Chicago Dermatological Society

Monthly Educational Conference

Program Information
CME Certification
and
Case Presentations

Wednesday, October 13, 2010

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

Program

Committees & Registration

8:00 a.m. - 9:00 a.m.	CDS Plans & Policies Committee
9:00 a.m. - 10:00 a.m.	IDS Board Meeting

Program Activities

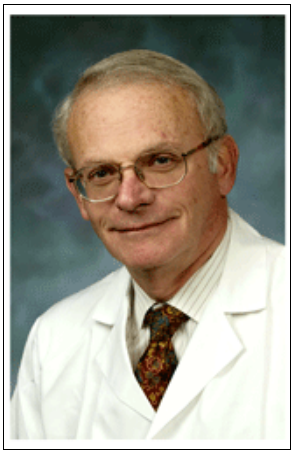
8:00 a.m.	Registration & Continental Breakfast; visit with exhibitors *Feinberg "A" Foyer – 3rd Floor of the Feinberg Pavilion*
9:00 a.m. - 10:00 a.m.	RESIDENT LECTURE The Role of Microbial Organisms in Wound Healing: New Molecular Approaches *Speaker:* Gerald Lazarus, MD *Feinberg "A" – 3rd Floor of the Feinberg Pavilion*
9:30 a.m. - 11:00 a.m.	CLINICAL ROUNDS – *Dermatology Clinic; 676 N. St. Clair Street, Suite 1600* • Patient Viewing • Slide Viewing
11:00 a.m. - 12:15 p.m.	GENERAL SESSION *Feinberg "A" – 3rd Floor of the Feinberg Pavilion* *BLUEFARB LECTURE* – "Cutaneous Ulcers for Dermatologists, an Exciting Opportunity" *Speaker:* Gerald Lazarus, MD
12:15 p.m. - 12:45 p.m.	Lunch & visit with exhibitors *Feinberg Pavilion Atrium - 3rd Floor*
12:45 p.m. - 1:00 p.m.	CDS Business Meeting *Feinberg "A" – 3rd Floor of the Feinberg Pavilion*
1:00 p.m. - 2:30 p.m.	Case Discussions *Feinberg "A" – 3rd Floor of the Feinberg Pavilion*
2:30 p.m.	Meeting adjourns

Mark the Date!

Next CDS monthly meeting – Wednesday, November 10, 2010
at the University of Chicago; Edward V. Maytin, MD PhD

Watch for details on the CDS website: www.ChicagoDerm.org

Guest Speaker



Gerald Lazarus, MD

Dr. Lazarus is Professor of Dermatology at the Johns Hopkins University School of Medicine and is chair of the Department of Dermatology at Johns Hopkins Bayview Medical Center. He also is director of the Wound Center at Hopkins. Dr. Lazarus was a visiting professor at the Peking Union Medical College and Hospital in Beijing, China. He earned his medical degree at The George Washington University, Washington, DC (1963) and he completed a medical internship/residency at the University of Michigan Medical Center, Ann Arbor (1965), served as a clinical research associate in the Department of Dermatology at Harvard Medical School (1969) and was chief resident in Dermatology at Harvard (1969-70). Dr. Lazarus has an extensive academic and medical career that has taken him to New York, North Carolina and California. He also is the author of numerous peer reviewed and basic research papers.

Educational Items

Course Director: Shelley Halper, MD

Target Audience: Practicing dermatologists, dermatology residents and fellows

Objectives:

At the conclusion of this learning activity, the participant should be able to:

1. Discuss the clinical aspects of cutaneous ulcers and related diagnostic factors.
2. Describe how new microbial methods can be employed in dermatological investigation.
3. Explain how these methods can be utilized in a dermatological practice for treatment of patients with cutaneous ulcers.

CME Statement

This activity has been planned and implemented in accordance with the Essential Areas and policies of the Accreditation Council for Continuing Medical Education (ACCME) through joint sponsorship of the Colorado Foundation for Medical Care, Office of Continuing Education (CFMC OCE) and the Chicago Dermatological Society. CFMC is accredited by the ACCME to provide continuing medical education for physicians.

