Chicago Dermatological Society

Monthly Educational Conference

Program Information
CME Certification
and
Case Presentations

Wednesday, November 14, 2018
Gleacher Center – Chicago, IL

Conference Host:
Department of Dermatology
Feinberg School of Medicine
Northwestern University
Chicago, Illinois

Program

Host: Northwestern University
Wednesday, November 14, 2018
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*
9:00 a.m. - 10:30 a.m.	**Clinical Rounds** Slide Viewing/Posters and Patient Viewing
9:00 a.m. - 10:00 a.m.	**Basic Science/Residents Lecture** "Applying Population Data To Address Clinical Dilemmas in Medical Dermatology" *Amit Garg, 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** • **Medical Student Mentoring Lunch** - Room 602
12:45 p.m. - 1:00 p.m.	**CDS Business Meeting**
1:00 p.m. - 2:00 p.m.	**General Session** BLUEFARB LECTURE - "Hidradenitis Suppurativa: Using Big Data to Unravel a Complex Disease" *Amit Garg, MD*
2:00 p.m.	**Meeting adjourns**

Mark the Date!
Next CDS monthly meeting – Hosted by the University of Chicago
Wednesday, December 5th; Gleacher Center, Chicago

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

Guest Speaker

AMIT GARG, MD

Professor and the Founding Chair for the Department of Dermatology at the Hofstra Northwell School of Medicine and Northwell Health; Lake Success, NY

Dr. Garg is board certified in Dermatology by the American Board of Dermatology. He went to the Northwell Health from Boston University Medical Center, where he directed the Residency Training Program in Dermatology as well as the undergraduate medical curricula in dermatology for the school of medicine. Dr. Garg has achieved international recognition as a skilled medical dermatologist, a thought leader in psoriasis, and a medical educator.

Dr. Garg earned his medical degree at the University of Massachusetts, Boston, in 2000 and completed his dermatology residency at the University of Illinois at Chicago in 2004 where he served as chief resident. His subspecialty expertise is interdisciplinary based in caring for patients with autoimmune and inflammatory conditions including psoriasis, lupus, dermatomyositis, and vasculitis.

Dr. Garg's research interests include developing instruments and assessing clinical and patient centered outcomes in psoriasis and hidradenitis suppurativa. He also has developed innovative teaching strategies to improve training and education outcomes. His recent research has focused on improving teaching and assessment methods in undergraduate and graduate medical education, as well as narrowing the practice gaps related to the skin cancer examination through increasing awareness of high risk patient groups, promoting integration of the skin cancer exam into the routine or focused physical exam, and enabling detection of suspicious pigmented lesions.

Leadership roles held by Dr. Garg include the American Academy of Dermatology, the American Board of Dermatology, the Association of Professors of Dermatology, the Medical Dermatological Society, the National Psoriasis Foundation, the Hidradenitis Suppurativa Foundation, the Group for Research and Assessment of Psoriasis and Psoriatic Arthritis, and the International Dermatology Outcome Measures group. He is a member of Dermatology s Residency Review Committee of ACGME.

Dr. Garg has served on editorial boards for journals as well as American Academy of Dermatology based publications. He also is editor-in-chief of the forthcoming first edition book on Rheumatic Skin Diseases. He has published a number of articles in the peer-reviewed literature and has authored several book chapters. Dr. Garg has been awarded the 2016 Thomas G. Pearson, EdD Memorial Education Award by the American Academy of Dermatology.

CME Information

11.14.2018

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.

The guest speaker, Amit Garg, MD, has disclosed the following potential conflicts of interest: Grants/Research Support - UCB, National Psoriasis Foundation, AbbVie; Consulting fees - Asana Biosciences, UCB, AbbVie, Pfizer. None of the planning committee members 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.

NORTHWESTERN UNIVERSITY
FEINBERG SCHOOL OF MEDICINE
DEPARTMENT OF DERMATOLOGY

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CHICAGO DERMATOLOGICAL SOCIETY **Case 1**

Presented by Andrew Para, MD, Lida Zheng, MD, Christina Clarke, MD
Department of Dermatology, Feinberg School of Medicine, Northwestern University

HISTORY OF PRESENT ILLNESS

A 55-year-old Caucasian woman presented to Northwestern Memorial Hospital with a progressive vesiculobullous eruption. Seven months prior to presentation, the patient developed widespread, mildly pruritic bullae that evolved into painful ulcerations. The lesions were predominantly distributed on her proximal arms, chest, abdomen, thighs, and distal legs. She also experienced painful oral erosions. She noted atrophic scarring at sites of prior lesions. The patient was biopsied and diagnosed with bullous pemphigoid. She was treated with systemic corticosteroids and azathioprine with minimal improvement. Given the refractory nature of her disease, she was transferred to NMH for further management.

The patient was otherwise in her usual state of health. She was not up to date on her routine cancer screening, including no recent mammography, Pap smear, or colonoscopy. She had started taking oral lithium for mood stabilization around the time her cutaneous eruption began but denied other new pharmacologic exposures.

PAST MEDICAL AND SURGICAL HISTORY

CKD stage III, essential hypertension, morbid obesity (BMI 50 kg/m2), obstructive sleep apnea, dermatillomania, generalized anxiety disorder, major depressive disorder
Cesarean sections x2, carpal tunnel release surgery, tonsillectomy

FAMILY AND SOCIAL HISTORY

The patient is adopted. Her biologic family medical history is unknown. She lives with her husband and adult son. She has a 30 pack year history of tobacco use and quit smoking 2.5 years prior to presentation. She reports rare alcohol consumption. She previously worked at an office desk job.

MEDICATIONS

Azathioprine, bupropion, buspirone, cyanocobalamin, fexofenadine, gabapentin, lamotrigine, lithium, losartan, metformin, methylprednisolone, metoprolol tartrate, venlafaxine

PHYSICAL EXAM

Labial, buccal, and hard palatal mucosae with well-demarcated erosions. Conjunctival, anorectal, and vulvar mucosae intact without abnormalities. Upper arms, chest, hips, thighs, and distal legs with sharply-demarcated, large (several centimeter), indurated ulcerations with beefy red granulation tissue and scant fibrinous debris at bases. Scant purulence and bleeding noted in some of the lesions. An intact, clear fluid-filled, tense bulla was noted on the right medial thigh. BSA involvement was ~10%. No cervical, axillary, or inguinal lymphadenopathy was palpated. Atrophic scarring was noted at sites of resolved blisters.

