Chicago Dermatological Society

September 2019 Educational Conference

Program & Speaker Information
CME Certification
Case Presentations

Wednesday, September 11, 2019
Stephens Convention Center – Rosemont, IL

Conference Host:
Division of Dermatology
Loyola University Medical Center

LOYOLA MEDICINE
We also treat the human spirit.®

Program

Host: Loyola University
Wednesday, September 11, 2019
Stephens Convention Center, Rosemont

8:00 a.m.	**Registration & Continental Breakfast with Exhibitors** *Ballroom #42 & 41*
8:30 a.m. - 10:30 a.m.	**Clinical Rounds** Slide viewing and posters - *Ballroom 41*
9:00 a.m. - 10:00 a.m.	**Basic Science/Residents Lecture** - *Ballroom 42* "Eleven Commandments for Avoiding Serious Drug Interactions" *Stephen Wolverton, MD*
10:00 a.m. - 10:30 a.m.	**Break and Visit with Exhibitors** - *Ballroom 41*
10:30 a.m. - 12:15 p.m.	**Resident Case Presentations & Discussion;** **MOC Self-Assessment Questions** - *Ballroom 42*
12:15 p.m. - 12:45 p.m.	**Box Lunches & visit with exhibitors** - *Ballroom 41*
12:55 p.m. - 1:00 p.m.	**CDS Business Meeting** - *Ballroom 42*
1:00 p.m. - 2:00 p.m.	**General Session** - *Ballroom 42* “Biologics: Avoiding the Most Serious Adverse Effects” *Stephen Wolverton, MD*
2:00 p.m.	**Meeting adjourns**

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

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

Mark the Date!

Next CDS meeting will be on Wednesday, October 16th at the Gleacher Center downtown.

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

Guest Speaker

STEPHEN WOLVERTON, MD

Theodore Arlook Professor of Dermatology
Indiana University School of Medicine
Indianapolis, IN

After receiving his undergraduate degree at Ball State University in 1975, Dr. Wolverton attended medical school at Indiana University School of Medicine and received his MD degree in 1979. Dr. Wolverton initially pursued a career in Family Practice, completing his residency at St. Elizabeth Medical Center in Dayton, Ohio, in 1982. This residency was followed by a year in a junior faculty position at the same FP residency program.

Dr. Wolverton initiated his dermatology career completing his residency at Wright State University in Dayton, Ohio, from 1983 to 1985. Subsequent faculty positions have included Wright State University (Fellow Instructor 1986-1987), Ohio State University (1987-1990, including a year as Acting Division Director), and the long-term faculty position in the Dermatology Department at the Indiana University School of Medicine (1990-present). His current position is Theodore Arlook Professor of Clinical Dermatology and Professor of Clinical Dermatology.

Dr. Wolverton's long-term academic interest has been systemic drug use in dermatology, focusing on all aspects of drug safety, including a more recent focus in the complex area of drug interactions. He is best known for his series of four books concerning Dermatologic Drug Therapy: Systemic Drugs for Skin Diseases (published in 1991) and Comprehensive Dermatologic Drug Therapy (initially published in 2001, 2nd edition published in February 2007, with the 3rd edition of this title published late Fall 2012).

In addition, for 20 years he has been the Course Director for the Introduction to Cutaneous Biology course for dermatology residents throughout the US and Canada that is sponsored by the Indiana University Department of Dermatology.

Dr. Wolverton is a frequent visiting professor at various dermatology residency programs, along with various state and local dermatologic medical societies. He continues his strong interest in dermatology resident education full-time at IU and during many of the visiting professorships.

Chicago Dermatological Society
Patient Privacy and HIPAA Compliance

APPROVED
June 3, 2015

Purpose

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

Background

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

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

Policy

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

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

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

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

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

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

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

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

CME Information

September 11, 2019

Overview

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

Target Audience

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

Learning Objectives

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

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

Physician Accreditation Statement

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

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

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

Disclosure of Conflicts of Interest

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

The guest speaker, Stephen Wolverton, MD, has no relevant conflicts of interest to disclose. He does intend to discuss off-label and/or investigative uses of commercial products. None of the planning committee members have any relevant conflicts of interest to disclose.

Continued next page

Contact Information

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

Americans with Disabilities Act

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

Disclaimer

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

Dislosure of Unlabeled Use

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

Table of Contents

Chicago Dermatological Society **Case #1**

[1]Adam Vaudreuil MD, [1]David Rosenfeld MD, [3]Kimberly Sable BS, [2]Jodi Speiser MD, and [1]Eden Lake MD

[1]Division of Dermatology, Loyola University Medical Center

[2]Department of Pathology, Loyola University Medical Center

[3]Loyola University, Stritch School of Medicine

HISTORY OF PRESENT ILLNESS

A 21-year-old woman with a 5-year history of p155/140 (TIF1-gamma) positive juvenile dermatomyositis (JDM) was admitted to the hospital for two weeks of fever, fatigue, muscle pain and new-onset tender swelling of the face, periorbital region and bilateral upper and lower extremities. Review of systems was positive for weakness, fatigue, lightheadedness, and decreased appetite. Previous treatments for her JDM included: intravenous immunoglobulin (IVIg), methotrexate, and mycophenolate mofetil; previous treatments were complicated by chronic pancytopenia and multiple episodes of neutropenic fever (all with negative infectious workups), and were therefore discontinued.

PAST MEDICAL HISTORY

Juvenile dermatomyositis, chronic pancytopenia, fever of unknown origin, psoriasis

MEDICATIONS

Acetaminophen, ibuprofen

ALLERGIES

No known drug allergies

FAMILY HISTORY

No pertinent family history

SOCIAL HISTORY

Non-smoker, no alcohol use, no illicit drug use

PHYSICAL EXAMINATION

The patient was ill-appearing. On the face there was prominent facial and periorbital edema with thin, scaly, erythematous plaques. Tender, non-pitting edema was noted involving the bilateral upper and lower extremities with faint erythematous to hyperpigmented, indurated nodules on the shins.

DERMATOPATHOLOGY

Punch biopsy performed of the right shin showed lobular panniculitis with fat necrosis, mixed inflammation with neutrophils and peri-eccrine involvement, and an overlying interface dermatitis.

ADDITIONAL STUDIES

A complete blood count demonstrated pancytopenia: leukopenia at 2.7 (3.5 - 10.5 K/μL), decreased red blood count at 2.37 (3.80 – 5.20 M/μL), decreased hemoglobin at 7.0 (11.5 – 15.5 gm/dL), and thrombocytopenia at 112 (150 – 400 K/μL). A complete metabolic panel demonstrated hyponatremia at 128 (136 – 144 mmol/L), hypocalcemia at 7.8 (8.9 – 10.3 mg/dL), hypoalbuminemia at 2.6 (3.6 – 5.0 g/dL), and mild transaminitis with elevated AST at 40 (7 – 35 U/L), and ALT at 74 (10 – 40 U/L). Creatinine kinase was decreased at 27 (35 – 200 U/L). Erythrocyte sedimentation rate was elevated at 74 (0 – 20 mm). Blood cultures and urinalysis were unremarkable.

DIAGNOSIS

Juvenile dermatomyositis (JDM) associated panniculitis

TREATMENT AND COURSE

The patient was started on oral prednisone with improvement in her symptoms and subsequently discharged from the hospital. At outpatient follow-up, a trial of rituximab was initiated. Although the patient's symptoms initially improved, she failed to demonstrate a sustained response and remains on oral steroids to maintain disease suppression. An additional infusion of rituximab recently yielded improved symptoms.

DISCUSSION

Juvenile dermatomyositis (JDM) is a disorder of autoimmune pathogenesis with childhood onset that involves systemic inflammation of the muscles and characteristic cutaneous findings. When compared with adult-onset dermatomyositis (DM), the juvenile form is not associated with an increased risk of malignancy but does have an increased incidence of calcinosis cutis and associated small vessel vasculitis. It can present a diagnostic challenge, with MRI, EMG or muscle biopsy often required to confirm the diagnosis. Skin manifestations include heliotrope rash, V-sign, Shawl sign, Gottron's papules, periorbital edema and infrequently panniculitis.

Panniculitis is an uncommon clinical presentation of DM with most studies involving case reports. One study found histologic evidence of panniculitis in approximately 10% of skin biopsies in DM patients. Panniculitis is often considered a precursor to calcinosis cutis, which may occur in roughly 46% (25-70%) of JDM patients and can cause significant morbidity.

Anti-p155/140 autoantibodies have been associated with more extensive cutaneous disease, calcinosis, and peripheral edema in JDM patients. These antibodies have also been associated with a higher risk of malignancy in adult DM patients, with roughly 80% of malignancy-associated DM patients with positive anti-p155 or p140 antibodies.

Subcutaneous edema is rarely described in DM, present in only 6% of patients in one study. The pathophysiology of DM may include antibodies that target endothelial cells and activate complement, resulting in activation of the membranolytic attack complex, leading to micro-ischemia and micro-infarction of the muscle fibers, which may result in edema of the subcutaneous tissue. Micro-infarction is found 2.3 times more often in

edematous DM compared to non-edematous DM, thus subcutaneous edema may be a presentation of DM that arises more quickly and with severe disease activity.

Due to the severity of edematous and/or subcutaneous DM, aggressive therapy may be required. First-line therapy consists of corticosteroids. Addition of other immunosuppressive or immunomodulatory agents, such as methotrexate, azathioprine, IVIg, or mycophenolate mofetil, may be required if disease suppression is not achieved with corticosteroids alone. Of note, recent studies have investigated the effectiveness of rituximab in DM. The RIM trial assessed rituximab's efficacy in refractory compared with early-onset inflammatory myopathies. Overall 83% of patients, including the JDM subset, met the definition of improvement. In another study re-examining the RIM trial data with additional cases, an overall response rate of 78.3% was observed with 52.1% of DM patients reporting improvement in skin lesions. Further analysis of the RIM data revealed that panniculitis affected 10.4% of JDM patients at baseline and decreased to 6.8% at 36 weeks after rituximab.

Subcutaneous tissue involvement (including edema, calcinosis cutis, and panniculitis) is seen more often in JDM than adult DM. Our patient also had antibody positivity to p155/p140 which likely predisposed her to a more severe disease course. Initiating aggressive therapy early in disease course may be beneficial in this subset of patients.

