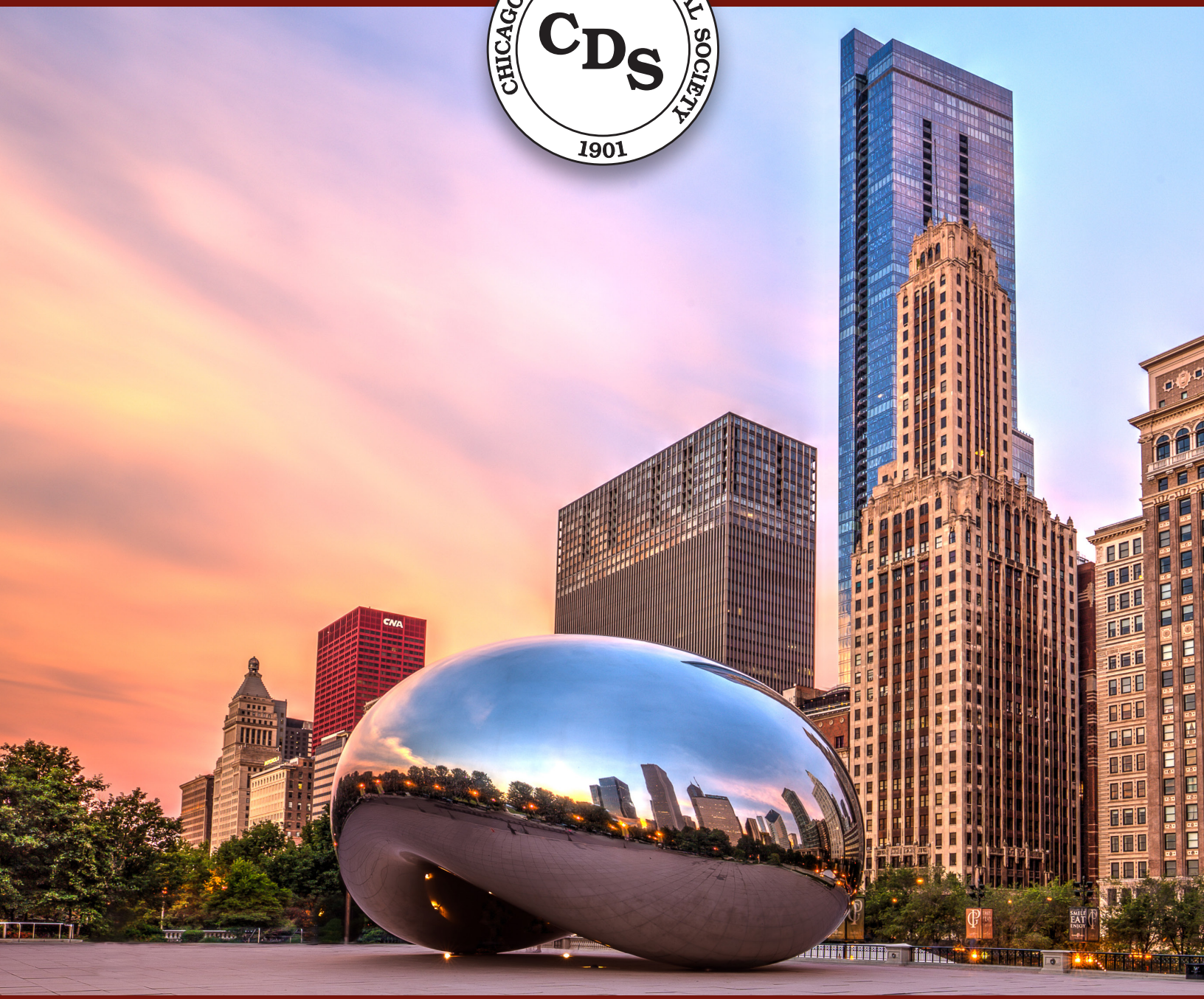
PROTOCOL BOOK • NOVEMBER 6, 2024

CHICAGO DERMATOLOGICAL SOCIETY

Monthly Meeting

Co-hosted by Northwestern University Feinberg School of Medicine Department of Dermatology



Chicago Dermatological Society

PROTOCOL BOOK
November 6, 2024

Co-hosted by
Northwestern University Feinberg School of Medicine
Department of Dermatology

Guest Speaker: **Jenny Murase, MD**
Director of Medical Consultative Dermatology
Palo Alto Foundation Medical Group
Associate Clinical Professor
University of California, San Francisco

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INVITED GUEST LECTURER

Jenny Murase, MD

Dr. Jenny Murase is the Director of Medical Consultative Dermatology for the Palo Alto Foundation Medical Group and an Associate Clinical Professor at the University of California, San Francisco. Dr. Murase has authored over 180 peer reviewed publications and book chapters and given over 400 international, national and regional presentations, specializing in the management of recalcitrant dermatitis/pruritus, consultative dermatology, patch testing, and women's health issues in dermatology. Dr. Murase served as Secretary of the Women's Dermatologic Society and co-Editor in Chief of the International Journal of Women's Dermatology, receiving a WDS Presidential Citation. She also served on the Board of Directors for the American Contact Dermatitis Society and received an ACDS Presidential Citation. She is the founder and chair of the American Academy of Dermatology Women's Health Expert Resource Group, and has served on multiple committees for the academy, including the Council on Education and Maintenance of Certification, the Employer Engagement Strategy Workgroup and the Clinical Guidelines Committee. Dr. Murase is a Councilor of the International Eczema Council and a member of the AAD Atopic Dermatitis Expert Resource Group. She received the Volunteer Faculty of the Year award in 2010 and 2020 from the UCSF Department of Dermatology residents for her teaching, and has directed over 30 symposiums for the American Academy of Dermatology, the European Society of Dermatology and Venerology, and the World Congress.

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PROGRAM

Co-hosted by
Northwestern University Feinberg School of Medicine
Department of Dermatology

November 6, 2024
Gleacher Conference Center

8:00 a.m.	**Registration & Continental Breakfast with Exhibitors**
8:30 a.m. - 10:15 a.m.	**Clinical Rounds** *Slide viewing/posters – ongoing through the early morning*
9:00 a.m.	**Welcome and Opening Comments** *Claudia Hernandez, MD - CDS President*
9:00 a.m. - 10:00 a.m.	**Morning Lecture: Tales of a Rash Whisperer: Untangling the Mystery of Adult Recalcitrant Eczematous Dermatitis** *Jenny Murase, MD*
10:00 a.m. - 10:30 a.m.	**Break and Visit with Exhibitors**
10:30 a.m. - 12:00 p.m.	**Resident Case Presentations & Discussion**
12:00 p.m. - 12:30 p.m.	**Box Lunches & Visit with Exhibitors**
12:30 p.m. - 1:00 p.m.	**CDS Business Meeting**
1:00 p.m. - 2:00 p.m.	**Afternoon Lecture: Consultative Dermatology for the Medical Dermatologist** *Jenny Murase, MD*
2:00 p.m.	**Program adjourns**

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Northwestern University Feinberg School of Medicine
Department of Dermatology

Chicago Dermatological Society Meeting
November 6, 2024

Dermatology Residents

Second Year
Jaimie Lin, MD
Anjani Sheth, MD, MPH

First Year
Nonye Ogbuefi, MD
Nicole (Nikki) Trupiano, MD
Madison Ernst, MD
Madeline Hooper, MD
Karishma Daftary, MD
Jonathan Park, MD, PhD
Morgan (Ella) Belina, MD

TABLE OF CONTENTS

Resident Case Presentations & Discussion

CHICAGO DERMATOLOGICAL SOCIETY **Case #1**

Presented by **Anjani Sheth**, MD, MPH, **Roopal V. Kundu**, MD
Department of Dermatology, Feinberg School of Medicine, Northwestern University

HISTORY OF PRESENT ILLNESS

A 53-year-old South Asian woman presented with progressive hyperpigmented lesions involving the neck, trunk, and upper extremities. Three years prior (2021), she developed a few hyperpigmented patches on her back one month after receiving the Pfizer-BioNTech SARS-CoV-2 vaccination. The lesions did not improve with topical steroids, topical calcineurin inhibitors, or ketoconazole shampoo but remained stable until mid-2023 when several new lesions appeared on the left lower back, upper extremity, and neck. New lesions were pink, slightly scaly, and mildly pruritic but turned darker, flatter, and asymptomatic after a few weeks.