PERTINENT LABS

Dermatologic Evaluation: Anti-BP180 IgG 0 (0-9 units), anti-BP230 IgG 1 (0-9 units), anti-collagen VII IgG 0 (0-6 units), skin swab HSV-1/-2 PCR negative
Oncologic Evaluation: CA-125 1922.9 (0-30.2 units/mL), Carcinoantigen (CEA) 4.4 (0-3 ng/mL), Human epididymis protein 4 (EP4) 460.3 (0-70 pmol/L)
Rheumatologic Evaluation: ANA 1:1,280 (speckled), anti-histone Abs 1.1 (0.0-0.9 units), anti-dsDNA negative, anti-Smith negative, anti-SSa/Ro negative, anti-SSb/La negative, C3 226 (75-176 mg/dL), C4 36 (10-40 mg/dL)

PERTINENT IMAGING

Transvaginal ultrasound: Normal R ovary. L ovary is not imaged but is normal in size on CT. Small soft tissue nodules in the cul-de-sac suspicious for peritoneal implants.

CT chest, abdomen, pelvis: Mild to moderate amount of ascites, mesenteric edema, patchy omental fat stranding.

PET/CT: No definitive evidence of occult neoplastic involvement. There is relatively extensive mildly hypermetabolic findings noted in the cutaneous tissues of the trunk, RUE, and proximal LEs.

HISTOPATHOLOGY

H&E: Subepidermal bulla. Unremarkable epidermis with some spongiosis but no acantholysis. Blister cavity is paucicellular. Dermis with mostly perivascular lymphohistiocytic infiltrate.

DIF: Linear IgG and C3 deposition along the dermal-epidermal junction. Salt-split demonstrated staining along the dermal component (floor).

Transvaginal culdocentesis with cytologic analysis of fluid: Positive for adenocarcinoma, consistent with high-grade serous carcinoma.

DIAGNOSIS

Paraneoplastic pemphigoid disorder. Unknown specific antigenic target. Differential diagnosis includes anti-laminin 332 cicatricial pemphigoid, anti-p200 pemphigoid, and anti-p105 pemphigoid.

TREATMENT AND COURSE

Treatment was first directed toward a primary vesiculobullous disease process. Intravenous immunoglobulin (IVIg), rituximab, and dapsone were initiated. She was continued on systemic corticosteroids. Unfortunately, her mucocutaneous disease failed to improve.

One month later, the patient was admitted to the Northwestern CCU with a submassive pulmonary embolism. Her occult ovarian malignancy was diagnosed during this subsequent admission via sampling of the free fluid in the rectouterine pouch. The patient was eventually transferred to the inpatient oncologic ward and initiated on a conventional systemic chemotherapeutic regimen consisting of carboplatin and paclitaxil.

The patient's pemphigoid disorder drastically improved after completing four cycles of carboplatin and paclitaxil. Her CA-125 levels declined concurrently. Due to toxicity, her chemotherapeutic regimen was decreased to single-agent carboplatin, of which she completed five additional cycles. Her corticosteroid regimen is slowly being tapered. Atrophic scarring remains at sites of prior lesions. Her gynecologic oncologists completed an abdominal debulking procedure earlier this month.

DISCUSSION

The pemphigoid group of mucocutaneous diseases is characterized by subepidermal blister formation due to the binding of autoantibodies to molecular components of the dermoepidermal junction (DEJ). Antigenic targets of molecularly identifiable proteins include BP180 (type XVII collagen), BP230, laminin 332 (previously laminin 5, epiligrin), integrin α6β4, and type VII collagen. p200 and p105 are antigenic targets of two other unique pemphigoid disorders.

Our patient's vesiculobullous disease remains undifferentiated; however, we have significantly narrowed the differential diagnosis. First, H&E demonstrated a subepidermal split and the DIF showed linear immunofluorescence of IgG and C3 at the DEJ, which confined the diagnosis to the pemphigoid group. Second, IgA-related disease (i.e. LABD) was ruled out as only IgG (and C3) was identified along the DEJ on DIF. Third, on salt-split skin analysis, the antibodies were bound to the dermal side (floor) of the specimen, ruling out bullous pemphigoid (BP) and anti-integrin

a6β4 mucous membrane pemphigoid. Further, negative BP180/BP230 IgG by ELISA confirmed that the patient's disease was not BP. Fourth, collagen VII IgG was negative, ruling out bullous systemic lupus erythematosus and epidermolysis bullosa acquisita. The remaining entities on our differential are anti-laminin 332 cicatricial pemphigoid, anti-p200 pemphigoid, and anti-p105 pemphigoid.

Mucous membrane (cicatricial) pemphigoid is an umbrella term that describes a heterogeneous group of pemphigoid disorders with predominantly mucosal disease. The term 'cicatricial pemphigoid' best describes the rare instances in which these conditions manifest primarily with cutaneous instead of mucosal disease. Laminin 332 is a molecular target within the MMP group. Cutaneous lesions are present in roughly one-third of cases. Scarring is usually noted after resolution of both mucosal and cutaneous lesions. An association with malignancy has been reported. Conjunctival scarring and irreversible ophthalmologic sequelae are characteristic of ocular MMP, which involves antibodies against the β4 subunit of integrin a6β4.

Anti-p200 pemphigoid is a rare vesiculobullous condition with only ~50 cases documented in the literature. It has recently been shown that 90% of anti-p200 pemphigoid patients have serum antibodies that target the C-terminus of laminin γ1. However, antibodies targeting laminin γ1 do not exhibit pathogenic activity, so the exact molecular target of this disease remains unclear. Laminin γ1 is a component of multiple laminin proteins at the DEJ. The clinical presentation of anti-laminin γ1 pemphigoid is highly variable. Lesions usually heal without scarring. Mucosal involvement is present in a minority of patients. A possible association with psoriasis has been reported in Japanese patients. Histopathologically, a neutrophilic inflammatory infiltrate is often noted. Anti-p105 pemphigoid is even less understood, and its clinical presentation is variable in the few documented cases. No molecular target has been identified in this disease.

KEY POINTS

1. The pemphigoid group of vesiculobullous diseases is defined by subepidermal blister formation secondary to autoantibodies targeting various molecular components of the DEJ.
2. Consider a paraneoplastic etiology when a disease process is refractory to standard treatment regimens.

REFERENCES

1. Schmidt E, et al. Pemphigoid diseases. Lancet. 2013. 381(9863):320-32.
2. Goletz S, et al. Anti-p200 pemphigoid. J Am Acad Dermatol. 2014. 71(1):185-91.
3. Egan CA, et al. Anti-epiligrin cicatricial pemphigoid and relative risk for cancer. Lancet. 2001. 357(9271):1850-1.

