Chicago Dermatological Society

November 2020
Monthly Educational Conference

Program Information
CME Certification
and
Case Presentations

Wednesday, November 11, 2020
Online via Zoom

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

Program

Host: University of Illinois at Chicago
Wednesday, October 14, 2020
Online Conference

8:30 a.m.	**Sign-in and Member Visitation Time**
9:00 a.m.	**Welcome & Introduction** *David Mann, MD - CDS President*
9:05 a.m. - 9:40 a.m.	**Guest Lecture #1** "Sometimes stepping back is better than a closer look" This examines the need for the "low power" clinical exam to appreciate patterns *Jean Bolognia, MD*
9:40 a.m. - 9:50 a.m.	**Questions & Answers**
9:50 a.m. - 10:35 a.m.	**Resident Case Presentations & Discussion** *Northwestern Residents*
10:35 a.m. - 10:50 a.m.	**Guest Lecture #2** "Re-examining the guidelines for treatment of cutaneous side effects due to immune checkpoint-blocking antibodies" *Jean Bolognia, MD*
10:50 a.m. - 11:00 a.m.	**Questions & Answers**
11:00 a.m.	**Closing Remarks and Introduction of Discussion Breakout Rooms** *David Mann, MD*
11:00 a.m. - 12:00 p.m.	**Breakout Rooms*** • Medical Students • Case Discussions • Practice Challenges • Residents Forum
12:00 p.m.	**Meeting adjourns**

* Four breakout sessions will commence at the conclusion of the second guest lecture. They are scheduled for approximately one hour (ending by 12 noon) and are intended to be open discussion with a moderator to facilitate the conversation. Meeting attendees were asked to indicate their choice of breakout session when first registering for the Zoom meeting.

Mark the Date!

Next CDS virtual meeting will be on Wednesday, December 2 – Co-hosted by the University of Chicago – Watch for details on the CDS website: www.ChicagoDerm.org

Guest Speaker

JEAN BOLOGNIA, MD

Professor of Dermatology and Vice-chair for Clinical Affairs, Department of Dermatology; Yale University School of Medicine; New Haven, CT

Dr. Jean Bolognia has served as President of the Medical Dermatology Society, the Women's Dermatologic Society and the American Dermatological Association, in addition to serving as Vice-President of the Society of Investigative Dermatology, the American Board of Dermatology, and the International Society of Dermatology. She has also been elected to serve on the Board of Directors of the American Academy of Dermatology and the International League of Dermatological Societies. In the latter organization, Dr. Bolognia served as Secretary-General. She also is the senior editor of the textbook Dermatology, which is now in its fourth edition, and Dermatology Essentials.

Dr. Bolognia earned her medical degree at Yale University in 1980 where she also completed a post-doctoral fellowship and her residency training. Her research involves clinicopathologic correlations regarding various types of melanocytic nevi (moles) and melanoma, as well as the cutaneous side effects of chemotherapy. Her clinical interests are focused on melanoma; pigmentation disorders; skin diseases; and skin neoplasms.

CME Information

November 11, 2020

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. During the coronavirus pandemic, CDS has continued to organize our regular educational conferences, but in a half-day "virtual" online live setting.

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 2020/21 series of meetings, the participant should be able to:

1. Describe how a clinician can appreciate patterns when observing a patient in a broader sense and how this technique might reveal clinical findings that otherwise might not be readily apparent.
2. Discuss how immune checkpoint-blocking antibodies work to help the body attack cancer cells and list several checkpoint inhibitor drugs that are commonly used.
3. Describe the cutaneous side-effects observed with checkpoint inhibitor drugs and discuss the guidelines that a clinician can turn to when using these medications.

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 2 *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 an online CME claim form after the completion of the conference. A link to this form along with the online evaluation form will be sent to each conference attendee after 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. None of the participants in this conference have disclosed relevant potential conflicts of interest.

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

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Americans with Disabilities Act

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

Disclaimer

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

Dislosure of Unlabeled Use

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

CHICAGO DERMATOLOGICAL SOCIETY **Case 1**

Presented by **Rachel Eisenstadt**, MD, **Emily Merkel**, MD, **Pedram Yazdan**, MD
Department of Dermatology, Feinberg School of Medicine, Northwestern University

HISTORY OF PRESENT ILLNESS

A 63-year-old female presented for evaluation of an eruption over the ears, face, and arms present for 4 months via televisit in setting of the COVID-19 pandemic. Her eruption initially began in November 2019 with erythema and swelling of the bilateral ears, which was presumed to be an allergic contact dermatitis. She was treated with oral prednisone, topical steroids, and oral anti-histamines without a robust response. Biopsies were then performed for further evaluation in April 2020. Initial biopsies of arm and ear lesions demonstrated granulomatous dermatitis with negative infectious stains, thought to be most consistent with cutaneous sarcoidosis for which the patient was initiated on methotrexate and hydroxychloroquine without significant improvement. In July 2020, her cutaneous eruption progressively worsened, and development of numbness and tingling in a stocking-and-glove distribution was noted. At this time, her cutaneous biopsies were re-evaluated.

PAST MEDICAL/SURGICAL HISTORY

Coronary artery disease, hyperlipidemia, hypertension, hypothyroidism, osteoarthritis, osteoporosis

FAMILY AND SOCIAL HISTORY

No family history of rheumatologic disease. She is originally from the Gujarat region of India and moved to the United States approximately 11 years prior to presentation. Her last visit to India was over 3 years previously. She denied tobacco, alcohol, or illicit drug use.

MEDICATIONS

Alendronate, atorvastatin, diclofenac gel, diltiazem, isosorbide mononitrate, levothyroxine, metoprolol, methotrexate, hydroxychloroquine

PHYSICAL EXAM

Edematous pink plaques distorting normal architecture were noted over the lobules and inferior helices of the bilateral ears. Scattered annular pink patches and edematous plaques without scale were noted over the bilateral cheeks, dorsal forearms, and anterior leg.