Colorado Foundation for Medical Care designates this educational activity for a maximum of 4.75 AMA PRA Category 1 Credits™. Physicians should only claim credit commensurate with the extent of their participation in the activity.

CFMC has no financial responsibility for this activity.

Commercial Support

Exhibitors – We gratefully acknowledge the support from our sponsors for this conference who have paid a fee to CDS for their exhibit space.

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CHICAGO DERMATOLOGICAL SOCIETY **CASE # 1**

Presented by Elizabeth Grossman, MD and Joaquin Brieva, MD
Department of Dermatology, Feinberg School of Medicine, Northwestern University

HISTORY OF PRESENT ILLNESS

A 37 year old Caucasian female with a history of asthma was transferred from an outside hospital in acute liver failure. Her aminotransferases were elevated to above 7000. Two weeks prior to presentation the patient had experienced shortness of breath and was treated for a presumed asthma exacerbation with prednisone. One week prior to presentation the patient developed fever and labial lesions; her primary obstetrician initiated her on valacyclovir 500 mg twice daily at that time. Her review of systems was positive for fever, abdominal pain, constipation, cough and shortness of breath, for which she had been treated with dexamethasone and prednisone. The patient denied any previous history of oral or genital herpes simplex viral infection.

PAST MEDICAL HISTORY

Asthma, seasonal Allergies

MEDICATIONS

azithromycin, ceftriazone, ipratropium, albuterol, acetylcysteine, valacyclovir, vitamin K, oral contraceptive pill

FAMILY HISTORY

Noncontributory

SOCIAL HISTORY

Married, denies new sexual partners

PHYSICAL EXAM

The patient was anicteric. Her left inferior labia majora had 3 punched out erosions. Throughout the vaginal mucosa were large, tender erosions. There was a cluster of tender, punched out erosions on the perineum. There were no intact vesicles or oral mucosal lesions.

LABS

Abnormal:
Blood HSV 2 PCR: 6.5 x 10^7 copies/mL
Vesicle HSV direct fluorescence antibody: positive
VZV IgG: positive, EBV IgG: positive, IgM negative, Toxoplasma IgG: positive, IgM negative,
AST: 6611 unit/L [ref 0-40], ALT: 8126 unit/L [ref 0-48], Alkaline phosphatase: 215 unit/L [ref 30-115], Albumin: 2.2 g/dL [ref 2.5-5.0], Total bilirubin: 3.8 mg/dL [ref 0-1.3], Direct bilirubin: 2.5 mg/dL [0-0.2], Total protein: 4.7 gm/dL [ref 6.0-8.0], INR: 1.7 seconds [ref 1.0-1.2], PT: 18.5 seconds [ref 12.0-15.0], Creatinine: 2.86 mg/dL [ref 0.00-1.70], Sodium: 129 mEq/L [ref 135-148], Bicarbonate 23 mEq/L [ref 24-32], Blood urea nitrogen: 25 mg/dL [ref 0-20], White blood count: 2.7 K/UL [ref 3.5-10.5], Platelets: 21 K/UL [ref 40-390]
Negative/Normal: serum HSV 1 PCR, Hepatitis B sAg, sAb, cAb, Hepatitis C Ab, Hepatitis A Ab, HIV Ab and PCR, CMV PCR negative
Abdominal CT: Liver measures 21 cm in length. There is diffuse fatty infiltration of the liver, no masses.
Abdominal ultrasound: Liver enlarged to 20. 6 cm, no nodularity
Chest CT: focal consolidation in the right middle lobe, scattered clusters of micronodules, some of which have a tree in bud configuration in the right middle and left upper lobes, and a 4-mm ground glass nodule in the superior right lower lobe.