CHICAGO DERMATOLOGICAL SOCIETY **Case 2**

Presented by Jennifer Shastry, MD, Duri Yun, MD, and Amy Paller, MD
Department of Dermatology, Feinberg School of Medicine, Northwestern University
Division of Dermatology, Ann & Robert H. Lurie Children's Hospital of Chicago

HISTORY OF PRESENT ILLNESS

A 1-day-old female born at 39 weeks gestation to a 21-year-old G3P3 mother was transferred from an outside hospital for evaluation and management of tense blisters noted at birth on both hands, the umbilical stump, and left hip. The patient was afebrile, breathing comfortably on room air, and tolerating oral feeds.

PAST MEDICAL/PRENATAL HISTORY

The patient was born with a birth weight of 2710 g (11%ile) via repeat Cesarean section. The patient's delivery was complicated by meconium-stained amniotic fluid. APGAR scores were 9 and 9 at 1 and 5 minutes, respectively. The patient's mother reported routine prenatal care without illnesses during her pregnancy. Prenatal labs were notable for being HIV negative, HBs Ag negative, syphilis/gonorrhea/chlamydia negative, and rubella immune. Maternal Group B *Streptococcus* status was positive, for which she was appropriately treated. The mother took a prenatal vitamin. There was no history of drug, alcohol or tobacco exposure.

FAMILY HISTORY

The patient's mother and father are from Mali, without known consanguinity. The patient had an older sibling who passed away at 40 days of life due to complications from a severe, generalized skin blistering disorder in Mali. There is one living, healthy sibling.

MEDICATIONS

Morphine, maintenance IV fluids

PHYSICAL EXAM

The patient was well-appearing, in no apparent distress, and breathing comfortably on room air without stridor. On the right nasal ala there was a focal erosion. Erosions were noted on the soft palate of the oral mucosa. On the dorsal aspect of the right hand was a large bulla with de-gloving extending to the index finger. Erosions were noted on the eponychium of the right thumb and left distal index finger. Subtle blistering was noted on the proximal nail folds of all ten fingers with nail dystrophy. Granulation tissue was noted on the peri-umbilical skin. Erosions were noted on the soft palate of the oral mucosa.

LABS/IMAGING

Genetic testing utilizing the Epidermolysis Bullosa Panel Plus by Blueprint Genetics demonstrated a homozygous nonsense c.349C > T mutation in the *LAMB3* gene, resulting in a premature stop codon and protein truncation.

DIAGNOSIS

Junctional epidermolysis bullosa, generalized-severe subtype

TREATMENT AND COURSE

During the patient's hospitalization, efforts were made to minimize trauma and friction to the skin. The patient's blisters and erosions were treated with non-stick Polymem® dressings. She eventually developed difficulty with oral feeds due to pain. At 38 days of age, she was noted to have respiratory stridor. On microlaryngoscopy, the patient was found to have severe subglottic stenosis, with narrowing to a diameter of less than 2.7 mm. Otolaryngology recommended symptomatic management with ranitidine, racemic epinephrine and dexamethasone. Given

these findings in the setting of her underlying disease, prognosis and goals of care were discussed, and the family elected for DNR/DNI status. The patient was discharged with hospice care at 10 weeks of life. She was subsequently readmitted three times due to sepsis and acute hypoxemic respiratory failure.

DISCUSSION

Epidermolysis bullosa is a heterogeneous group of mechanobullous disorders involving genetic mutations in proteins which make up the basement membrane zone. Junctional EB (JEB) results from fragility at the level of the lamina lucida. The most common defect in JEB is found in laminin-332, a heterotrimer anchoring protein encoded by the genes *LAMA3, LAMB3*, and *LAMC2*. JEB caused by autosomal recessive mutations in the laminin-332 protein is subdivided into generalized severe (JEB-gen sev), generalized intermediate, localized and laryngoonychocutaneous syndrome. In JEB-gen sev, the function of laminin-332 is severely compromised, while it is variably decreased in the other forms. *LAMB3* is the most commonly mutated gene in JEB-gen sev.

JEB-gen sev, formerly referred to as the Herlitz subtype, is characterized by severe generalized blistering, failure to thrive, and early airway compromise. The incidence of JEB-gen sev has been estimated at 1 in 150,000 to 1 in 500,000 live births. It presents with blistering of the skin and mucous membranes at birth, with frequent involvement of the scalp, perioral skin, trunk, and buttocks. Blistering of the fingertips with nail sloughing, formation of granulation tissue, and dental hypoplasia are characteristic. Blistering may heal with atrophic scarring. Laryngeal involvement presents with early hoarseness and often progresses to tracheolaryngeal stenosis. Disruption of the skin barrier leads to loss of proteins, fluid, and iron, contributing to patients' failure to thrive. The prognosis of JEB-gen sev is poor, and the extent of cutaneous blistering is not predictive of the outcome. The mean age of death is 5-6.5 months, and most patients succumb before the age of 3 years. Respiratory complications and infections are the most common causes of early death.

No cure exists for JEB-gen sev; therefore, management is supportive. Goals of care discussions with the family should be initiated early in the course of JEB-gen sev patients. Appropriate wound care with lancing of blisters and non-adherent dressings is important for prevention of complications. Stridor can be treated with dexamethasone and nebulized epinephrine. Invasive measures such as intubations, tracheostomies, gastrostomy tube placements, and central line placements have not been shown to improve survival. There are case reports of treating JEB-gen sev with stem cell transplantation (SCT), but skin fragility returned and the patients ultimately died from complications of their underlying disease.

KEY POINTS

1. JEB-gen sev is an autosomal recessive disorder most commonly caused by mutations in the genes encoding laminin-332, leading to blistering of the lamina lucida.
2. Affected individuals present with blistering of the skin and mucous membranes at birth, often involving the trunk, perioral skin, and hands. The prognosis is poor; most patients die in early infancy due to failure to thrive, infection, and/or respiratory involvement.

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3. Yang C, Kroshinksy D, Cummings B. Neonatal Junctional Epidermolysis Bullosa: Treatment Conundrums and Ethical Decision Making. Am J Clin Dermatol 2014; 15:445-450.
4. Kelly-Mancuso G, Kopelan B, Azizkhan R, Lucky A. Junctional Epidermolysis Bullosa Incidence and Survival: 5-Year Experience of the Dystrophic Epidermolysis Bullosa Research Association of America (DebRA) Nurse Educator, 2007 to 2011. Ped Dermatol. 2013; 31(2): 159-162.