LABS/IMAGING

ESR 44 mm/hour (1-20)
Normal/Negative:

- Complete blood count, basic metabolic panel
- Rheumatoid factor, anti-citric citrullinated peptide (CCP) antibody
- Hepatitis B, C serologies
- Quantiferon Gold
- Chest X-Ray

HISTOPATHOLOGY

Dermal aggregates of epithelioid histiocytes with numerous Langhans' type multinucleated giant cells and scattered lymphocytes were seen. DPAS, AFB stains were negative. Upon re-evaluation of initial biopsies in July 2020, Fite stain was performed and was notable for numerous small bacilli within granulomatous inflammation.

DIAGNOSIS

Multibacillary leprosy

TREATMENT AND COURSE

Methotrexate and hydroxychloroquine were discontinued, and the patient established care at the University of Illinois at Chicago's Regional Hansen's Disease Center for treatment of presumed multibacillary leprosy. Preliminary results from confirmatory PCR testing at the CDC demonstrated presence of *Mycobacterium leprae*. She was initiated on minocycline 100 mg PO nightly, rifampin 600 mg monthly, and dapsone 50 mg daily. Additionally, the patient was noted to have persistent arthralgias and joint swelling as well as persistent subcutaneous nodules on the anterior leg concerning for potential erythema nodosum leprosum, for which she received a prolonged oral prednisone taper.

DISCUSSION

Leprosy, or Hansen's disease, is caused by the slow-growing obligate intracellular mycobacteria *Mycobacterium leprae* and *Mycobacterium lepromatosis*. With fewer than 1 case per 10,000, the World Health Organization declared leprosy to be eliminated in 2000, but a number of new cases are still noted each year in endemic and non-endemic locations. In 2017, 210,671 cases were reported in a total of 150 countries. Endemic locations include India, Brazil, and Indonesia, which collectively represent 80.2% of reported cases. In the United States, 185 cases of leprosy were diagnosed in 2017, with Arkansas, California, Florida, Hawaii, Louisiana, and New York reporting the highest prevalence among states with a known diagnosis.

The most common mode of transmission is via respiratory droplet, though the culprit mycobacteria may also be transferred via broken skin barrier. In the Unites States, armadillos serve as a zoonotic host for *Mycobacterium leprae*. The incubation period varies from months to >30 years, with an average incubation of 4-10 years. The risk of acquisition among household contacts has been reported to be as high as 25%.

Classification of leprosy as a disease process involves identification of the patient's immunologic response to infection. The Ridley-Jopling classification system classifies individuals into either tuberculoid leprosy, borderline tuberculoid leprosy, mid-borderline leprosy, borderline lepromatous leprosy, and lepromatous leprosy based on clinical and histological features, as well as bacterial index. Tuberculoid leprosy is categorized by a robust Th1-dominant cell-mediated response with less severe disease comprised of hypo- or hyperpigmented annular plaques that may be associated with anesthesia, anhidrosis, and alopecia within the lesions themselves. Lepromatous leprosy is categorized by a Th2-dominant humoral response which clinically may present with poorly defined macules, papules, nodules, and plaques. Peripheral nerve involvement is not isolated to cutaneous lesions and may instead present as a stocking-and-glove neuropathy. Late sequelae of lepromatous leprosy include earlobe infiltration, saddle nose deformity, leonine facies, and madarosis. Given the multiple intermediary subtypes, another classification system by the WHO utilizes features bacterial index (either density of bacilli, or number of skin lesions) to classify disease as either paucibacillary (1-5 lesions) or multibacillary (>5 lesions).

Multidrug therapy (MDT) with rifampin, dapsone, and clofazimine is the standard of treatment for both paucibacillary and multibacillary disease per the WHO guidelines. Paucibacillary disease is typically treated for at least 6 months, while multibacillary disease is typically treated for at least 12 months. The National Hansen Disease Program also notes that minocycline, clarithromycin, and ofloxacin can be used as part of a multidrug therapy regimen. Treatment may be complicated by cell-mediated and humoral immune reactions to the mycobacterium. One such example is erythema nodosum leprosum, a type 2 immune mediated response leading to painful subcutaneous nodules in the setting of upregulated TNF-alpha, neutrophil, and complement activity. Erythema nodosum leprosum may be associated with worsening

peripheral neuropathy or systemic symptoms, such as fever, neuritis, orchitis, iritis, lymphadenitis, glomerulonephritis, and tibial periostitis. These presentations often necessitate the use of anti-inflammatory medications, oral corticosteroids, or thalidomide. Following MDT, relapse rates are 0.77% for multibacillary disease and 1.07% for paucibacillary disease.

KEY POINTS

1. Leprosy is caused by infection with the slow-growing obligate intracellular mycobacteria *Mycobacterium leprae* and *Mycobacterium lepromatosis.*
2. Diagnosis is confirmed with presence of acid-fast bacilli on slit-skin smear examination, positive Fite stain, or confirmation of *Mycobacterium* via PCR evaluation.
3. Leprosy may be classified by WHO criteria into pauci- or multibacillary disease by number of lesions and density of mycobacteria or by the Ridley-Jopling classification, which is based on a patient's immunologic response.
4. Multidrug therapy with rifampicin, dapsone, and clofazimine is the standard of care for treating leprosy.

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CHICAGO DERMATOLOGICAL SOCIETY **Case 2**

Presented by **Laura Walsh**, MD, **Molly Stout**, MD, **Emily Keimig**, MD
Department of Dermatology, Feinberg School of Medicine, Northwestern University

HISTORY OF PRESENT ILLNESS

A 44-year-old female presented to dermatology clinic with tender, pink-yellow papules coalescing into plaques present for two months. The eruption began on her cheeks and progressed to involve the nose, left helix, dorsal forearms, upper chest, and lower extremities. The cutaneous eruption was associated with polyuria, polydipsia, frontal headache, fatigue, and sore throat.

