PROTOCOL BOOK • DECEMBER 6, 2023

CHICAGO DERMATOLOGICAL SOCIETY 2023

Monthly Meeting

Co-hosted by University of Chicago Department of Dermatology

Chicago Dermatological Society

PROTOCOL BOOK
December 6, 2023

Co-hosted by
University of Chicago Department of Dermatology

Guest Speaker: **Melissa Mauskar, MD**
Department of Dermatology
Department of Obstetrics and Gynecology
UT Southwestern Medical Center

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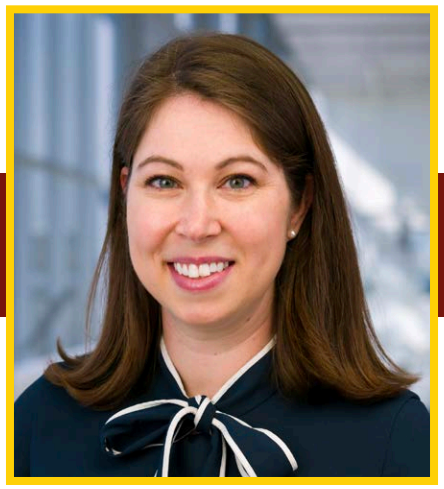
INVITED GUEST LECTURER

Melissa Mauskar, MD



Melissa Mauskar, MD, is an Associate Professor in the Department of Dermatology and the Department of Obstetrics and Gynecology at UT Southwestern Medical Center. Her clinical practice focuses on complex medical dermatology and vulvar dermatoses. She is the founder and Director of the Gynecologic Dermatology Clinic at UT Southwestern, a tertiary referral center for gynecologists, dermatologists, and primary care physicians serving Texas and surrounding states.

Dr. Mauskar earned her medical degree at the University of Texas Health Science Center at San Antonio. She completed her residency in dermatology at Georgetown University Hospital and MedStar Washington Hospital Center and is certified by the American Board of Dermatology. She is a fellow of the International Society for the Study of Vulvovaginal Disease (ISSVD) and serves on the Board of Directors for the North American Chapter of the ISSVD.

Dr. Mauskar began her tenure at UT Southwestern as a member of the Dermatology Inpatient Consultation team, specializing in treating patients with severe cutaneous drug eruptions. Most of Dr. Mauskar's clinical practice now focuses on Vulvar dermatology and women's health. She lectures worldwide on vulvar dermatoses and is passionate about educational initiatives to improve the recognition, diagnosis, and treatment of patients with vulvar conditions. In addition to inspiring dermatologists and gynecologists to champion women's health, she aims to collaborate with colleagues and improve clinical research initiatives for women with lichen sclerosus. The Dermatology Foundation has funded her research, and she is a co-founder of the Vulvar Dermatoses Research Consortium.

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PROGRAM

Co-hosted by
University of Chicago Department of Dermatology

December 6, 2023
University of Chicago Gleacher 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** *CDS President, Dr. Morayo Adisa*
9:00 a.m. - 10:00 a.m.	**Morning Lecture** The Mauskar Collection *Dr. Melissa Mauskar*
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, MOC**
12:00 p.m. - 12:30 p.m.	**Boxed 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** Vulvar Dermatoses - Lessons Learned *Dr. Melissa Mauskar*
2:00 p.m.	*Program adjourns*

AT THE FOREFRONT
UChicago Medicine

University of Chicago Department of Dermatology

Chicago Dermatological Society Meeting
December 6, 2023

Dermatology Residents

Third Year
Brooke Cui, MD
Ekene Ezenwa, MD
Umar Sheikh, MD

Second Year
Gaurav Agnihotri, MD
Colton Funkhouser, MD
Liesl Schroedl, MD
Sarah Semaan, MD

First Year
Kelsey Gradwohl, MD
Victoria Lee, MD, PhD
Mina-Abena Maranga, MD, MSc

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Resident Case Presentations & Discussion

PRESENTERS
Victoria Lee MD, PhD; Christopher R. Shea MD; Oluwakemi Onajin MD

HISTORY OF PRESENT ILLNESS
A 44-year-old female with a twenty-year history of hidradenitis suppurativa (HS) Hurley stage 3 and rheumatoid arthritis presented to our dermatology clinic for evaluation. She reported active flares in the groin, abdominal fold, intergluteal cleft, and buttocks. Her treatment regimen for HS at that time included silver sulfadiazine cream, clindamycin gel, and chlorhexidine gluconate 4% wash.

Prior medical therapies for HS included topical silver sulfadiazine, oral antibiotics (sulfamethoxazole trimethoprim, clindamycin, rifampin), and biologics (infliximab, adalimumab, etanercept). Excision of sinus tracts in her bilateral axillae 15 years ago healed well without recurrence. She underwent surgical excisions of sinus tracts in the groin and buttocks on two separate occasions, one 8 years prior then again 1 year ago, but the scattered papules persisted in the groin area.

The patient reported that she was previously on weekly adalimumab therapy for rheumatoid arthritis, and had noted some improvement in the HS, but she had been off therapy for one year. The patient denied a history of diabetes, inflammatory bowel diseases, irregular menses or acne. She was not on any oral contraceptive medications. She reported that her flares of HS did not coincide with her menses.

PAST MEDICAL HISTORY
Hidradenitis suppurativa (Hurley stage III), rheumatoid arthritis on chronic low-dose prednisone, hypertension, anemia and chronic hematochezia, obesity with BMI ~50 kg/m^2

FAMILY HISTORY
No pertinent family history

SOCIAL HISTORY
Former smoker who quit 8 years ago

MEDICATIONS
Prednisone 10mg PO daily, hydrochlorothiazide 12.5 mg PO daily

ALLERGIES
No known drug allergies

PHYSICAL EXAMINATION
Physical examination revealed multiple erythematous papulonodules, interconnect sinus tracts, and hypertrophic scarring near the labia majora and mons pubis with scattered papillomatous pearly-pink to brown papules and plaques.

DERMATOPATHOLOGY
Histopathologic analysis of a shave biopsy specimen taken from a pearly-pink papule near the mons pubis demonstrated widely dilated lymphatic vessels in the dermis, consistent with acquired lymphangioma circumscriptum of the vulva.

DIAGNOSIS
Acquired lymphangioma circumscriptum of the vulva in a patient with hidradenitis suppurativa

TREATMENT & COURSE

The patient deferred treatment for acquired lymphangioma circumscriptum since she was asymptomatic. She remained asymptomatic at subsequent clinic visits. She was encouraged to follow up with her gynecologist for annual examination and pap smear.

For her HS, she was restarted on adalimumab therapy with maintenance dose 40mg weekly, topical clindamycin gel, daily chlorhexidine gluconate 4% wash, and wound care. In the interim prior to starting adalimumab therapy, the patient was treated with oral clindamycin 300mg twice daily and oral rifampin 300mg every 12 hours.

Two months later, the patient developed a severe flare of hidradenitis suppurativa and rheumatoid arthritis while on adalimumab therapy, requiring an admission to the hospital. At her follow-up appointment with dermatology four months later, she was switched from adalimumab to infliximab therapy with maintenance dose 5mg/kg every 8 weeks. She was also started on weekly methotrexate 7.5mg to reduce the risk of developing human antichimeric antibody and resistance to infliximab. The plan was to increase the dose of infliximab to 10mg/kg every 4 weeks, but the patient was lost to follow-up.

DISCUSSION

Lymphangioma circumscriptum is a rare benign disorder that consists of dilated superficial lymphatic channels or large cysts filled with lymphatic fluid. This condition is classified into congenital and acquired forms. Congenital lymphangioma circumscriptum occurs as a result of developmental malformations of local sequestrated lymphatic cisterns in the reticular dermis, forming abnormal connections and dilated channels to the superficial lymphatics.[1] While the etiology of acquired lymphangioma circumscriptum (ALC) is not fully understood, it is proposed that an architectural disruption of previously normal lymphatic channels leads to lymphatic obstruction, thus triggering a compensatory sequestration and saccular dilatation of the thin superficial lymphatics.[1]

Clinically, the dilated superficial lymphatic channels manifest as clustered or diffuse translucent-to-red vesicle-like papules that sometimes ooze clear or bloody fluid.[2] In addition, ALC lesions may develop hyperkeratosis over time, leading to a verrucous appearance.[2] Their variable presentation poses a diagnostic challenge and misdiagnosis is common. The differential diagnosis often includes herpes simplex virus infection, verruca vulgaris, condyloma acuminata, molluscum contagiosum, irritant or allergic contact dermatitis, and soft-tissue neoplasms including leiomyomas, cellular angiofibromas, angiomyofibroblastomas, angiomyxomas, or non-melanoma skin cancers.[3,4] Furthermore, the differential diagnosis of neoplasms in regions affected by HS include keloids and granulation tissue, in addition to lymphangioma circumscriptum. Lastly, it is important to rule-out squamous cell carcinomas in long-standing HS.