Presented by Raj Chovatiya, MD, PhD and Jennifer Choi, MD
Department of Dermatology, Feinberg School of Medicine, Northwestern University

UNKNOWN

A 57-year-old male presented with three weeks of worsening erythema, pain, and tenderness of the right chest and flank

CHICAGO DERMATOLOGICAL SOCIETY **Case 4**

Presented by Molly Stout, MD and Lauren Guggina, MD
Department of Dermatology, Feinberg School of Medicine, Northwestern University

HISTORY OF PRESENT ILLNESS

A 66-year-old female presented with tender, indurated plaques over the abdomen. Lesions initially appeared 1.5 years prior to evaluation and were attributed to warfarin therapy. At that time, her anticoagulation medication was switched to apixaban with no improvement in skin lesions. In the months prior to our evaluation, she experienced acute worsening pain of her abdomen associated with the development of new lesions on the abdomen and pannus. She was hospitalized twice for presumed cellulitis but did not improve with antibiotics.

PAST MEDICAL/SURGICAL HISTORY

Atrial fibrillation, congestive heart failure, hypothyroidism, type 2 diabetes mellitus
Cesarean section, knee surgery

FAMILY/SOCIAL HISTORY

She lived in a nursing home. She denied smoking or alcohol use.

MEDICATIONS

Albuterol, amlodipine, apixaban, atorvastatin, carvedilol, gabapentin, glipizide, hydrocodone-acetaminophen, levothyroxine, metformin, pantoprazole, torsemide

PHYSICAL EXAM

Abdomen and anterior pannus with severely tender, violaceous purpuric patches with necrosis and central ulceration. Underside of pannus with severely tender, well-demarcated, medium depth ulcer with yellow fibrinous exudate at the base and serous drainage.

LABS/IMAGING

Abnormal

WBC 14.9 (3.5-10.5 K/uL), 73% PMNs, hemoglobin: 9.4 (13.0-17.5 g/dL), platelets 634 (140-390 K/uL), sodium 130 (133-146 mEq/L), CO2 34 (21-31 mEq/L), BUN 33 (2-25 mg/dL), albumin 2.5 (3.5-5.7 g/dL), AST 54 (0-39 U/L), alk phos 500 (32-104 U/L)
A nuclear medicine bone scan demonstrated abnormal activity in the soft tissues of the abdomen, particularly severe in the skin over the patient's panniculus.

Normal/Negative

Calcium, creatinine, ionized calcium, Phosphorus, PTH

HISTOPATHOLOGY

Two punch biopsies from the abdomen showed a thrombotic vaso-occlusive process, with multiple vessels in the subcutaneous tissue with fibrin clots. Von Kossa stains were negative for calcium deposits.
Subsequent excisional wedge biopsy revealed a calcifying and necrotizing panniculitis with thrombi. Prominent background diffuse dermal angiomatosis was noted. A von Kossa stain was positive for calcium deposits.

DIAGNOSIS

Non-uremic calciphylaxis

TREATMENT AND COURSE

The patient was treated with sodium thiosulfate 12.5 g intravenous (IV) four times weekly. She also received intralesional sodium thiosulfate once during her hospitalization but was unable to tolerate further intralesional treatment due to significant pain. She received narcotics for pain control and wound care for ulcerated lesions with improvement.

DISCUSSION

Calciphylaxis presents with exquisitely painful skin lesions, often starting as retiform purpura and evolving to necrotic ulcers or plaques most often in areas with the greatest adipose tissue, including the thighs, abdomen, and buttocks. Calciphylaxis develops as a result of calcification of arterioles in the dermis and subcutaneous adipose tissue, with subsequent thrombosis and necrosis of the surrounding tissue.

Calciphylaxis typically affects patients with end-stage renal disease (ESRD) but can occur in patients without renal disease and is likely underdiagnosed in this population. As with uremic calciphylaxis, non-uremic calciphylaxis is more commonly seen in Caucasian females. Risk factors include primary hyperparathyroidism, malignancy, alcoholic liver disease, connective tissue disease, protein C and S deficiency, and Crohn's disease. A review of 15 non-ESRD calciphylaxis patients revealed 80% had received glucocorticoids prior to development of skin lesions, 60% were on warfarin, and 60% had an underlying autoimmune disorder.

Calciphylaxis is often a clinical diagnosis in patients with a typical cutaneous presentation and a history of ESRD. In patients without ESRD, a skin biopsy is often critical to establishing a definitive diagnosis. The diagnostic yield is maximized by biopsy site selection at the margin of a necrotic lesion, with an appropriate depth to ensure adequate sampling of subcutaneous fat. A von Kossa stain can help to confirm calcium deposits. Worsening ulceration and pain with biopsy must be weighed against adequate tissue sampling for diagnosis and is an important aspect of patient counseling.

Among patients in whom a biopsy is non-diagnostic or refused, imaging may support the diagnosis of calciphylaxis. Imaging modalities may include plain radiographs, mammography, high-resolution computed tomography (CT), and bone scan.

The mainstay of treatment for calciphylaxis is aggressive wound care, pain control, and IV sodium thiosulfate. In patients without ESRD, the accepted regimen for patients with a normal GFR is 25 g of sodium thiosulfate intravenously three to five times weekly, with close monitoring for the development of adverse effects such as metabolic acidosis or hypotension. Other adverse effects include nausea, vomiting, hypocalcemia, QT prolongation, and volume overload.

KEY POINTS

1. Non-uremic calciphylaxis is an important differential diagnosis for patients without renal disease who present with painful necrotic ulcers or plaques in adipose-rich areas.
2. Risk factors for non-uremic calciphylaxis include medications such as glucocorticoids and warfarin, diabetes mellitus, and other autoimmune and connective tissue diseases.
3. Wedge or excisional biopsy may be needed to diagnose calciphylaxis if a more superficial biopsy is non-diagnostic but may have more complications such as delayed wound healing.
4. The mainstay of calciphylaxis treatment is aggressive wound care, pain control, and sodium thiosulfate.

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CHICAGO DERMATOLOGICAL SOCIETY **Case 5**

Presented by Olivia Schenck, MD and Lacey Kruse, MD
Department of Dermatology, Feinberg School of Medicine, Northwestern University
Division of Dermatology, Ann & Robert H. Lurie Children's Hospital of Chicago

HISTORY OF PRESENT ILLNESS

An 8-day-old healthy female presented for evaluation of three, asymptomatic skin lesions located on her right forehead, posterior neck, and left calf present since birth. In the 2 days prior to presentation, the lesion on the posterior neck had developed ulceration and crusting. Review of systems was negative; she was feeding well and gaining weight.

PAST MEDICAL HISTORY

Born at 39 weeks gestation via repeat Cesarean section with no pregnancy or delivery complications

FAMILY AND SOCIAL HISTORY

No pertinent family history. She lives with her parents and healthy 5-year-old sister.