Over the subsequent two months after initial presentation, the cutaneous eruption spread to her arms, trunk, back, and legs. She also developed night sweats and intermittent fevers. She was started on topical triamcinolone 0.1% ointment BID for 5 days without improvement. After an initial biopsy showed granulomatous dermatitis, she was started on prednisone 40 milligrams daily for two weeks. She had improvement in her extracutaneous symptoms but not of her cutaneous eruption. As prednisone was tapered, her fevers, night sweats, fatigue and skin lesions recurred. She was started on hydroxychloroquine 200 milligrams twice daily and referred to Northwestern Dermatology for further workup and management of her refractory disease.

PAST MEDICAL AND SURGICAL HISTORY

The patient had a past medical history of hypothyroidism, anxiety, and major depressive disorder. She had a past surgical history of cholecystectomy and hysterectomy.

FAMILY AND SOCIAL HISTORY

Her maternal grandfather had acute myeloid leukemia; paternal grandmother had a history of breast cancer; paternal grandfather had a history of chronic lymphocytic leukemia; and an aunt had history of lymphoma. She had a 15 pack-year smoking history.

MEDICATIONS

Notable medications include hydroxychloroquine 200 mg daily and triamcinolone 0.1% ointment twice daily.

PHYSICAL EXAM

The patient was tired-appearing. Cutaneous examination was notable for pink-yellow papules coalescing into plaques involving the malar cheeks, nasal tip, left helix, dorsal forearms, and medial superior breasts. Discrete papules were noted on the bilateral shins and knees.

DERMATOPATHOLOGY

Biopsy of axillary and neck plaques showed deep infiltration of histiocytes extending into the subcutaneous tissue with Touton giant cells and xanthomatous changes. There were also numerous eosinophils present. Atypia was absent and Ki67 showed low proliferative activity within the biopsied area. Immunohistochemisty was notable for CD163 positivity of tumor cells; BRAF-V600E was negative.

LABS/IMAGING

PERTINENT LABS

Negative or within normal limits: CBC, CMP, ANA, T-cell rearrangement off peripheral tissue, ESR, quantitative immunoglobulins, serum free light chains, ACTH/cortisol, serum protein electrophoresis, serum osmolality, infectious workup (HCV Ab, CMV IgG, HHV-6, Lyme serologies, RPR, HIV, EBV PCR, Quantiferon Gold, urine histoplasmosis/blastomyces antigens, *Cryptococcus* Ab, *Coccidioides* Ab)

Pertinent positive studies:

- CRP 43.13 mg/L (nl 0-10.00)
- 24-hour urine protein 0.3 g/24 hours (0.01-0.15)
- Urine osmolality 86 mOsm/L (390-1090)
- Prolactin 122 ng/mL (4.79-23.3)

PERTINENT IMAGING

Whole-body Nuclear Bone Scan: mild-to-moderate increased uptake identified in the distal femoral metaphysis and in the bilateral tibias, greater in the proximal metaphyses

PET-CT: hypermetabolic activity of the pituitary, T12 of the spinal cord, multiple patchy hypermetabolic areas of the skin and musculature, hypermetabolic foci of L femoral head and R iliac bone

Chest X-Ray, Cardiac MRI: unremarkable

DIAGNOSIS

Erdheim-Chester disease (ECD)

TREATMENT AND COURSE

After skin biopsy was strongly suggestive of a non-Langerhans cell histiocytosis such as Erdheim-Chester disease, the above imaging and laboratory workup was completed and confirmed the diagnosis. The patient was then referred to hematology/oncology for malignancy evaluation given the increased incidence of myeloid neoplasms in patients with ECD. Bone marrow biopsy was negative for hematologic malignancy. She was started on cobimetinib 60 mg daily for 21 days out of 28 with good response, though her dose was reduced due to nausea, vomiting, and diarrhea. She developed an acneiform drug eruption thought to be secondary to cobimetinib, which was managed with topical steroids, topical clindamycin, and oral minocycline.

Additionally, she was referred to endocrinology given the new diagnosis of ECD with associated polyuria and polydipsia. Laboratory findings were consistent with diabetes insipidus and she was started on desmopressin (DDAVP). Pituitary MRI was completed given elevated prolactin and showed a 6 mm area of hypoenhancement in the left lateral pituitary adenohypophysis thought to be consistent with a pituitary microadenoma, which is being closely monitored.

DISCUSSION

Erdheim-Chester disease (ECD) is a rare non-Langerhans histiocytic disorder with multisystem involvement. The disorder is commonly characterized by multifocal osteosclerotic lesions of the long bones, which show sheets of foamy histiocytes on biopsy with or without histiocytic infiltration of extraskeletal tissues. 95% of patients with ECD show long bone involvement, and osteosclerosis around the knees is pathognomonic. 59% of cases have maxillary sinus, large vessel or retroperitoneal infiltration. Vascular involvement typically manifests as periarterial infiltration involving the aorta or other vessels. Retroperitoneal infiltration can be seen as wispy perinephric infiltration dubbed 'hairy kidney' or can present as adrenal infiltration. Cardiac involvement can be seen in 57% of cases, most typically of the atrioventricular groove and right atrial wall. Pulmonary and central nervous system involvement is seen in 46% and 41% of patients respectively. Pulmonary involvement is primarily pleural. Sites of the CNS most commonly involved are the dura, parenchyma, spinal cord, or nerve roots. Pituitary gland involvement, as demonstrated in our patient, is seen in 22% of cases. The most common endocrine manifestation is diabetes insipidus, which typically precedes diagnosis of ECD. Additionally, up to 10% of patients with ECD can also have an overlapping myeloid neoplasm ranging from myelodysplastic syndrome to chronic myelogenous leukemia. Lastly, cutaneous involvement is less common and is seen in 27% of patients. A recent review described skin manifestations

ranging from facial xanthelasma-like lesions, subcutaneous nodules, and granuloma annulare-like lesions.