REFERENCES

- Aggarwal R, Loganathan P, Koontz D, et al. Cutaneous improvement in refractory adult and juvenile dermatomyositis after treatment with rituximab. *Rheumatology*. 2017(56)2:247-254.
- Dalakas MC, Hohlfeld R. Polymyositis and dermatomyositis. Lancet 2003; 362:971-82.
- Fasano S, Gordon P, Hajji R, et al. Rituximab in the treatment of inflammatory myopathies: a review. *Rheumatology.* 2016;56(1):26-36.
- Fujimoto M, Watanabe R, Ishitsuka Y, Okiyama N. Recent advances in dermatomyositis-specific autoantibodies. *Curr Opin Rheumatol.* 2016;28:636-644
- Gunawardena H, Wedderburn LR, North J et al. "Clinical associations of Autoantibodies to a p155/140kDa doublet protein in juvenile dermatomyositis." *Rheumatology*. 2008;47:324-328.
- Janis JF, Winkelmann RK. Histopathology of the skin in dermatomyositis. A histopathologic study of 55cases. *Arch Dermatol* 1968;97:640-50.
- Milisenda JC, Doti PI, Prieto-Gonzalez S, Grau JM. Dermatomyositis presenting with severe subcutaneous edema: Five additional cases and review of the literature." *Seminars in Arthritis and Rheumatism*. 2014:44(2):228-233.
- Oddis CV, Reed AM, Aggarwal, et al. Rituximab in the treatment of refractory adult and juvenile dermatomyositis and adult polymyositis: A randomized, placebo-phase trial." *Arthritis & Rheumatism*. 2013;65(2):314–324.
- Robinson AB, Reed AM. Clinical features, pathogenesis and treatment of juvenile and adult dermatomyositis. *Nature Reviews Rheumatology*. 2011;7(11):664-675.

- Sakurai N, Hino-Shishikura A, Nozawa T, et al. Clinical significance of subcutaneous fat and fascial involvement in juvenile dermatomyositis. [online]. *Modern Rheumatology*. 18 Oct 2018.
- Santos-Briz A, Calle A, Linos K, et al. Dermatomyositis Panniculitis: a Clinicopathological and Immunohistochemical Study of 18 Cases. *Journal of the European Academy of Dermatology and Venereology*, 2018;32:1352-1359.
- Tansley SL, McHugh NJ, Wedderburn LR. Adult and juvenile dermatomyositis: are the distinct clinical features explained by our current understanding of serological subgroups and pathogenic mechanisms? *Arthritis Research & Therapy*. 2013;15:211.
- Van Dongen HM, van Vugt RM, Stoof TJ. Extensive persistent panniculitis in the context of dermatomyositis. [published online ahead of print]. *Journal of Clinical Rheumatology.* 2019.
- Watanabe M, Natsuga K, Arita K, Abe R, Shimizu H. Generalized acute subcutaneous edema as a rare cutaneous manifestation of severe dermatomyositis. *J Eur Acad Dermatol Venereol.* 2016 Nov;30(11):e151-e152.

Chicago Dermatological Society **Case #2**

[1]David Rosenfeld MD, [2]Adam Rosenfeld BS, [1]Adam Vaudreuil MD, and [1]Eden Lake MD
[1]Division of Dermatology, Loyola University Medical Center
[2]University of Missouri School of Medicine

HISTORY OF PRESENT ILLNESS

A 19-year-old transgender man (female to male) presented to the Loyola Dermatology clinic for evaluation of acne. A few months earlier, he began the process of transitioning with weekly testosterone injections and was now recovering from a recent bilateral mastectomy. The patient endorsed a history of mild facial acne that began two years ago. Since receiving testosterone therapy, his acne dramatically worsened and progressed to involve his chest and back. The acne was characterized predominantly by inflammatory nodules and pustules as well as a mix of both black- and whiteheads. He had just completed a trial of clindamycin 1% lotion, tretinoin 0.1% cream, benzoyl peroxide wash and a 3-month course of oral doxcycyline. He noted no significant improvement and was concerned about the scarring-nature of his acne. The patient denied any other cutaneous concerns or pertinent dermatologic history.

PAST MEDICAL HISTORY

Major depressive disorder, generalized anxiety disorder, asthma

PAST SURGICAL HISTORY

Bilateral mastectomy

MEDICATIONS

Testosterone injections, clindamycin 1% lotion, tretinoin 0.1% cream, doxycycline, venlafaxine, albuterol

ALLERGIES

Cats, dust, pollen

FAMILY HISTORY

None pertinent

SOCIAL HISTORY

Denies alcohol, tobacco, or illicit drug use
Sexually active only with women

PHYSICAL EXAMINATION

The patient was in no acute distress. Cutaneous examination revealed scattered erythematous papules and pustules on the bilateral cheeks, forehead and chin as well

as open and closed comedones. There was background ice pick atrophic scarring. There were similar erythematous papules and pustules on the back and chest.

DIAGNOSIS

Severe nodulocystic acne in a transgender patient on testosterone therapy

TREATMENT

After extensive patient counseling, the decision was made to initiate isotretinoin therapy. The patient had a history of depression and anxiety managed by his primary care physician, but no contraindications to isotretinoin were identified. The patient was scheduled for a hysterectomy the day after his clinic visit and his gynecologist cleared him for therapy despite theoretical post-operative healing risks. He was registered in the iPLEDGE® program as a “Female Patient Who Cannot Get Pregnant” due to the hysterectomy. Although the patient identifies as a male, he was agreeable to a female assignment for the purposes of treatment.

ADDITIONAL STUDIES

Routine laboratory tests for isotretinoin initiation were obtained, including a complete metabolic panel, complete blood count and lipid panel. Abnormalities included a decreased HDL of 34 (> 39 mg/dL) and an increased LDL 110 (< 100 mg/dL). The remaining laboratory work-up was unremarkable. Neither a urine or serum beta human chorionic gonadotropin (hCG) was obtained.

DISEASE COURSE

Due to the severe inflammatory nature of his acne as well as the inability to start prednisone post-hysterectomy, the patient was started on a low dose of isotretinoin at 20mg daily. At the initial follow-up, he was tolerating the medicine well with no significant adverse effects. There was no change in his baseline depression or mood status. Isotretinoin was increased to 20mg twice daily and has been maintained on this dose. The patient continues to endorse significant improvement in his acne and overall satisfaction with the treatment course.

DISCUSSION

Acne vulgaris is a common inflammatory condition of the pilosebaceous unit with a wide spectrum of clinical disease. While it typically presents in puberty as a result of androgen stimulation and changes in keratinization, a number of medications can trigger the disease. Among these is exogenous testosterone, which is commonly used in female to male transition therapy. It is evident that testosterone injections increase sebum production and therefore increase the risk of acne in transgender males. In one study of 20 transgender men initiating testosterone treatment, the prevalence of acne increased from 35% at baseline to 82% after only six months of treatment. After one

year, acne remained on the face in 55% of patients and on the back and chest in 50%. Although topical retinoids and oral antibiotics are considered first-line treatment, these may be insufficient for management of androgen-induced acne. As a result, isotretinoin remains a valuable intervention, particularly considering the lifelong requirements of testosterone therapy in this population.

All patients who are on isotretinoin must be registered in the iPLEDGE® program, which is a risk-management program mandated by the Food and Drug Administration (FDA) to protect against preventable birth defects and other pregnancy-related effects of isotretinoin. Currently, there are only three identification options for patient registration: “Females of Reproductive Potential,” “Females Who Cannot Get Pregnant” and “Males.” This is problematic for transgender patients who either do not identify with their assigned gender from birth or do not identify with a gender at all. If patients are not registered appropriately, they are at risk for citation and possible termination from the program. This also presents a challenge for dermatologists who wish to respect the autonomy and gender expression of their patients while at the same time adhere to the guidelines of the iPLEDGE® program.

In 2014, there were approximately 1.4 million transgender persons in the United States and that number has been increasing. The National Academies of Science, Engineering and Medicine have highlighted gaps in understanding transgender health concerns and are emphasizing ways in which those gaps can be bridged. However, until iPLEDGE® is modified for greater inclusion, dermatologists must continue to have difficult conversations with these patients.

From an ethical standpoint, given current restrictions, it is recommended that transgender patients be registered as their assigned gender at birth. Theoretically, transgender women (male to female), could be registered as “Females Who Cannot Get Pregnant.” They have no reproductive potential, and therefore, possess no pregnancy risk. Transgender men (female to male) who have had a hysterectomy, bilateral oophorectomy, are menopausal or have premature ovarian failure also have no child-bearing potential. Therefore, they too could be safely registered by their preferred pronoun, “Males.” However, in both cases, this is considered unethical and not recommended. For transgender men who still have child-bearing potential, there is no safe and inclusive option for them, such as “Males of Reproductive Potential.” As a result, they must register against their preferred pronoun as “Females of Reproductive Potential” or not register at all.

For male transgender patients, dermatologists should inquire if they are interested or planning on scheduling a hysterectomy of bilateral oophorectomy as part of their transition. In these cases, isotretinoin initiation may be delayed until after surgery.

Traditionally, it is recommended that surgeries be delayed 6 to 12 months after completing isotretinoin due to concern of poor wound healing and scarring. However, recent data suggests this may be unnecessary. Additional studies are still needed to re-evaluate this practice.

If patients do not intend on a transitional surgery, they must be counseled on appropriate contraceptive measures. Testosterone injections are not considered adequate contraception, and for transgender men receiving these, traditional hormonal contraceptives are contraindicated. The remaining highly effective primary forms of contraception according to iPLEDGE® include tubal ligation, partner's vasectomy, non-hormonal intrauterine devices and complete abstinence. Secondary forms include male latex condoms, diaphragms, cervical caps and vaginal sponges.

For transgender men who are uncomfortable identifying as female through iPLEDGE®, they may unfortunately choose to defer otherwise medically-indicated treatment. This may cause significant scarring and profound social and psychological effects creating an unnecessary burden on an already marginalized community.

Recommendations have been made to exclude gender classification from the registration process all together as child-bearing potential is the only relevant criteria. Registration options could simply include "Person Who Can Get Pregnant" and "Person Who Cannot Get Pregnant." A gender-neutral approach to iPLEDGE® would create congruity with patients' preferred gender pronouns and a broader sense of inclusivity within the health care system. Given the frequency of iPLEDGE® use and a growing transgender population, it is important for dermatologists to participate in patient advocacy. Both the American Academy of Dermatology and the American Medical Association have supported this gender-neutral categorization model, and recently, the Society for Pediatric Dermatology has formally requested the FDA and iPLEDGE® to endorse it.

REFERENCES

- Boos MD, Ginsberg BA, Peebles JK. Prescribing isotretinoin for transgender youth: A pledge for more inclusive care. *Pediatric Dermatology.* 2018;*36*(1): 169-171.
- Ginsberg BA, Calderon M, Seminara NM, Day D. A potential role for the dermatologist in the physical transformation of transgender people: A survey of attitudes and practices within the transgender community. *Journal of the American Academy of Dermatology.* 2016;74:303-308.
- Katz KA. Transgender Patients, Isotretinoin, and US Food and Drug Administration–Mandated Risk Evaluation and Mitigation Strategies. *JAMA Dermatology.* 2016;*152*(5):513.