MEDICATIONS

Vitamin D supplement

PHYSICAL EXAM

Right forehead with a well-circumscribed 1 cm firm, round subcutaneous nodule without overlying skin changes. Posterior neck with a 2 cm erythematous nodule with central ulceration and a medial vascular stain clinically consistent with a nevus simplex. Left calf with a plate-like firm 3 cm subcutaneous nodule. No palpable cervical, axillary, or inguinal lymphadenopathy. No hepatosplenomegaly.

LABS

Abnormal: CBC with RBC 3.02 (3.60-6.20 x 10^9/uL), Hgb 10.0 (12.5-20.5 g/dL), Hct 29.8 (39-63%), Plt 519 (150-450 K/uL)
Normal/Negative: WBC, CMP, calcium

IMAGING

Ultrasound: 14.7 x 11.3 x 12.6 mm irregular, hypoechoic soft tissue lesion with calcification and a hyperechoic rim on the posterior neck, and a 28.0 x 15.5 x 24.9 mm intramuscular soft tissue mass with a large cystic component on the left posterior calf muscle.
X-ray skeletal survey: multiple (>8) focal lytic lesions, most prominently involving the right tibia proximally and distally, as well as multiple pulmonary nodules.
CT of the chest, abdomen, and pelvis: right retroperitoneal, right paraspinal, and left inguinal soft tissue masses, multiple bilateral pulmonary nodules, and multiple lytic bone lesions.

HISTOPATHOLOGY

Punch biopsy of the ulcerated nodule on the right posterior neck revealed a biphasic well-circumscribed multinodular dermal tumor composed of fascicles of myofibroblasts embedded in a myxoid stroma and irregular arborizing vascular channels of hemangiopericytoma-like spaces with some immature vascular areas. Atypia was not identified.

DIAGNOSIS

Generalized infantile myofibromatosis

TREATMENT AND COURSE

Our patient was referred to oncology. Given her visceral involvement, particularly of her lungs and the risk for respiratory compromise in the setting of potential myofibroma enlargement, our patient was started on systemic treatment with methotrexate (1 mg/kg) and vinblastine (0.16 mg/kg). On follow-up imaging 3 months after initiation of therapy, there was a decrease in the size of her pulmonary and soft

tissue myofibromas. During the course of treatment, she developed a vertebral compression fracture at the site of a lytic bone lesion but did not require intervention given proper vertebral alignment and stability. She had complete resolution of her cutaneous disease. Following cessation of treatment after one year, she has continued to have stable imaging findings, now most recently at her 2-year post-therapy follow-up.

DISCUSSION

Infantile myofibromatosis (IM) is a rare, benign disorder of fibroblastic/myofibroblastic proliferation yet represents the most common fibrous tumor of infancy. IM has been classified into 3 clinical types: 1) solitary form presenting with a single cutaneous nodule; 2) multicentric form involving skin, subcutaneous tissues, muscle, and bone; and 3) multicentric form with visceral involvement, involving most commonly the lungs, gastrointestinal tract, heart, and liver. The majority of cutaneous lesions in all forms are located on the head, neck, or trunk. Solitary IM, the most common type, tends to occur later in life than multicentric forms. Most cases are sporadic, though familial cases have been described.

Clinically, IM presents as firm, rubbery, skin-colored to violaceous nodules; ulceration is common in the multicentric form. IM may be initially mistaken for hemangiomas given their prominent vascularity. The clinical differential diagnosis also includes neurofibromas, leiomyomas, sarcomas, and metastatic neuroblastoma. Diagnosis is made through histopathological examination with classic findings of a dermal nodule with a periphery of spindle-shaped cells arranged in smooth muscle-like bundles or hyalinized fascicles and a central area of vascular hemangiopericytoma-like proliferations. These spindle-shaped cells stain positively for smooth muscle actin and vimentin, indicating their myofibroblastic origin. Further evaluation with thorough physical examination, skeletal radiographs, ultrasound or CT imaging, and EKG are needed to assess for systemic involvement.

Both solitary and multicentric IM follow a benign course, typically with spontaneous regression of tumors over 12 to 24 months. Both of these forms can often be managed with observation alone. Their mortality rates have been reported as 0-1%. Surgical excision can be considered for solitary myofibromas, though recurrence rates of almost 10% have been reported. Generalized IM can have a poor prognosis due to mass effect and compromise of vital organs, with untreated mortality rates ranging from 73-93%.

Given the rarity of this condition, treatment for generalized IM has been based on therapies used for other infantile connective tissue tumors, such as desmoid tumors and infantile fibrosarcomas. Vinblastine-methotrexate therapy, as used in our patient, was first reported in 2000 and has been reported to have clinical benefit over other chemotherapy regimens. Patients with the generalized form of IM should be followed long-term, as late and recurrent nodules have been reported.

KEY POINTS

1. Infantile myofibromatosis is a rare disorder yet represents the most common fibrous tumor of infancy and presents as firm, rubbery, skin-colored to violaceous nodules.
2. Pediatric patients presenting with multiple myofibromas should undergo a thorough assessment for visceral disease given the difference in prognosis and treatment options for multicentric forms with visceral involvement.

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Presented by Namita Jain, MD, MPH and Lauren Guggina, MD
Department of Dermatology, Feinberg School of Medicine, Northwestern University

UNKNOWN

A 32-year-old male presented with fevers, neck swelling, and an asymptomatic eruption on the trunk and extremities over the course of one week.

CHICAGO DERMATOLOGICAL SOCIETY **Case 7**

Presented by Parul Goyal, MD; Joan Guitart, MD; Emily Keimig, MD
Department of Dermatology, Feinberg School of Medicine, Northwestern University

HISTORY OF PRESENT ILLNESS

A 61-year-old Caucasian woman presented for evaluation and treatment of a persistent lesion on the left elbow. Ten months prior to presentation, the patient noted a lesion which she described as a "mosquito bite" on the left elbow. The lesion grew in size and ulcerated over the following seven months. Three skin biopsies demonstrated granulomatous dermatitis. Evaluation for an infectious etiology, including Gram, AFB, and Fite stains and tissue cultures, was negative. She was treated with 100 mg minocycline BID for 30 days without improvement. Repeat biopsy again demonstrated granulomatous dermatitis. She was then treated with oral prednisone (dose varying between 40 mg and 60 mg) and two doses of intralesional triamcinolone; however, the lesion continued to enlarge, ulcerate and drain. The patient presented to the Northwestern Sarcoidosis clinic for a second opinion. Repeat skin biopsy and tissue culture were performed.