As ECD is a myeloid progenitor cell malignancy, patients have a clonal proliferation of myeloid progenitor cells. This malignant process is usually driven by a somatic mutation in BRAF or MAPK signaling pathways. These mutations result in increased proinflammatory cytokines and chemokines that accelerate recruitment and activation of histocytes. The characteristic mutation is BRAF-V600E, which is found in CD34+ cells of up to half of affected individuals.

Overall, if a histiocytic neoplasm such as ECD is suspected, the recommended workup is full body PET-CT (vertex to toes) as well as a biopsy of lesional skin or tissue. BRAF-V600E mutational testing can be performed on tissue, and next-generation sequencing for MAP-kinase or other mutations can be considered. If ECD is confirmed, labs including CBC, CMP, LDH, and CRP; imaging including MRI Brain, Cardiac MRI, and high-resolution Chest CT; and referral to endocrinology for specialized endocrine testing should be performed.

Treatment depends on the driving mutation. If the BRAF-V600E mutation is present, targeted inhibitors for BRAF have shown efficacy. If the mutation is not present, MEK inhibitors have emerged as a viable therapeutic choice. Glucocorticoids have shown efficacy in decreasing clinical manifestations but have not shown a benefit in survival. Many other systemic agents, such as methotrexate, IL-1R antagonists, sirolimus, and infliximab, have been reported in case studies. Radiation and surgery have been used to address mechanical complications but overall have limited roles in treatment of ECD.

KEY POINTS

1. Erdheim-Chester disease (ECD) is a rare non-Langerhans histiocytic disorder that affects multiple organ systems, including the bones and skin, and is associated with an increased incidence of myeloid neoplasms.
2. The characteristic mutation associated with ECD is BRAFV600E, which is found in CD34+ cells of up to half of affected individuals.

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CHICAGO DERMATOLOGICAL SOCIETY **Case 3**

Presented by **Samantha Venkatesh**, MD, **Molly Stout**, MD, **Maria Colavincenzo**, MD, **Lida Zheng**, MD
Department of Dermatology, Feinberg School of Medicine, Northwestern University

HISTORY OF PRESENT ILLNESS

A 58-year-old female with chronic sinusitis and a remote history of systemic lupus erythematosus was admitted to the hospital from dermatology clinic with rapidly enlarging purulent cutaneous ulcerations on the scalp and lower extremities. She had a history of prior similar ulceration in 2015, starting after she developed a pustule on her L occipital scalp with purulent drainage. In August 2017, she developed painful pustules on her right temporal scalp, left occiput, and nose which all eventually ulcerated with purulent drainage. Tissue cultures were negative throughout her course. The diagnosis was presumed to be pyoderma gangrenosum, and she was started on dapsone 50 mg daily as well as topical betamethasone dipropionate 0.05% cream, silver sulfadiazine 1% cream, and chlorhexidine washes. The patient declined systemic steroids due to concern for side effects. In January 2018, the patient developed a rapidly expanding ulceration on her right calf without preceding trauma which prompted dermatology evaluation at Northwestern. The patient denied fevers, chills, oral lesions, photosensitivity, hematuria, or other systemic symptoms.

PAST MEDICAL AND SURGICAL HISTORY

The patient reported a history of hypertension, chronic sinusitis, and a remote history of systemic lupus erythematosus. Surgical history included excision of a benign breast cyst and seton placement in 2015 for purulent abscesses, nodules, and fistulas of the buttocks.

FAMILY AND SOCIAL HISTORY

The patient reported a 35-year pack history of tobacco use. She denied alcohol use. She reported cocaine use.

MEDICATIONS

Dapsone 50 mg daily, betamethasone dipropionate 0.05% cream daily, silver sulfadiazine 1% cream daily, chlorhexidine washes daily

PHYSICAL EXAMINATION

On the right temporal scalp, a 7 x 7 cm ulceration with copious yellow purulent and malodorous drainage was present. She was noted to have prominent saddle nose deformity. On the left nasal dorsum and sidewall extending to the nasal tip, there was a 1.5 cm erythematous edematous plaque with yellow crust. On the L medial buttock, three well-defined superficial 1 cm ulcerations and a single sinus tract were visualized. On the right medial calf, there was a 6 x 5 cm ulcer with violaceous and undermined borders with serous and purulent drainage.

LABS/IMAGING

PERTINENT LABS

Dermatologic Evaluation: Punch biopsy from the right shin at the edge of the ulcer demonstrated a dermal abscess with fibrinoid necrosis and inflammation of deep and superficial dermal blood vessels consistent with a necrotizing vasculitis. Special stains for microorganisms were negative. Wound culture and tissue culture were negative for bacterial and fungal organisms.

Rheumatologic Evaluation: BMP normal, WBC 23.2 (H), Hemoglobin 9.3, Platelets 641 (H), ESR 115 (H), CRP 14.0 (H), ANA negative, RF negative, CCP negative, C3 normal, C4 normal, p-ANCA <40, MPO (-), c-ANCA 1:2560 (H), PR3 38 (H), urine toxicology screen positive for cocaine.

PERTINENT IMAGING
CT Face with Contrast: Extensive bilateral sinusitis
Chest X-Ray: Few scattered bilateral linear opacities

DIAGNOSIS
Granulomatosis with polyangiitis (GPA) presenting as pyoderma gangrenosum

TREATMENT AND COURSE
For her GPA, the patient was started on methylprednisolone 1g IV for 5 days while inpatient and then transitioned to prednisone 60 mg. She also received her first dose of rituximab 1g IV while inpatient, which was well tolerated with plans for rituximab infusions every 6 months. The patient's dapsone was increased to 100 mg daily for PJP prophylaxis while receiving steroids and rituximab.