PAST MEDICAL AND SURGICAL HISTORY

Eczematous dermatitis, lichen simplex chronicus, allergic rhinitis, subclinical hypothyroidism

FAMILY AND SOCIAL HISTORY

The patient's father has a history of type 2 diabetes mellitus, and the patient's mother died from pulmonary fibrosis at age 65. She has a sister who is healthy. She works as a consultant for a financial services company. She drinks three glasses of wine per week and is a non-smoker.

MEDICATIONS

Calcium, glucosamine, multivitamin, vitamin B12, vitamin D3

PHYSICAL EXAM

The patient was well-appearing and in no apparent distress. Involving the neck, posterior shoulders, left back extending down to left hip, left arm, and central chest, there were hyperpigmented (gray-brown) macules and patches. On the left side of the trunk, the patches were organized in a blaschkoid pattern and wrapped around from the back to the left flank. Dermoscopy showed an even peppering of perifollicular blue-gray granules. There was no perceptible erythema or scale. The oral mucosa was clear. Fingernails were polished, but there were no perceptible textural changes.

LABS/IMAGING

CBC with differential and BMP from six months prior to presentation were within normal limits. The patient had also undergone an extensive thyroid panel due to elevated TSH (6.15 μIU/mL) two months prior to presentation, but T3, reverse T3, T4, thyroglobulin antibody, thyroid peroxidase antibody, and thyroxine binding globulin were all within normal limits.

DERMATOPATHOLOGY

Histopathology demonstrated a slightly acanthotic epidermis with parakeratosis, a superficial band-like lymphohistiocytic infiltrate with focal squamatization of the basal layer with occasional necrotic keratinocytes, and numerous melanin laden macrophages, consistent with a lichenoid dermatitis with prominent melanoderma.

DIAGNOSIS

Blaschkoid lichen planus pigmentosus due to Covid-19 vaccination

TREATMENT AND COURSE

The patient was initiated on clobetasol 0.05% ointment BID for three weeks to halt any ongoing subclinical inflammation. After three weeks, the patient switched to tacrolimus 0.1% ointment BID. At this time, the patient also initiated a compounded lightening agent nightly for 3 months consisting of tranexamic acid 7%, hydroquinone 8%, kojic acid 2%, and hydrocortisone 2.5%. The patient was counseled on the importance of diligent sun protection with tinted mineral sunscreens.

DISCUSSION

Lichen planus is classically characterized by pruritic, polygonal, purple papules on the extremities. There are numerous variants or subtypes that vary in morphology, including lichen planus pigmentosus, hypertrophic lichen planus, and atrophic lichen planus.[1] The histologic appearance, however, is quite universal and generally shows hyperkeratosis, wedge-shaped hypergranulosis, "saw-tooth" irregular acanthosis, vacuolar degeneration of basal keratinocytes, and a band-like lymphohistiocytic infiltrate in the papillary dermis.[2] The term lichenoid dermatoses refers to distinct clinical entities whose clinical or pathologic features overlap with lichen planus.[1]

Rarely, lichen planus and other lichenoid dermatoses can occur in a blaschkoid pattern. With the exception of lichen striatus, this is not a typical distribution for these dermatoses.[2,3] There are several reports of lichen planus pigmentosus occurring in a blaschkoid distribution, particularly on the trunk, which deviates from its typical presentation in sun-exposed areas.[3] Because there is overlap in histology between lichen striatus, adult blaschkitis, and other blaschkoid lichenoid eruptions, the unifying term "blaschkolinear acquired inflammatory skin eruptions" (BLAISE) has been proposed.[2,4]

The etiology of lichen planus and lichenoid eruptions is not fully understood, but medications, infections, and even vaccines are known triggers.[1,2] A recent case series highlighted cases of Covid-vaccine-induced lichenoid eruptions, including classic lichen planus, inverse lichen planus, a solitary lichen planus lesion (forme fruste presentation), lichen striatus, and an eruption of lichenoid keratoses. The case series focused particularly on lichenoid eruptions that occurred in a blaschkoid distribution. Seven of the 46 cases of Covid-vaccine-induced lichenoid eruptions (15.2%) occurred in the blaschkoid distribution. In general, only an estimated 0.24-0.62% cases of lichen planus occur in a blaschkoid distribution, suggesting that the Covid-19 mRNA vaccine may be associated with increased incidence of a blaschkoid pattern of lichenoid dermatoses.[2]

Lichen planus and other lichenoid reactions represent only a fraction of the cutaneous eruptions related to Covid-19. Since the identification of this new infectious respiratory pathogen in 2019, numerous cutaneous manifestations have been attributed to both primary infection with the virus and vaccination against it. Covid-toes, or chilblain-like skin eruptions, quickly became known as a cutaneous reaction to infection with the Covid-19 virus. Patients have also demonstrated urticarial, papular, vesicular, purpuric, livedoid, and necrotic eruptions during active Covid-19 infection.[5] Following Covid-19 vaccination, local injection site reactions (immediate or delayed type IV hypersensitivity reactions) are the most common cutaneous reactions, followed by urticaria and angioedema (type I hypersensitivity reactions). Herpes zoster, pityriasis rosea, and vasculopathic processes like pernio, purpuric eruptions, and vasculitis have also been described after Covid-19 vaccination.[6] Most of the information regarding these cutaneous reactions come from case reports; thus, additional research is needed to further elucidate the role of COVID-19 infection and vaccination in triggering these eruptions.

KEY POINTS

1. Covid-19 mRNA vaccination has been associated with lichenoid eruptions, including blaschkoid lichenoid eruptions.
2. Treatment may require halting any active or subclinical inflammation with anti-inflammatory agents prior to treating with lightening agents via monotherapy or combination therapy.

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CHICAGO DERMATOLOGICAL SOCIETY **Case #2**

Presented by **Madeline Hooper**, MD, **Rachel Lipman**, MD and **Lida Zheng**, MD
Department of Dermatology, Feinberg School of Medicine, Northwestern University

HISTORY OF PRESENT ILLNESS

A 53-year-old male presented for evaluation of new left testicular swelling and a worsening pruritic eruption on the right proximal thigh. The rash first developed 5 years earlier and biopsy at that time was consistent with Majocchi's granuloma. However, the rash progressed despite treatment with terbinafine (with course complicated by transaminitis), ciclopirox cream, topical antihistamines, hydrocortisone 1% cream, and various home remedies.

Ten days prior to presentation, the patient developed tender left testicular swelling. He denied preceding testicular trauma, fevers, gastrointestinal upset, dysuria, hematuria, or penile discharge. He was otherwise in his normal state of health, without night sweats, cough, or weight loss.

PAST MEDICAL AND SURGICAL HISTORY

The patient completed a 6-month course of treatment for pulmonary tuberculosis 26 years prior to presentation, and a 2-month course of treatment (early self-discontinuation due to gastrointestinal upset) for latent tuberculosis 4 years prior to presentation.

FAMILY AND SOCIAL HISTORY

The patient was born in Ecuador and had lived in Chicago for 20 years.

MEDICATIONS

None

PHYSICAL EXAM

On the right medial thigh, there were pink to brown dermal papules with overlying scale coalescing to form annular plaques. The left hemiscrotum was markedly edematous with a 2x4 cm area of induration with distinct erythema involving the posterior aspect. There was no crepitus or fluctuance. Testicles were mildly tender to palpation.