- Lee YH, Scharnitz TP, Muscat J, Chen A, Gupta-Elera G, Kirby JS. Laboratory Monitoring During Isotretinoin Therapy for Acne. *JAMA Dermatology.* 2016;*152*(1):35.
- Motosko C, Zakhem G, Pomeranz M, Hazen A. Acne: A side-effect of masculinizing hormonal therapy in transgender patients. *British Journal of Dermatology.* 2018;*180*(1): 26-30.
- Park et al. Risk factors for acne development in the first 2 years after initiating masculinizing testosterone therapy among transgender men. *Journal of the American Academy of Dermatology.* 2019;*81(2)*:617-618.
- Spring, L. K. et al. Isotretinoin and Timing of Procedural Interventions. *JAMA Dermatology.* 2017;*153*(8):802.
- Stoff, Ben. *Ethics in Acne: Transgender Patients and iPLEDGE*. Presented at the American Academy of Dermatology Annual Meeting. 2018. San Diego, CA.
- Sullivan et al. Issues in transgender dermatology. A systematic review of the literature. *Journal of the American Academy of Dermatology.* 2019;81*(2)*:438-447.
- Tolkachjov SN, Sahoo A, Patel NG, Lohse CM, Murray JA, Tollefson MM. Surgical outcomes of patients on isotretinoin in the perioperative period: A single-center, retrospective analysis. *Journal of the American Academy of Dermatology.* 2017;*77*(1): 159-161.
- Yeung H, Chen SC, Katz KA, Stoff BK. Prescribing isotretinoin in the United States for transgender individuals: Ethical considerations. *Journal of the American Academy of Dermatology.* 2016;*75*(3):648-651.

Chicago Dermatological Society **Case #3**

[1]Jeave Reserva MD, [1]David Rosenfeld MD, [2]Olaoluwa Bode-Omoleye MD, [3]Madhu Dahiya MD, and [4]David Eilers MD

[1]Division of Dermatology & [2]Department of Pathology, Loyola University Medical Center

[3]Department of Pathology & [4]Section of Dermatology, Edward Hines Jr. Veterans Affairs Hospital

HISTORY OF PRESENT ILLNESS

A 72-year-old male with history of stage IA mycosis fungoides (MF) presented with a 3-day old painful nodule on his left dorsal foot. He has uncontrolled diabetes mellitus complicated by peripheral neuropathy and was uncertain of recent trauma to the affected area. Six months prior to presentation, he developed a red papule on the left medial ankle that enlarged and ulcerated thought to possibly be trauma-induced. Over several months, the ulcer eventually healed after sharp debridement and weekly Unna boot dressing changes with silver impregnated calcium alginate applied to the wound base and triamcinolone acetonide 0.1% ointment to the surrounding skin. His review of systems was otherwise unremarkable.

PAST MEDICAL HISTORY

Diabetes mellitus type II complicated by peripheral neuropathy, hyperlipidemia, hypertension, osteoarthritis, gastroesophageal reflux disease, benign prostate hyperplasia, post-traumatic stress disorder

MEDICATIONS

Metformin, glipizide, insulin, pravastatin, meloxicam, gabapentin

ALLERGIES

Amitriptyline

FAMILY HISTORY

No pertinent family history

SOCIAL HISTORY

No past or current use of alcohol, tobacco, or illicit drugs

PHYSICAL EXAMINATION

The patient was well-appearing. On the left dorsal foot, there was a 1.5 cm tender deeply violaceous, crusted nodule with a well-demarcated peripheral rim of erythema and focal fine scaling. A pink scar was noted on the left medial malleolus. Over the left proximal lateral thigh and left lateral suprapubic, there were large, pink to red, slightly wrinkled, and finely scaly patches.

DERMATOPATHOLOGY

Biopsy of the nodule showed epidermal spongiosis with microvesiculation and a dense superficial and deep dermal lymphoid infiltrate comprised of large, atypical lymphocytes

with brisk mitotic rate. Admixed in the background were small, more mature-appearing lymphocytes and scattered eosinophils, neutrophils and histiocytes.

The atypical cells strongly expressed CD30, CD2, and, to a lesser extent, CD3, but were negative for CD5 and CD7. The background population of small lymphocytes expressed CD3 with scattered CD20 and CD8 immunoreactivity, suggesting a reactive population admixed with the atypical proliferation.

ADDITIONAL STUDIES

Complete blood count with differential and peripheral blood smear were unremarkable. Computed tomography of the chest, abdomen, and pelvis showed no lymphadenopathy. Whole body positron emission tomography showed no abnormal fluorodeoxyglucose uptake.

DIAGNOSIS

Primary cutaneous anaplastic large cell lymphoma (pcALCL)

TREATMENT AND COURSE

Two monthly intralesional triamcinolone acetonide (40mg/mL) injections were performed which resulted in complete clinical resolution. Similar solitary lesions on the right thigh and left buttock were noted at 12- & 15-months after presentation, which also completely resolved after intralesional corticosteroid injections. The patient is closely followed up by the hematology/oncology service, and to date, has not shown any evidence of extracutaneous involvement.

DISCUSSION

Primary cutaneous anaplastic large cell lymphoma (pcALCL) is one of the primary cutaneous CD30+ T-cell lymphoproliferative disorders (CD30+ LPD). CD30+LPD are the second most common form of primary cutaneous T-cell lymphomas (CTCL) and includes pcALCL, lymphomatoid papulosis (LyP), and borderline lesions. These neoplasms' common phenotypic hallmark is the expression of CD30, a cytokine receptor belonging to the tumor necrosis factor receptor superfamily involved in the control of tumor cell growth.

Primary cutaneous anaplastic large cell lymphoma classically presents as solitary, grouped or multifocal nodules on the head, neck, or extremities that persist for at least 3 to 4 weeks, with a fifth of cases showing multifocal cutaneous involvement. Typically affecting males in their 60s, these nodules tend to ulcerate but also not infrequently spontaneously regress (20%-42% of cases). Five-year survival rates for early stage disease ranges between 90% and 97.5%, with only 10% of cases showing extra cutaneous spread to regional lymph nodes. Despite favorable prognosis, recurrences after spontaneous regression are common, and complete remission without therapeutic intervention is the exception.

Histologically, pcALCL manifests as a circumscribed nodular cohesive infiltrate of large lymphoid cells extending into the deep dermis or subcutis. The tumor cells have round, irregularly shaped nuclei and abundant pale cytoplasm thus exhibiting pleomorphic,

anaplastic, or an immunoblastic morphology. Few reactive cells such as neutrophils or eosinophils may be present, although these cells may be abundant in immunodeficient patients with pcALCL. By definition, at least 75% of the tumor cells must express CD30 and anaplastic lymphoma kinase (ALK) is almost always negative, in contrast with systemic ALCL.

As with other CD30+LPD, the diagnosis of pcALCL relies heavily on clinicopathologic correlation and staging, given the potential morphologic, clinical and molecular overlap with the other cutaneous CD30+ LPD, LyP, and more aggressive hematolymphoid neoplasms. Notably, a biopsy of LyP type C may be indistinguishable from pcALCL; but its clinical behavior of recurrent and regressing crops of smaller (<1cm) papules and nodules assists in its distinction from pcALCL.

CD30-rich MF with large cell transformation (MF-LCT or T-MF) is an important differential diagnosis of pcALCL. MF-LCT patients typically present with long-standing classic lesions of MF with the development of tumor nodules. MF-LCT histologically tends to have epidermotropic CD30+ tumor cells which occur less frequently in pcALCL. Perforin expression favors pcALCL, while GATA3+ expression is seen more often in MF-LCT. The importance of distinguishing between CD30-rich MF-LCT from pcALCL is highlighted by their differences in disease-free 5-year survival rates, which is 65% in MF-LCT and >95% in pcALCL. Co-existence of CD30+LPD, such as pcALCL and LyP, with MF in the same patient is a known phenomenon. Longitudinal clinicopathologic correlation is often necessary in differentiating between CD30-rich MF-LCT and CD30+LPDs.

Treatment of solitary or grouped pcALCL includes surgical excision and/or radiotherapy. Skin directed therapies such as intralesional methotrexate and topical imiquimod have also been reported. Intralesional corticosteroid has been reported to result in complete remission in a patient with multifocal skin relapse. Multiagent chemotherapy is reserved for disseminated disease beyond locoregional lymph nodes. In addition, targeted therapy such as brentuximab vedotin, an anti-CD30 monoclonal antibody, has shown favorable outcomes over standard systemic therapies that include methotrexate and bexarotene.

REFERENCES

- Agar NS, Wedgeworth E, Crichton S, Mitchell TJ, et al. Survival outcomes and prognostic factors in mycosis fungoides/Sézary syndrome: validation of the revised International Society for Cutaneous Lymphomas/European Organisation for Research and Treatment of Cancer staging proposal. *J Clin Oncol.* 2010;28:4730–9.
- Brown RA, Fernandez-Pol S, Kim J. Primary cutaneous anaplastic large cell lymphoma. *J Cutan Pathol.* 2017 Jun;44(6):570-577.
- Cieza-Díaz DE, Prieto-Torres L, Rodríguez-Pinilla SM, Córdoba Mascuñano R, et al. Mycosis Fungoides Associated with Lesions in the Spectrum of Primary Cutaneous CD30+Lymphoproliferative Disorders: The Same Process or 3 Coexisting Lymphomas? *Am JDermatopathol.* 2019 Mar 29. doi: 10.1097/DAD.0000000000001423. [Epub ahead of print].

- Fauconneau A, Pham-Ledard A, Cappellen D, Frison E, et al. Assessment of diagnostic criteria between primary cutaneous anaplastic large-cell lymphoma and CD30-rich transformed mycosis fungoides; a study of 66 cases. *Br J Dermatol.* 2015 Jun;172(6):1547-1554.
- Goyal A, Carter JB, Duncan LM. Chapter 2: Introduction to Cutaneous Lymphomas. In: Carter JB, Goyal A, Duncan LM, eds. *Atlas of Cutaneous Lymphomas: Classification and Differential Diagnosis.* Cham: Springer; 2015. pp. 5-12.
- Goyal A, Carter JB, Duncan LM. Chapter 4: Introduction to the T-Cell Lymphomas. In: Carter JB, Goyal A, Duncan LM, eds. *Atlas of Cutaneous Lymphomas: Classification and Differential Diagnosis.* Cham: Springer; 2015. pp. 23-29.
- Kang SK, Chang SE, Choi JH, Sung KJ, Moon KC, Koh JK. Coexistence of CD30-positive anaplastic large cell lymphoma and mycosis fungoides. *Clin Exp Dermatol.* 2002 May;27(3):212-5.
- Kempf W, Kerl K, Mitteldorf C. Cutaneous CD30-positive T-cell lymphoproliferative disorders-clinical and histopathologic features, differential diagnosis, and treatment. *Semin Cutan Med Surg.* 2018 Mar;37(1):24-29.
- McCalmont TH. Maximizing the clinical utility of descriptive lymphoid pathology reporting. *Semin Cutan Med Surg*. 2018 Mar;37(1):75-80.
- Melchers RC, Willemze R, Bekkenk MW, de Haas ERM, et al. Evaluation of treatment results in multifocal primary cutaneous anaplastic large cell lymphoma: report of the Dutch Cutaneous Lymphoma Group. *Br J Dermatol.* 2018 Sep;179(3):724-731.
- Sauder MB, O'Malley JT, LeBoeuf NR. CD30(+) Lymphoproliferative Disorders of the Skin. *Hematol Oncol Clin North Am*. 2017 Apr;31(2):317-334.
- Shinohara MM, Shustov A. How I treat primary cutaneous CD30(+) lymphoproliferative disorders. *Blood.* 2019 Aug 8;134(6):515-524.
- Vu K, Ai W. Update on the Treatment of Anaplastic Large Cell Lymphoma. *Curr Hematol Malig Rep*. 2018 Apr;13(2):135-141.
- Wieser I, Tetzlaff MT, Torres Cabala CA, Duvic M. Primary cutaneous CD30(+) lymphoproliferative disorders. *J Dtsch Dermatol Ges.* 2016 Aug;14(8):767-82.