Definitive diagnosis is made via skin biopsy and histopathological examination, which demonstrates numerous dilated thin-walled lymphatic channels in the superficial dermis with possible expansion of narrow lumen vessels to the reticular dermis and subcutaneous tissue.[5] Associated acanthosis, overlying hyperkeratosis, and the presence of capillary tufts, has been reported. Immunohistochemical staining of lymphatic markers, such as lymphatic endothelial receptor 1, vascular endothelial growth factor C, and D2-40 can differentiate lymphatic channels from blood vessels.[5,6] Extravasation of white or red blood cells may be seen in lymphatic channels.[5]

While ALC can occur anywhere in the body (most often cited sites involve the chest, thighs, and buttocks), ALC of the vulva (ALV) is rare.[3,7] As a result, the diagnosis of ALV may be underreported as it is often not considered in the initial differential. ALV has been associated with various predisposing conditions, including surgery or radiation therapy for cervical and endometrial neoplasms, genital tuberculosis, and Crohn's disease with vulvar or peritoneal fistulae formation.[3,8] Though ALV has been reported in the context of patients who carry a diagnosis of HS, these are reported with much less frequency.[3] In the case of our patient, it is possible that the chronic development of inflammatory nodules, sinus tracts, and scarring in the vulvar and groin areas due to extensive HS disease created an environment conducive to disruption and obstruction of the underlying lymphatic architecture. In addition, the patient underwent multiple prior excisions for HS in the vulvar and groin area, which may have led to damage and obstruction of underlying lymphatic structures. Both of these processes may have contributed to the development of ALV in this patient. Similarly to our patient, in rare case reports of HS-associated ALV, the labia majora was the most common site involved, and several patients had undergone surgical excisions of sinus tracts years prior to the diagnosis of ALV.[9-11] Interestingly, cases of ALV associated with HS were more likely to have severe, treatment-resistant forms of HS, some of which required surgical intervention.[9,11]

To date, while there are no current treatment guidelines for ALV, wide local surgical excision remains the treatment of choice, should treatment be desired.[12,13] Of note, surgical excision requires the removal of the deep-feeding lymphatic cisterns to prevent recurrence of the disease.[13,14] Despite this, recurrence is common and patients often require re-excision.[5,6,8] Depending on the extent of disease and patient preference, other treatment options include conservative management by observation and close follow-up, abrasive modalities such as carbon dioxide and Nd:YAG laser therapy, cryotherapy, electrocoagulation, sclerotherapy, superficial radiotherapy, and pulsed dye laser therapy or intense pulsed light therapy for smaller superficial cutaneous blebs.[2-5,7,10,15] It is important to note that recurrence rate is high with all therapeutic modalities.[5] Eroded lesions should be monitored for the development of secondary infections.[7] Additionally, while malignant transformation is very rare, few cases of lymphangiosarcoma have been reported to arise at the site of preexisting lymphangioma circumscriptum, usually in relation to local radiotherapy.[7] Lastly, it is important to note that special considerations should be undertaken when treating patients with darker skin tones, as hypopigmentation is more frequent and prominent following cryotherapy in these patients, as well as scarring and dyspigmentation following any form of laser therapy or sclerotherapy.

We present this case to emphasize that early recognition and management of both genital and extragenital HS may reduce the likelihood of potentially severe and debilitating sequelae from chronic lymphatic obstruction. In addition, this case highlights the diagnostic challenge of identifying and managing patients with a coexistence of ALV within affected areas of HS in the anogenital region. Clinicians must maintain a high index of suspicion for ALV when evaluating patients with HS in the anogenital region, as the characteristic vesicle-like or sometimes verrucous papules of ALV may be overshadowed by the more prominent nodules, abscesses, and sinus tracts of HS. Managing the coexistence of HS and ALV in the anogenital region requires a comprehensive and multidisciplinary approach. The primary goal of treatment is to alleviate symptoms, improve quality of life, and minimize recurrence. The aesthetic appearance and psychosexual implications of ALV are also important factors to consider.[8] It is essential for clinicians to weigh the risks and benefits of each treatment modality carefully, considering the impact on both HS, ALV, and skin of color. There remains a need for further research into the mechanism, risk factors, and treatment of ALV in the setting of HS.

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PRESENTERS
Ekene Ezenwa MD; Christopher R. Shea; Mark D. Hoffman, MD

HISTORY OF PRESENT ILLNESS
A 43-year-old woman with a history of pruritic rashes of the face, hands, and torso ongoing for two years presented with worsening skin disease, including newer involvement of the eyelids and scalp. There were now associated fatigue, proximal muscle weakness, and joint stiffness. She had a history of ductal breast carcinoma that had been diagnosed two years earlier - with regional lymph node metastases at presentation and mediastinal lymph node metastases occurring a year later - which had been treated with chemotherapy and radiation therapy, resulting in largely stable non-progressive disease that was being managed palliatively.

This clinical history, laboratory work, punch biopsy findings, and imaging were consistent with a diagnosis of dermatomyositis. Treatment was initiated with hydroxychloroquine 200 mg daily (approximately 5 mg/kg/day), but after two weeks she developed a morbilliform (presumably drug-induced) eruption of the torso and extremities leading to its discontinuation. Topical agents including corticosteroids, tacrolimus, and ruxolitinib had negligible effects. Prednisone was administered at 1 mg/kg/day, which ameliorated the skin manifestations, but cutaneous signs and symptoms remained severe and extracutaneous disease was progressive. IVIG dosed at 2 g/kg monthly was initiated, and after 5 cycles muscle symptoms had improved, but there was little change in the skin lesions and only modest improvement in the pruritus. Anifrolumab 300 mg monthly was then begun (and IVIG discontinued), chosen based on its rapid effect when used for cutaneous lupus, and its promising safety data.

PAST MEDICAL HISTORY
Invasive ductal breast carcinoma with metastasis to the mediastinal lymph nodes s/p chemotherapy and radiation therapy, on palliative radiotherapy
Ulcerative colitis not on systemic therapies

MEDICATIONS
Albuterol inhaler PRN
Metoprolol 25mg daily
Omeprazole 40mg daily
Tetrahydrocannabinol (THC) edibles qHS

ALLERGIES
Sulfonamides

PHYSICAL EXAMINATION
Violaceous patches and plaques: on the face, including a heliotrope discoloration of the eyelids; on the fingers, with Gottron papules; and on the chest, back, lateral hips and thighs.

LABORATORY RESULTS

Laboratory Study	Patient Result	Reference Range
CPK	202 U/L	9 – 185 U/L
Aldolase	7.2 U/L	2 - 8 U/L
ANA	1:160, speckled pattern	1:80
Anti-RNP	1.2	<1.0
Myomarker TIF-1γ:	34 U	<20 U

IMAGING

Magnetic Resonance Imaging, Left and Right Femurs

Mild edema-like signal with postcontrast enhancement involving the right quadratus femoris and left abductor muscles.

DERMATOPATHOLOGY

Histopathologic analysis of punch biopsy specimens from the right hand and right scapula showed an atrophic epidermis with focal basal vacuolization. The dermis had a superficial and deep perivascular and periadnexal infiltrate of lymphocytes and plasma cells, with increased mucin.

DIAGNOSIS

Refractory Paraneoplastic Dermatomyositis Responsive to Anifrolumab

TREATMENT & COURSE

Anifrolumab administration resulted in marked skin improvement of the torso that was apparent after the first injection, and it was continued for an additional three monthly doses leading to near-clearing of the facial and trunk activity. She also noted reduced pruritus and improved myalgias, as the patient could now ambulate easily. At that time, imaging identified progressive metastatic hepatic, osseous, and lymph node disease and chemotherapy was then reinstituted, and the decision was made to pause treatment with anifrolumab during chemotherapy. Skin disease remained under excellent control for 2 months after the last anifrolumab injection, at which point the face, scalp, neck, and chest flared with an eruption similar to the patient's initial presentation, which resolved approximately 1 week after anifrolumab reinstitution.

DISCUSSION

Dermatomyositis (DM) is a connective tissue disorder with dermatologic and/or extracutaneous manifestations. Although DM primarily affects skin and muscle, it can also affect other organs such as the lungs, and may be associated with malignancy. Various treatments are deployed in DM management, but their effects are inconsistent. Skin disease can be refractory to therapy, even when other involved organ systems are responsive. Interferons (IFNs) are believed to play a role in driving DM disease activity, and medications targeting IFN pathways are both available and under development.

Treatments for DM can include topical, oral, and intravenous medications. The selection of specific agents depends on an individual patient's disease activity, co-morbidities, and risk tolerance[1,2].

Newer targeted therapies continue to develop as more is discovered about DM-associated inflammatory pathways. IFNs are a family of cytokines theorized to play a role in driving DM disease activity. To date, there are three known groups of human IFNs: type I including numerous IFNαs as well as IFNβ, IFNε, IFNκ, and IFNω, all of which bind to the same receptor complex having IFN-αR1 (aka IFNAR1) and IFNAR2 components; type II, whose single member is IFNγ; and type III, comprising several IFNλs[3]. Serologic and gene expression studies have found a positive correlation between levels of IFNβ and DM disease and its activity[4,5]. These findings collectively support the notion that aberrant IFNβ signaling is involved in the pathophysiology of DM.