DIAGNOSIS

Disseminated herpes simplex virus hepatitis from primary HSV 2 infection

TREATMENT AND COURSE

The patient was started on IV acyclovir, renally dosed; however, she remained febrile with significant abdominal pain. Her transaminitis began to resolve slowly over her hospital course. Due to the significant viral load, and her expected prolonged viremia from her hepatitis, she was discharged home with a three week course of IV acyclovir to be administered through a PICC line. At time of discharge her liver function was stable, her leukopenia and thrombocytopenia had resolved and her kidney function was improving.

DISCUSSION

In the United States, among people aged 14-49, the estimated seroprevalence for herpes simplex virus (HSV) 2 is 17.2%; for HSV-1 the seroprevalence is 62%. HSV infections in healthy adults are usually restricted to mucocutaneous lesions and associated neural ganglia. Frequently the infection is subclinical.

Asymptomatic hepatitis with slight elevation in the aminotransferase levels may occur in 14% of healthy young adults who have acute HSV-2. However, disseminated herpes simplex hepatitis is a rare complication. Acute liver failure from HSV most commonly affects individuals who are immunosuppressed or females in the third trimester of pregnancy, although 25% of reported cases are in immunocompetent adults. Clinically, patients present with fever, malaise and abdominal pain; they are most often anicteric. Serologic abnormalities include transaminitis, leukopenia, thrombocytopenia, coagulopathy and acute renal failure. The aminotransferase levels may be 100 to 1,000 times normal with a minimal bilirubin elevation. Complicating the diagnosis may be the lack of cutaneous findings. Of cases reported to date in the literature, only 44% of individuals had cutaneous herpetic lesions.

Acute liver failure has been seen with both HSV strains and with both primary and reactivation infection. In the immunocompetent host, only primary HSV infection leads to hepatitis, and it is most commonly infection with HSV-2. Although the pathogenesis of HSV hepatitis is unknown, there are several proposed mechanisms: impaired processing of HSV antigen by T-cell and/or macrophages, high viral inoculums, superinfection with a second strain of HSV or infection with a hepatovirulent strain of HSV.

The course of herpes simplex hepatitis is typically fulminant and the prognosis is poor. Outcomes frequently are liver transplantation or death. Although the mortality is high, herpes simplex hepatitis is one of the few treatable causes of acute liver failure. Early treatment with acyclovir 10mg/kg intravenously every 8 hours is the standard of care and leads to improved survival rates.

REFERENCES

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CHICAGO DERMATOLOGICAL SOCIETY **CASE # 2**

Presented by Sarah Baker, MD, Joaquin Brieva, MD, and Mary Martini, MD
Department of Dermatology, Feinberg School of Medicine, Northwestern University

HISTORY OF PRESENT ILLNESS

A 43 year old previously healthy male presented to the emergency department with new onset left ankle pain and swelling, high fevers to 103.7°, diffuse myalgias, night sweats, and tender erythematous, edematous papules and plaques on his trunk and extremities. Several of the lesions were also noted to have a vesicular appearance. The fevers and rash began approximately 3-4 days prior to presentation. Review of systems was negative for cough, diarrhea, urethral discharge, sore throat or recent unexplained weight loss, and the patient denied recent travel or sick contacts.

PAST MEDICAL HISTORY

Occasional sinusitis

MEDICATIONS

Multivitamins

ALLERGIES

Penicillin

PHYSICAL EXAM

Upon initial evaluation, the patient was ill-appearing with shaking chills. He had no lymphadenopathy, and his lungs were clear to auscultation. Mucocutaneous examination revealed numerous, diffuse erythematous, edematous papules on the scalp, neck, upper back and extremities. Many of these lesions had central vesiculation filled with yellowish-gray fluid. There was a shallow ulceration with fibrinous exudate on the right lower labial mucosa.