LABS/IMAGING

Microbiologic evaluation:

- Wound cultures: Anaerobic/aerobic bacterial culture negative at 72 hours; acid-fast bacilli and fungal cultures negative
- Tissue culture: Methicillin-sensitive *Staphylococcus aureus*
- Scrotal abscess culture: *Mycobacterium tuberculosis* positive at 4 weeks, methicillin-sensitive *Staphylococcus aureus*

Scrotal ultrasound: Normal testicular size. No intratesticular mass. Thickened scrotal wall suggestive of edema/cellulitis and a 4.7cm heterogenous structure of the left scrotum consistent with an abscess.

DERMATOPATHOLOGY

Histopathology demonstrated a granulomatous and suppurative dermatitis with dermal fibroplasia. DPAS, Gram, Fite, and acid-fast bacilli stains were all negative for microorganisms.

DIAGNOSIS

Cutaneous tuberculosis (lupus vulgaris) with testicular tuberculosis

TREATMENT AND COURSE

Urology performed a beside incision and drainage of the scrotal abscess, and the patient was empirically started on a 2-week course of trimethoprim-sulfamethoxazole. Four weeks later, the scrotal abscess culture grew *Mycobacterium tuberculosis*, alongside methicillin-sensitive *Staphylococcus aureus*. The patient started rifampin, isoniazid, pyrazinamide, and ethambutol (RIPE therapy), but treatment was aborted by the patient after only 6 weeks due to gastrointestinal upset.

DISCUSSION

Cutaneous tuberculosis (CTB) is a rare manifestation of *Mycobacterium tuberculosis* infection, comprising between 1% and 2% of all tuberculosis (TB) cases worldwide. Infection can occur via direct exogenous inoculation, contiguous (endogenous) extension, and hematogenous spread – each route resulting in unique clinical presentations. The myriad manifestations of CTB complicate easy recognition of this condition.

Exogenous CTB is often secondary to a preceding injury as acid-fast bacilli cannot penetrate the skin barrier de novo. Examples of exogenous spread include tuberculous chancres in cases of primary infections and TB verrucosa cutis, a hyperkeratotic variant in patients with some immunological memory to TB. Contiguous (endogenous) CTB is characterized by lesions overlying a deeper tuberculoid focus and often presents with sinus tracts, nonhealing ulcers, and abscesses, as seen in scrofuloderma and orificial TB. Hematogenous CTB occurs when a primary infection spreads to distant parts of the body. Examples include lupus vulgaris, acute miliary TB, and metastatic TB abscesses. Lupus vulgaris, the most common type, presents as red-brown papules and plaques. This is more common in patients with malignancy and disfiguration but can also occur in immunocompetent individuals during reinfection, reactivation if latent TB, or after BCG activation. In contrast, immunocompromised individuals are more likely to develop acute miliary TB and metastatic TB abscesses. If our case had involved CTB in the skin adjacent to the testicular TB abscess, it could reasonably be classified as scrofuloderma; however, the chronicity of the cutaneous eruption, smoldering natural history, and noncontiguous location to the left hemiscrotum is more consistent with lupus vulgaris.

Diagnosis of CTB can be additionally challenging as the lesions themselves may evade confirmatory studies due to low microbial loads. Tissue culture, nucleic acid amplification test, and acid-fast staining of skin biopsies can be falsely negative, as in our case. Nonetheless, histopathological evaluation of suspected CTB is warranted. Characteristic histological features are specific to each CTB subtype. For example, tuberculous chancres are multibacillary and predominantly neutrophilic with necrosis. Scrofuloderma commonly reveals many bacilli amongst suppurative granulomas, necrosis, and neutrophilic abscesses. Lupus vulgaris is typically paucibacillary and demonstrates upper dermal epithelioid granulomas or a confluent granulomatous infiltrate in the papillary dermis.

Monoclonal antibody assays and PCR amplification may also be helpful in diagnosis of CTB, in addition to immunologic tests like the tuberculin skin test (specificity 63%, sensitivity 33-95% for CTB) and interferon gamma release assay (specificity 75%, sensitivity 92% for CTB). Chest radiography and additional tests based on review of systems and exam should be included to evaluate for systemic involvement and immunocompromised states. Like pulmonary TB, CTB treatment involves a 2-month intensive phase with RIPE, followed by at least 4 months of isoniazid and rifampin. A proposed diagnostic algorithm published in the JAAD recommends a trial of therapy in cases of high clinical suspicion despite inconclusive histology and microbial studies. Lack of response to treatment after 4 to 6 weeks may indicate drug resistance or improper diagnosis.

KEY POINTS

1. Cutaneous tuberculosis can mimic many other dermatoses, and its presentation is determined by the route of infection: exogenous inoculation presents as singular lesions in areas of prior trauma, whereas regional and hematogenous spread are more often characterized by multiple papulonodules, plaques, and abscesses.

2. Evaluation for systemic disease such as malignancy and immunocompromise is paramount in cases of cutaneous tuberculosis as this often affects the type and severity of presentation.
3. Diagnosis is tricky as cutaneous tuberculosis can evade microbiological confirmation, sometimes requiring PCR, tuberculin skin tests, and interferon gamma release assays. In situations of high clinical suspicion and indeterminate culture or histopathology data, a trial of antitubercular treatment and workup for systemic tuberculosis can be pursued.

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CHICAGO DERMATOLOGICAL SOCIETY **Case #3**

Presented by **Nicole Trupiano,** MD, **Cuong V. Nguyen**, MD, and **Maria L. Colavincenzo**, MD
Department of Dermatology, Feinberg School of Medicine, Northwestern University

UNKNOWN

A 35-year-old female with a history of hidradenitis suppurativa presented to the emergency department with 4 weeks of rash on the face and trunk.

CHICAGO DERMATOLOGICAL SOCIETY **Case #4**

Presented by **Madison Ernst**, MD and **Paras Vakharia**, MD, PharmD
Department of Dermatology, Feinberg School of Medicine, Northwestern University

HISTORY OF PRESENT ILLNESS

A 28-year-old man presented for evaluation of multiple facial lesions. The patient reported that a cyst on the left cheek had been present for 1 year. A week prior to presentation, the cyst became hard, red, and painful. The patient reported a history of multiple facial milia and cysts, which he attributed to a genetic diagnosis. The patient was otherwise in his usual state of health.

PAST MEDICAL AND SURGICAL HISTORY

The patient reported a personal history of a genetic syndrome, ADHD, and chronic low back pain secondary to lumbar disc herniation, which had been treated with two hemilaminectomies.

FAMILY AND SOCIAL HISTORY

The patient reported that his mother also shared his genetic condition. His mother, several cousins, and other family members had been diagnosed with "dozens to hundreds" of basal cell carcinomas as well as milia.

MEDICATIONS

Lisdexamfetamine, meloxicam

PHYSICAL EXAM

There was a 1.6 cm smooth, compressible nodule on the patient's left superior cheek with two puncta and overlying erythema. Numerous milia as well as atrophic scars were noted on the bilateral cheeks. On the left lateral lower eyelid, there were two tan papules with blue-gray ovoid nests. On his right inferior lateral orbital rim, he had a 2 mm papule with brown pigment and telangiectasias on dermoscopy. His frontal hairline was sparse. His dorsal hands and forearms demonstrated follicular atrophoderma.

LABS/IMAGING

No labs or imaging were obtained. Patient declined genetic testing for basal cell tumor syndromes.