Her prednisone was tapered off in July 2018. Due to flare of symptoms with this taper, the patient was restarted on dapsone 100 mg daily. She has since received 5 total doses of rituximab 1g IV with significant improvement of her ulcerations with plans to continue IV rituximab infusions every 6 months indefinitely. She has been followed by closely by dermatology and rheumatology in the outpatient setting.

DISCUSSION
The diagnosis of GPA, according to the American College of Rheumatology, is made with two of four criteria, including nasal or oral inflammation, abnormal chest imaging, urinary sample with red blood cells or casts, and granulomatous inflammation on kidney biopsy. A positive ANCA titer is not required for diagnosis, though it is frequently present. c-ANCA and its antigen PR3 are positive in over 84% of cases of confirmed GPA. Cutaneous manifestations of GPA are seen in 9 to 25% of cases, typically as leukocytoclastic vasculitis. The presentation of pyoderma gangrenosum-like lesions has been reported infrequently in the literature. In a recent retrospective analysis of 743 patients with cutaneous manifestations of GPA, only 1.1% exhibited PG-like lesions.

Complicating this diagnosis was the patient's history of cocaine use, as adverse effects of cocaine abuse may mimic rheumatologic conditions including GPA. Cocaine adulterated with levamisole, in particular, is known to cause agranulocytosis and vasculitis. In a case series of 8 patients with levamisole-induced pyoderma gangrenosum, serologic studies were notable for positive p-ANCA antibodies. Additionally, in a review of 30 patients with ANCA positivity and cocaine exposure, titers of p-ANCA and its antigen MPO were 15 times higher in patients with levamisole-induced vasculitis compared to idiopathic ANCA-associated vasculitis. In this case, therefore, the patient's strongly positive c-ANCA titers with positive PR3 antigen supported a diagnosis of GPA.

There is a paucity of literature regarding the treatment of pyoderma gangrenosum in GPA, though few case reports have described the efficacy of rituximab. In a recent case report describing a 50-year-old male with GPA who developed pyoderma-like ulcerations, the patient relapsed after steroid taper and was treated with rituximab with remission of pulmonary nodules and skin disease. A review of pediatric cases of PG-like ulcerations in the setting of GPA evaluated eight cases, which also demonstrated treatment response to rituximab.

The patient described above achieved clinical remission of her lesions with rituximab infusions and is continuing on maintenance therapy. This case highlights the presentation of GPA with PG as a rare cutaneous manifestation and the utility of rituximab as a treatment modality.

KEY POINTS

1. Pyoderma gangrenosum is a rare cutaneous presentation of granulomatosis with polyangiitis (GPA).
2. Levamisole-induced vasculitis is difficult to differentiate from ANCA-associated vasculitis, though anti-MPO (P-ANCA) antibody titers are commonly elevated to a higher degree than anti-PR3 (C-ANCA) antibody titers.
3. Given its rare clinical presentation, treatment for GPA-associated PG is poorly described in the literature, though case reports have highlighted the efficacy of rituximab.

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Presented by **Zachary Solomon**, MD, **Emily Merkel**, MD, **Jennifer Choi**, MD
Department of Dermatology, Feinberg School of Medicine, Northwestern University

UNKNOWN

A 62-year-old female presented with blurred vision, eyelid swelling, and a worsening scalp wound

CHICAGO DERMATOLOGICAL SOCIETY **Case 5**

Presented by **Victor Quan**, MD, **Derek Hsu**, MD, **Xiaolong Alan Zhou**, MD, MSc, **Julia Mhlaba**, MD
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HISTORY OF PRESENT ILLNESS

A 34-year-old female with Vogt-Koyanagi-Harada (VKH) syndrome with refractory uveitis presented with a two-week history of a generalized eruption.

In the four years prior to presentation, her uveitis was treated with mycophenolate mofetil and adalimumab. However, due to persistent ocular symptoms with weekly dosing of adalimumab, she was transitioned to infliximab. Two weeks after initiation of infliximab, she developed "blisters" on her bilateral toes, which spread to her legs, trunk, and arms. She presented to the ED for further workup and management given this new eruption and persistent, significant pain with ambulation.

PAST MEDICAL AND SURGICAL HISTORY

The patient was diagnosed with Vogt-Koyanagi-Harada (VKH) syndrome in her early twenties after a three-year course of persistent uveitis complicated by glaucoma and cataracts. The patient also endorsed a history of intermittent growth of patches of white hair since childhood and white spots on her face for several years, though she had never been formally evaluated by a dermatologist previously. She denied a history of auditory abnormalities. Past history was otherwise notable for hypertension. The patient's surgical history was significant for surgical management of glaucoma and bilateral cataracts.

FAMILY AND SOCIAL HISTORY

There was no family history of VKH syndrome, psoriasis, vitiligo, or other autoimmune conditions. The patient was on disability and lived with her mother and sister.

MEDICATIONS

Acetazolamide 500 mg BID, brimonidine 0.1% eyedrops BID, hydrochlorothiazide 25 mg daily, lisinopril 10 mg daily, mycophenolate mofetil 1500mg BID, prednisolone acetate 1% eyedrops daily, timolol 0.5% eyedrops nightly.

PHYSICAL EXAM

The patient was a well-appearing female in no apparent distress. On her trunk and extremities, there were diffuse pink and scaly annular plaques with peripheral pustules. On the palms and soles, there were hyperkeratotic erythematous plaques and fissures. Her forehead, cheeks, and chin had hypopigmented patches with foci of re-pigmentation.