Chicago Dermatological Society **Case #4**

[1]Brooke Vasicek MD and [1]Wendy Kim DO
[1]Division of Dermatology, Loyola University Medical Center

HISTORY OF PRESENT ILLNESS

A 3-year-old otherwise healthy male was referred to our clinic for evaluation of a red rash on the trunk, face, and axillae. The rash had been present since infancy. Since that time, he had been treated for atopic dermatitis with hydrocortisone 2.5% ointment during flares and liberal use of emollients daily with limited improvement. He had mild associated pruritus, but never required oral antihistamines. Mom noted that some areas of the rash would grow and shrink in size, and eventually clear, only to appear in another area. He had previously had skin prick testing with negative results. There was no family history of atopic dermatitis or asthma. Review of systems was negative.

PAST MEDICAL HISTORY

Full term birth via cesarean delivery

MEDICATIONS

Hydrocortisone 2.5% ointment twice daily to affected areas of the skin

ALLERGIES

No known drug allergies

FAMILY HISTORY

Seasonal allergies – father

SOCIAL HISTORY

Lives with his mother, father, and younger sister, two cats and one dog in the home, attends preschool

PHYSICAL EXAMINATION

The patient was a well-appearing young male with well demarcated, pink-yellow patches with a slightly brighter pink, finely scaling, thin plaque at the periphery creating a geographic border over the bilateral cheeks to the nasal bridge (with sparing of the melolabial folds), chin, bilateral axillae, abdomen, anterior chest, and lower back. There was slight scaling on the dorsal feet. The remainder of the exam, including the palms, soles, hair, and teeth, was unremarkable.

DERMATOPATHOLOGY

None

ADDITIONAL STUDIES

None

DIAGNOSIS

Erythrokeratodermia variabilis (EKV)

TREATMENT AND COURSE

A skin biopsy and genetic testing were offered but given the chronic and asymptomatic nature of rash, the family elected for empiric treatment with the option for further work-up if treatment results were unsatisfactory. In addition to a gentle skin care regimen, Mom was instructed to apply ammonium lactate 12% lotion twice daily to red skin. At his follow-up visit three months later, he had significant improvement with nearly complete clearance of his rash. The family was very pleased with the treatment outcome and declined further work-up. Mom continues to apply ammonium lactate lotion twice daily to red areas and once daily to the entire body. He has remained clear or nearly clear for five months with this regimen.

DISCUSSION

Erythrokeratodermia variabilis is a rare, primarily genetic, erythrokeratoderma often seen in Caucasian individuals. While autosomal recessive and sporadic cases are reported, inheritance is classically autosomal dominant with complete penetrance. Erythrokeratodermia variabilis is caused by mutations in gap junction proteins. Mutations in genes GJB3, GJB4, and occasionally GJA1, which encode for gap junction proteins connexin 31, 30.3, and 43, lead to the formation of altered intercellular channels and subsequently defective epidermal differentiation.

Affected individuals present with transient, well-demarcated, erythematous, patches shortly after birth or within the first year of life. The patches can be found anywhere on the body and often have a geographic, circinate, or target-like morphology, occasionally coalescing into very large patches. Erythema often varies in intensity, lasts minutes to days prior to fading, and may have a blanching halo surrounding the patch. A minority of patients experience localized burning prior to, or at the time of, a patch developing.

With age, erythema slowly subsides and well-demarcated, yellow-brown to pink-brown hyperkeratotic plaques begin to appear. The plaques may have a velvety or ridged surface and/or a collarette of desquamation or fine, adherent scales. Typically, plaques are symmetrically distributed over the trunk, buttocks, and distal extremities with sparing of the flexures, face, and scalp. Half of all patients will have an associated palmoplantar keratoderma. Generalized hyperkeratosis, hypertrichosis, and hystrix-like plaques can be seen in severe cases.

Erythrokeratodermia variabilis tends to be progressive during childhood and stabilizes after puberty. Skin lesions may clear periodically and the condition generally improves with time. Common exacerbating factors include stress, rapid temperature changes, friction, and ultraviolet radiation.

Erythrokeratodermia variabilis has genetic and clinical overlap with another erythrokeratoderma - progressive symmetric erythrokeratoderma (PSEK). Two families affected by PSEK, a genetically heterogeneous condition, were found to have mutations in GJB4. This discovery raised a debate if EKV and PSEK are different manifestations of the same inherited condition. Similar to EKV, PSEK presents in infancy or early childhood with symmetric, fixed, hyperkeratotic plaques on an erythematous base on the extremities and buttocks which increase in size and number during childhood,

stabilizing during puberty. However, PSEK lacks the transient erythematous patches seen in EKV, more commonly involves the face, and less frequently affects the trunk. Given these similarities, some have suggested the term erythrokeratodermia variabilis et progressiva be used to include both entities.

Erythrokeratodermia variabilis is a clinical diagnosis. Histological findings are nonspecific but may demonstrate basket-weave orthokeratosis, acanthosis with a prominent granular layer, and papillomatosis. Although non-specific, skin biopsy may prove useful in excluding other conditions on the differential diagnosis such as pityriasis rubra pilaris. Additionally, genetic testing can be used to support a diagnosis of EKV.

Treatment of EKV is aimed at symptom control. For mild cases, topical keratolytics, humectants, and/or retinoids can be used. While typically reserved for more extensive disease, systemic retinoids or PUVA can result in significant reduction, or even complete clearing, of both the hyperkeratotic and erythematous lesions. Erythematous patches recalcitrant to treatment can be camouflaged with make-up if cosmetically bothersome.

REFERENCES

- Dieter M, Vinzenz O. Disorders of keratinization. In: Calonje E, Brenn T, Lazar AJ, Billings SD. Eds. *McKee's Pathology of the Skin,* 5th Ed. Edinburgh: Elsevier/Saunders; 2020. p53-117.
- Ishida-Yamamoto A. Erythrokeratodermia variabilis et progressiva. *Journal of Dermatology* 2016;43:280-5.
- Karadag AS, Bilgili SG, Calka O, Bayram I. Erythrokeratodermia variabilis: Two case reports. *Indian Dermatology Online Journal* 2013;4(4):340-3.
- Patterson J. Disorders of epidermal maturation and keratinization. In: Patterson J, Hossler G, eds. *Weedon's Skin Pathology,* 4th Ed. Philadelphia: Elsevier; 2016. p281-320.
- Richard G. Connexin disorders of the skin. *Clinics in Dermatology* 2005;23-32.
- Richard, G, Brown, N, Rouan, F, Van der Schroeff, JG, Bijlsma, E, Eichenfield, LF, Sybert, VP, Greer, KE, Hogan, P, Campanelli, C, Compton, JG, Bale, SJ, DiGiovanna, JJ, Uitto, J. Genetic heterogeneity in erythrokeratodermia variabilis: novel mutations in the connexin gene GJB4 (Cx30.3) and genotype-phenotype correlations. *Journal of Investigative Dermatology* 2003;120:601-609.
- Richard G and Ringpfeil F. Ichthyoses, Erythrokeratodermas, and Related Disorders. In: Bolognia J, Schaffer J, Cerroni L, eds. *Dermatology*, 4th Ed. Phiadelphia Elsevier; 2018. p888-923.
- Sbidian E, Bousseloua N, Jonard L, Leclerc-Mercier S, Bodemer C, Hadj-Rabia S. Novel Mutation in GJB4 Gene (Connexin 30.3) in a Family with Erythrokeratodermia Variabilis. *Advances in Dermatology and Venereology* 2013;93(2):193-5.
- van Steensel MAM, Oranje AP, van der Schroeff JG, Wagner A, van Geel M. The Missense Mutation G12D in Connexin30.3 Can Cause Both Erythrokeratodermia Variabilis of Mendes da Costa and Progressive Symmetric Erythrokeratodermia of Gottron. *American Journal of Medical Genetics Part A* 2009;149A:657-661.
- Yoshikata-Isokawa Y, Itoh M, and Nakagawa H. Japanese sporadic case of erythrokeratodermia variabilis caused by the connexin-30.3 (GJB4) mutation: Is Glycine 12 a mutational hotspot in the connexin family? *Journal of Dermatology* 2016;43(7):830-1.

Chicago Dermatological Society **Case #5**

[1]Ada Agidi MD, [1]Ashish Arshanapalli MD, [1]Jayla Gray MD, [2]Kumaran Mudaliar MD, and [1]Wendy Kim DO

[1]Division of Dermatology, Loyola University Medical Center

[2]Department of Pathology, Loyola University Medical Center

HISTORY OF PRESENT ILLNESS

A 56-year-old Caucasian female presented to clinic with non-healing wounds on the back and knee. Three years prior to presentation, she had a cyst-like lesion on the back that was debrided. The wound did not heal and continued to enlarge. In November 2018, plastic surgery closed the wound with flap placement. The patient later developed wounds along the incision sites and reported multiple failed flap placements. She endorsed severe pain and drainage, 100-pound weight loss over the last year, night sweats, chills, nausea, vomiting, bilateral shoulder arthralgias, chills, and cough. She denied fevers, headaches, decreased appetite, diarrhea, hematuria, hematochezia, and overseas travel prior to onset of symptoms. The patient also reported a history knee replacement complicated by ulcers along the incision line which led to infected hardware.

PAST MEDICAL HISTORY

Rheumatoid arthritis, chronic sinusitis, essential hypertension, hypothyroidism

MEDICATIONS

Levothyroxine, silver sulfadiazine 1% cream TID to ulcers, vancomycin 1000 mg IV BID, doxycycline 100 mg BID

ALLERGIES

Cefdinir, codeine, lisinopril, penicillin

FAMILY HISTORY

No pertinent family history

SOCIAL HISTORY

Patient had a 60-pack year smoking history and reported one alcoholic beverage per week. She denied illicit drug use.

