermatology consult.

PAST MEDICAL HISTORY

Diabetes
Essential thrombocytosis

MEDICATIONS

Metformin
Hydroxyurea

ALLERGIES

Sulfonamide antibiotics

FAMILY HISTORY

Mother: diabetes

SOCIAL HISTORY

Non-smoker

PHYSICAL EXAM

Examination of the left knee revealed a 21 cm x 18 cm ulceration with a violaceous rim and sharp jagged edges due to debridement. The patellar tendon was visible.

HISTOPATHOLOGY

Left knee: ulcerated and necrotic skin down to muscle with marked neutrophilic exudate

LABORATORY RESULTS

Arthrocentesis: 52,000 white blood cells, 88% polymorphonuclear cells, no organisms seen on Gram stain
Wound culture: 1 of 4 tubes positive for mild *Staphylococcus epidermidis*
Tissue cultures for anaerobic bacteria, acid-fast bacilli, fungal cultures negative x 2
Aerobic bacterial tissue culture initially negative, repeat positive for *Staphylococcus haemolyticus* x 1 colony
Leukocytosis to 40,000

RADIOLOGY

Left lower extremity ultrasound negative for deep venous thrombosis

TREATMENT AND COURSE

The patient was started on prednisone 1 mg/kg/day by dermatology with significant improvement in pain within 3-4 days. After one month of prednisone, the ulcer was granulating and the pain had resolved. The patient was transitioned to cyclosporine 3 mg/kg/day. Given the extent of the ulceration with new indwelling hardware, the patient was placed on 10 weeks of IV antibiotics per infectious disease. The patient continued to follow up with dermatology, orthopedic surgery and plastic surgery. During this time dehydrated human amnion/chorion allograft was placed weekly by dermatology. Given the improvement in pain and evidence of rapid healing, a successful case was made to forgo a gastrocnemius flap with plastic surgery as well as an arthrocentesis with orthopedics. Five months after initiation of systemic immunosuppressants, the patient's ulceration had decreased from 21 cm x 18 cm to 16 cm x 14.5 cm with peripheral epithelialization. Granulation tissue had filled in the wound.

DIAGNOSIS

Pyoderma gangrenosum

DISCUSSION

Pyoderma gangrenosum is a chronic, recurrent ulcerative disease. Estimated incidence is 3-10 cases per million people per year. It is most commonly seen in middle-aged adults, more often in females. Fifty percent of patients have associated medical comorbidities, most commonly inflammatory bowel disease followed by hematologic malignancies. Twenty to thirty percent of cases exhibit pathergy, with antecedent trauma, such as surgery, as seen in our patient.

Originally described in 1930, pyoderma gangrenosum was thought to be infectious in etiology. Despite being well known in dermatology, this diagnosis is often missed. While some inflammatory disorders may resolve spontaneously, pyoderma gangrenosum usually requires treatment to achieve remission, as well as avoidance of debridement. Thus, delays in diagnosis and treatment can lead to significant patient morbidity and mortality.

The pathogenesis of neutrophilic dermatoses remains unknown. Despite being categorized by a sterile, predominately neutrophilic infiltrate, neutrophilic dermatoses remain heterogeneous in their presentation. Three main processes are believed to be responsible for the development of disease: genetic predisposition, altered expression of inflammatory effector molecules, and

abnormal neutrophil function. The hematopoietic growth factor G-CSF has been shown to be elevated in neutrophilic dermatoses and correlates with disease activity. Other cytokines have also been shown to be elevated including IL-1α, IL-1β, IL-2, and interferon γ. The role of these effector molecules is unclear. While no triggers have been identified, these changes may be due to associated systemic disease states.

Treatment of pyoderma gangrenosum occurs in two phases: halting the inflammatory process followed by healing of the wound. Pyoderma gangrenosum responds rapidly to systemic immunosuppressants, such as prednisone, cyclosporine, and anti-TNF-α agents. Reduction in pain, erythema, and exudate can be seen in as little as one to two weeks. Transition to chronic immunosuppression is often required. After remission of inflammation, wound healing begins and is often prolonged.

Special considerations arise when disease overlies the joint space. Rarely reported, there is no standard or validated management for these difficult cases. Case reports have shown success with muscle flaps while on systemic immunosuppression after inflammatory activity has been halted. Improvement has also been reported with hyperbaric oxygen and negative pressure therapy, however these treatment modalities are limited and expensive. In this case, dehydrated human amnion/chorion allograft was placed around the edge of the ulcer weekly to aid in peripheral epithelialization. Human placental tissue allograft was placed directly on the patellar tendon to aid in soft tissue regeneration. Thirteen applications of the human amnion/chorion allograft and two applications of the human placental tissue allograft were placed during the course of two and a half months of cyclosporine with a reduction in ulcer size by five centimeters. Wound depth improved from exposed patellar tendon to granulation tissue abutting the epithelial edge. It is important to note that throughout application of these allografts, the patient remained on chronic immunosuppression, so it is unclear what role these products played in deep wound healing.

Dehydrated human amnion and chorion and placental tissue allografts have been used for healing chronic wounds in other specialties. These allografts have been shown to retain cytokines and growth factors to promote wound healing. These molecules are believed to be responsible for mesenchymal progenitor cell recruitment to the site of implantation as well as increased angiogenesis.

Since other specialties often have little experience in diagnosing and treating pyoderma gangrenosum, the condition is often exacerbated by debridement and treatment as infection rather than inappropriate inflammation. Additionally, the potential for healing of deep wounds is often underestimated, leading to early decisions for aggressive surgical procedures, including amputations or as in this case complicated skin/muscle flap procedure for wound closure. This is a condition which deserves our continued efforts to educate our colleagues, and often requires our being a strong advocate for the patient to allow a sufficient period of time to demonstrate healing potential before any significant surgical procedure is performed.

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