LABS/IMAGING

WBC 13.5 (3.5-10.5K/uL). Hgb 10.1 (11.6-15.4 g/dL).
Comprehensive metabolic panel, uric acid, and magnesium within normal limits.
Lipid panel within normal limits except triglycerides 201(<100 mg/dL).
ANA 1:160 (homogenous/speckled), negative autoimmune disease panel, C3 142.3 (81-157 mg/dL), C4 22.8 (12-39 mg/dL)

Punch biopsy, right abdomen: H&E sections showed confluent parakeratosis with absence of the granular cell layer. Crust with numerous neutrophils was noted. There was acanthosis with thinning of the suprapapillary plates. Capillary loops within the dermal papillae were dilated and tortuous. There was mild dermal edema with a mixed inflammatory infiltrate composed of mononuclear cells with numerous neutrophils. Marked neutrophilic exocytosis with microabscess formation was noted. Significant

eosinophils were not identified. DPAS stain was negative for fungi. Perilesional DIF was without evidence of immune deposits. Findings were consistent with a diagnosis of pustular psoriasis.

DIAGNOSIS

TNF-a inhibitor-induced generalized pustular psoriasis in a patient with underlying Vogt-Koyanagi-Harada (VKH) syndrome

TREATMENT AND COURSE

For treatment of the generalized pustular psoriasis, the patient was initiated on cyclosporine 300 mg PO (2.5 mg/kg/day) with close monitoring for hypertension and topical triamcinolone 0.1% ointment BID to the affected areas.

At one-week follow-up, she was noted to have 80% improvement in her skin lesions and was continued on cyclosporine 300 mg daily. For diffuse scalp scaling, she started fluocinonide 0.05% solution and ketoconazole 2% shampoo daily. A multi-disciplinary discussion with rheumatology and ophthalmology is ongoing to determine optimal alternate therapy for uveitis.

DISCUSSION

Vogt-Koyanagi-Harada (VKH) syndrome is an autoimmune inflammatory condition characterized by severe bilateral granulomatous posterior or pan-uveitis and variable extraocular symptoms, including vitiligo with associated poliosis, auditory symptoms, and in some cases a prodromal aseptic meningitis.

VKH syndrome most commonly occurs in Asia, Latin America, and the Middle East. It most commonly presents during the third and fourth decade of life, with a slight predominance in female patients and in patients of Hispanic descent. It is proposed that CD4+ T cells target melanocytes in the autoimmune inflammatory process of VKH syndrome.

Patients present in several phases. Some patients have a prodromal phase with headache, meningismus, fever, nausea, and vertigo. All patients present with an acute uveitic phase characterized by sudden onset bilateral granulomatous uveitis. Uveitis can become chronic with recurrent exacerbations. The convalescent phase has a variable presentation, with auditory symptoms of sensorineural hearing loss or tinnitus and depigmentation of the choroid, skin, and hair occurring in 30% of patients.

Acute uveitis is treated with high-dose systemic steroids. The majority of young patients have some residual visual deficits due to cataracts, glaucoma, choroidal neovascularization, and subretinal fibrosis. Long-term management can include immunosuppressive agents such as mycophenolate mofetil, cyclosporine, and methotrexate, and more recently, rituximab, adalimumab, and infliximab. Reversal of poliosis and vitiligo can occur in some patients and is associated with younger age and good prognosis.

TNF-a inhibitors can effectively treat multiple inflammatory and autoimmune conditions. However, the paradoxical induction of psoriasis is well described, with the most common subtypes being plaque, palmoplantar pustular, and generalized pustular. This phenomenon has been reported with both infliximab and adalimumab. On average, the onset is 14 months after initiation of therapy.

In the literature, there are fewer than 15 case reports of VKH syndrome and psoriasis. In most cases, psoriasis precedes VKH syndrome, presents as plaque psoriasis, and may even occur at sites of vitiligo. There has been some association with specific HLA genotypes HLA-DR4, HLA-

DR53, and HLA-Cw6. This is the first reported case of generalized pustular psoriasis in a patient with VKH syndrome treated with a TNF-a inhibitor.

KEY POINTS

1. VKH syndrome is an autoimmune inflammatory syndrome characterized by severe bilateral granulomatous posterior or pan-uveitis and variable extraocular symptoms, including vitiligo with associated poliosis, auditory symptoms, and in some cases a prodromal aseptic meningitis.
2. TNF-a inhibitors including adalimumab and infliximab are highly effective monoclonal antibody therapies, although these medications can paradoxically induce psoriasis. Most often this is plaque psoriasis, but cases of palmoplantar or generalized pustular psoriasis have also been reported.

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CHICAGO DERMATOLOGICAL SOCIETY **Case 6**

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

HISTORY OF PRESENT ILLNESS

A 7-year-old female presented to Lurie Children's Dermatology for a lesion on the right cheek. The lesion was first observed at 1 year of age, and the patient developed a similar lesion on the left shoulder several months prior to presentation. The lesions were asymptomatic and had never bled, and the patient had no history of epistaxis.

PAST MEDICAL/SURGICAL HISTORY

Tonsillectomy at 4 years of age, otherwise healthy.

FAMILY AND SOCIAL HISTORY

No known history of vascular lesions, although limited examination of mother revealed two faint pink stains on her forearms.

MEDICATIONS

None

PHYSICAL EXAM

The patient was well-appearing and in no apparent distress. On the right cheek, there was a 3 x 2 cm telangiectatic patch. On the left cheek and right neck, there were small telangiectasias. On the left shoulder, there was a 3 x 2 cm telangiectatic patch. On the right lateral back, there was a 1 x 2 cm faint telangiectatic patch with peripheral pallor. On the hands, there were telangiectatic macules. None of the lesions had associated swelling, thrill, or bruit.