DERMATOPATHOLOGY

Histopathology of the superior left lateral eyelid lesion demonstrated large, irregular lobules of basaloid cells with hyperchromatic nuclei and scant cytoplasm within the dermis. At the periphery of the lobules, there was palisading of cells with stromal retraction. The stroma demonstrated fibromyxoid changes with variable lymphohistiocytic infiltrate. The lesion was diagnosed as a nodular BCC. The inferior left lateral eyelid lesion was consistent with a milium. Histopathology of the right lower inferior eyelid was consistent with nodular BCC as well as a milium.

DIAGNOSIS

Hereditary basal cell tumor syndrome, likely Bazex-Dupre-Christol syndrome

TREATMENT AND COURSE

Both basal cell carcinomas were treated with Mohs micrographic surgery. The patient has since been lost to follow up.

DISCUSSION

This 28-year-old patient's presentation with multiple BCCs, milia, congenital hypotrichosis, self-reported hypo/anhidrosis, and follicular atrophoderma is most consistent with Bazex-Dupre-Christol syndrome (BDCS). BDCS is as a rare ectodermal dysplasia and hereditary tumor syndrome. It was first described in 1964 and has been reported in about 30 families worldwide. It follows an X-linked dominant inheritance pattern. Classically, BCDS presents with a triad of hypotrichosis, follicular atrophoderma, and BCCs. Hypotrichosis and follicular atrophoderma typically develop at or around birth. BCCs often develop in the

second decade of life but have occurred in patients as young as 3 years old. Additional associations include hypohidrosis, facial hyperpigmentation, trichoepitheliomas, and hair shaft dystrophies.[2] BDCS is not associated with systemic symptoms or internal malignancies.

The diagnosis of BDCS is clinical. It should be considered in young patients with a personal and family history of BCCs. The differential diagnosis includes other hereditary BCC syndromes, such as Basal cell nevus syndrome and Rombo Syndrome, follicular disorders, and ectodermal dysplasias such as multiple basaloid follicular hamartoma syndrome. Of note, BDCS should not be confused with Bazex Syndrome (acrokeratosis paraneoplastica), which describes a rare acral psoriasiform dermatosis associated with internal malignancies.

The underlying genetic mechanism of BDCS is an active area of research. For many years, BDCS had been associated with an unknown mutation within an 11.4 Mb interval on Chromosome Xq25-q27.1. Studies over the past 3 years now suggest that BDCS is more specifically related to small tandem non-coding intergenic duplications on chromosome Xq26.1.[3,6] It has been suggested that these duplications dysregulate one of the surrounding genes, such as the flanking centromeric genes ARHGAP36 or ACTRT1.[4] ARHGAP36 is a known positive regulator of the Sonic Hedgehog pathway in some tumors.[4] Its expression is upregulated in the BCCs of BDCS patients as well as in many sporadic BCCs.[3] *ACTRT1* regulates the tumor suppressor ARP-T1, a non-coding mRNA required for assembly of cilia.[4]

While there is no cure for BDCS, early diagnosis is important for the timely treatment of the associated BCCs as well as for genetic counseling. Management involves diligent sun protective measures, regular self-skin examinations and total body skin exams with a dermatologist starting in childhood, and treatment of BCCs.

KEY POINTS

1. Bazex-Dupre-Christol syndrome is an X-linked dominant disorder that presents in children and young adults with the triad of congenital hypotrichosis, follicular atrophoderma, and multiple BCCs.
2. Early diagnosis is important for treatment of BCCs and genetic counseling.

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CHICAGO DERMATOLOGICAL SOCIETY

Presented by **Jonathan Park**, MD, PhD, **Jennifer Choi,** MD, **Cuong Nguyen**, MD, **Lida Zheng**, MD
Department of Dermatology, Feinberg School of Medicine, Northwestern University

HISTORY OF PRESENT ILLNESS

Case 1: A 69-year-old woman with stage IV lung adenocarcinoma with an EGFR mutation on amivantamab (EGFR/MET inhibitor) and osimertinib (EGFR inhibitor) presented with an asteatotic eczema-like rash on the face, arms, and back with full body dryness 1-2 months after initiating amivantamab. She trialed courses of betamethasone dipropionate 0.05% cream, doxycycline, and cephalexin with some overall improvement. However, 1.5 months after initial presentation, she developed ulcers involving her upper back, arms, lateral breasts, chest, posterior thighs, and abdomen. Her cancer-directed treatment was held pending further workup and management.

Case 2: A 73-year-old man with stage IIB lung adenocarcinoma with an EGFR mutation status post right upper lobe lobectomy and adjuvant chemotherapy was started on amivantamab and osimertinib for recurrent and metastatic disease. The patient was being followed in oncodermatology clinic for significant xerosis and fissuring of the fingers when he developed painful scattered punched-out ulcerations on the extremities, back, and lower legs. His cancer-directed treatment was held pending further workup and management.

PAST MEDICAL AND SURGICAL HISTORY

Case 1:
The patient had a medical history of vitamin B12 deficiency and GERD.

Case 2:
The patient had a medical history of type 2 diabetes mellitus, GERD, and hypertension. Past surgical history was notable for inguinal hernia repair and tear duct repair.

FAMILY AND SOCIAL HISTORY

Case 1:
There was no notable family or social history.

Case 2:
There was no notable family or social history.

MEDICATIONS

Case 1:
Acetaminophen, denosumab, dexamethasone elixir, ibuprofen, omeprazole, ondansetron, tramadol, osimertinib, and amivantamab

Case 2:
Albuterol, apixaban, carvedilol, cyclobenzaprine, doxycycline, dulaglutide, esomeprazole, insulin, lisinopril, montelukast, prochlorperazine, rosuvastatin, osimertinib, and amivantamab.

PHYSICAL EXAM

Case 1:
The patient was well-appearing and in no apparent distress. The patient's extensor arms had numerous round-oval punched-out ulcers with central crusting/hyperkeratosis. Involving her posterior upper thighs extending onto the buttocks, there were numerous 2-6 mm round punched-out ulcerations, some with hyperkeratotic and crusted centers. The upper back and posterior shoulders had thin healing crusted oval erosions.

Case 2:
The patient was well-appearing and in no apparent distress. Scattered hemorrhagic crusted ulcerations were noted on the extremities, back, and lower legs. Patient also had diffuse xerosis, yellow discoloration of the nails of the hands, and fissures on the distal fingertips.

LABS/IMAGING

Case 1:
HSV/VZV PCRs, fungal cultures, and superficial wound cultures were negative. Tissue culture grew moderate *Pseudomonas aeruginosa*.

Case 2:
Acid-fast bacilli cultures, fungal cultures, and superficial wound cultures were negative. Tissue culture grew few *Pseudomonas aeruginosa*.

DERMATOPATHOLOGY

Case 1:
Histopathology of the left arm demonstrated a central ulcer covered by a serosanguinous exudate with numerous bacterial colonies noted within the cornified layer. No vasculitis was observed. Viral cytopathic changes were not observed. EBER-1 in situ hybridization was negative for Epstein-Barr mRNA.

Case 2:
Histopathology of the left arm demonstrated a central ulcer covered by a neutrophilic scale-crust with adjacent epidermal spongiosis. No vasculitis was observed. Some bacterial colonies were identified within a follicular infundibulum but were absent on Gram staining. DPAS stain was negative for fungal organisms.

DIAGNOSIS

Ecthyma-like pseudomonal ulcers in the setting of EGFR/MET inhibition

TREATMENT AND COURSE

Case 1:
The patient was started on oral ciprofloxacin 500 mg BID, topical gentamicin 0.1% ointment BID to the affected areas, and dilute hypochlorous acid body wash during showers, which improved her rash. The patient was restarted on amivantamab and osimertinib after a 17-day course of ciprofloxacin that was stopped given drug interaction with osimertinib. Repeat superficial aerobic/anaerobic wound cultures were obtained which were negative. The patient remains on cancer-directed treatment.