LABS

Abnormal: sedimentation rate 23mm/hr [ref 3-10]; C-reactive protein 10.7 mg/dL [ref <0.8]; Neutrophils 80% [ref 34-73%]; peripheral smear-rare giant platelets, neutrophilia, no blasts; SPEP-accentuated alpha 2 band, no restricted bands in gamma region; UPEP-polyclonal gammopathy, no restricted bands
Negative/normal: RPR; ANA; dsDNA antibodies; HIV 1&2 antibodies; Hepatitis A/B/C panels; herpes simplex and varicella zoster direct fluorescent antibodies; tissue, blood, & urine cultures; AST, ALT, creatinine, UA; pANCA, cANCA; WBC
Chest X-ray 7/10/2010: normal, **Chest X-ray 7/12/2010:** bilateral lower lobe infiltrates
CT angiography, chest 7/12/2010: Significant consolidation of bilateral lower lobes
Transthoracic echocardiogram: Trace tricuspid regurgitation, small pericardial effusion

HISTOPATHOLOGY

Back: The epidermis shows mild spongiosis. In the papillary dermis there is marked edema and a dense collection of neutrophils and nuclear debris. Vasculitis is not identified. Gram, DPAS, and AFB stains are negative, and immunohistochemistry is negative for HSV or VZV.

DIAGNOSIS

Bullous Sweet syndrome with neutrophilic alveolitis

TREATMENT AND COURSE

The patient was admitted to the hospital, and given his high fevers, he was initially placed on broad spectrum antimicrobial therapy with vancomycin, cefipime, doxycycline and azithromycin. Two days following admission, the patient developed acute shortness of breath and chest pain. Imaging

revealed consolidation of bilateral pulmonary lower lobes. He remained febrile without leukocytosis and continued to develop new skin lesions. Blood, urine and tissue cultures were negative. Skin biopsy revealed a suppurative neutrophilic dermatitis. Given the high suspicion for Sweet syndrome, the patient was begun on methylprednisolone 60mg IV twice daily. His skin lesions improved rapidly and repeat chest X-ray 72 hours following initation of corticosteroids showed marked improvement of his pulmonary infiltrates. Antimicrobial therapy was discontinued with the exception of azithromycin, and the patient was discharged on a prednisone taper. At his one week follow up visit, all of his skin lesions had resolved.

DISCUSSION

Sweet syndrome, also known as acute febrile neutrophilic dermatosis, is a reactive neutrophilic process characterized by fever, peripheral neutrophilia, and tender erythematous plaques and nodules on the face, extremities and trunk. Occasionally, lesions may appear bullous, pustular or ulcerated. Neutrophilic infiltrates are largely confined to the skin in Sweet syndrome; however they may also invade extracutaneous sites such as the abdominal viscera, lymph nodes, bone, central nervous system, kidneys, lungs, ocular mucosa and the heart. Pulmonary involvement is rare in Sweet syndrome, with fewer than 25 cases reported in the literature to date.

Young to middle-aged females are most commonly affected by Sweet syndrome, and three variants of Sweet syndrome have been proposed. The classic form is seen in conjunction with GI or respiratory infections, pregnancy, and inflammatory bowel disease. The medication-induced form is most commonly associated with granulocyte colony stimulating factor, and a final subtype is associated with malignancies. Malignancy-associated Sweet syndrome is most often seen with hematologic malignancies (85%) but may also be seen with solid organ tumors (15%) such as genitourinary, breast and gastrointestinal malignancies. It has been suggested that patients with malignancy-associated sweet syndrome have more severe cutaneous manifestations, and it may precede the diagnosis of the underlying malignancy. Approximately half of all patients with malignancy-associated Sweet syndrome display extracutaneous manifestations.

Laboratory abnormalities such as leukocytosis, left shift, and elevated sedimentation are often seen with Sweet syndrome. Classic histologic findings in Sweet syndrome include a relatively normal epidermis with papillary dermal edema and occasional sub-epidermal vesiculation. A dense neutrophilic infiltrate is seen in the dermis and/or subcutis, demonstrating leukocytoclasis but generally no frank vasculitis. Left untreated, lesions may persist for weeks to months; however, Sweet syndrome typically responds rapidly to corticosteroids, which are the mainstay of treatment. Other treatment alternatives include dapsone, colchicine, and potassium iodide. More recently, TNF antagonists have proven successful in the management of Sweet syndrome. Relapse is noted in up to one third of patients.