PAST MEDICAL/SURGICAL HISTORY

Hypertension, cardiovascular disease

FAMILY AND SOCIAL HISTORY

A sister with a history of uterine cancer had recently died due to mantle cell lymphoma. A brother had rheumatoid arthritis. She denied tobacco, alcohol, or illicit drug use.

MEDICATIONS

Amlodipine, aspirin, losartan, ranitidine, oral conjugated estrogen

PHYSICAL EXAM

Left upper arm and elbow with a 12 cm friable, ulcerated pink tumor with surrounding induration and satellite pink nodules. Right shoulder with a few faint pink macules, including scar at the site of the prior biopsy. No palpable cervical, axillary, or inguinal lymphadenopathy.

LABS/IMAGING

Abnormal:

SPEP: polyclonal increase in gamma region and alpha 1 region, increased total protein
ESR 76 (0-30) and CRP 1.7 (0-3.0)

Normal/Negative:

ACE level 25, LDH 211, CBC, CMP, *Blastomyces* urine antigen
CXR: No hilar or mediastinal enlargement, no evidence of interstitial lung disease, no pulmonary nodules.
PET-CT: PET-positive neoplasia within atypically located lymph nodes and subcutaneous soft tissue masses scattered throughout the neck, chest, abdomen, pelvis, left arm, and left leg.

HISTOPATHOLOGY

Diffuse, dense, sheet-like and deep infiltrate composed of atypical pleomorphic cells with many histiocytes. Numerous mitotic figures noted. Special stains (DPAS, Gram and acid fast bacilli) were negative. The tumor cells stain positively for CD3, CD2, CD30 and TIA-1 and negatively for CD4, CD5, CD7, CD8, CD20, CD56, ALK1, TCR-delta, Beta-F1, EBER-1, CD45RA and EMA.

DIAGNOSIS

Anaplastic lymphoma kinase (ALK)-negative primary systemic anaplastic large cell lymphoma

TREATMENT AND COURSE

The patient underwent radiation therapy to the left elbow lesion and six cycles of CHOEP (cyclophosphamide, doxorubicin, etoposide, vincristine, and prednisone) chemotherapy. Post-chemotherapy PET/CT scan showed a positive response with dramatically decreased hypermetabolic activity in the left posterior elbow soft tissue mass as well as resolution of previously noted PET-positive neoplasms in the neck, chest, abdomen, pelvis, left leg, and remainder of the left arm. The patient achieved complete clinical remission with resolution of her skin ulceration and tumor.

DISCUSSION

Anaplastic large cell lymphoma (ALCL) is a subset of peripheral T-cell lymphoma that accounts for approximately 2% of adult non-Hodgkin lymphoma (NHL). Four clinical subtypes of ALCL have been identified: ALK-positive primary systemic ALCL, ALK-negative primary systemic ALCL, primary cutaneous ALCL, and breast implant-associated ALCL. ALK-positive lymphomas commonly express the t(2;5)(p23;q25) translocation, leading to a constitutively active tyrosine kinase. ALK positivity has been identified in multiple retrospective analyses to be a positive prognostic factor. Up to 30% of ALK-negative lymphomas express the t(6;7)(p25.3;q32.3) translocation, which is associated with decreased expression of the cytotoxic markers TIA-1 and granzyme B and confers a more favorable prognosis in ALK-negative lymphomas.

The typical lymphoid cells seen in ALCL are large and pleomorphic with horseshoe-shaped nuclei and abundant cytoplasm. Approximately 60% of ALCL tumors express one or more surface antigens associated with T cells, while 40% express neither T nor B cell antigens. ALK-positive ALCL typically demonstrates universal expression of CD30; high rates of epithelial membrane antigen (EMA) expression, TIA1, granzyme B, and perforin; and variable expression of CD43, CD4, and CD2. ALK-negative ALCL also demonstrates universal expression of CD30; frequent expression of TIA1, granzyme B, perforin, and CD2; and variable expression of CD43, CD3, EMA, and CD4. Both ALK-positive and ALK-negative tumors have low rates of expression of CD8 and CD56.

The two most important prognostic factors in patients with primary systemic ALCL are the International Prognostic Index and, as discussed above, the tumor's ALK status. The International Prognostic Index was created to help predict survival in patients who were diagnosed with aggressive NHL and were treated with chemotherapy regimens containing doxorubicin. The patient's age, Eastern Cooperative Oncology Group (ECOG) performance status, serum lactate dehydrogenase level, Ann Arbor clinical stage, and the number of extranodal sites involved at the time of diagnosis all influence the index. The index is then able to stratify these patients into four risk groups, with low risk being an IPI score of 0-1; low-intermediate risk being an IPI score of 2; high-intermediate risk being an IPI score of 3; and high risk being an IPI score of 4-5. In the original group of patients used to create and validate the index, an IPI score of 0 to 1 predicted a five-year survival rate of 73 percent while an IPI score of 4 to 5 predicted a five-year survival rate of 26 percent.

Induction therapy for systemic ALCL most commonly consists of either CHOP (cyclophosphamide, doxorubicin, vincristine, prednisone) or CHOEP (cyclophosphamide, doxorubicin, vincristine, etoposide, prednisone) regimens. Radiation therapy given in combination with induction chemotherapy has not definitively been shown to be advantageous in patients with early stage ALCL. Once induction chemotherapy is completed, hematopoietic stem cell transplantation (HSCT) is typically considered as consolidation therapy. The decision as to whether or not to proceed with HSCT is controversial and depends on the patient's age, ALK status, and IPI score.

KEY POINTS

1. The two most important prognostic factors in patients with primary systemic ALCL are the International Prognostic Index and the ALK status. A higher IPI score portends a lower five-year survival rate. ALK positivity predicts a more favorable prognosis than ALK negativity.
2. Up to 30% of ALK-negative primary systemic large cell lymphomas express the t(6;7)(p25.3;q32.3) translocation. This leads to decreased presence of the cytotoxic markers TIA-1 and granzyme B, imparting a favorable prognosis.
3. Induction therapy for primary systemic ALCL consists of either the CHOP or CHOEP regimens. Radiation therapy has not been definitively shown to be advantageous as a component of induction therapy in patients with early stage disease. The decision as to whether or not to proceed with HSCT is controversial and depends on the patient's age, ALK status, and IPI score.