PERTINENT LABS

Genetic testing using the *RASA1* Gene Next Generation Sequencing identified no pathogenic mutations. Genetic testing using the *EPHB4* Single Gene Test Plus demonstrated a heterozygous frameshift variant *EPHB4* c.452del,p(Pro151Leufs*9), resulting in a premature stop codon and loss of normal protein function either through protein truncation or nonsense-mediated mRNA decay.

PERTINENT IMAGING

MRA of the head and MRI of the brain and spine with and without contrast were completed to evaluate for CNS arteriovenous malformations and were all unremarkable.

DIAGNOSIS

Capillary Malformation-Arteriovenous Malformation (CM-AVM) Syndrome Type II

TREATMENT AND COURSE

The patient underwent four rounds of pulsed dye laser therapy (settings: 595nm, 9.25-11J/cm^2, 7mm spot, 0.45-1.5msec pulse duration) to the left cheek, right cheek, and anterior neck, which resulted in marked improvement in the size and appearance of the treated lesions. Following initial brain and spine imaging, she has developed no symptoms to warrant repeating imaging to date. However, longitudinal clinical and radiologic surveillance will be performed, and genetic testing for her mother and siblings was encouraged.

DISCUSSION

Capillary malformation-arteriovenous malformation (CM-AVM) syndrome is an autosomal dominant disorder characterized by multifocal capillary malformations (CMs), intra- and extra-cranial arteriovenous malformations (AVMs), and arteriovenous fistulae (AVFs). Depending on the genetic mutation and clinical features, CM-AVM can be delineated into two separate types (CM-AVM1 and CM-AVM2). Recent studies have demonstrated that many patients presumed to have CM-AVM1 do not harbor the expected heterozygous loss-of-function mutations in *RASA1* but instead demonstrate loss-of-function mutations in *EPHB4*, leading to the designation of CM-AVM2 as a separate clinical entity. *EPHB4* is an upstream transmembrane tyrosine kinase receptor expressed in venous endothelial cells during vascular development that activates *RASA1*, which encodes the p120RasGAP protein and inhibits the MAPK pathway. Inactivating mutations in *RASA1* or *EPHB4* lead to uncontrolled activation of MAPK, resulting in dysregulated angiogenesis and vascular overgrowth, implicating the EPHB4-RAS-ERK signaling pathway as a cause of AVMs in both CM-AVM1 and CM-AVM2.

The presentation of CM-AVM2 is similar to both hereditary hemorrhagic telangiectasia (HHT, also known as Osler-Weber-Rendu syndrome) and CM-AVM1, though several differences exist. While HHT is also inherited in an autosomal dominant pattern, frequent epistaxis is more common, patients lack capillary malformations, and the disorder is caused by mutations in one of three TGF-b HHT genes (*ENG*, *ACVRL1*, or *SMAD4*). AVMs of the central nervous system are found in both HHT and CM-AVM, but pulmonary and hepatic AVMs are considered more characteristic of HHT. CMs in both CM-AVM1 and CM-AVM2 often have a peripheral white halo, and patients often present with a congenital CM and develop new CMs during adolescence, which is a key clinical feature that should prompt consideration of this diagnosis. Telangiectasias, which can be observed on the lips, in the perioral region, and on the upper thorax in CM-AVM2, are not a typical feature of CM-AVM1. Bier spots (vasospastic macules) are seen more frequently in CM-AVM2, while fast-flow vascular malformations are more common in CM-AVM1. Finally, Parks-Weber syndrome should be included in the differential; however, this syndrome is more commonly associated with limb and bone hypertrophy in addition to CMs and AVMs of the affected limb.

At the time of CM-AVM2 diagnosis, imaging of the brain and spine is recommended given the associated risk of central nervous system AVMs that can be life-threatening. If symptoms such as seizures, headaches, neurologic deficits, hydrocephalus, or heart failure occur, imaging should be repeated. Pulsed dye laser (PDL) therapy, which allows for selective photothermolysis of vessels, was previously contraindicated for the treatment of fast-flow lesions due to fear of accelerating the progression of AVMs; however, recent publications have shown successful treatment without evidence of progression. Finally, genetic counseling is recommended to assist patients and families in clarifying genetic status as well as in making informed medical and personal decisions.

KEY POINTS

1. CM-AVM2 is caused by loss-of-function mutations in *EPHB4*, which leads to dysregulated angiogenesis. In contrast, CM-AVM1 is caused by loss-of-function mutations in *RASA1*.
2. The presence of telangiectasias and Bier spots is more consistent with CM-AVM2 than CM-AVM1. Patients with HHT do not have CMs and are more likely to have a history of frequent epistaxis than patients with CM-AVM2.
3. Patients diagnosed with CM-AVM2 should be evaluated for possible central nervous syndrome AVMs with brain and spine imaging.
4. PDL therapy may be an effective treatment for select CMs in CM-AVM2.

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Presented by **Spencer Ng**, MD, **Simran Chadha**, BS, **Derek Y.** Hsu, MD, **Lauren M. Guggina**, MD, and **Cuong V. Nguyen**, MD
Department of Dermatology, Feinberg School of Medicine, Northwestern University

UNKNOWN

A 26-year-old female with a history of HIV/AIDS presented with three months of progressive, pruritic, and purulent skin erosions and ulcerations

CHICAGO DERMATOLOGICAL SOCIETY **Case 8**

Presented by **Alvin Li**, MD, **Jessica Labadie**, MD, **Amy S. Paller**, MD
Department of Dermatology, Feinberg School of Medicine, Northwestern University

HISTORY OF PRESENT ILLNESS

A 5-year-old female first presented to Lurie Children's Hospital in August 2018 with a one-year history of red, scaly, thin pruritic plaques on the face, elbows, and legs. She had been treated previously with a course of oral cephalexin for a presumed infectious process without improvement. She denied fever, chills, fatigue, joint pain, or swelling.