We report an individual with DM whose IVIG-refractory skin disease responded to the IFNAR1-blocking antibody anifrolumab. Anifrolumab was first approved in 2021 for the treatment of moderate to severe systemic lupus erythematosus (SLE)[6], and may result in rapid cutaneous improvement in SLE, reported as quickly as 4 weeks following initiation in refractory cases[7].

Moreover, the safety profile has shown comparable rates of serious opportunistic infection and malignancy relative to placebo[8]. SLE and DM share several features including their involvement of the skin and potential for extracutaneous manifestations, and both diseases have been linked to dysregulation primarily assigned to type I IFN pathways[5]. In contrast to DM and the role imputed to IFNβ, the pathophysiology of SLE is more closely tied to IFNα[9]. Though different IFNs have been implicated in these two diseases, they act through a common receptor. Accordingly, anifrolumab may have applications in the management of recalcitrant DM.

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PRESENTERS
Abby Maranga, MD, MSc; Arlene Ruiz de Luzuriaga, MD, MPH, MBA; Amy Xu, MD, MA

HISTORY OF PRESENT ILLNESS
A 30-year-old female with a history of polycystic ovarian syndrome (PCOS) presented to the University of Chicago Dermatology clinic for evaluation of facial lesions that had been present for years. Her most recent flare had begun a year prior as closed comedones and pruritic pustules. The lesions were limited to her face and had been managed as acne without success. At the time she was using over-the-counter acne washes, moisturizers, and combination benzoyl peroxide and clindamycin gel. She had also been on spironolactone for several years for PCOS before self-discontinuing. At a prior dermatology visit, she had been prescribed ketoconazole 2% cream for possible pityrosporum folliculitis; however, use led to worsening of her facial lesions. She thus presented to the clinic for further management.

PAST MEDICAL HISTORY
Polycystic ovarian syndrome

PAST SURGICAL HISTORY
None.

FAMILY HISTORY
No pertinent family history.

SOCIAL HISTORY
Denies tobacco or recreational drug use.

MEDICATIONS
Spironolactone 50mg daily, clindamycin and benzoyl peroxide 1/5% gel daily, ketoconazole 2% cream daily

ALLERGIES
None

PHYSICAL EXAM
Multiple pink edematous papules and pustules on bilateral cheeks, jawline, and postauricular neck

LABORATORY RESULTS
HIV Ab/Ag: Negative

IMAGING
n/a

DERMATOPATHOLOGY

Histopathological analysis of a punch biopsy from the left jawline demonstrated follicular mucinosis, numerous intrafollicular eosinophils, and few neutrophils with a mixed perifollicular inflammatory infiltrate. There was no significant cytologic atypia and the methenamine silver stain was negative for fungi.

DIAGNOSIS

Eosinophilic pustular folliculitis (Ofuji's disease)

TREATMENT & COURSE

The patient was empirically started on hydrocortisone 2.5% ointment daily and with some interval improvement. After receiving biopsy results she was started on indomethacin 500mg daily and switched from hydrocortisone to tacrolimus 0.1% ointment daily with marked improvement at her three month follow-up visit.

DISCUSSION

Eosinophilic pustular folliculitis (EPF) was first described by Drs. Seiichi Ise and Shiego Ofuji in a middle-aged woman with recurring small pustular lesions on the face, trunk, and upper extremities without systemic symptoms. It was initially thought to be a follicular variant of subcorneal pustular dermatosis; however, histology of subsequent cases consistently demonstrated a mixed inflammatory infiltrate with eosinophils localized to the hair follicles, and the condition was distinguished as a separate entity. EPF classically presents as edematous papulopustules on the face, trunk, and extensor surfaces of the arms, but lesions have also been described on the acral surface of hands and feet. These lesions tend to appear in clusters and often coalesce to form larger, edematous, erythematous plaques. The lesions can be intensely pruritic, and the disease course is often chronic and relapsing. Due to the morphologic similarities to other disorders, EPF is frequently misdiagnosed on clinical assessment, and case series have reported initial diagnoses of acne, eczema, cellulitis, folliculitis, urticaria, seborrheic dermatitis, and other infiltrative and/or papulopustular disorders.

There are several variants of the disease that have been identified in the literature, the most common being immunosuppression-associated EPF typically associated with HIV infection. Other variants include infancy-associated EPF which appears in immunocompetent children under the age of 1 years old but typically presents exclusively on the scalp. Less common variants involve immunogenic triggers, such as cancer-associated EPF and medication-associated EPF. The variant seen among immunocompetent adults without significant past medical history or comorbid conditions is a rare form known as classic EPF, and eponymously referred to as Ofuji disease. Classic EPF is mainly seen in individuals of East Asian descent; however, there are case reports of the condition described in individuals of other ethinic backgrounds.

Histologically, EPF is differentiated from other conditions by the presence of infundibular eosinophilic pustules; epidermal and dermal inflammatory infiltrates with eosinophils and lymphocytes can also be observed in these lesions. Although peripheral eosinophilia was observed in most of the classic cases identified by Ofuji et al, it is not always present. To date, its etiology remains unknown; it is hypothesized that prostaglandin D2 plays a role in EPF by causing sebocytes to produce eotaxin-3, which leads to infiltration of eosinophils around the pilosebaceous unit.

There are a variety of treatments that have been used for EPF. All variants respond to topical or oral corticosteroids, which was the mainstay of treatment for several years to varying degrees. Other common medications used for EPF included tacrolimus, pimecrolimus, antibiotics, antifungals, NSAIDs, cyclosporin, UV radiation, and retinoids. A review comparing various treatment regimens for all variants of EPF found that 84% of cases of classic EPF had a partial or complete response to systemic or topical indomethacin, compared to 40% of cases treated with topical steroids and 75% of cases treated with systemic steroids. The effectiveness of indomethacin, a cyclooxygenase inhibitor, in treating EPF is likely related to reducing production of prostaglandins. The review found that efficacy differed by EPF variant – immunosuppression-associated EPF was less responsive to indomethacin and more responsive to topical tacrolimus, systemic retinoids, and UV therapy, while infancy-associated EPF was responsive to topical tacrolimus and systemic antibiotics.

We present this case to highlight a rare diagnosis in an immunocompetent patient that can masquerade as the common clinical complaint of acne.

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PRESENTERS
Liesl Schroedl, MD, Adena Rosenblatt, MD, PhD, Sarah Stein, MD

HISTORY OF PRESENT ILLNESS
A one-day-old male infant born at 29 weeks 6 days' gestation via spontaneous vaginal delivery was transferred to Comer Children's Hospital for management of absence of skin affecting 40-50% body surface area. At delivery, the infant's APGARs were 7 and 8 at 1 and 5 minutes, respectively. Upon arrival he was noted to exhibit increased work of breathing with retractions. He failed noninvasive mechanical ventilation and was intubated. Once hemodynamically stable, dermatology was consulted for diffuse absence of skin.

BIRTH HISTORY
The patient's mother had received prenatal care in the United Arab Emirates, where she resided. She was visiting her husband, who lives in Illinois, at the time of delivery. There were no reported prenatal complications. The mother had negative HIV and syphilis serologies, but her GBS, hepatitis B, gonorrhea, and chlamydia status remained unknown.
Consequently, she had received one dose of ampicillin prior to delivery; she also received a dose of betamethasone for fetal lung maturation.

FAMILY HISTORY
There was no known family history of genetic or dermatologic conditions and no known history of consanguinity.

SOCIAL HISTORY
The patient's mother reported no alcohol, tobacco, or illicit drug use.

MEDICATIONS
None prior to admission.

ALLERGIES
None.

PHYSICAL EXAM
The infant was ill-appearing, intubated, and sedated with an umbilical venous catheter in place. Micrognathia, broad nasal root, and bilateral hypoplastic ears were noted, with right external ear structures significantly smaller and more rudimentary than the left. Scalp examination revealed normal hair shaft density without evidence of erosion or atrophic plaque. Oral and genital mucosae were intact. Bilateral cheeks and temples exhibited well-demarcated translucent moist deeply eroded plaques. Bilateral upper extremities, chest, and abdomen demonstrated scattered discrete erythematous oval-shaped deep erosions. Bilateral lower extremities from anterior knees and shins extending to dorsal and medial aspects of the feet demonstrated translucent moist deeply eroded plaques. No nail abnormalities were observed.

LABORATORY DATA

WBC (on admission): 3.0 4.0-11.0k/µl)
Platelets (on admission): 146 (150-450k/µl)
Blood culture (obtained on hospital day 10): Positive for *Enterococcus faecalis*
Microarray (obtained on admission): Normal
Chromosomal analysis (obtained on admission): Normal
Epidermolysis bullosa genetic panel: Homozygosity for variant in *ITGB4* gene, c.2114-1 G>A

IMAGING

Chest X-ray performed on admission
Diffuse bilateral pulmonary haziness. No evidence of bowel obstruction or necrotizing enterocolitis.