Case 2:
The patient was started on oral ciprofloxacin 500mg BID. The patient's rash improved, and antibiotics were de-escalated from oral therapy to topical gentamicin ointment. Osimertinib was resumed. At the most recent visit, the patient's rash had resolved off all treatment, leaving hyperpigmented macules at prior sites of ulcerations.

DISCUSSION

Amivantamab is an epidermal growth factor receptor (EGFR) and mesenchymal–epithelial transition factor (MET) bispecific antibody with multiple mechanisms of action including ligand blocking, receptor degradation, and immune cell-directing activity. It was recently approved for EGFR exon 20 insertion-mutated non-small cell lung cancer (NSCLC) and was also shown to improve survival for patients with exon 19 deletions.[1,2] During the clinical trials for amivantamab, the majority of grade 3 or higher adverse events were found to be skin-related EGFR inhibitor toxic effects such as xerotic dermatitis, paronychia, and papulopustular eruptions.[3,4] Similarly, the most common adverse events observed with osimertinib, a third generation EGFR tyrosine kinase inhibitor approved for NSCLC with EGFR exon 19 deletions or exon 21 L858R mutations, were diarrhea, rash, dry skin, and paronychia.[5] Skin toxicities associated with

EGFR targeted therapeutics can become severe enough to interrupt anticancer treatment regimens as observed in the cases above.

The relative frequency by which EGFR targeted therapies lead to dermatologic toxicities is likely due to the key role that EGFR signaling plays in skin homeostasis.[6] EGFR is widely expressed in normal skin tissue and cells including the epidermis, sebaceous glands, eccrine glands, and dendritic cells, and plays an important role in keratinocyte differentiation and migration to the skin surface.[7] Inhibition of EGFR signaling can lead to premature differentiation, inflammation, apoptosis, and atrophy, which in turn leads to disruption of the skin barrier and skin homeostasis. The resulting inflamed skin can become affected by secondary infection, which was observed in both cases.[8]

To our knowledge, these cases are the first descriptions of a novel morphology of ecthyma-like punched-out ulcers associated with EGFR/MET inhibition. Cutaneous ulceration in general has been very rarely associated with EGFR inhibition[9], which suggests that MET inhibition may play a role, especially given the ulcers developed after starting amivantamab in both cases. While recent reports have described ulcers with EGFR/MET inhibition on the scalp and genitals,[10,11] the distribution, morphology, and association with pseudomonal infection has not been previously described. The pathogenesis of these ulcers is not clear. Given the ecthyma-like morphology, the etiology may be due to a vaso-occlusive process as seen in ecthyma gangrenosum; however, these patients were not septic at presentation and vasculitis was not observed on histopathology. Alternatively, the lesions may be caused by skin necrosis secondary to severe cutaneous inflammation. C-MET is known to play a key role in wound healing,[12] so use of amivantamab may lead to impaired wound healing. *Pseudomonas* itself may drive ulcer formation through the production of exotoxins, supported by the fact that both patients improved after anti-pseudomonal therapy. Given the negative superficial wound cultures and improvement only after antibiotic initiation, these cases highlight the importance of obtaining biopsy for tissue culture for patients on EGFR/MET targeted therapies with cutaneous ulcers.

As EGFR and EGFR/MET targeted agents are more commonly used, it is important for dermatologists to become familiar with the clinical presentation of their associated toxicities and management. These cases highlight the importance of close collaboration with medical oncologists and with patients to ensure anticancer treatment is held when necessary and resumed once able.

KEY POINTS

1. Novel EGFR and EGFR/MET targeted therapies including amivantamab and osimertinib are commonly being used for NSCLC patients, and often lead to dermatologic toxicities due to the role of EGFR signaling in normal skin homeostasis.
2. A novel toxicity of EGFR/MET inhibition is ecthyma-like punched-out ulcerations secondary to *Pseudomonas aeruginosa.*
3. Superficial wound cultures may be negative, and tissue culture should be pursued in the setting of clinical suspicion.

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CHICAGO DERMATOLOGICAL SOCIETY **Case #6**

Presented by **Nonye Ogbuefi**, MD, **Xiaolong (Alan) Zhou**, MD, and **Amy Paller**, MD
Department of Dermatology, Feinberg School of Medicine, Northwestern University

HISTORY OF PRESENT ILLNESS

A 34-year-old man with a history of xeroderma pigmentosum presented for evaluation of a nodule on his right abdomen.

The patient was diagnosed at age 3 with xeroderma pigmentosum type C, at which time skin pigmentary changes and eye sensitivity to light and sun had prompted a genetics evaluation. He was found to be homozygous for the XPC c.1677C>G XPC; p.(Y559*) allele. He was very diligent about sun protection and treated potential pre-cancerous lesions with imiquimod. Thus, his xeroderma pigmentosum was not complicated by numerous skin cancers and he only had a history of one basal cell carcinoma on his nose in 2016.

The patient was in his usual state of health until October 2023 when he presented to the emergency room with headaches. He was found to have a right frontal hemorrhagic mass. He underwent frontal craniotomy and resection with pathology consistent with DICER1-altered primary intracranial sarcoma. Sequencing also showed pathogenic variants in ATRX, PDGFRA, and XPC, with high tumor mutational burden (19.2). PET-CT scan demonstrated multiple osseous lesions and hypermetabolic activity in the pancreas, liver, and right abdominal wall. The patient then presented to clinic for biopsy of the abdominal nodule, which was neither pruritic nor tender.

PAST MEDICAL AND SURGICAL HISTORY

The patient's past medical history included an imperforate anus, early onset hypertension, subclinical hypothyroidism, hypogonadism, type 2 diabetes mellitus, hyperaldosteronism, thrombocytopenia with a positive auto-platelet antibody test, and a cerebral aneurysm. There was concern that the aneurysm may represent a connective tissue disorder, such as Loeys-Dietz Syndrome, which shares similar features with Marfan syndrome. Comparative genomic hybridization detected the presence of allelic homozygosity in some chromosomes, which indicated some degree of consanguinity in inheritance, including in the LDS locus on chromosome 3p. However, the patient was never confirmed to have Loeys-Dietz Syndrome.

Past surgical history included surgical clipping of his cerebral aneurysm complicated by a left PCA stroke in 2007, a cholecystectomy in 2009 for gallbladder polyps, and electrohydraulic lithotripsy (EHL) for bladder stone removal in 2017.

FAMILY AND SOCIAL HISTORY

The patient's family is from India. His father has a history of sarcoidosis. His sister is a carrier for xeroderma pigmentosum.

MEDICATIONS

Acyclovir, amlodipine, dexamethasone, glipizide, lacosamide, levofloxacin, metformin, posaconazole, and spironolactone

PHYSICAL EXAM

The patient is Fitzpatrick Phototype IV. Exam was notable for a 2x1.4 cm firm subcutaneous nodule over the right epigastric area on a diffuse background of lentigines.

DERMATOPATHOLOGY

Histopathology of the right abdomen demonstrated a low-grade spindle cell neoplasm with a molecular profile that was markedly different than his previously diagnosed DICER1-altered intracranial sarcoma. A DICER1 gene variant was not identified in the skin biopsy. CD163 was positive. An expanded NGS panel was performed and the following variants of known or potential clinical significance

were identified: XPC p.(Y559*), NF1 c.586+1G>T, CBL p.(H398P), CBL p.(K477*). The only shared mutation between the spindle cell neoplasm and the intracranial sarcoma was XPC.

DIAGNOSIS

Abdominal wall spindle cell neoplasm suspicious for a second primary sarcoma given the distinct mutational profile

TREATMENT AND COURSE

The patient's clinical course was further complicated by a new diagnosis of mixed phenotype leukemia in February 2024. He was started on azacitidine and venetoclax and achieved remission after cycle 1. He was considered for allogeneic hematopoietic stem cell transplant, but he was not a candidate due to his synchronous sarcoma.