PHYSICAL EXAMINATION

The patient was well-appearing. On the back, there were linear geometric ulcers following incision lines with violaceous overhanging undermined borders. Some were cribriform in shape, and with healthy granulation tissue at the base with yellow fibrinous drainage. The left knee was not examined due to knee dressing; however she provided

a photo showing two cribriform ulcerations with undermined borders and violaceous edges within linear scar.

DERMATOPATHOLOGY

Punch biopsy showed dense epidermal and dermal inflammatory infiltrate with numerous eosinophils admixed with neutrophils, plasma cells, and scattered giant cells. There were fibrinoid changes in some vessels.

ADDITIONAL STUDIES

A complete blood count demonstrated a decreased hemoglobin at 10.6 (11.5-15.5 gm/dL). Complete metabolic panel was unremarkable. Cytoplasmic antineutrophilic cytoplasmic antibodies (c-ANCA) titers were elevated at 1:160 (<1:20) and proteinase-3 (PR3) antibody was elevated at 4.1 (<1.0 AI). Perinuclear antineutrophilic cytoplasmic antibodies (p-ANCA) and neutrophil myeloperoxidase (MPO) antibodies were within normal limits. Protein/creatinine ratio was 0.18 (<0.16 mg/mg). Cryoglobulins were absent. ANA, dsDNA, Sm, SSA, SSB, RNP, Scl70, RF, and CCP antibodies were all negative. Immunofixation was unremarkable. Coccidioides, blastomycosis, and histoplasma serologies were negative. Tissue culture was negative for bacteria, fungus, and acid fast bacilli. CT chest showed scattered bilateral subcentimeter pulmonary nodules.

DIAGNOSIS

Atypical eosinophilic granulomatosis with polyangiitis (EGPA) associated with pyoderma gangrenosum(PG)-like ulcers

TREATMENT AND COURSE

The patient was started on a prednisone taper and timolol 0.5% TID to the deepest areas of the ulcers. Recommendations were given to avoid further debridement or surgery to prevent pathergy. At follow up about one month later, patient reported improvement in wounds and pain. Pulmonary nodules also decreased in size, further supporting our diagnosis of EGPA. She was then started on azathioprine 50 mg daily.

DISCUSSION

Eosinophilic granulomatosis with polyangiitis (EGPA), formerly known as Churg-Strauss syndrome, is a systemic small-and-medium-sized vessel necrotizing vasculitis characterized by chronic rhinosinusitis, asthma, and peripheral eosinophilia. Pathogenesis is not well elucidated; it is thought to be a result of complex interactions of genetic and environmental factors that lead to an inflammatory response, mainly involving eosinophils, T, and B lymphocytes. Genetically implicated factors include *HLA-DRB1*04* and **07, HLA-DRB4,* and IL10.2 haplotype of the IL-10 promoter gene.

Acquired pathogenic factors include exposure to different allergens, infections, vaccinations, drugs, and silica exposure.

Eosinophilic granulomatosis with polyangiitis most commonly involves the lungs; other frequently involved organs include the heart, upper respiratory tract, and skin. The clinical features of EGPA develop over three evolutionary phases. In the first phase, patients present with upper respiratory manifestations such as asthma, allergic rhinitis, and/or nasal polyps. During the second or eosinophilic phase, there is peripheral and tissue eosinophilia due to eosinophilic infiltration of multiple organs primarily affecting the lungs, intestines, and heart. In the third phase, there is presence of systemic vasculitis affecting the peripheral nervous system, kidneys, and skin.

Cutaneous findings are present in about 50-66% of patients with EGPA. Patients present with subcutaneous nodules on extensor surfaces, hemorrhagic lesions such as purpura, petechiae, ecchymosis, hemorrhagic bullae, urticaria, erythematous macules, livedo reticularis, and rarely cutaneous ulcers. There have been only a few reported cases of ulcerations in EGPA with one report of PG-like ulcerations. The association of PG-like ulcers with systemic granulomatosis is well recognized in granulomatosis with polyangiitis but not in the context of EGPA. Similar to PG, affected patients can present with evolution of ulcer after minor trauma, a phenomenon known as pathergy.

The prototypical laboratory finding in EGPA is peripheral eosinophilia, which is present in 80-100% of cases. ANCA is positive in about 40-75% of EGPA patients. Eosinophilic granulomatosis with polyangiitis is most commonly characterized by p-ANCA on immunofluorescence assay and antibodies directed against the MPO on enzyme-linked immunosorbent assay. However, c-ANCA pattern and detection of PR3 antibodies have also been reported in <5% of cases. Patients may also show increased IgG4 blood levels. Histologic features include interstitial and vascular granulomatous inflammation composed of eosinophilic necrotic matrix surrounded by giant cells and palisading lymphocytes. There may also be presence of fibrinoid necrosis of the vessel wall with or without the presence of a granuloma or eosinophilic infiltrates.

Treatment of EGPA involves use of systemic glucocorticoids in order to achieve remission. Patients with life threatening disease or severe organ involvement should be started on a combination of glucocorticoids and another immunosuppressive agent like cyclophosphamide. Maintenance therapy with azathioprine or methotrexate is recommended after remission-induction therapy to prevent relapse and allow for glucocorticoid tapering. Rituximab, intravenous immunoglobulins, interferon alpha, or plasmapheresis may be considered for refractory disease.

Skin involvement is not rare in EGPA, and therefore must be included in the differential diagnosis of necrotizing ulceration. Pyoderma gangrenosum is a diagnosis of exclusion and similar lesions can present with underlying pathologic processes like vasculitis, malignancy, infection, drug-induced processes, or exogenous tissue injury. As a result, when faced with PG-like lesions, an underlying disease must be considered.

REFERENCES

- Boudny, Clara, Helga Nievergelt, Lasse R. Braathen, and Dagmar Simon. "Wegener's granulomatosis presenting as pyoderma gangrenosum." *JDDG: Journal der Deutschen Dermatologischen Gesellschaft* 6, no. 6 (2008): 477-479.
- Chakraborty, Rebanta K., and Narothama Reddy Aeddula. "Churg Strauss Syndrome (Allergic Granulomatosis)." In *StatPearls [Internet]*. StatPearls Publishing, 2019.
- Chen, Ko-Ron, and J. Andrew Carlson. "Clinical approach to cutaneous vasculitis." *American journal of clinical dermatology* 9, no. 2 (2008): 71-92.
- Dejardin, A. Botelho, F. Delesalle, E. Delaporte, and B. Wallaert. "Pyoderma gangrenosum and Churg-Strauss syndrome." *La Revue de* medecine interne 28, no. 8 (2007): 564-565.
- Frumholtz, Laure, Sara Laurent-Roussel, Olivier Aumaître, François Maurier, Guillaume Le Guenno, Agnes Carlotti, Alexiane Dallot et al. "Clinical and pathological significance of cutaneous manifestations in ANCA-associated vasculitides." Autoimmunity reviews 16, no. 11 (2017): 1138-1146.
- Gioffredi, Andrea, Federica Maritati, Elena Oliva, and Carlo Buzio. "Eosinophilic granulomatosis with polyangiitis: an overview." *Frontiers in immunology* 5 (2014): 549.
- Groh, Matthieu, Christian Pagnoux, Chiara Baldini, Elisabeth Bel, Paolo Bottero, Vincent Cottin, Klaus Dalhoff et al. "Eosinophilic granulomatosis with polyangiitis (Churg–Strauss)(EGPA) Consensus Task Force recommendations for evaluation and management." *European journal of internal medicine* 26, no. 7 (2015): 545-553.
- Hayami, Chisako, Naoko Ishiguro, Yasuko Fukuya, Yoshiki Tokura, and Makoto Kawashima. "Churg-Strauss syndrome presenting with severe cutaneous and intestinal ulcers." *European Journal of Dermatology* 22, no. 3 (2012): 397-399.
- Hoffman, Mark D. "Pyoderma gangrenosum associated with c-ANCA (h-lamp-2)." *International journal of dermatology* 40, no. 2 (2001): 135-137.
- Marques, Camila Carneiro, Elizabeth Leocadia Fernandes, Gabriela Momente Miquelin, and Mariana Morais Tavares Colferai. "Cutaneous manifestations of Churg-Strauss syndrome: key to diagnosis." *Anais brasileiros de dermatologia* 92, no. 5 (2017): 56-58.

Chicago Dermatological Society **Case #6**

[1]Mathew Joseph MD, [2]Jodi Speiser MD, and [1]Kristin Lee MD
[1]Division of Dermatology, Loyola University Medical Center
[2]Department of Pathology, Loyola University Medical Center

UNKNOWN

Chicago Dermatological Society **Case #7**

[1]Maureen Riegert MD, [1]Laryn Steadman MD, [1]Brooke Vasicek MD, [1]Wendy Kim DO, [2]Jodi Speiser MD, and [1]Eden Lake MD
[1]Division of Dermatology, Loyola University Medical Center
[2]Department of Pathology, Loyola University Medical Center

HISTORY OF PRESENT ILLNESS

A 20-year-old male presented to the emergency department with fever, persistent productive cough for 1.5 weeks, decreased appetite, and conjunctival injection. Two days later, he developed typical and atypical, edematous targetoid lesions on the arms and legs and violaceous patches with serous and hemorrhagic crust on the periorbital skin. The external eyelids, mouth, extremities, and urethra demonstrated erosions and red papules with central bullae. He denied previous cold sores, genital ulcers, or new medications. He did, however, report history of a similar rash that previously required hospitalization.

PAST MEDICAL HISTORY

Stevens-Johnson syndrome (SJS)

MEDICATIONS

Clarithromycin

ALLERGIES

Amoxicillin-Clavulanate, cephalosporins, ibuprofen, penicillin G

FAMILY HISTORY

No pertinent family history

SOCIAL HISTORY

Social alcohol use, denies smoking or illicit drugs

PHYSICAL EXAMINATION

The patient was intubated and sedated. The eyelids, eyes, mouth, and urethra initially had erosions and red annular papules with bullae centrally. Similar lesions were present on his extremities, though these were more nummular, pink, and homogenous.

DERMATOPATHOLOGY

Histologic sections from a punch biopsy showed an interface dermatitis with apoptotic keratinocytes and adjacent subepidermal bullae.

ADDITIONAL STUDIES

Pertinent positives: A complete blood count demonstrated an elevated white blood count at 12 (3.5 - 10.5 K/µL), *Mycoplasma pneumoniae* IgG, respiratory polymerase chain reaction (PCR) was positive for adenovirus, respiratory tracheal aspirate grew methicillin-resistant *Staphylococcus aureus* (MRSA).