Pediatric Abdominal Ultrasound performed on hospital day six
Ascites and abnormal appearance of stomach and bowel wall with increased wall thickening and echogenicity and may be secondary to inflammation.

Abdominal X-ray performed on hospital day eight
Three mild to moderately dilated bowel loops are in the lower central abdomen. No pneumatosis, pneumoperitoneum, or portal venous gas.

DIAGNOSIS

ITGB4-related junctional epidermolysis bullosa with congenital absence of skin, pyloric atresia spectrum; homozygous pathogenic *ITGB4* variant, c.2114-1 G>A.

COURSE

The patient was managed according to anti-shear protocol including avoidance of all adhesives. Liberal use of petroleum jelly covered with Mepilex followed by Kerlix wraps and overlying stockinette dressings were maintained. Bullae greater than one centimeter were drained with sterile 21-gauge needle. Fluid, nutritional, and temperature status were monitored closely and repletion was performed as necessary to address insensible losses. On hospital day eight, the patient's respiratory status had improved, so he was extubated; however, he was observed to have increasing abdominal distension. It was noted that he had one bowel movement shortly after birth, but had not had another subsequently. Abdominal x-ray at that time showed abnormal bowel gas pattern with moderately dilated loops of bowel, but there was no evidence of gastric distension or "single bubble" sign to suggest the presence of pyloric atresia. Subsequently, a nasogastric tube was placed for decompression and was removed several days later due to diminishing output and return of bowel movements. Despite this, his abdominal distension progressed, and he was found to have *E. faecalis* bacteremia on hospital day ten. Emergency exploratory laparotomy was performed due to concern for necrotizing enterocolitis, revealing an intraabdominal abscess. His bacteremia persisted despite drainage of the abscess and continued antibiotic and antifungal therapy. Eventually, the decision was made by the patient's parents to pursue palliative care. The patient received appropriate medication for comfort and control of pain and passed away on day of life fifteen.

DISCUSSION

Epidermolysis bullosa (EB) is a clinically heterogeneous genetic disorder resulting in skin fragility and bulla formation with minor trauma. According to a recent consensus reclassification, there are four main classical types of EB (simplex, junctional, dystrophic, and Kindler), which are delineated on the basis of location of epidermal or dermal cleavage.[1] Congenital absence of skin (CAS), also referred to as aplasia cutis congenita, has been associated with EB in rare cases.[2] Bart et. al first described congenital absence of skin associated with epidermolysis bullosa and nail abnormalities in five generations of one family in 1966;[3] this constellation of features therefore came to be known as Bart's syndrome. While this eponym is no longer in use, cases of EB with concomitant CAS have been increasingly recognized in recent years. Clinically, EB with CAS tends to present with erosion or ulceration on the lower extremities which is often bilateral. Involvement of upper extremities, trunk, head, neck, and genitalia has also been reported, albeit with lower frequency. Anonychia or nail dystrophy can also be present; one review found nail abnormalities were present in roughly one-third of patients with EB with CAS.[8] Extracutaneous features observed in patients with EB with CAS include pyloric atresia, external ear deformities, and skeletal deformities. Diagnosis involves a combination of clinical and genetic data. Management involves local wound care and protective dressings. In some cases, skin grafting or debridement may be performed.[4]

EB with CAS has been noted in association with all four types of EB in the setting of both dominant and recessive inheritance patterns. The majority of cases of EB with CAS have been associated with dystrophic EB and thereby collagen VII mutations. EB with CAS has also been reported in junctional EB and EB simplex.[4] The most cases of CAS associated with junctional EB were found to have mutations in integrin subunit beta 4, integrin subunit alpha 6, or less commonly, laminin-332. EB simplex-associated CAS has occurred in patients with mutations in keratin 5, keratin 14, plectin, and kelch-like protein 24.[5] Several theories have been posited regarding the pathophysiology of EB with CAS. One hypothesis is that friction from movement in utero contributes to bulla formation and subsequent CAS at birth.[4] Chiaverini et al. found that, in patients with dystrophic EB, a glycine substitution in collagen VII creates a thermolabile version of the protein which becomes unstable in warmer body regions, including the legs when friction from rubbing occurs.[6] Another group postulated that CAS may follow lines of Blaschko.[7] To date, the exact mechanism underlying CAS in EB remains to be elucidated.

Junctional EB with pyloric atresia presenting with CAS is a rare phenomenon. Caused by mutations in *ITGA6* and *ITGB4,* which encode a structural transmembrane polypeptide*,* junctional EB with pyloric atresia in and of itself is rare. It is less common than junctional EB-intermediate and junctional EB-severe subtypes due to variants in laminin-332 or collagen XVII, and it confers a more severe phenotype than these other forms. Junctional EB with pyloric atresia has been associated with higher frequency of CAS as compared to other forms of junctional EB. It has also been associated with more widespread, extensive CAS and overall poor prognosis relative to other forms of junctional EB.[5] One study found that 50% of patients with junctional EB-pyloric atresia and CAS died within the first year of life.[8] Another retrospective analysis revealed that

the majority of patients with junctional EB with pyloric atresia and CAS possessed an *ITGB4* variant resulting in premature termination codons, a proposed explanation for the severe phenotype observed in this particular form of EB.[5]

Our case expands the small but growing literature-reported inventory of cases of junctional EB with pyloric atresia presenting with CAS; only about 100 cases have been described thus far.[5] This case encompasses several classic features of this rare condition, including bilateral lower extremity absence of skin, external ear abnormalities, and high mortality. While ultimately genetic testing was consistent with the phenotype associated with pyloric atresia, the myriad concomitant gastrointestinal pathologies and lack of typical pyloric atresia imaging findings made it difficult to confirm this feature. Our case as well as those reported in the literature illustrate that comprehensive genetic evaluation proves crucial for diagnosis and prognostication in patients with EB with CAS. If performed early, this information can help to guide counseling of family members and clinical management.

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PRESENTERS
Umar Sheikh, MD; Christopher Shea, MD; Angad Chadha, MD

HISTORY OF PRESENT ILLNESS
A 50-year-old female presented to the University of Chicago Emergency Room with two days of right hand swelling, pain, and ulceration after cutting herself with a knife while cooking. She was found to have elevated inflammatory markers and an elevated blood glucose to the 500's. She was admitted for further workup. The patient was febrile to a Tmax of 39.7C (103.5F), had a leukocytosis to a peak WBC of 43.1 $x10^9$ per L and tachycardia to a peak of 135 BPM. The patient was repeatedly taken to the operating room by orthopedic surgery for debridement; multiple sets of tissue cultures were negative. Five days later, despite adequate antibiotic coverage (empiric vancomycin, cefepime, metronidazole) the patient continued to be febrile with had a persistent leukemoid reaction and persistent tachycardia.

Dermatology was consulted for possible alternate diagnoses and recommended a wedge biopsy of the edge of the ulcer on the third finger down to bone while the patient was in the operating room with orthopedic surgery.

The patient notably had no personal history of hematologic malignancy, rheumatologic or autoimmune disease or inflammatory bowel disease.

PAST MEDICAL HISTORY
Type 2 Diabetes Mellitus, Diabetic Retinopathy, Hypertension

FAMILY HISTORY
Family history of asthma in sister

SOCIAL HISTORY
Lives at home with daughter

MEDICATIONS
Insulin

ALLERGIES
No Known Drug Allergies

PHYSICAL EXAMINATION
Right hand with diffuse edema and palmar surface with large ulcerated plaque from mid-palm extending to proximal fingers 2-5. Edges of ulcer with violaceous discoloration.

LABORATORY RESULTS AT PEAK PRESENTATION

Peak WBC 43.1 $x10^9$ per L	(4.5-11.0 x 109 per L)
Peak Tachycardia 135 BPM	(60-100 BPM)
Tmax 39.7ºC	(36.1C- 37.2C)
C-Reactive Protein 356 mg/L	(<5 mg/L)
Erythrocyte Sedimentation Rate 120 mm/HR	(1-41 mm/HR)

Negative blood cultures

Negative tissue cultures on hospital day 4, 6, and 7

IMAGING

MRI Right Hand

Impression: Extensive soft tissue infection/cellulitis as above with fluid collection/abscess dorsal to the second metacarpal extending into the soft tissue crease between the second and third metacarpals. No findings of osteomyelitis

MRI Right Forearm

Impression: Extension of soft tissue edema proximally, including the superficial and deep fascia of the forearm, with some reactive muscle edema. However, there is no abscess or underlying osteomyelitis.

DERMATOPATHOLOGY

Middle finger skin wedge biopsy: Neutrophilic dermatitis with ulcer – The biopsy shows a dense neutrophilic infiltrate in the dermis and subcutis

Palmar skin biopsy: Neutrophilic dermatitis and panniculitis with ulcer – The dense neutrophilic infiltrate with basophilic strands in the deep dermis extends throughout the fat lobules. There is fibrin deposition within the blood vessels.