For his DICER1-altered primary intracranial sarcoma, the patient completed adjuvant intracranial proton radiotherapy in February 2024. He unfortunately developed intracranial progression of disease in April 2024, requiring repeat resection and stereotactic radiosurgery. He was then started on doxorubicin and pembrolizumab due to the aggressive presentation, high tumor mutation burden, and the patient's DNA repair deficiency. The patient is now on pembrolizumab monotherapy due to cytopenia secondary to the doxorubicin. His disease is currently stable with no change in size of the abdominal nodule.

At this point, the patient has concern for three possible distinct cancers in the setting of xeroderma pigmentosum type C: the mixed phenotype leukemia, the DICER1-altered intracranial sarcoma, and the abdominal wall spindle cell neoplasm.

DISCUSSION

Xeroderma pigmentosum (XP) is a rare autosomal recessive genodermatosis that results from pathogenic variants in nucleotide excision repair (NER) leading to defective DNA repair. The disease presents in early childhood and is characterized by cutaneous photosensitivity and pigmentary changes in UV exposed areas of the body, as well as ocular abnormalities.[1] Some XP patients have progressive neurologic involvement, and an increased susceptibility to neoplasms of the central nervous system has been described.[1-2]

Individuals affected by XP are born with normal-appearing skin. In 40% of cases, patients present with sunburn reactions in the first few weeks of life, while the other 60% of patients present with an increased number of lentigines in sun-exposed areas by the age of two years.[2] With increased sun exposure, the skin becomes dry, rough, and atrophic. XP patients have an estimated 10,000-fold increased risk of the development of non-melanoma skin cancer and a 2,000-fold increased risk of cutaneous melanoma.[3-4]

Eight gene variants have been identified in XP and correlate with different subtypes and clinical presentations of the disease. Seven of the gene variants (XPA through XPG) involve a defect in NER, while the eighth gene variant (XPV) encodes for a defective DNA polymerase η involved in DNA synthesis.[1]

The subtype identified in our patient is xeroderma pigmentosum complementation group C (XPC). XPC is the most common subtype in the United States. Patients present with classic XP skin manifestations, including photosensitivity and the development of early dermatologic malignancies.[3,5] Interestingly, individuals with the XPC subtype do not typically develop the extreme sunburn reactions or neurodegenerative abnormalities found in other subtypes. However, patients with XPC have a 10-20-fold increased risk of developing internal neoplasms.[2] Since these areas are not exposed to the UV radiation, it is thought that exposure to genotoxins, such as dietary carcinogens, free radicals, and aldehydes, induces unique genetic variants that lead to the development of these internal neoplasms.[3-4,6]

The NER system normally removes UV-damaged DNA by two mechanisms: i) designated transcription-coupled repair, which rapidly repairs errors of DNA transcription to RNA; and ii) global genome repair,

which more slowly repairs DNA in the rest of the genome.[1] A recent study demonstrated that patients with XPC have constitutive deficiency of global genome nucleotide excision repair (GG-NER), while the transcription-coupled nucleotide excision repair (TC-NER) is unaffected. This results in an excess of unrepaired bulky DNA lesions on the untranscribed strands of a gene, which is unable to be repaired by global genome- nucleotide excision repair; lesions on the transcribed strands are effectively repaired by transcription coupled- nucleotide excision repair. This asymmetry is unique to XPC tumors and may explain the increased susceptibility of individuals with XPC to internal neoplasms.[5,6]

This patient presented a treatment dilemma because of the required chemotherapy and radiation therapy for treatment of the sarcoma and leukemia. Although patients with XP have inadequate repair of UV-damaged DNA, patients with XP have normal cellular and clinical responses to radiation therapy, likely because ionizing radiation is repaired through base excision repair rather than NER. Therefore, radiation therapy can be used as adjuvant treatment without complications in XP patients, as seen in our patient who successfully underwent adjuvant radiation therapy for his intracranial sarcoma.[7] Despite concern about the use of platinum-based chemotherapy agents, because repair of bulky DNA lesions after this chemotherapy occurs through TC-NER rather than GG-NER, patients with XPC do not have issues with these therapies. However, cytotoxicity is increased in other XP subtypes.[5,8-9]

While there is no cure for xeroderma pigmentosum, skin effects can be minimized with early diagnosis, stringent UV protection, and early removal of precancerous and cancerous lesions. Patients should avoid cigarette smoke and other environmental carcinogens, which can induce DNA damage. Finally, clinical research suggests the use of long-term oral isotretinoin as chemoprevention in XP patients. Enzyme and gene therapy also show future potential for a cure.[10]

KEY POINTS

1. Xeroderma pigmentosum (XP) is a rare autosomal recessive genodermatosis that results from pathogenic variants in nucleotide excision repair leading to defective DNA repair and malignancy development. The different variants of nucleotide excision repair result in various subtypes and clinical presentations of the disease.
2. While patients with the XPC subtype do not develop extreme sunburn reactions or neurodegenerative changes, XPC deficiency results in unique pathogenic variations that lead to an increased susceptibility to internal malignancies.
3. Patients with XPC can tolerate radiation therapy and platinum-based chemotherapy.

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CHICAGO DERMATOLOGICAL SOCIETY **Case #7**

Presented by **Prachi Aggarwal,** MD, **Jaimie Lin,** MD, **Paras Vakharia,** MD, PharmD
Department of Dermatology, Feinberg School of Medicine, Northwestern University

HISTORY OF PRESENT ILLNESS

A 43-year-old woman with a history of keloidal acne scarring and fibroids status-post laparoscopic surgery presented for a lesion of concern on her umbilicus. The patient reported noticing a growth at her umbilicus over the past 2 years with periodic bleeding, discomfort, and increased sensitivity. She underwent laparoscopic surgery in 2007 to treat uterine fibroids with an entry point through her umbilicus. The patient was otherwise in her usual state of health.

PAST MEDICAL AND SURGICAL HISTORY

In 2007, the patient underwent laparoscopic surgery for a right ovarian cyst and fibroids within the uterine muscle. Pathology from the procedure demonstrated endometriosis. She was otherwise healthy with no other reported medical conditions.

MEDICATIONS

Oral contraceptive (desogestrel and ethinyl estradiol)

PHYSICAL EXAM

The patient was well-appearing and in no apparent distress. Within the umbilicus, there was a 2 cm dark brown, bleeding nodule that was firm but compressible.

IMAGING

MRI demonstrated a 1.9 x 1.6 cm enhancing lesion near the umbilicus and T1 hyperintensity between the left uterine body and the urinary bladder, concerning for deep infiltrating endometriosis.

DERMATOPATHOLOGY

Histopathology demonstrated prominent fibroplasia with glandular structures surrounded by a loose stroma and some decidual changes in the reticular dermis. Hemorrhage, necrosis, and a patchy lymphoplasmacytic infiltrate were focally noted.

DIAGNOSIS

Cutaneous endometriosis

TREATMENT AND COURSE

The patient was referred to gynecology to discuss various treatment options. Given that she was already on continuous oral contraceptives and was mainly symptomatic from one focus of endometriosis, the team decided to proceed with surgical removal of the umbilical lesion with reconstruction by plastic surgery.

DISCUSSION

Endometriosis refers to the decidualization of endometrial tissue under hormonal influences outside of the uterine cavity. Cutaneous endometriosis occurs when endometrial tissue becomes embedded in the skin. The most common cause of cutaneous endometriosis is thought to be iatrogenic implantation of detached endometrial tissue at a prior surgical incision site. The most common surgical procedure associated with cutaneous endometriosis is cesarean section, followed by episiotomy. Studies have shown an incidence as high as 0.25% in all patients that have undergone cesarean section.

The average reported time between surgical procedure and onset of cutaneous endometriosis ranges between 3.7-4.5 years. Thus, it is important to obtain a thorough surgical and past medical history when these patients present to the office.