Pertinent negatives: Blood cultures had no growth, herpes simplex virus (HSV) 1&2 DNA PCR penile swabs, HSV 1&2 DNA PCR blood, HSV 1&2 IgG, cytomegalovirus PCR, *M. pneumoniae* IgM, Monospot, human immunodeficiency virus, syphilis screening, *Neisseria gonorrhoeae*, and *Chlamydia trachomatis*.

DIAGNOSIS

Recurrent erythema multiforme major (EMM)

TREATMENT AND COURSE

The patient was started on IV acyclovir 400 mg q8 hours for empiric treatment of HSV and intravenous immunoglobulin 60g daily for three days for treatment of presumed SJS by the primary team. He was also started on triamcinolone 0.1% ointment to symptomatic lesions. His present hospital course was complicated by secondary MRSA pneumonia, which was treated with vancomycin and ultimately required 28 days of hospitalization and tracheostomy. Ophthalmology, infectious disease, otolaryngology, and gastroenterology were consulted during his hospital course. He was discharged without permanent sequelae. From the patient's history, as dermatology was not consulted on previous episodes, the similar presentation was likely EMM in the past as well. Lab testing during that encounter demonstrated a respiratory panel positive for influenza B, and negative labs for HSV 1&2 and *M. pneumoniae* IgM antibodies.

Although HSV was not a causative agent in the patient's episodes of EMM, we recommended long-term prophylactic antiviral therapy with valacyclovir 500 mg daily given the recurrent nature of his EMM and the severe complications of the most recent admission as well as the variable causative etiologies.

DISCUSSION

Once thought to exist on a spectrum with SJS, erythema multiforme (EM) is now largely considered a distinct entity. Erythema multiforme is due to an underlying infectious cause, most notably HSV, in greater than 90% of cases. Stevens-Johnson syndrome, however, is most commonly a reaction to a medication. Recurrent EM has been reported in association with HSV, *M. pneumoniae*, hepatitis C infection, menstruation, malignancy, sarcoidosis, inflammatory bowel disease, radiation, and drugs, amongst other causes.

Studies investigating the pathogenesis of EM have primarily focused on herpes-associated EM (HAEM). It is thought that HSV DNA is transported from keratinocytes by peripheral blood mononuclear cells which initiate an inflammatory response with recruitment of CD4+ Th1 cells. The generated IFN-γ leads to amplification of the inflammatory response. The mechanism of autoimmune cross-reactivity in HAEM has been suggested as shared peptide sequences between oral mucosa and HSV. Genetic susceptibility has also been proposed to underlie HAEM, with the HLA-DQB1 allele identified in patients with a susceptibility to EM. Additionally, dysregulation of the Janus kinase-signal transducer and activator of transcription (JAK-STAT) signaling contributed to recurrence of EM in one reported patient. This suggests that dysregulation of inflammatory signaling could contribute to EM pathogenesis independent of HSV infection.

Erythema multiforme is a self-limited eruption of targetoid lesions in an acrofacial distribution which mostly affects young adults, with a male predominance noted in the pediatric population. Erythema multiforme major is distinguished by its severe mucosal involvement and frequent prodromal symptoms such as fever and arthralgia. Cutaneous involvement in EM typically manifests as targetoid lesions, characterized by three distinct zones of color: central duskiness with or without a blister, a surrounding ring of edema, and an erythematous zone at the periphery. Atypical lesions with two or fewer indistinct zones of color may also be present, and evolution of lesions is common. Oral mucosal involvement is seen in two-thirds of patients, with a smaller percentage experiencing ocular or genital involvement. Our patient had extensive mucocutaneous lesions with primarily atypical targetoid lesions as well as typical targetoid lesions on the lower extremities.

The main differential diagnoses for EM are SJS and *Mycoplasma pneumoniae*-induced rash and mucositis (MIRM). Stevens-Johnson syndrome is classified on a spectrum with toxic epidermal necrolysis (TEN); they are distinguished by the percentage of the patient's body surface area with epidermal detachment. Stevens-Johnson syndrome/toxic epidermal necrolysis has a "flu-like" prodrome with ocular, oral, and/or genital involvement typically occurring 4-28 days after ingestion of a drug. In our patient, new medications were excluded as a potential trigger. *Mycoplasma pneumoniae*-induced rash and mucositis was previously classified as a subset of the EM spectrum of disease but can be distinguished by the presence of *M. pneumoniae* IgM antibodies or the growth of *M. pneumoniae* in oropharyngeal or bullae cultures or PCR positivity. Our patient had negative *M. pneumoniae* IgM and negative *M. pneumoniae* respiratory viral PCR during both episodes of EMM.

Antiviral therapy has been studied as a suppressive treatment in recurrent EM with moderate success, even in patients without clinical evidence of HSV. Despite lacking

adequate randomized controlled drug trials for patients with recurrent EM without HSV, suppressive antiviral therapy is still recommended. We recommended it for our patient after discussing the relatively low side effect profile of antiviral medications and the potential sequelae of another recurrence of EMM. Corticosteroids can be considered in the treatment of an acute episode. However, patients may worsen with withdrawal. Due our patient's respiratory infection, steroids were not considered. Other reported treatments for recurrent EM include dapsone, thalidomide, lenalidomide, levamisole, and tofacitinib, amongst others. The establishment of treatment guidelines for recurrent EM due to non-HSV viral triggers is necessary to improve outcomes for patients with recurrent EM. Further randomized controlled trials are required to create an appropriate treatment algorithm.

REFERENCES

- Aurelian L, Ono F, Burnett J. Herpes simplex virus (HSV)-associated erythema multiforme (HAEM): a viral disease with an autoimmune component. Dermatol Online J. 2003;9:1.
- Canavan T, Mathes EF, Frieden I, Shinkai K. *Mycoplasma pneumoniae*-induced rash and mucositis as a syndrome distinct from Stevens-Johnson syndrome and erythema multiforme: A systematic review. J Am Acad Dermatol. 2015;72:239-245.
- Damsky W, King BA. Idiopathic erythema multiforme: Evidence of underlying Janus kinase-signal transducer and activator transcription activation and successful treatment with tofacitinib. JAAD Case Reports. 2016;2:502-4.
- Dodiuk-Gad RP, Chung WH, Valeyrie-Allanore L, Shear NH. Stevens-Johnson Syndrome and Toxic Epidermal Necrolysis: An Update. Am J Clin Dermatol. 2015;16:475-93.
- Drahy F, Ingen-Housz-Oro S, Grootenboer-Mignot S, Wolkenstein P, Chosidow O. Lenalidomide as an Alternative to Thalidomide for Treatment of Recurrent Erythema Multiforme. JAMA Dermatology. 2018;154:487-9.
- Heinze, A., Tollefson, M., Holland, K. E., & Chiu, Y. E. (2017). Characteristics of pediatric recurrent erythema multiforme. *Pediatric Dermatology, 35*(1), 97-103.
- Hozenecker W, Prins C, French LE. Erythema Multiforme, Stevens-Johnson Syndrome, and Toxic Epidermal Necrolysis. In: Bolognia JL, Schafer JV, Cerroni L. Dermatology, 4th edition. Philadelphia, PA: Elsevier Limited; 332-347.e2.
- Khalil I, Lepage V, Douay C, et al. HLA DQB1*0301 Allele is Involved in the Susceptibility to Erythema Multiforme. Journal of Investigative Dermatology. 1991;97:697-700.
- Levin J, Hofstra T. Recurrent Erythema Multiforme. JAMA. 2014;312:426-427.
- Liu RF, Chen CB, Hui RCY, Kuan YZ, Chung WH. The effect of levamisole in the treatment of recalcitrant recurrent erythema multiforme major: An observational study. Journal of Dermatological Science. 2018;92:38-44.
- Lucchese A. From HSV infection to erythema multiforme through autoimmune crossreactivity. Autoimmunity Reviews. 2018;17:576-81.

- Oak ASW, Seminario-Vidal L, Sami N. Treatment of antiviral-resistant recurrent erythema multiforme with dapsone. Dermatologic Therapy. 2017;30:e12449.
- Sokumbi O, Wetter DA. Clinical features, diagnosis, and treatment of erythema multiforme: A review for the practicing dermatologist. International Journal of Dermatology. 2012;51:889-902.
- Tatnall FM, Schofield JK, Leigh IM. A double-blind, placebo-controlled trial of continuous acyclovir therapy in recurrent erythema multiforme. British Journal of Dermatology. 1995;132:267-270.
- Wetter DA, Davis MDP. Recurrent erythema multiforme: Clinical characteristics, etiologic associations, and treatment in a series of 48 patients at Mayo Clinic, 2000 to 2007. J Am Acad Dermatol. 2010;62:45-53.

Chicago Dermatological Society **Case #8**

[1]Lauren Moy MD and [2]Wendy Kim DO
[1]Division of Dermatology, Loyola University Medical Center

HISTORY OF PRESENT ILLNESS

An 11-year-old Caucasian boy presented to dermatology clinic accompanied by his mother with the chief complaint of "alopecia." Mom stated that the patient had the condition for about 6-8 years. Mom said that when the patient was in kindergarten, parents noticed a small lighter patch of hair that fell out and left a bald patch. The patient was evaluated by multiple dermatologists and had a biopsy in 2016. Treatments tried were topical minoxidil, topical corticosteroids, topical calcineurin inhibitors, and intralesional steroid injections with no improvement. The patient was otherwise healthy and denied any fevers, chills, headaches, nausea, vomiting, recent illnesses, or any other symptoms.

PAST MEDICAL HISTORY

Born full term vaginally with no complications
Petit mal seizures with abnormal EEG and normal MRI findings
History of Erythema Minor at 18 months old from amoxicillin

MEDICATIONS

None

ALLERGIES

Amoxicillin

FAMILY HISTORY

Maternal uncle with juvenile arthritis, Mom reported "staring spells" that ran in the family

SOCIAL HISTORY

Lived at home with both parents and a sibling

PHYSICAL EXAMINATION

The patient was well-appearing. Faint linear hair loss at lateral edge of left eyebrow and left lateral lash line with no inflammation or scarring noted. Left vertex scalp with a well demarcated alopecic plaque with sparse thin hairs in the center and a mild depression from biopsy site. Mild linear depression seen on superior aspect of left forehead going back into the hairline.

DERMATOPATHOLOGY

Histologic sections from the initial punch biopsy by an outside facility of the left scalp in 2016 showed decreased number of terminal anagen hair follicles and sebaceous glands with a lymphocytic infiltrate around a terminal anagen hair bulb. Focal perivascular lymphohistiocytic inflammation was present and PAS stains showed focal Pityrosporum yeast forms in follicular ostia. Movat stains showed retained elastic fibers without evidence of scarring and no significant increased dermal mucin.