REFERENCES

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CHICAGO DERMATOLOGICAL SOCIETY **CASE # 3**

Presented by Sandra Han, MD, Mario Lacouture, MD, and Maria Colavincenzo, MD
Department of Dermatology, Feinberg School of Medicine, Northwestern University

HISTORY OF PRESENT ILLNESS

The patient is a 71 year old Caucasian female initially diagnosed with early small lymphocytic lymphoma (SLL) in December 2005. Six months after her diagnosis, the patient presented to dermatology with numerous pruritic, erythematous papules involving her face and neck. Biopsy revealed Demodex folliculitis. She was treated with 40% sulfur cream with some improvement.

She presented a year later with similar, but more numerous lesions, now involving her arms and trunk. Biopsy of the wrist showed leukemia cutis with infiltrating lymphoma cells from her underlying SLL. She continued to develop new lesions, and three biopsies over the next year, including one on the neck, demonstrated arthropod bite reactions coexisting with leukemia cutis. She did not, however, recall having any insect bites. She presented again in May 2010 with new lesions of her scalp and abdomen, which were more edematous and intensely pruritic than previous lesions. Biopsy of two lesions, including one on the ear, revealed follicular mucinosis. In addition to these cutaneous findings, the patient also developed orbital cellulitis in May 2008 and herpes zoster of her left flank and abdomen in July 2008. These resolved with appropriate antibiotic and antiviral regimens.

PAST MEDICAL HISTORY

Hypertension, hyerplipidemia, hypothyroidism, diabetes mellitus, degenerative joint disease

MEDICATIONS

Metoprolol, amlodipine, ezetimibe, fish oil, levothyroxin, insulin, metformin, escitalopram

FAMILY HISTORY

The patient's brother is deceased from chronic lymphocytic leukemia.

SOCIAL HISTORY

The patient is married. She is a retired school teacher. No tobacco. Occasional alcohol.

PHYSICAL EXAM

Scalp, face, arms, and abdomen with scattered 3-8 mm pink, dome-shaped, monomorphic, slightly rubbery papules. No alopecia is noted within the lesions.

LABS

Abnormal: LDH (12/2005): 202 U/L [ref 100-190], LDH (5/2010): 224 U/L, CBC (5/2010): Hb 11.2 g/dL [ref 11.6-15.4], Hct 32.8% [ref 34-45%], lym 54% [ref 15-50%], eos 10% [ref 0-8%], absolute lym 4.4 K/uL [ref 1.0-4.0], abs eos 0.8 [ref 0.0-0.6]
Negative/normal: CBC (12/2005): WBC 9.1, Hb 12.8, Hct 37.3, Plt 247 (Lym 31%; PMN 59%, Eo 4%, Mo 5%, Ba 1%); CBC (5/2010): WBC 8.2, Plt 141 (PMN 31%, Mo 5%, Ba 1%)
Lymph node biopsy 12/2005: Immunophenotypic analysis shows mixed population of T and B-cells with ratio of 1.2:1. The T cells are antigenically normal. The B cells express CD19+, CD20+, CD23+, HLADR+ and dim CD5+. Surface membrane light chain immunoglobulins are monoclonal for kappa.
Bone marrow biopsy 1/2006: Clonal CD19+ B-cell population with dim kappa-restricted surface immunoglobulin light chain. The cells are dim CD5+, CD10-, CD23+, FMC7-, CD79b+, CD20+. The cells are also CD38- and Zap70-.

HISTOPATHOLOGY

Wrist, right: Unremarkable epidermis. Dermis reveals a dense and diffuse infiltrate of small, round cells with scant cytoplasm. No evidence of epidermotropism or germinal centers. Immunohistochemistry (IHC) demonstrates infiltrating cells that are strongly CD20+ and CD23+ but negative for kappa, lambda, and CD5.