The presentation of cutaneous endometriosis can vary, posing a diagnostic dilemma in patients presenting with pain, swelling, or discoloration around surgical incision sites. The differential diagnosis for

umbilical lesions includes a keloidal scar, dermatofibrosarcoma protuberans, pyogenic granuloma, melanoma, umbilical hernia, urachal duct cyst, and cutaneous metastases such as those seen with abdominal malignancies. Non-invasive imaging techniques such as computed tomography, ultrasound with or without Doppler, or magnetic resonance imaging may be helpful in facilitating the diagnosis but often can be inconclusive. Skin biopsies and fine-needle aspiration may also be helpful tools used to establish the diagnosis.

Surgical excision with 1 cm margins is the most effective treatment with reported postoperative recurrence rate of less than 9%. For those wishing to pursue medical therapy, oral contraceptives, progesterone, or danazol may help with symptom control by inhibiting cyclical endometrial proliferation. However, recurrence is often noted with hormonal therapies.

KEY POINTS

1. Cutaneous endometriosis is often iatrogenic and occurs when ectopic endometrial tissue is embedded in the skin. Symptoms include pain, swelling, and cyclical bleeding, especially at sites of previous gynecologic surgeries.
2. Symptoms of cutaneous endometriosis may present years after an inciting procedure and a thorough surgical and past medical history may help reach the correct diagnosis. For patients failing medical management, surgical excision is recommended to reduce recurrence risk and provide symptomatic relief.

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CHICAGO DERMATOLOGICAL SOCIETY **Case #8**

Presented by **Karishma Daftary**, MD, and **Lida Zheng**, MD
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HISTORY OF PRESENT ILLNESS

A 44-year-old female was referred by rheumatology for a 5-year history of urticarial lesions, night sweats, low-grade fevers, joint pains, muscle weakness, and fatigue. The urticarial lesions were primarily distributed on the upper and lower extremities and typically resolved with bruising in 3-4 days. She had an external biopsy 4 years prior demonstrating urticaria without evidence of vasculitis; however, she had been diagnosed clinically with urticarial vasculitis given the appearance of her lesions. She had tried numerous treatments prior to her presentation without significant improvement in her symptoms, including golimumab, adalimumab, methotrexate, etanercept, dapsone, and multiple courses of prednisone. Given the refractory nature of her disease, she was referred for a second opinion for further management.

PAST MEDICAL AND SURGICAL HISTORY

The patient's past medical history included seronegative rheumatoid arthritis, essential hypertension, and obesity. Her surgical history included two cesarean section deliveries.

FAMILY AND SOCIAL HISTORY

The patient's father had a history of colon cancer. The patient denied any history of autoimmune disease, skin disorders, or other relevant family history. The patient denied tobacco and recreational drug use. She endorsed occasional alcohol use.

MEDICATIONS

Dapsone, etanercept, hydrochlorothiazide, lisinopril, methotrexate, prednisone

PHYSICAL EXAM

On the arms, abdomen, and legs, there were numerous edematous red papules with rims of pallor and red brown patches and thin plaques. There were also faintly purpuric patches on the lower legs.

LABS

Normal: WBC 10.4 (4.8-10.8 K/µL), ANA, ANCA, tryptase 2.5 (<11mcg/L), LDH 205 (140-271 units/L), C3 191 (87-200 mg/dL), Anti-SS-A 2(0-19 u), Anti-SS-B 2 (0-19 u), TSH 1.82 (0.30-5.33 µIU/mL)

Abnormal: ESR 29 (0-20 mm/hr), CRP 14.9 (0-8 mg/L), C4 56 (19-52 mg/dL), absolute neutrophils 8.7 (1.9-8.0 K/µL)

SPEP: M Spike 0.4 g/dL and IgG monoclonal protein with lambda light chain specificity

Bone marrow biopsy: Normocellular marrow, <5% polyclonal plasma cells

DERMATOPATHOLOGY

Histopathology demonstrated a perivascular and interstitial infiltrate composed of numerous neutrophils and histiocytes. There was no significant karyorrhexis or fibrinoid necrosis of the vessels. These findings were noted to be most consistent with urticarial dermatosis including neutrophil-rich urticaria or neutrophilic urticarial dermatosis.

DIAGNOSIS

Schnitzler syndrome

TREATMENT AND COURSE

After the initial diagnosis of Schnitzler syndrome, the patient was co-managed by dermatology and rheumatology. In addition to her therapy for rheumatoid arthritis (methotrexate and etanercept), she was initially treated with dapsone, prednisone, cetirizine, triamcinolone 0.1% cream to the body, and hydrocortisone 1% cream to the face. However, the patient continued to have new lesions, joint pains, night sweats, fevers, progressive muscle weakness, and fatigue. Based on the initial serum protein electrophoresis and bone marrow biopsy results, the patient was diagnosed with a monoclonal gammopathy of unknown significance (MGUS) and continued surveillance with oncology.

Over the following 2 years, the patient received multiple treatments including canakinumab, colchicine, and tocilizumab; however, her symptoms remained uncontrolled requiring frequent and prolonged prednisone tapers. The initiation of rituximab was considered, but prior to starting the medication the patient was referred to Northwestern Dermatology for a second opinion.

At Northwestern Dermatology, the patient had a recalcitrant urticarial rash and repeat skin biopsy again demonstrated urticarial dermatosis with numerous neutrophils and no evidence of immune deposits. She was found to have elevated IL-6 (123 pg/mL, reference < 5 pg/mL) despite treatment with tocilizumab. Given the constellation of findings, the patient was referred to oncology to be reevaluated for concomitant lymphoproliferative disease. Repeat bone marrow biopsy was indicative of a plasma cell neoplasm with 1-2% monotypic lambda-restricted CD38+, CD138+, CD19- plasma cells. The patient is currently being transitioned to therapy with daratumumab and prednisone.

DISCUSSION

Schnitzler syndrome, first described by French dermatologist Liliane Schnitzler in 1972, is a rare acquired autoinflammatory syndrome with ~300 cases reported in the literature. The syndrome is characterized by recurrent, non-pruritic urticarial lesions typically on the trunk and limbs, intermittent fevers, bone pain, arthralgia, increased ESR, and monoclonal gammopathy (typically IgM kappa light chain). Typical age of onset is 50-55 years of age with slight male predominance.

The Strasbourg diagnostic criteria, established by Lipsker et al. in 2001 and revised in 2013, may be used to help differentiate from conditions with overlapping features, including cryopyrin-associated periodic syndrome (CAPS), adult-onset Still's disease, and Waldenström's disease. Obligate criteria include a chronic urticarial rash and a monoclonal IgG or IgM gammopathy, of which both must be met for definite diagnosis. Minor criteria include recurrent fevers, objective findings of abnormal bone remodeling with or without bone pain, neutrophilic dermal infiltrate on skin biopsy, and leukocytosis and/or elevated CRP. For a definite diagnosis, two minor criteria must be met for patients with IgM gammopathy, whereas three must be met for patients with IgG gammopathy.

The pathophysiology of Schnitzer syndrome is not completely understood. Though the syndrome shares many features with CAPS, which is caused by an activating mutation in NLRP3, no somatic or germline variations of NLRP3 were identified by next-generation sequencing in two cohorts of patients with Schnitzler syndrome. IL-1β and IL-6 have been implicated in the pathogenesis of the syndrome in multiple studies, which is underscored by successful treatment of patients by IL-1β blockade. It is theorized that systemic overproduction of IL-1β, possibly by dermal mast cells, results in loss of anti-inflammatory Th17 cell activity leading to the clinical features of the syndrome. Furthermore, IL-6 levels positively correlate with disease activity. The role of IgM paraprotein is unknown. Further research needs to be done to elucidate the pathophysiology of this syndrome.