ADDITIONAL STUDIES

Complete blood count, complete metabolic panel, and thyroid function tests were within normal limits

DIAGNOSIS

Linear morphea or En coup de sabre (ECDS)

TREATMENT AND COURSE

Our patient saw an outside hospital pediatric rheumatologist to establish care and has been started on prednisone 40mg taper (stopped 7/12/2019) and methotrexate 20mg weekly. A recent magnetic resonance imaging (MRI) of brain was normal. The patient is currently being followed by pediatric dermatology, rheumatology, neurology, and ophthalmology.

DISCUSSION

The differential diagnosis for ECDS includes steroid atrophy, alopecia areata, Parry Romberg Syndrome (PRS)/progressive hemifacial atrophy, lupus profundus, and focal dermal hypoplasia. En coup de sabre is a variant of linear morphea that presents with a unilateral, sclerotic plaque with variable localized atrophy on the paramedian forehead and/or frontal scalp. It is associated with neurological findings in 18% to 47% of cases which includes complex partial seizures, hemiparesis and muscle weakness, personality changes, intellectual deterioration, and headaches. Magnetic resonance imaging abnormalities have been found in 85% to 90% of patients even in the absence of clinical neurologic symptoms. Currently, there are no standardized radiologic screening guidelines.

The pathogenesis is unclear but is thought to be due to genetic, environmental, immune mediated alterations, or injury to local vasculature. The diagnosis is usually made on the basis of clinical and histopathological findings. Serum autoantibodies are not sensitive or specific to morphea, but ANA titer is positive in most children with frequent positive dsDNA. Histologic findings vary depending on the stage of disease and depth of the biopsy. Classically, histopathology findings include collagen deposition in the dermis and subcutis, vascular and adnexal structure changes and inflammatory infiltrated. Pierre-Louis et al determined that unique atrophic follicular remnants indicated an end-stage process or permanent alopecia. In the past these findings were reported in chemotherapy-induced permanent alopecia but not in alopecia secondary to morphea or other cicatricial alopecias.

At present, there is no current standardized treatment for ECDS. Possible medical treatments include topical corticosteroids, intralesional steroid injections, oral corticosteroids, methotrexate, hydroxychloroquine, excimer laser, phototherapy, and mycophenolate mofetil. Cosmetic treatments include neurotoxin injections, polymethylmethacrylate or hyaluronic acid fillers, surgical grafting, and fat transfer. Pequet et al retrospectively reviewed 114 patients with onset of morphea prior to 18 years of age. The authors concluded that the linear morphea variant and onset at 10 years or younger were at higher risk of developing extracutaneous involvement. In contrast, Zulian et al looked at 750 children with morphea and found no difference in the

mean age of onset and extracutaneous involvement. A possible discrepancy between these studies could be that Zulian's study had a broader definition of extracutaneous manifestations, including autoimmune diseases such as diabetes mellitus and thyroid disease, and may have captured rare overlap syndromes including cardiac, renal, and respiratory involvement, which are rarely seen in morphea.

There have been three similar pediatric cases reported in Milwaukee, WI from the departments of pediatric dermatology and rheumatology. The authors noted that the patients with ECDS presented with neurologic abnormalities before or concurrently with the diagnosis of skin disease and that complex partial seizures were most frequent neurologic condition reported. Because of the morbidity associated with joint and neurologic complications, the authors recommended early intervention with systemic therapies. The largest study to date on long-term expectations was conducted by Condie et al. Their cross-sectional study showed that pediatric onset of ECDS had similar levels of cutaneous severity as adult onset. However, pediatric onset had increased levels of extracutaneous damage and a trend toward more functional impairment. The authors concluded that that pediatric onset linear morphea patients can experience active disease that persists into adulthood and should have regular follow up with dermatology, rheumatology, and neurology.

REFERENCES

- Condie D, Grabell, Jacobe H. Comparison of Outcomes in Adults with Pediatric-Onset Morphea and Those With Adult-Onset Morphea: A Cross-Sectional Study From the Morphea in Adults and Children Cohort. Ped Rheum. 6;12 Dec 2014. 3496-3504.
- Pequet MS, Holland KE, Zhao S, et. al. Risk Factors for Morphoea Disease Severity: A Retrospective Review of 114 Paediatric Patients. Br J Dermatol. 2014 Apr; 170(4):895-900.
- Franco JP, Serra MS, Lima RB, et al. Scleroderma en coup de sabre treated with polymethylmethacrylate – Case Report. An Bras Dermatol. 2016 Apr;91(2):209-11.
- Rimoin L, Arbiser J. Improvement of "En Coupe de Sabre" Morphea and Associated Headaches with Botulinum Toxin Injections. Dermatol Surg. 2016 Oct; 42(10):1216-9.
- Thareja SK, Sadhwani D, Fenske A. En coup de sabre morphea treated with hyaluronic acid filler. Report of a case and review of the literature. Int J Dermatol. 2015 Jul; 54(7):823-6.
- Polcari I, Moon A, Mathes E, et. al. Headaches as a Presenting Symptom of Linear Morphea en Coup de Sabre. Ped. 134(6) Dec 2014.
- Tolkachjov SN, Patel NG, Tollefson MM. Progressive hemifacial atrophy: a review.*Orphanet J Rare Dis. 2015 Apr 1; 10:39.*
- Khamaganova I. Progressive Hemifacial Atrophy and Linear Scleroderma En Coup de Sabre: A Spectrum of the Same Disease? Front Med (Lausanne) 2017; 4:258.
- Pierre-Louis M, Sperling L, Wilke M, et al. Distinctive histopathologic findings in linear morphea *(en coup de sabre)* alopecia. J of Cutaneous Path. 2013 June;40(6):580-584.
- Holland K, Steffes B, Nocton J, et al. Linear Scleroderma en coup de sabre With Associated Neurologic Abnormalities. Pediatrics. 2006 January;117:1.

Chicago Dermatological Society **Case #9**

[1]Michael Knabel MD, [1]Brooke Vasicek MD, [2]Kumaran Mudaliar MD, and [1]Eden Lake MD

[1]Division of Dermatology, Loyola University Medical Center

[2]Department of Pathology, Loyola University Medical Center

HISTORY OF PRESENT ILLNESS

A 43-year-old male presented with an enlarging growth on his right hand for 16 months. The lesion began as a pustule that progressively increased in size. The lesion was initially asymptomatic; however, the patient began to have pain in the area several weeks prior to presentation. He was evaluated by hand surgery due to concern for osteomyelitis. Hand surgery team sent him to dermatology for suspicion of pyoderma gangrenosum. He was previously treated with topical as well as oral antibiotics without improvement. The only previous diagnostic studies per the patient were superficial bacterial swabs for culture. Additionally, the patient reported daily wound care with hydrogen peroxide and baking soda followed by application of silver sulfadiazine cream. He denied pruritus, bleeding or drainage, fevers, chills, weight loss, fatigue, trauma to the area, recent travel or pets at home. The patient worked in construction and was at a job site in a dirty canal when the lesion was first noted.

PAST MEDICAL HISTORY

No past medical history

MEDICATIONS

No medications

ALLERGIES

No known drug allergies

FAMILY HISTORY

No pertinent family history

SOCIAL HISTORY

Patient was an every day smoker, endorsed social alcohol and denied illicit drug use. He worked in construction.

PHYSICAL EXAMINATION

The patient was well-appearing. On the right dorsal hand there was a 10.5 x 7 cm erythematous, friable plaque with areas of pink sclerotic papules. The medial aspect of the wound had a violaceous boarder with peripheral erythema extending to the proximal 3th and 4rd digits.

On the right 5th digit there was an erythematous indurated plaque and limited flexion of the distal interphalangeal, proximal interphalangeal, and metacarpophalangeal joints.

DERMATOPATHOLOGY

Punch biopsy showed pseudoepitheliomatous hyperplasia, acute and chronic inflammation with small abscess formation.
There were scattered fungal organisms with broad based budding yeast on Grocott methenamine silver stain.

ADDITIONAL STUDIES

Fungal culture was positive for *Blastomyces dermatitidis*. DNA probe assay and fungal smear identified moderate budding yeast. Complete blood count with differential, complete metabolic panel, hepatitis B, human immunodeficiency virus (HIV), Gram stain and culture, acid fast bacilli stain and culture were unremarkable.

DIAGNOSIS

Primary cutaneous blastomycosis

TREATMENT AND COURSE

The patient was referred to Infectious Disease (ID) for management and started on itraconazole 200mg three times daily (TID) for 3 days, followed by 200mg twice daily (BID) for 12 months of therapy. He follows with ID for routine complete blood count, complete metabolic panel, and itraconazole serum level. Liver functions test are monitored monthly. At last follow up the patient reported significantly improved range of motion in the 5^{th} digit of the right hand.

DISCUSSION

Blastomyces is a thermally dimorphic fungus existing as a filamentous mold in the environment and when above 35^0 C in tissue, broad-based budding yeast with double retractile cell wall unique among dimorphic fungi. The Blastomyces family is made up of *B. dermatitidis and B. gilchristii*, which are endemic to the Mississippi and Ohio River valleys of the Midwest and Great Lakes adjacent to the Saint Lawrence Seaway. Infection occurs through aerosolization of conidia after disruption of soil and decaying wood or direct inoculation of tissue following trauma; as a result, those with occupational or recreational exposure have a higher risk for infection. Conidia are phagocytized by macrophages and converted to yeast allowing for evasion of host immune defenses through the inhibition of cytokine production, suppression of nitric oxide production, and impairment of CD4+ T cell activation.

Termed “the great pretender” blastomycosis mimics malignancy, inflammatory dermatoses and other infectious processes that often contribute to a delay in diagnosis. Most patients present with primary pulmonary disease, ranging from mild pneumonia to acute respiratory distress syndrome. Approximately 25-40% of infected patients exhibit extra-pulmonary manifestations mostly commonly involving the skin, bone, and genitourinary tract. Cutaneous disease typically presents as papulopustular lesions progressing to irregular, verrucous and ulcerative plaques.

Although blastomycosis is not an opportunistic agent, iatrogenic immunosuppression in solid organ transplant patients, HIV with CD4 counts less than 200 cells/mm^3, and diabetes predispose patients to more severe disease and disseminated infection.

Additionally, increased use of TNF-alpha inhibitors presents a risk for severe infection.

Definitive diagnosis is made by fungal culture, although DNA probe assay can rapidly identify blastomycosis to aid in diagnosis. Microscopic evaluation can also expedite diagnosis and initial of therapy; neutrophilic infiltration with non-caseating granulomas is suggestive. Yeast is visualized with periodic acid-Schiff, methenamine silver, 10% KOH or calcofluor white stains.