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CHICAGO DERMATOLOGICAL SOCIETY **Case 8**

Presented by Derek Hsu, MD, Emily Merkel, MD, Lauren Guggina, MD and Joaquin Brieva, MD
Department of Dermatology, Feinberg School of Medicine, Northwestern University

Patient A

HISTORY OF PRESENT ILLNESS

A 57-year-old Caucasian female with a history of marginal zone lymphoma with rapid transformation to stage 4 diffuse large B cell lymphoma (DLBCL) was admitted for haploidentical hematopoietic stem cell transplantation (HSCT). Following HSCT, the patient's course was complicated by numerous events, including *Clostridium difficile* colitis, cardiac arrest, failure to engraft, *Enterococcus faecium* bacteremia, acute renal failure requiring hemodialysis, and atypical hemolytic uremic syndrome requiring eculizumab. The patient eventually required tracheostomy for persistent respiratory failure.

Approximately six weeks following admission, the patient was noted to have a necrotic wound involving the left lower extremity, which expanded over the subsequent 2 weeks.

PAST MEDICAL/SURGICAL HISTORY

Marginal zone lymphoma with rapid transformation to stage 4 DLBCL
Splenectomy
Breast cancer s/p chemotherapy, radiation therapy, and right lumpectomy
RLE DVT and PE
Cardiomyopathy following anthracycline treatment
Depression

MEDICATIONS

Acyclovir, amphotericin B nasal inhalation spray, atovaquone, cefepime, eculizumab, isavuconazonium sulfate, IVIG, linezolid, methylprednisolone, micafungin, TBO-filgrastim, vancomycin

FAMILY/SOCIAL HISTORY

No tobacco, alcohol, or illicit drug use

PHYSICAL EXAM

General: Intubated, obtunded
Skin: On the left lower extremity, from the lateral mid-thigh to proximal leg, there is a well-demarcated, 20 cm deeply violaceous to centrally black plaque with a peripheral 2-3 cm red-violaceous annulus. There is surrounding desquamation and necrosis of the overlying skin. Lower legs with livedo reticularis.
Vascular: Left popliteal, dorsalis pedis, and posterior tibialis pulses absent; left leg cool to touch.

HISTOPATHOLOGY

The deep dermis shows marked hemorrhage with neutrophils and nuclear debris. In the deep vessels and perivascular dermis, there are broad non-septated hyphal forms. DPAS is positive for non-septated hyphae.

LABS

Abnormal: WBC 0.3 (3.5-10.5 K/uL), Absolute neutrophils 0.3 (1.5-8.0 K/uL), Hemoglobin 9.9 (13.0-17.5 g/dL), creatinine 1.8 (0.60-1.30 mg/dL)
Tissue culture: *Rhizopus* spp.
Normal/negative: blood cultures

TREATMENT AND COURSE
The patient was diagnosed with angioinvasive mucormycosis with ischemic complications of the left lower extremity. She was started on IV amphotericin B. The patient was deemed to be a poor candidate for surgical revascularization. She remained severely encephalopathic, requiring mechanical ventilation and pressor support. In accordance with the family's wishes, the patient was transitioned to comfort care and died shortly thereafter.

FINAL DIAGNOSIS
Angioinvasive mucormycosis, *Rhizopus* spp., complicated by left leg ischemia

Patient B
HISTORY OF PRESENT ILLNESS
A 34-year-old Caucasian male with a history of primary refractory DLBCL status-post HSCT was admitted for fevers, chills and cough productive of brown sputum. He was found to have MSSA bacteremia, *Pseudomonas putida* pneumonia, and extended spectrum β lactamase-producing *Klebsiella pneumoniae* bacteriuria. The patient was treated with meropenem and linezolid, with initial improvement. However, he then developed recurrent fevers and worsening malaise. His antimicrobial therapy was broadened to include posaconazole and amphotericin B.

One week after admission, he was noted to have a lesion on the right arm which, per the patient, began as a "pimple" 6 weeks prior to admission. The skin lesion had been evaluated during an outpatient hematology appointment and treated with a 7-day course of linezolid for presumed bacterial cellulitis. The patient endorsed intermittent purulent drainage from the right arm lesion, which improved after antibiotic treatment.

PAST MEDICAL/SURGICAL HISTORY
Primary refractory DLBCL s/p allogeneic MUD HSCT
Chronic, severe GVHD with skin, ocular, oral and +/- liver involvement
Transplant-associated thrombotic microangiopathy treated with eculizumab
Hemorrhagic cystitis secondary to BK virus, complicated by hydronephrosis
Recurrent *Klebsiella pneumoniae* urinary tract infections, complicated by sepsis
CMV viremia, CKD, HTN, DVT

MEDICATIONS
Acetylcysteine, allopurinol, amlodipine, eculizumab, ibrutinib, metoprolol succinate, pentamidine, prednisone, rituximab, triamcinolone, ursodiol, valacyclovir, voriconazole

FAMILY/SOCIAL HISTORY
Former smoker (1.5 pack year history; quit 2014)
Camping trip to Wisconsin, 2 weeks prior to admission

PHYSICAL EXAM
General: Ill-appearing, somnolent Caucasian male
Skin/mucosa: Numerous erosions in the oropharynx. Arms, legs, chest and face with numerous scaly erythematous macules and thin papules coalescing into larger patches and thin plaques involving >50% BSA. Right posterior upper arm with 2.5 cm necrotic eschar with irregular borders and surrounding erythema and induration.

HISTOPATHOLOGY
There is a necrotic ulcer. The deep dermis shows marked hemorrhage with neutrophils and nuclear debris. In the perivascular dermis, large irregular non-septated hyphal forms are noted, including the presence of angioinvasion. The DPAS stain highlights the fungal forms.

LABS

Abnormal: Hemoglobin 9.0 (13.0 - 17.5 g/dL), platelets 62 (140 - 390 K/UL), creatinine 3.5 (0.60 – 1.30 mg/dL)

Normal/negative: WBC, cryptococcal antigen, *blastomyces* antibody

TREATMENT AND COURSE

The patient was maintained on broad spectrum antibacterial and antifungal coverage. On the evening following dermatologic evaluation, the patient reported blurry vision and lethargy. CT brain revealed a large intraparenchymal hemorrhage. The patient was intubated for airway protection and transferred to the ICU. Over the next few days, the patient failed to improve. Following discussions with family, the patient was terminally extubated and died shortly thereafter.

ADDITIONAL STUDIES

Skin tissue and sputum culture with *Rhizopus oryzae*

FINAL DIAGNOSIS

Disseminated *Rhizopus* with skin, lung, and suspected brain involvement

DISCUSSION

Mucormycosis is a broad term referring to rare, invasive fungal infections with high mortality. The most common agents causing human disease belong to the order of Mucorales and the genera *Rhizopus, Mucor, and Rhizomucor.* These organisms are distributed worldwide where they are found in soil or decaying vegetation. Infection occurs via inhalation of spores or direct inoculation. In susceptible hosts, neutropenia contributes to the development of disseminated disease.