DIAGNOSIS

Necrotizing Neutrophilic Dermatosis

TREATMENT & COURSE

The patient's ulcer was consistent with necrotizing neutrophilic dermatitis (NND) in light of biopsy findings with a dense neutrophilic infiltrate in the deep dermis along with negative tissue cultures, fevers, leukocytosis and tachycardia. The patient was started on prednisone 60mg daily with rapid improvement in her physiologic parameters within 24 hours. The patient was continued on a prednisone taper and mycophenolate mofetil was added on discharge from the hospital. The patient was unable to tolerate mycophenolate mofetil due to side effects of diarrhea and was transitioned to infliximab 5mg/kg in the outpatient setting. After stabilization of the NND, the patient's third finger necessitated eventual amputation due to necrosis resulting from the NND as well as surgical interventions . The patient was unfortunately also unable to tolerate infliximab for more than a month due to worsening dyspnea on exertion. The patient was continued on a prednisone taper alone along with rigorous wound care. The ulcer healed up by six months after diagnosis and the patient was able to wean off all immunosuppressive medications without recurrence of the NND.

DISCUSSION

Neutrophilic dermatoses are a group of inflammatory skin disorders of uncertain etiology defined by necrotizing, pathologic, and sterile neutrophilic inflammation of the skin and subcutis. The diagnostic entity of neutrophilic dermatosis has two prototypical examples: pyoderma gangrenosum (PG) and Sweet syndrome (SS; acute febrile neutrophilic dermatosis). PG is classically a painful, progressive, cribiform ulcer while SS features tender, infiltrative, edematous, almost cellulitis-like plaques(s) with or without pustule and bulla formation.

The term necrotizing neutrophilic dermatosis (NND) has been used to describe form of neutrophilic dermatoses that mimic features of necrotizing fasciitis, a rapidly progressing soft tissue infection that often leads to rapid clinical deterioration. In NND, the classic cutaneous

features of neutrophilic dermatoses are present but are usually much more robust and are accompanied by signs of severe infection including sepsis parameters, hypotension or shock, and severe leukemoid reactions. Given the clinical overlap with necrotizing soft tissue infection, misdiagnosis is common and can lead to medical and surgical morbidity for patients. A multi-institutional study reported that in patients presenting with NND, debridement was performed in 78% of patients, antibiotics were administered in 91%, and limb amputations were performed in 7% with many of these interventions being unnecessary. [3]

Sweet's Syndrome has well-defined diagnostic criteria that may overlap clinically with Necrotizing Neutrophilic Dermatosis Criteria. Diagnostic criteria for Sweet's Syndrome include a sudden onset of tender, erythematous plaques or nodules as well as a dense neutrophilic infiltrate in the upper dermis, fever, a rapid response to systemic corticosteroids as well a strong association with underlying malignancy, inflammatory disease, pregnancy, or preceding infection or vaccination. [1] Necrotizing neutrophilic dermatoses on the other hand present with systemic symptoms that are typically not seen in classic Sweet syndrome, including fever, hypotension or shock, and severe leukemoid reactions. The neutrophilic infiltration can be deeper, involving the dermis, subcutaneous fat, and even the fascia and skeletal muscle. [3]

Sanchez et al. has proposed a set of diagnostic criteria to assist with the differentiation of NND from necrotizing fasciitis. Clinically this includes the presence of erythematous or ulcerative plaques with violaceous borders; multisystem involvement resembling shock with fevers and lack of identifiable infectious source; and lack of crepitus. Histopathologic features include neutrophilic infiltration and necrosis involving the fascia and/or muscle. Treatment course includes a lack of clinical improvement or worsening in clinical picture seen with antibiotics or surgical intervention as well as a rapid response to systemic steroids. Lastly a presence of other known comorbidity or associations including malignancies, hematologic disorders, inflammatory bowel disease or history of pathergy, are also features supportive of necrotizing neutrophilic dermatoses.[3]

The treatment of neutrophilic dermatosis differs dramatically from that of soft-tissue infections. Surgical debridement is typically discouraged because of the risk of pathergy (pathologic spread of the neutrophilic dermatosis to areas of surgical trauma). Medical management centers around the use of high dose oral corticosteroids (prednisone 1-2mg/kg equivalent) to control the aberrant, pathologic inflammation. Steroid-sparing immunosuppressants may be added for recalcitrant cases or for longer term control. Some experts advocate for empiric initiation of systemic steroids while awaiting cultures and biopsy, especially in cases of ill patients with no clear evidence of infection (e.g. negative infectious stains and tissue cultures) or those who fail to improve with appropriate antimicrobial coverage. Concomitant treatment with corticosteroids and antimicrobials may be a potentially important lifesaving compromise of management. (ref 3).

Necrotizing neutrophilic dermatoses are rare diagnoses and usually not considered by other medical specialties.[1] While NND is increasingly well documented in the dermatology literature, there is a paucity of publications on NND in the literature of other specialties likely to encounter the diagnosis such as surgery, infectious disease, oncology, and gastroenterology. This likely leads to under-diagnosis, delays in diagnosis, and further morbidity for patients with NND.

Prompt recognition of necrotizing neutrophilic dermatoses with initiation of systemic therapy can prevent unnecessary surgical interventions and morbidity.[1,2,3,4] This case demonstrates the importance of early dermatological consultation in cases of severe soft-tissue infection that do not respond to usual treatment within a few days.

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PRESENTERS
Kelsey Gradwohl MD; Christopher R. Shea MD; Amy Xu MD, MA

HISTORY OF PRESENT ILLNESS
A 63-year-old male presented to the University of Chicago Dermatology clinic for a rash on his trunk present for 1 year. He noted crops of slightly pruritic pustules on the inframammary area and bilateral flanks that would appear and then regress over several days leaving behind hyperpigmentation and scale. New lesions would occasionally produce scant discharge. He had not tried previous treatment. The patient denied joint pain, fever, or night sweats.

PAST MEDICAL HISTORY
Type II diabetes mellitus complicated by neuropathy and toe amputation, history of stroke, and hypertension.

FAMILY HISTORY
No family history of autoimmune conditions or psoriasis.

SOCIAL HISTORY
Former smoker.

MEDICATIONS
Insulin, atorvastatin, dulaglutide, amlodipine, pregabalin, and clopidogrel.
No new medications.

ALLERGIES
No known drug allergies.

PHYSICAL EXAMINATION
On exam on bilateral flanks and inframammary area there were ovoid thin plaques with fine scale, mixed with several larger flaccid pustules. Dermoscopy of the plaques revealed that each was studded at the periphery with superficial pinpoint pustules. There was no palmoplantar, mucosal or nail involvement.

LABORATORY RESULTS

Laboratory Study	Patient Result	Reference Range
Protein electrophoresis w/ reflex to immunofixation	No monoclonal detected by capillary electrophoresis	
Glucose-6-phosphate dehydrogenase (G6PD)	7.5 u/g Hb (75% mean of normal)	8.0-11.9 U/g Hb (>60% mean of normal considered adequate and not supportive of G6PD deficiency)
QuantiFERON- TB Gold	Negative	
Hepatitis B surface antigen Hepatitis B core antibody Hepatitis C virus antibody screen with reflex to viral load	Non-reactive	Non-reactive

IMAGING
None

DERMATOPATHOLOGY
The epidermis was acanthotic with spongiosis and mild compact hyperkeratosis. There was presence of neutrophilic exocytosis with formation of large subcorneal collections of neutrophils consistent with pustules. Sparce lymphocytic infiltrate was noted in the upper dermis. Methenamine silver stain was negative for fungi.

Direct immunofluorescence studies were non-specific.

DIAGNOSIS
Subcorneal pustular dermatosis / Sneddon-Wilkinson disease.

TREATMENT & COURSE
At the time of biopsy, the patient was started on topical triamcinolone 0.1% ointment twice daily. After 2 months of intermittent use with difficulty reaching the lesions on the posterior flank, the patient did not experience improvement and developed new lesions on his back. The patient was then started on dapsone 25mg daily.