Guidelines set forth by the Infectious Disease Society of America state all infected patients should receive antifungal therapy regardless of clinical severity due to likelihood of progression and/or recurrence. For mild to moderate disease oral itraconazole is first-line therapy. Treatment regimen includes a loading dose of 200mg TID for 3 days followed by 200mg BID for 12 months. Other azole agents may be used if itraconazole is not tolerated. Moderately severe to severe blastomycosis, as well as disease in immunocompromised and organ transplant patients, should be treated with a lipid formulation of amphotericin B at 3 to 5 mg/kg/d until noted clinical improvement with step-down to oral itraconazole for 12 months duration. Amphotericin remains the drug of choice for treatment in pregnancy as -azoles are teratogenic,

REFERENCES

- Baumgardner DJ, Buggy BP, Mattson BJ, et al. Epidemiology of blastomycosis in a region of high endemicity in north central Wisconsin. *Clin Infect Dis* 1992; 15:629-35.
- Castillo CG, Kauffman CA, Miceli MH. Blastomycosis. *Infect Dis Clin North Am*. 2016 Mar; 30(1):247-64.
- Chapman SW, Dismukes WI, Proia LA, et al. Infectious Disease Society of America. Clinical practice guidelines for the management of blastomycosis: 2008 updated by the Infectious Disease Society of America. *Clin Infect Dis*. 2008; 46(12): 1801-1811.
- Fang W, Washington L, Kumar N. Imaging manifestations of blastomycosis: a pulmonary infection with potential dissemination. *Radiographics*. 2007; 27(3):541-655.
- Goico A, Henao J, Tejada K. Disseminated blastomycosis in a 36-year-old immunocompetent male from Chicago, IL. *Oxf Med Case Reports*. 2018 Sep 24;2018(10).
- Krumpelbeck E, Tang J, Ellis MW, Georgescu C. Disseminated blastomycosis with cutaneous lesions mimicking tuberculosis. *Lancet Infect Dis*. 2018 Dec; 18(12):1410.
- Lemos LB, Baliga M, Guo M. Blastomycosis: the great pretender can also be an opportunist. initial clinical diagnosis and underlying diseases in 123 patients. *Ann Diagn Pathol*. 2002;6:194-203.
- McBride JA, Gauthier GM, Klein BS. Clinical Manifestations and Treatment of Blastomycosis. *Clin Chest Med*. 2017 Sep;38(3):435-449.
- Pappas PG, Pottage JC, Powderly WG, et al. Blastomycosis in patients with the acquired immunodeficiency syndrom. *Ann Int Med* 1992; 116:847-53.
- Saccente M, Woods GL. Clinical and laboratory update on blastomycosis. *Clin Microbiol Rev*. 2010; 23(2):367-381.
- Smith JA, Kauffman CA. Endemic fungal infections in patients receiving tumor necrosis factor-alpha inhibitor therapy. *Drugs* 2009;69: 1403-15.
- Smith JA, Riddell J IV, Kauffman CA. Cutanerous manifestations of endemic mycosis. *Curr Infect Dis Rep*. 2013; 15(5):440-449.

Chicago Dermatological Society **Case #10**

[1]David Surprenant MD, [1]Jeave Reserva MD, [1]Rebecca Tung MD, and [1]David Eilers MD
[1]Division of Dermatology, Loyola University Medical Center

Patient 1:

HISTORY OF PRESENT ILLNESS

A 36-year-old female with an enlarging right parotid mass was referred preoperatively for removal of a lumbar transdermal piercing prior to planned right parotidectomy. The patient had two lumbar transdermal piercings placed on her lower back approximately ten years prior. Only one piercing remained as the other had fallen out inadvertently several years prior. The surgical team felt the remaining transdermal piercing represented a potential hazard to the patient and requested removal by dermatology prior to proceeding with parotidectomy.

PAST MEDICAL HISTORY

Recently identified and enlarging parotid mass requiring surgical removal

PHYSICAL EXAMINATION

On the right lumbar back there was a 0.5 cm circular metal frame containing a pink crystal jewel.

DIAGNOSIS

Intradermal piercing

TREATMENT AND COURSE

The transdermal piercing was removed via wide local excision utilizing local anesthesia without incident.

Patient 2:

HISTORY OF PRESENT ILLNESS

A 61-year-old male with multiple sclerosis presented as a consultation to dermatology clinic for shrapnel removal. The patient was wheelchair-bound due to progressive multiple sclerosis, and the neurology service required magnetic resonance imaging (MRI) of the brain for diagnostic purposes. An MRI of the brain several years prior was significantly degraded by a large amount of magnetic susceptibility artifact from suspected metal shrapnel in the left frontal scalp. During a repeat MRI attempt, the ferromagnetic shrapnel began to visibly move beneath the skin, and the scan attempt was terminated. The patient had no recollection of injury or exposure to shrapnel in the military or otherwise. The patient was not able to pinpoint the specific location of the shrapnel. The supposed piece of shrapnel required removal prior to further MRI attempts.

PAST MEDICAL HISTORY
Progressive multiple sclerosis requiring MRI imaging for diagnostic and therapeutic planning purposes.

PHYSICAL EXAMINATION
The cutaneous exam was unremarkable. There was no identifiable scar or skin surface change in the area of concern. Extensive and thorough palpation failed to identify any foreign subcutaneous object or mass.

ADDITIONAL STUDIES
A plain radiograph of the head did not identify any foreign objects. Computerized tomography (CT) scan imaging of the head revealed a 5 mm metallic foreign body in the left frontal scalp.

DIAGNOSIS
Metallic ferromagnetic foreign body

TREATMENT AND COURSE
The foreign body was not identifiable with inspection or palpation. The CT scan images were utilized to triangulate the suspected location of the foreign object using bony and surface anatomy landmarks. An implantable cardioverter defibrillator (ICD) detection donut magnet (Medtronic, 90 Gauss) was then placed in the suspected area, resulting in levitation of the foreign body and clear identification of its location. With the magnet overlying the identified object, the skin was marked with a surgical marker. The area was then numbed with local anesthetic (1% lidocaine) and the lesion was excised without incident.

DISCUSSION
The removal of foreign bodies in the dermis and subcutaneous tissue is occasionally necessary. Dermatologists are the specialists of choice for execution of these procedures.

The first case presented was referred to dermatology for removal of a transdermal piercing, with concern it may represent a surgical hazard. Referred to as dermal piercings, transdermal implants, microdermal implants, dermal anchors, single-point piercings, and skin divers—this type of body piercing consists of an L-shaped footplate and post that is implanted approximately 2.5 mm under the skin. The individual may then select a decorative jewel to screw into the post protruding from the skin.

Dermal piercings carry several risks including infection, metal sensitivity reactions, delayed wound healing, and hemorrhage. Further, they represent a potential barrier to future diagnostic and therapeutic medical interventions. While many piercings are made from surgical grade titanium, lower quality piercings may be made of ferromagnetic surgical steel—a particular problem for MRI imaging. Surgically, transdermal piercings represent a nidus for infection, a potential source of pressure injury, and a possible burn risk with the use of electrosurgery. Burn risk with electrosurgery is highest when the

dispersive electrode is within 10 mm of a piercing and when a piercing is located between active and dispersive electrodes.

Dermal piercings are considered permanent and are not easily removed. While these piercings can occasionally be removed with a manual rocking motion, surgical excision is often required, particularly as longstanding piercings tend to become embedded in the surrounding tissue. In the presented case, excisional removal with narrow (3 mm) margins was utilized for removal. It is important for the modern-day dermatologist to be aware of the practice of transdermal piercings, the associated clinical risks, as well as indications and techniques for removal.

The second case presented represents a challenge in identifying small foreign bodies embedded in the dermis and subcutaneous tissue. Such implanted foreign bodies are particularly problematic with MRI imaging. All metal objects scatter MRI magnetic fields, creating image artifact that often impedes accurate image interpretation. Additionally, implanted ferromagnetic material poses a burn risk via radiofrequency-induced thermal heating as well as projectile injury risk secondary to movement induced by the magnetic field.

Localization of embedded metallic foreign bodies can be difficult, particularly when small in size and in the absence of visible scarring. In some cases, patients lack recollection of any prior injuries or accidents. Adjuvant imaging modalities can prove useful in identifying the location of hard-to-identify foreign bodies. Metallic objects are easily identifiable on CT scan imaging. With a knowledge of internal and surface anatomy, CT scan imaging may be utilized to approximate the location of very small metallic objects. Once an area of interest is better approximated, a magnet can assist in precise localization of ferromagnetic objects. Found in many health clinics, implantable cardioverter-defibrillator (ICD) detection donut magnets are utilized to interrogate pacemakers/ICDs or inhibit the delivery of shock therapy from a device. Placement of an ICD detection magnet over a suspected location of interest can induce slight movement in ferromagnetic foreign objects, thus allowing for precise localization.

In conclusion, an understanding of transdermal piercings as well as their potential risks and removal techniques is essential for the modern dermatologist. With a strong understanding and appreciation of anatomy, basic radiological knowledge, and some ingenuity, dermatologists are capable of identifying small ferromagnetic foreign bodies and ensuring their safe removal. As the leading experts in the diagnosis and treatment of all conditions skin-related, dermatologists are best served to assist patients with the many issues associated with cutaneous and subcutaneous foreign bodies.

REFERENCES

- Beers M, Meires J, Loriz L. Body piercing: coming to a patient near you. *The Nurse Practitioner Journal.* 2007;32:55-60.
- Deml M, Goost H, Schyma C, Kabir K, Hoppe S, Deborre C. Thermic effect on metal body piercing by electrosurgery: An ex vivo study on pig skin and bovine liver. *Technology and Health Care.* 2018;26:239-247.

- Govers D. What happens if it won't come out? Caring for patients with sub-dermal, trans-dermal, or micro-dermal piercings & implants in the operating room. *The Dissector*. 2016;44:27-30.
- Kim YH, Choi M, Kim JW. Are titanium implants actually safe for magnetic resonance imaging examinations? *Archives of Plastic Surgery*. 2019;46:96-97.
- Parkins G, Porter M. Dermal piercings: unregulated high street surgery? *British Journal of Dermatology*. 2014;171:1236-1276.
- Smith F. Caring for surgical patients with piercings. *Association of Perioperative Registered Nurses Journal*. 2016;103:584-593.
- Taheri A, Mansoori P, Sandoval LF, Feldman SR, Pearce D & Williford PM. Electrosurgery: part I. Basics and principles. *Journal of the American Academy of Dermatology*. 2014;70(4):591-e1.
- Taheri A, Mansoori P, Sandoval LF, Feldman SR, Pearce D & Williford PM. Electrosurgery: part II. Technology, applications, and safety of electrosurgical devices. *Journal of the American Academy of Dermatology.* 2014;70(4):607-e1.
- Wanzer L, Hicks R. Identifying and minimizing risks for patients with dermal implants. *Association of Perioperative Registered Nurses Journal*. 2012;96:C5-C6.
- Winn A, Rivard S, Gratrix M. Dermal piercing removal: searching for an optimal technique. *Dermatologic Surgery*. 2017;43:1507-1508.