Of the six clinical presentations, cutaneous mucormycosis is the second most common and generally results from direct inoculation of spores into the dermis. Patients typically present with a single, tender, indurated papule that develops into an ecthyma-like lesion. The lesion can progress rapidly, reflecting infarction and subsequent tissue necrosis.

Diagnosis can be challenging and requires a high index of suspicion. In the absence of standardized blood tests or standardized PCR, obtaining tissue for histopathology and culture is of critical importance. Hyphae with an irregular branching angle greater than 90 degrees may be visualized under microscopy and is specific for the diagnosis of mucormycosis.

This presentation highlights two cases of mucormycosis in patients with a history of hematologic malignancy and HSCT who were receiving antifungal prophylaxis. The incidence of mucormycosis is estimated to be between 1-2% among such patients.

Treatment of mucormycosis relies on surgical debridement combined with high-dose, systemic antifungal therapy. Amphotericin B is considered the treatment of choice and has the largest spectrum of antifungal activity. For those unable to tolerate amphotericin B, posaconazole and isavuconazole, iron chelators, and echinocandins represent additional therapeutic options.

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CHICAGO DERMATOLOGICAL SOCIETY **Case 9**

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

UNKNOWN

A 10-year-old Hispanic male presented for evaluation of "bruising" on the left lower leg.

CHICAGO DERMATOLOGICAL SOCIETY **Case 10**

Presented by Julia Mhlaba, MD and Xiaolong (Alan) Zhou, MD
Department of Dermatology, Feinberg School of Medicine, Northwestern University

HISTORY OF PRESENT ILLNESS

A 53-year-old Japanese male presented with a six-month history of worsening hand dermatitis associated with severe pruritus. The patient was treated with clobetasol 0.05% ointment twice daily without significant improvement. On follow-up, he noted progression of his lesions to involve his face, trunk, arms and feet. Review of systems was negative for fevers, chills, weight loss, fatigue or night sweats.

PAST MEDICAL/SURGICAL HISTORY

None

FAMILY/SOCIAL HISTORY

Father with history of hepatocellular carcinoma. Emigrated from Japan 10 years prior to presentation but denied recent travel. Works as a biochemical researcher.

MEDICATIONS

None

PHYSICAL EXAM

Face, trunk, arms, palms and soles with numerous, 1-2 mm erythematous papules and pustules coalescing into large, partially-indurated plaques with centrifugal extension and occasional central clearing.

LABS/IMAGING

Abnormal: Absolute eosinophils 1.1 (0.0-0.6 K/uL)

Normal/Negative: CBC, CMP, LDH, Flow cytometry, T-Cell gene rearrangement (blood and tissue), HIV Ab/Ag, Syphilis, *Neisseria gonorrhoeae*, *Chlamydia*, Quantiferon gold, Hepatitis C serology panel

HISTOPATHOLOGY

Perivascular and periadnexal eosinophilic and lymphocytic infiltrate concentrated at the follicular isthmus and sebaceous glands. A plaque on the glabrous right plantar foot showed eosinophilic spongiosis and subcorneal and intraepidermal pustules. Tissue stains and cultures were negative for bacterial, mycobacterial, and fungal organisms.

DIAGNOSIS

Eosinophilic Pustular Folliculitis / Ofuji's disease

TREATMENT AND COURSE

The patient was subsequently started on indomethacin 50 mg daily. Within one month, the patient demonstrated near complete resolution of all lesions with improvement in pruritus and resolution of eosinophilia. After three months on indomethacin, the patient developed recurrent lesions on palms and soles. He was then started on acitretin 25 mg daily with improvement.

DISCUSSION

Eosinophilic pustular folliculitis (EPF) is a noninfectious inflammatory dermatosis first characterized in Japan in 1970 by Ofuji et al. Over 300 cases of EPF have been reported, with more than 100 cases occurring in Japanese patients. EPF is classified into three variants: classic EPF (Ofuji's

disease) which typically affects healthy Japanese adults; immunosuppression-associated EPF (IS-EPF) which is often associated with HIV; and infancy-associated EPF (I-EPF). Classic EPF peaks in incidence during the third and fourth decades of life. Among Japanese patients, the male-to-female ratio approximates 5 to 1.

Clinically, classic EPF appears as recurrent papules and pustules on an erythematous base, which gradually become confluent to form indurated, annular plaques. Eruptions most commonly occur on the face (>80%), with frequent involvement of the trunk and extremities. Palmoplantar pustules occur in approximately one-fifth of patients despite the lack of follicles in these areas. There is no systemic involvement. Individual plaques typically persist for 7 to 10 days, recur every 3 to 4 weeks and are often pruritic.

General diagnostic evaluation includes complete blood count with differential, human immunodeficiency virus (HIV) testing, and skin punch biopsy. Laboratory findings in classic EPF include leukocytosis with eosinophilia in up to 35% of patients, which normalize as skin lesions improve. On histology, there is a periadnexal infiltrate of eosinophils and lymphocytes primarily involving the follicular isthmus, infundibulum and sebaceous glands. On follicle-bearing areas, this infiltrate may form eosinophilic microabscesses, invade the pilosebaceous unit, and lead to destruction of the follicles in advanced cases. On follicle-free palmoplantar surfaces, histology demonstrates eosinophilic spongiosis and subcorneal and intraepidermal pustules with eosinophils and neutrophils.

While the etiology of EPF is uncertain, it has been proposed to be the result of immune dysregulation surrounding sebocytes, with excess prostaglandin D2 (PGD_2) stimulating sebocyte release of eosinophil chemoattractant, eotaxin-3. Indomethacin inhibits cyclooxygenase and arachidonic acid metabolites, including PGD_2, thus disrupting this process. Oral indomethacin (25-75 mg/day) is suggested as first-line treatment for classic EPF, demonstrating clinical efficacy in numerous cases. The time to initial response on oral indomethacin has been noted to range from several days to 2-6 weeks. In patients with kidney failure or peptic ulcers, topical indomethacin can be considered as an alternative first-line treatment.

KEY POINTS

1. Classic eosinophilic pustular folliculitis is a noninfectious inflammatory dermatitis that presents as pruritic plaques studded with papules and pustules and commonly affects Japanese patients.
2. Diagnosis is made via clinical presentation and histopathology demonstrating eosinophilic infiltrate surrounding the follicles at the level of the isthmus and sebaceous glands, eosinophilic spongiosis and subcorneal pustules.
3. Indomethacin is the first-line treatment for EPF and exhibits benefit within six weeks of initiation.

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