PAST MEDICAL AND SURGICAL HISTORY

The patient's past medical history was significant for developmental delay, for which she was currently receiving speech and occupational therapy.

FAMILY AND SOCIAL HISTORY

The patient's mother was previously diagnosed with plaque psoriasis of the scalp.

MEDICATIONS

None

PHYSICAL EXAMINATION

The patient appeared well nourished and in no apparent distress. Physical examination was notable for erythematous, mildly scaly and discrete hyperpigmented patches on the bilateral cheeks. There were few scattered erythematous plaques with overlying scale and crust on the arms, elbows, and legs. Additionally, numerous flat-topped shiny, skin colored papules, some with umbilication, were noted in a linear pattern over the arms and legs.

LABS/IMAGING

Punch biopsy, left upper arm (performed at Ohio State University): H&E demonstrated a lichenoid infiltrate with some spongiosis and crusting in the epidermis. Prominent lymphocyte exocytosis and keratinocyte necrosis with dyskeratosis were noted at higher magnification.

Genetic testing for NLRP1 and exome sequencing was sent to Dr. Keith Choate at Yale and is currently pending. Material for genetic testing and cytokine profiling was also sent to the autoinflammatory group at the NIH (PI Ivona Aksentijevich).

DIAGNOSIS

Keratosis lichenoides chronica

TREATMENT AND COURSE

At time of initial presentation, the patient started tretinoin 0.05% cream nightly to the extremities and tacrolimus 0.03% ointment twice daily to the extremities and face, leading to slight improvement of her face but exacerbation of her disease over the elbows and legs. She was then initiated on methotrexate 7.5 mg weekly (0.4 mg/kg) without significant response and was then uptitrated to methotrexate 10 mg weekly (0.5 mg/kg) with marked improvement of the face and later the extremities. Upon cessation of methotrexate, however, she again developed recurrent disease over the lower extremities and also developed an active eruption over the arms. She was evaluated at Lurie Children's Hospital in August 2018, and methotrexate 10 mg weekly was restarted with the addition of tacrolimus 0.1% ointment twice daily to the face and mometasone 0.1% ointment twice daily to the extremities. Despite this, her skin continued to worsen.

A short course of prednisolone 20 mg daily tapered over 6 weeks resulted in improvement, but unfortunately this was not sustained despite the concomitant initiation of mycophenolate mofetil 750 mg daily and hydroxychloroquine 100 mg daily. The initiation of acitretin was attempted but denied by the patient's insurance despite multiple appeals. In February 2020, she started a trial of NB-UVB, but this was discontinued in the setting of the COVID-19 pandemic. She was then switched to compounded topical ruxolitinib with clearance of facial lesions and improvement in the eruption over her extremities, but continuation of this treatment was limited by cost.

Methotrexate was then restarted at a higher dose (12.5 mg weekly, 0.6 mg/kg) and increased to 15 mg weekly (0.7 mg/kg) with subsequent improvement. At most recent follow up, the patient's mother notes that the patient's pruritus had improved and that the eruption overall appeared to be improving.

DISCUSSION

Keratosis lichenoides chronica (KLC) is a rare cutaneous disorder characterized by violaceous, keratotic papules distributed symmetrically on the trunk and extremities in a distinctive linear to reticular pattern. A concurrent facial eruption is common, presenting as greasy, centrofacial plaques resembling sebopsoriasis or rosacea in adults. As seen in our case, the facial eruption presents differently in pediatric KLC, with increased prominence of erythematous to purpuric macules. Given its rarity, diagnostic criteria are not well established.

The pathophysiology underlying KLC is currently unknown. Recent studies have linked one familial case of KLC with germline mutations in the nucleotide-binding domain, leucine-rich, repeat containing protein 1, or NLRP1. NLRP1 is an inflammasome sensor protein found predominantly in the skin that activates inflammatory cytokines. Mutations in NLRP1 thus predispose affected keratinocytes towards inflammasome formation and the release of tumor necrosis factor-alpha and keratinocyte growth factor, ultimately resulting in epidermal hyperplasia and hyperkeratosis.

Treatment of KLC is notoriously difficult. Current treatment regimens are based on limited case reports in the literature and include topical steroids, topical and systemic retinoids, calcineurin inhibitors, phototherapy and immunosuppressants. One review of KLC cases published in 2016 suggested oral retinoids and phototherapy, used either separately or in combination, are the most effective treatment options. Of the 30 patients who were treated with oral retinoids, 20% had partial responses and 37% had complete responses. If retinoids are not a practical option, as in our case, higher doses of methotrexate can be helpful in improving pruritus and skin lesions. While there have thus far been no published cases of KLC being treated with biologic drugs, the recent discovery of NLRP1 mutations as a major driver of familial KLC presents a potential targetable pathway. Given the potential value of JAK inhibition for lichenoid lesions and interferon-driven disorders, topical ruxolitinib was trialed in this case with promising results. A recently published abstract describes inhibition of the NLRP1 pathway in synovial fibroblasts from patients with rheumatoid arthritis after treatment with the JAK inhibitor baricitinib. Systemic JAK inhibitors are thus a potential future therapeutic option for this challenging condition.

KEY POINTS

1. Keratosis lichenoides chronica (KLC) is a rare cutaneous disorder characterized by violaceous, keratotic papules distributed symmetrically on the trunk and extremities in a distinctive linear to reticular pattern. There is often a concurrent sebopsoriasis-like facial rash.
2. While the pathophysiology underlying KLC is unknown, recent studies have linked familial cases of KLC with germline mutations in NLRP1, an inflammasome sensor protein.

3. Treatment of KLC is difficult. Based on limited data, oral retinoids and phototherapy are a reasonable first-line therapeutic option.

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