DISCUSSION

Subcorneal pustular dermatosis (SPD) or Sneddon-Wilkinson syndrome is a rare, chronic relapsing remitting condition first described by I.B. Sneddon and D.S. Wilkinson in 1956.[1] It is characterized by a symmetric outbreak of superficial pustules on the trunk in the axillary, inguinal and submammary regions. Palmoplantar involvement is rarely reported, and it classically spares the face and mucus membranes.[2] The pustules form over several days and spread in an annular, circinate or serpiginous pattern leaving a central clearing and a rim of peripheral pustules.[3] The pustules are flaccid and eventually rupture leaving post-inflammatory hyperpigmentation or hypopigmentation, and scale. The pustules can have a unique presentation of half pustular half clear fluid referred to as a hypopyon pustule.[3] Pruritus is occasionally reported, but lesions are generally asymptomatic. Patients are generally well-appearing and lack systemic symptoms.[4] It is most common in middle aged women in their 40-60's.[5]

The exact etiology and pathogenesis of SPD is overall unclear. One study demonstrated increased levels of TNF-alpha in the pustular fluid suggesting that it might play a chemotactic role in the accumulation of neutrophils in the upper layers of the epidermis resulting in subcorneal pustule formation.[6] The most well-documented co-morbid associations are monoclonal IgA gammopathy and IgA myeloma thus screening with serum protein electrophoresis is recommended.[2] Pyoderma gangrenosum, mycoplasma pneumonia, rheumatoid arthritis, hypothyroidism and hyperthyroidism, systemic lupus erythematous, Sjogren's, Crohn's, multiple sclerosis and SAPHO (synovitis, acne, pustulosis, hyperostosis, osteitis) syndrome are reported associations in the literature.[7,2] Other associated malignancies have also been reported including chronic lymphocytic lymphoma, metastatic thymoma, neuroendocrine tumors, and lung cancer.[2]

On histology, subcorneal pustules with neutrophils and occasional eosinophils with a mixed superficial perivascular infiltrate will be seen in SPD. Significant spongiosis or acanthosis is typically not observed, a feature that can help distinguish SPD from pustular psoriasis.[8] Clinical and histologic differential diagnoses for SPD range from inflammatory disorders like pustular

psoriasis and acute generalized exanthematous pustulosis both of which have a more acute onset and severe systemic symptoms, to infectious etiologies like impetigo.[9] However, the key entity on the differential diagnosis of SPD is IgA pemphigus subcorneal pustular dermatosis type (SPD-type), which can mimic SPD both clinically and histologically.[10] Acantholysis is typically absent in SPD and more likely to be seen in IgA pemphigus SPD-type, though acantholysis can be seen in older lesions of SPD.[11] Therefore, direct immunofluorescence (DIF) is the only definitive way to distinguish SPD from IgA pemphigus SPD-type. In SPD the DIF will be negative or non-specific, while IgA pemphigus SPD-type will show an increased deposition of IgA in the epidermis due to IgA autoantibodies targeting desmocollin-1 in the upper epidermis.[10,12]

The mainstay of treatment for SPD is oral dapsone often with improvement in four weeks.[3] Some have used ongoing low dose dapsone therapy to prevent recurrences.[13] The patient should be counseled about methemoglobinemia and aplastic anemia prior to initiation or dapsone.[2] Etretinate and acitretin (0.25 to 1mg/kg/day) have also been shown to be effective.[3] Some have used topical steroids alone or in combination with dapsone with success.[3] PUVA and NB-UVB have been utilized alone or in combination with topical steroids with success.[9] Short courses of oral steroids have been used with variable response, but at times have been reported to precipitate flares.[3, 9] Infliximab and adalimumab have been utilized in recalcitrant cases of SPD with some success.[14] Both medications inhibit TNF alpha as their primary mechanism and dapsone has been shown to also inhibit TNF alpha in vitro.[15] This in combination with SPD's association with other TNF alpha mediated diseases (pyoderma gangrenosum, rheumatoid arthritis, and irritable bowel disease) and studies showing increased TNF-alpha levels in the pustules of patients with SPD, suggests a possible mechanistic link to the role of TNF-alpha in the pathogenesis of SBD.[15]

We present this case to show a classic clinical presentation of a rare disease, to highlight the importance of direct immunofluorescence in distinguishing SPD from IgA pemphigus – SPD type, and to review treatment options.

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PRESENTERS
Sarah Semaan MD; Angad Chadha MD; Oluwakemi Onajin MD

HISTORY OF PRESENT ILLNESS
A 40-year-old female presented to the University of Chicago Dermatology clinic for evaluation and management of hidradenitis suppurativa (HS) and leg ulcerations. Past medical history was notable for HS since she was a teen with extensive involvement of bilateral axilla, inframammary folds, groin and buttock. She has been on multiple treatments in the past including topical, oral antibiotics: doxycycline, minocycline, linezolid and rifampin, and adalimumab which initially was helping but lost efficacy after few months, as well as many surgical interventions. Patient also had a history of bilateral leg ulcerations for 6 years that was biopsied at an outside institution and was consistent with pyoderma gangrenosum (PG).

REVIEW OF SYSTEM
Positive for blurry vision in the left eye

PAST MEDICAL HISTORY
Hidradenitis suppurativa, hypertension, and pyoderma gangrenosum

FAMILY HISTORY
Crohn's, ulcerative colitis, rheumatoid arthritis, and diabetes

SOCIAL HISTORY
Denies any smoking

MEDICATIONS
Lisinopril-hydrochlorothiazide, tirzepatide and medroxyprogesterone

ALLERGIES
Vancomycin (reaction: hives and pruritis)

PHYSICAL EXAMINATION
Bilateral lower legs with multiple ulcerations, draining papulonodules with circumferential shiny hyperpigmented patches.
Right inframammary fold with linear 3cm ulceration, sinus tract formation and active drainage.
Left eye with injected conjunctiva and a crescent shaped ulceration on the left side of cornea.

DIAGNOSIS
Peripheral ulcerative keratitis in a patient with pyoderma gangrenosum and hidradenitis suppurativa

TREATMENT AND COURSE

Syndromic HS was considered however patient did not have any symptoms of arthritis or acne on presentation.

The patient was seen by ophthalmology and diagnosed with peripheral ulcerative keratitis (PUK). She was started on tobramycin and dexamethasone eye drops. Given her worsening HS, PG and new diagnosis of PUK, she was started on oral prednisone course of 60mg daily with 10mg taper every week for 6 weeks. She was then bridged to infliximab 5mg/kg every 8 weeks which was subsequently increased to 7.5mg/kg every 6 weeks due to HS flaring. Patient was seen in dermatology clinic for follow up after 3 months with significant improvement of her HS and PG and full recovery of her PUK.

DISCUSSION

Peripheral ulcerative keratitis (PUK) is a rare but serious ocular condition that is an important clinical entity due to its ophthalmological and systemic implications. PUK has an average incidence of 0.2–3 individuals per million population[1]. It represents a spectrum of inflammatory diseases, characterized by cellular infiltration, corneal thinning, and ulceration. Patients may present with decreased visual acuity, blindness, eye pain, redness, or irritation. The diagnosis is often confirmed by slit lamp examination.

The differential diagnosis of a PUK includes infections, trauma, malignancies, autoimmune conditions and dermatologic conditions such as cicatricial pemphigoid and acne rosacea. The most frequent systemic noninfectious diseases associated with PUK are systemic collagen vascular diseases, accounting for nearly half of PUK cases. Around one-third of PUK cases is associated with Rheumatoid arthritis, followed by ANCA- vasculitis. Other associated diseases include systemic lupus arthritis, polyarteritis nodosa and its variants, sjorgren's syndrome, and eosinophilic granulomatosis with polyangiitis[2]. Much less commonly but can also be seen in psoriasis, hidradenitis suppurativa (HS) and pyoderma gangrenosum (PG). Left untreated, PUK can result in decreased visual acuity, corneal perforation and eventual blindness.

The exact etiology of PUK is poorly understood, the postulated reasons include autoimmune reactions to corneal antigens, circulating immunocomplex deposition, vasculitis, and hypersensitivity reactions to exogenous antigens. PUK may result from humoral or cell-mediated immune mechanisms or both, causing obliterative microangitis at the level of the limbal vascular arcades. Subsequent leakage of inflammatory cells with destructive collagenases and proteases leads to scleral inflammation and destruction[3].

Although rare, neutrophilic dermatoses have been associated with PUK including sweets and PG[4,5,6]. Most common ocular disease reported with PG is PUK with fewer repots of scleromalacia, ulcerative, necrotizing or nodular sclerites[4]. There have been only seven reported cases of PUK associated with PG. Presentation is often unilateral

and the left eye is more frequently affected[5]. Extracutaneous neutrophilic infiltrates may occur in patients with neutrophilic diseases and produce lesions in various sites such as the eyes, lungs, bones, digestive tract, and the central nervous system.

PUK has also been reported with hidradenitis suppurativa (HS). Coexistence of inflammatory eye disease and HS is very rare. In prior studies, the most common manifestation was anterior uveitis, followed by episcleritis/scleritis. Few reports presented cases of PUK that has been associated with severe, uncontrolled HS, without other concurrent autoimmune or rheumatologic disease making HS the likely cause[7]. It has been thought that underlying immune dysregulation in HS patients may be associated with the risk of severe ocular surface diseases. Among other dermatologic immune diseases, PUK has been reported in parallel to an exacerbation of psoriasis[8] which further support the immune dysregulation role in developing PUK.

The first line of treatment for PUK is topical and systemic corticosteroids. If these are unsuccessful, cytotoxic/immunosuppressive medications such as cyclophosphamide, azathioprine, methotrexate, or cyclosporine may be used. Anti-TNF drugs, including etanercept, infliximab, adalimumab has been successful in treating PUK, uveitis, and scleritis associated with immune diseases. In one study, severe and refractory PUK was more responsive to rituximab, tocilizumab, or belimumab compared to anti-TNF agents[9]. In our case, PUK was diagnosed in the setting of flaring HS and PG, switching to infliximab proved to be a very effective treatment for the PG, HS and PUK.