Treatment of Schnitzler syndrome is typically with IL-1 blockade, such as with anakinra, canakinumab, or rilonacept. The level of complete remission in patients treated with these therapies is ~83% at 36 months. Unfortunately, these medications are not curative, and symptoms will typically reoccur if the patient stops treatment. In refractory patients, anti-IL-6 blockade with tocilizumab can be effective. Prior to the advent of these therapies, other treatments such as colchicine, pefloxacin, interferon-alpha, and corticosteroids were used with less efficacy.

It is imperative to evaluate for and treat concomitant lymphoproliferative disorders. The development of lymphoproliferative disorders in patients with Schnitzler syndrome, most commonly Waldenström's macroglobulinemia, is well described in the literature. In one study, 35 of 281 patients (12%) developed a hematologic malignancy with a median follow up time of 8 years since disease onset. Long term surveillance of these patients is recommended for this reason. In our case, the patient had initially been diagnosed with MGUS. However, her refractory symptoms and recurrent skin lesions suggested an underlying lymphoproliferative disorder rather than MGUS, as MGUS by definition is asymptomatic. For this reason, the patient was referred to a myeloma specialist who repeated a bone marrow biopsy which was consistent with a plasma cell neoplasm, warranting additional treatment.

KEY POINTS

1. Schnitzler syndrome is characterized by recurrent, non-pruritic urticarial lesions, intermittent fevers, bone pain, arthralgia, increased ESR, and monoclonal gammopathy.
2. The syndrome is chronic/recurrent and requires long-term treatment with IL-1 blockade. IL-6 blockade may be used in refractory cases.
3. Patients with Schnitzler syndrome should undergo long term surveillance for lymphoproliferative disorders.

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CHICAGO DERMATOLOGICAL SOCIETY **Case #9**

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HISTORY OF PRESENT ILLNESS

A 53-year-old male with a history of type 2 diabetes mellitus and hyperlipidemia presented with a progressive, diffuse pruritic rash accompanied by muscle pain, weakness, fatigue, and unintentional weight loss. The rash began 9 months ago on his back and had since spread to his chest, abdomen, and arms. He also noted worsening exercise tolerance, thigh muscle pain, night sweats, and a 15-pound weight loss over the past 3 months. He was previously physically active and played volleyball multiple times per week; however, he recently had experienced difficulty even with simple daily activities like standing up from a chair and brushing his teeth.

The patient had started combination pill empagliflozin-linagliptin-metformin and atorvastatin 3 months prior to the onset of his rash but otherwise denied new pharmacologic or environmental exposures. He was initially seen by an outside dermatologist who performed a biopsy which was reportedly nondiagnostic. He was instructed to stop both the combination pill and atorvastatin in case the rash was drug-induced. Despite discontinuing both agents, his cutaneous and systemic symptoms persisted.

PAST MEDICAL AND SURGICAL HISTORY

The patient's past medical history included hyperlipidemia and type 2 diabetes mellitus.

FAMILY AND SOCIAL HISTORY

The patient has three living sisters, all healthy to his knowledge. His mother died suddenly at a young age, but he was unsure of her cause of death. He lives with his wife and three daughters in Chicago and has worked for most of his life as a mechanic. He did not drink alcohol or use illicit drugs; he was previously an occasional smoker but quit smoking the year prior.

MEDICATIONS

None

PHYSICAL EXAM

On the chest, abdomen, back, shoulders, upper and lower extremities, there were numerous erythematous to hyperpigmented smooth, edematous plaques and nodules varying between 1 and 3 cm in size. There was no lymphadenopathy. There was proximal muscle weakness in the hip and shoulder girdles, and he had difficulty standing up from a seated position.

LABS/IMAGING

Normal: Hepatitis panel, Syphilis, HIV, Lyme, TB, ANCA, Autoimmune/paraneoplastic myopathy and myositis-specific antibody panels

Abnormal: AST 434 (0-39 units/L), ALT 586 (0-52 units/L), CK 16,462 (39-308 units/L), Anti-HMGCR Ab > 200 (negative < 20)

CT brain, cervical spine, chest, abdomen, and pelvis: Unremarkable

Right deltoid muscle biopsy: Pauci-cellular necrotizing myopathy with MHC 1 upregulation consistent with immune-mediated necrotizing myopathy

DERMATOPATHOLOGY

Histopathology from the shoulder demonstrated a perivascular and periadnexal superficial and deep dermal lymphocytic dermatitis, consistent with Jessner's lymphocytic infiltrate.

DIAGNOSIS

Jessner's lymphocytic infiltrate related to statin-associated anti-HMGCR immune-mediated necrotizing myopathy

TREATMENT AND COURSE

The patient was treated with intravenous immunoglobulin (IVIG) and systemic steroids with some improvement in his strength and rash prior to discharge home. However, he subsequently developed progressive and recalcitrant myopathy with new dysphagia that continues to persistent despite additional treatment with IVIG, methotrexate, rituximab, and plasmapheresis. He is now being considered for a clinical trial with CAR-T therapy.

DISCUSSION

The immune-mediated necrotizing myopathies (IMNMs) are a group of acquired autoimmune conditions defined by rapidly progressive muscle fiber injury. These disorders have been categorized into three subtypes based on the associated autoantibody present: anti-signal recognition particle (anti-SRP) IMNM, anti-3-hydroxy-3-methylglutaryl-coenzyme A reductase (anti-HMGCR) IMNM, and seronegative IMNM.[1,2] While anti-HMGCR necrotizing myopathy has been linked to statin therapy, anti-HMGCR necrotizing myopathy may occur in statin-naive patients as well.[3-4] Development of statin-naive anti-HMGCR IMNM may be related to diets naturally rich in statin, such as those with mushrooms or red yeast rice, and it has been reported particularly in younger patients and patients of Asian descent.[4]

Anti-HMGCR necrotizing myopathy presents with proximal muscle weakness, elevated creatine kinase, and muscle biopsy with pauci-immune muscle fiber necrosis. The differential diagnosis in these patients may include dermatomyositis and other autoimmune idiopathic myopathies, overlap myositis and connective tissue diseases, sarcoidosis, amyloidosis, and infectious etiologies such as Lyme disease. Skin involvement has been reported in less than 10% of cases of anti-HMGCR IMNM; however, among those with cutaneous manifestations, a dermatomyositis-like eruption is typically noted.[5-10] Rarely, eruptions resembling Jessner's lymphocytic infiltrate or pseudolymphoma have been described.[11] This lymphocytic infiltrate, noted in our patient's cutaneous biopsy, consists of dermal perivascular and periadnexal CD8+ T cells. Jessner's infiltrate can be seen in isolation as well as in a variety of inflammatory skin disorders, including discoid lupus erythematosus, lymphocytic lymphomas, and polymorphous light eruption.

Treatment of anti-HMGCR necrotizing myopathy involves immediate statin discontinuation, if applicable, as well as immunosuppression with systemic steroids. Relapse of muscle disease with steroid weaning is commonly observed, and most patients are treated with additional steroid-sparing agents such as IVIG, methotrexate, cyclophosphamide, azathioprine, cyclosporine, and/or rituximab.[12] A small retrospective study by Landon-Cardinal et al. found improved muscle strength in patients with refractory anti-HMGCR necrotizing myopathy treated with rituximab, though the role of rituximab in these patients remains controversial.[11,13] Despite treatment, prognosis of anti-HMGCR necrotizing myopathy is guarded, with less than half of patients regaining normal muscle strength within 2 years of disease onset, although patients over the age of 60 may have a more favorable outcome with regards to muscle recovery.[11]

KEY POINTS

1. Anti-HMCGR necrotizing myopathy is an idiopathic inflammatory myopathy with rare cutaneous manifestations including dermatomyositis-like eruptions or Jessner's lymphocytic infiltrate.
2. This autoimmune myopathy is associated with current or previous statin use, especially in older adults.

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