We present this case for clinical interest and to highlight a rare but serious ocular manifestation that can be associated with common inflammatory dermatological disorders. Dermatologists should be aware of extra-cutaneous and ocular conditions that can be associated with pyoderma gangrenosum and hidradenitis suppurativa. This rare ocular manifestation has a serious sequela when left untreated which makes recognition and early treatment crucial. Further, coordination between ophthalmology, dermatology, and/or rheumatology is essential to ensure prompt diagnosis and treatment of inflammatory eye disease that are associated with chronic inflammatory dermatosis such as HS and PG.

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PRESENTERS
Colton Funkhouser MD, Oluwakemi Onajin MD, Arlene Ruiz de Luzuriaga MD, Amy Xu MD

HISTORY OF PRESENT ILLNESS
A 34-year-old female presented to the University of Chicago Dermatology clinic with a rash present for 3 months that started on her distal extremities and progressed to involve her chest, back, and proximal extremities. The rash waxed and waned, lasting for days to weeks at a time. It was associated with pruritus and burning. She had been treated at an outside urgent care with an intramuscular steroid injection and a methylprednisolone dose pack with improvement. She had also developed recurrent daily fevers up to 39.5°C, sore throat, and severe arthralgias and joint swelling involving her ankles, knees, wrists, elbows, and shoulders limiting her ability to ambulate.

PAST MEDICAL HISTORY
Anemia

FAMILY HISTORY
No family history of dermatologic or autoimmune conditions

MEDICATIONS
IM triamcinolone, methylprednisolone, hydroxyzine

ALLERGIES
No known drug allergies

PHYSICAL EXAMINATION
Bilateral upper and lower extremities, chest, and back with widespread erythematous edematous papules coalescing into larger plaques
Bilateral wrists and elbows with notable erythema, joint swelling, and tenderness to palpation
Skin warm to palpation

LABORATORY RESULTS

Laboratory Study	Patient Result	Reference Range
White blood cell count	7.5 x 10^3 /µL	3.5 - 11.0 10^3 /µL
ESR	120 mm/Hr	0-20 mm/Hr
CRP	44 mg/L	<5 mg/L
LDH	644 U/L	116-245 U/L
Ferritin	3600 ng/mL	10-220 ng/mL
ANA	1:160, speckled	<1:80
Interleukin-6	17 pg/mL	<6.4 pg/mL
Rheumatoid factor	18 iU/mL	<14 iU/mL

Comprehensive metabolic panel, C3, C4, IgE, SSA, SSB, anti-dsDNA, SM Ab, RNP Ab, SMRNP Ab, and CCP were within normal limits or negative. SPEP had a polyclonal distribution.

IMAGING
3-view x-rays of bilateral ankles, knees, wrists
Unremarkable, without evidence of fracture, malalignment, or definite erosions

DERMATOPATHOLOGY

Initial punch biopsy from the left arm demonstrated increased intravascular neutrophils with mild dermal edema consistent with neutrophilic urticaria. Two repeat punch biopsies were performed from the right leg and demonstrated a superficial perivascular and interstitial neutrophilic infiltrate, again most consistent with neutrophilic urticaria. In each of the biopsies there was no clear neutrophilic epitheliotropism or features diagnostic for neutrophilic vasculitis. Direct immunofluorescence was performed both times and was non-specific.

DIAGNOSIS

Adult-onset Still's disease

TREATMENT & COURSE

She initially presented to dermatology clinic and was treated with prednisone, naproxen, and referred to rheumatology. She continued to have persistence of her rash, fevers, and arthralgias and so was admitted to the University of Chicago Medical Center for expedited work up. While admitted, in conjunction with rheumatology, she was treated with 3 days of anakinra with complete resolution of arthralgias and fevers but persistence of her rash and pruritus. She was then transitioned to tocilizumab without effect. She remained on prednisone throughout this course and had improvement in her rash and arthralgias with increased dose of prednisone to 40mg daily. She was then started on canakinumab and colchicine while tapering the prednisone with significant improvement in her symptoms. She remains well controlled on canakinumab and colchicine.

DISCUSSION

Adult-onset Still's disease (AOSD) is a systemic inflammatory condition that typically affects young adults.[1] AOSD is rare, with an incidence that is estimated to range between 0.16 and 0.4/100,000 people.[2,3] Although the etiology of AOSD is unknown, it is thought to represent a continuum with systemic juvenile rheumatoid arthritis, delineated by age of onset.[4]

AOSD is characterized by the triad of a quotidian spiking fever, arthritis, and evanescent rash.[1–3] The fever in AOSD often precedes other manifestations and presents as a high spiking fever that generally exceeds 39°C and lasts less than 4 hours, with a quotidian or twice quotidian pattern. Most patients develop an evanescent salmon-pink erythema or erythematous eruption, often on the proximal limbs and trunk associated with febrile attacks.[1] Arthralgias and arthritis are another common symptom, typically involving the wrists, knees, and ankles. The arthritis may start mild but can progress to a destructive symmetrical polyarthritis.[1] Other features can include splenomegaly, lymph node involvement, hepatomegaly and elevated liver enzymes. Less commonly, patients with AOSD can develop an aseptic pharyngitis, pericarditis, pneumonitis, renal disease, or neurological manifestations. AOSD patients are also at risk for life threatening complications. Macrophage activation syndrome is considered the most severe complication and other life threatening complications include disseminated intravascular coagulopathy (DIC), thrombotic thrombocytopenic purpura, diffuse alveolar hemorrhage, pulmonary hypertension, and aseptic meningitis.[1]

Although the typical cutaneous manifestation in AOSD is an evanescent salmon-pink eruption, there are also several atypical cutaneous eruptions including neutrophilic urticarial dermatosis (NUD) and neutrophilic urticaria, as was seen in our case.[5–7] NUD presents with evanescent pink to red macules or plaques with associated fevers and arthralgias.[8] Histopathologically, NUD demonstrates a perivascular and interstitial neutrophilic infiltrate with leukocytoclasia but without vasculitis or dermal edema. NUD is often associated with systemic diseases such as AOSD, Schnitzler syndrome, systemic lupus erythematosus, Marshall's syndrome, and malignancy. NUD can also occur as an entity on its own without an associated systemic disease.[9,10] Neutrophilic urticaria histopathology demonstrates dermal edema with a

neutrophilic perivascular infiltrate that is often less intense to the infiltrate in NUD and lacks the leukocytoclasia and interstitial component present in NUD.[9]

AOSD is often diagnosed by rheumatologists, as arthritis is a common predominant symptom, however cutaneous findings may cause patients to present to dermatology. AOSD is a clinical diagnosis but thorough workup should be completed to exclude mimickers as the nonspecific symptoms may pose a diagnostic challenge. Laboratory findings in AOSD include elevated acute phase reactants such as ESR and CRP, leukocytosis with neutrophilia, anemia, and thrombocytosis.[1,11] Other common findings include transaminitis, hypertriglyceridemia, and hyperferritinemia, often higher than seen in other autoimmune or inflammatory conditions. A 5-fold increase in serum ferritin levels is strongly suggestive of AOSD.[1] Further workup often includes lab work to rule out other autoimmune conditions and imaging tests to rule out potential mimickers and evaluate any visceral or lymph node involvement.

The disease course in AOSD can have several clinical patterns, including a monocyclic, polycyclic, and chronic course. The monocyclic course involves one episode lasting between 2 months to 1 year followed by sustained remission. The polycyclic course has recurrent systemic flares with remission between flares, while the chronic course has one persistent episode lasting greater than one year and is often associated with a persistent polyarthritis.[11]

The initial treatment of AOSD involves glucocorticoids, which has been shown to lead to remission in 65% of patients.[12] NSAIDs are often used early in the disease process for symptom relief, however most patients do not achieve remission and adverse events are common. For patients with a polycyclic or chronic disease pattern, further treatment with other immunosuppressants or biologics may be needed. The first-line steroid sparing agent is methotrexate, while other options such as cyclosporine, azathioprine, hydroxychloroquine, leflunomide, and colchicine have been shown to have benefit.[12,13] For patients refractory to steroids and other disease modifying anti-inflammatory agents, biologics can be beneficial. The biologic selection is determined in-part by disease phenotype; arthritis symptom predominance has been associated with a significant response to IL-6 inhibition, whereas the systemic phenotype has been associated with a significant response to IL-1 inhibition.[11] The IL-1 inhibitor canakinumab is the only FDA-approved biologic in the US for the treatment of AOSD, while both canakinumab and anakinra are approved in Europe. Canakinumab has been shown to provide rapid and sustained efficacy, often leading to full clinical remission.[11]

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PRESENTERS
Gaurav Agnihotri MD, Arlene Ruiz de Luzuriaga MD MBA, Angad Chadha MD

HISTORY OF PRESENT ILLNESS
A 27-year-old male with a history of ulcerative colitis (UC) presented with a 10-month history of a worsening facial rash and 2-year history of mouth ulcers. His oral ulcers were attributed to his UC in the past and were not treated. His facial rash had been treated as a skin infection with oral antibiotics with no improvement. The patient stated that improvement of the rash was noted mostly when treated with systemic steroids for his UC. He reported being adherent to his UC medications and had an upcoming colectomy for uncontrolled diarrhea related to his UC.

REVIEW OF SYSTEMS
Positive for diarrhea. Negative for fevers/chills, headaches, joint pain.

PAST MEDICAL HISTORY
Ulcerative colitis

MEDICATIONS
Mesalamine (5-aminosalicylic acid) and ozanimod (sphingosine-1-phosphate receptor agonist)

ALLERGIES
None

FAMILY HISTORY
No pertinent history

PHYSICAL EXAM
Annular erythematous thin plaques studded with peripheral pustules and central erosion were noted on the right and left temples, parietal and occipital scalp, and nose. Confluent annular whitish eroded plaques and linear pustules were noted on the lower inner lip and hard palate.

LABORATORY AND IMAGING DATA
White blood cell count:11.2 x 10^3/μL [Reference: 3.5 – 11.0 x 10^3/μL]
Absolute eosinophil count:1.59 x 10^3/μL [Reference: 0.0 – 0.6 x 10^3/μL]
Bacterial and fungal tissues cultures negative
Herpes simplex virus PCR negative

HISTOPATHOLOGY
H&E from left temple demonstrated acanthosis with large intraepidermal pustules composed of neutrophils and eosinophils. Focal acantholysis was present. Within the dermis there was a diffuse inflammatory infiltrate composed predominantly of neutrophils and eosinophils.

DIF showed deposition of IgG and fibrinogen in the dermis and trace amounts of C3 at the dermal-epidermal junction. There was no evidence of any specific immune-mediated dermatosis.

DIAGNOSIS

Pyodermatitis-pyostomatitis vegetans

TREATMENT AND COURSE

The patient was initially treated with topical clobetasol ointment twice daily for the face, fluocinolone oil twice daily for the scalp, and triamcinolone dental paste twice daily for the mouth lesions. He was started on prednisone for his worsening UC by gastroenterology which led to significant improvement in his cutaneous disease as well. The patient had a complete proctocolectomy and was eventually tapered off the prednisone. Two days later there was a recurrence of the pyodermatitis- pyostomatitis vegetans, including new involvement of the peristomal site. He was restarted on prednisone and topical triamcinolone for the mouth and peristomal site. The patient's lesions again improved; however, the patient was unable to taper off prednisone without developing new lesions. Infliximab was then started with an eventual taper off prednisone. The patient's skin lesions were controlled with infliximab; however, the oral and peristomal site lesions have persisted. The plan is now to increase the frequency of infliximab and start fluocinonide gel to the affected mucosal areas.

DISCUSSION

Pyodermatitis-pyostomatitis vegetans (PPV) is a rare mucocutaneous disorder first described in 1898 by François Hallopeu. It is strongly associated with an underlying inflammatory bowel disease (IBD), in particular ulcerative colitis [1]. While many patients with PPV also have symptomatic IBD, few may have subclinical IBD thus warranting a gastroenterology referral for a thorough gastrointestinal screening history and exam [1]. PPV affects men more often and usually occurs between the ages of 20 and 60 [2]. Pediatric cases have been reported as well [3]. The pathogenesis is unknown.

PPV initially appear as confluent pustules that erode into shallow erosions and ulcers in a "snail track" pattern on mucosal surfaces [1]. Cutaneous lesions present as crusted, friable, papulopustules that coalesce into annular, exophytic plaques. They appear concurrently with oral lesions or after the development of oral disease. Lesions typically affect the face, scalp, axilla, and groin. Bacterial, fungal, and viral cultures are often negative [1,4]. Peripheral eosinophilia has been associated with PPV [5].

On histology, PPV presents with intra and subepithelial microabscesses of eosinophils and neutrophils [1,5]. Epidermal hyperplasia and focal acantholysis may also be seen, and is usually more notable in oral lesions. Some consider pyostomatitis vegetans to be the mucosal equivalent of pyoderma gangrenosum; however, Clark et al suggests that intraepidermal and dermal eosinophils may be a significant differentiating factor [2,5]. Negative immunofluorescence studies can help rule out pemphigus vegetans or IgA pemphigus, which are key differential diagnoses. PPV is usually characterized by a

negative direct immunofluorescence; however, a weakly positive direct immunofluorescence may also be seen [4,5].

Systemic corticosteroids are the first line of treatment. Topical steroids have also been successful used. If unable to withdraw or taper steroids, second line treatment options noted in the literature include dapsone, azathioprine, cyclosporine, mycophenolate mofetil, methotrexate, and infliximab – all with variable efficacy [1,4,5]. Management of the underlying IBD may also help treat PPV. There have been cases of clearance of PPV after total colectomy [6]. However, colectomy doesn't guarantee complete resolution of PPV, as in our patient's case.

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PRESENTERS
Brooke Cui, MD; Maria Estela Martinez-Escala, MD, PhD; Diana Bolotin, MD, PhD; Amy Xu, MD; Omar P. Sangüeza, MD; Christopher R. Shea, MD

HISTORY OF PRESENT ILLNESS
A 58-year-old male presented to the dermatology clinic with a papule on the scalp that had been present for an unknown duration. Patient notes the lesion had been removed in the distant past and recurred. Initial histopathology was reportedly benign.

PAST MEDICAL HISTORY
HTN, Chronic tension headaches

FAMILY HISTORY
No pertinent family history

SOCIAL HISTORY
No pertinent social history

MEDICATIONS
Amlodipine 5mg BID

ALLERGIES
No known drug allergies

PHYSICAL EXAMINATION
Left parietal scalp with a 6mm firm, brown, bound down papule

NOTABLE LABORATORY RESULTS
None

DERMATOPATHOLOGY
Punch biopsy demonstrated a dermal proliferation with multilobulated and infiltrative architecture, composed of various follicular-type structures. In the upper dermis, there were lobules of basaloid cells with peripheral palisading resembling follicular germ and myxoid stroma with central necrosis and prominent mitotic figures.

The neoplasm also had matrical differentiation, represented by the abrupt transition from basaloid cells to anucleate cells. Foci of sebaceous differentiation and several keratin-filled cysts reminiscent of follicular infundibula were present. There was also focal squamous differentiation shown by horn pearl formation.

The deeper portion of the tumor demonstrated prominent clear-cell changes consistent with trichilemmal differentiation within a desmoplastic stroma.

Perineural invasion involving a nerve with a diameter of 0.08mm is focally identified in step sections.

Immunohistochemical Stains
Bcl2: diffusely positive in the superficial component of the tumor

BerEP4: positive at the periphery of the lobules of the superficial component and weakly positive at the center of the lobules of the superficial component. The deeper component was negative.
Beta-catenin: variably nuclear, cytoplasmic or membranous staining of several tumoral cells
EMA: positive staining of foci with sebaceous differentiation in the tumor
Ki-67: positive nuclear staining in >60% of the nuclei of the tumor in the superficial portion and < 20% of the tumor in the deeper portion

DIAGNOSIS

Infiltrating Panfollicular Carcinoma

IMAGING

MRI of the brain and neck did not demonstrate large-caliber nerve involvement or evidence of metastatic disease.

TREATMENT & COURSE

Treatments options that were considered included excision vs mohs surgery vs slow mohs. Multiple factors were considered. In addition to the presence of perineural invasion, the infiltrative architecture of the deep portion of the neoplasm partially stained for pan-cytokeratin. Also slow Mohs offered the advantage of visualizing all the margins as opposed to a wide local excision. Ultimately slow Mohs was pursued. Complete removal of the tumor was achieved after 1 stage. No recurrence has been reported after 1 month of follow up.

DISCUSSION

Panfolliculoma is a benign neoplasm of follicular differentiation described in 1993, with histopathologic characteristics similar to trichoblastoma, but with differentiation towards all components of the hair follicle [1,5]. To date, there are only two published cases of its malignant counterpart, panfollicular carcinoma, published in the *Journal of Cutaneous Pathology* in 2013 by Fedeles et al. Their Case 1 presented a 48-year-old male with an ill-defined pink nodule on the left upper nose. Pathology demonstrated germinative-center-like islands, cords and strands, along with inner and outer sheath matrical differentiation. There was deep dermal extension and a mitotic index of 4 mitotic figures /10 high power fields. Their Case 2 described a 77-year-old male who presented with a pink papule on the left helical rim. Pathology was similar to case 1, in addition to showing sebaceous differentiation. Pathology likewise demonstrated deep dermal extension with a mitotic index of 20 mitotic figures/10 high power fields. Both patients underwent Mohs surgery for complete excision. Both cases had no recurrence after 2 years [4].

The differential diagnosis for a hair follicle neoplasm includes BCC with matrical differentiation, proliferating pilomatricoma, and pilomatrical carcinoma. Immunohistochemistry helps narrow the differential diagnosis and better characterize the neoplasm. Beta-catenin suggest pilomatrical origin. Staining for BerEP4 suggests follicular germinative cells. Both stains were congruent between the case series and our case [4].

We present this case of infiltrating panfollicular carcinoma to highlight a rare adnexal neoplasm.

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NOTES

NOTES

Thank You

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