Neck, right: Epidermis with central area of pseudoepitheliomatous hyperplasia. The dermis reveals a dense and diffuse infiltrate of monotonous lymphoid cells surrounded by a more heterogeneous infiltrate with many eosinophils. IHC demonstrates a collection of monotonous, CD20+, CD23+ cells in the center of the lesion. The majority of the infiltrate is CD3+ and surrounds the CD20+ cells. A lambda light chain restriction is noted.

Ear, right: Sections reveal slight spongiosis and hyperkeratosis with some exocytosis of mononuclear cells. The dermis shows prominent mucinous degeneration of the follicular epithelia with a modest periadnexal, perivascular and interstitial lymphohistioctyic infiltrate. Colloidal iron stain was performed and demonstrates significant deposits of acid mucopolysaccharides within the follicular units.

DIAGNOSIS

Small lymphocytic lymphoma/chronic lymphocytic leukemia with leukemia cutis, exaggerated arthropod bites, follicular mucinosis, and cutaneous infections

TREATMENT AND COURSE

The patient was prescribed fluocinonide 0.1% cream for leukemia cutis and arthropod bites, which provided minimal relief. Most recently, she was prescribed alclometasone 0.05% cream, which has helped with pruritus. Lesions have continued to wax and wane. The patient has been seen by her oncologist every three months. Serial CT scans evaluating lymph node involvement demonstrate disease progression, but with the exception of her skin lesions, she has remained symptom free. She has therefore not received any chemotherapy for her hematologic malignancy and declines any systemic medication for her skin lesions. Following her episode of herpes zoster, she was placed on prophylactic acyclovir without further recurrences.

DISCUSSION

Small lymphocytic lymphoma (SLL) is an indolent B-cell neoplasm characterized by the proliferation of a monoclonal population of lymphocytes. Chronic lymphocytic leukemia (CLL) is a pathologically and immunophenotypically identical condition, and distinction between these two is made by the presence of "B-symptoms" (fever, night sweats, weight loss, fatigue) and a greater number of absolute number of peripheral B lymphocytes in CLL. Most clinicians consider these to be the same condition on a shared clinical spectrum. CLL is the most common leukemia in Western countries. The prognosis of CLL is highly variable, but many run an indolent course, and chemotherapy is usually not indicated in patients with early and stable disease.

Cutaneous manifestations of CLL are uncommon, with 4-20% of patients having skin involvement. These can be categorized as "specific" or "non-specific" lesions, with the latter due to debility caused the disease or effects of treatment. Our patient manifested a variety of specific and non-specific lesions.

Leukemia cutis is a specific manifestation of CLL and represents infiltration of the skin by neoplastic clones of leukocytes. Lesions are variably pruritic and present most commonly as erythematous papules or nodules of the head and neck, but lesions may also be violaceous, hemorrhagic, or erosive. Histologically, three main architectural patterns are recognized: (a) perivascular and periadnexal, (b) nodular and diffuse, and (3) band-like. Cytologically, the infiltrating cells are small, uniform lymphoid cells with round nuclear contours and scant cytoplasm. In some patients, eosinophils arrange around blood vessels and adnexal structrure or dissect between collagen bundles.

Exaggerated arthropod bites in patients with CLL present as markedly pruritic or painful erythematous papules or nodules on exposed sites. Many, including our patient, do not recollect having any preceding insect bites. Histologically, these lesions display abundant dermal lymphoid cell and eosinophil infiltration. The infiltrates are composed of mixed B-cell and T-cell populations with aggregates of B-cells (CD20+) surrounded by T-cells (CD3+). These patients have been shown to have normal cutaneous reactivity to common antigens but hypersensitivity to mosquito antigen.

Follicular mucinosis is a cutaneous finding that may be seen in CLL. Based on Ackerman's characterization of the condition, follicular mucinosis is a secondary histologic reaction pattern in which mucin accumulates within the follicular epithelium. Its relationship to alopecia mucinosa and mycosis fungoides remains controversial. However, it has been described in association with both leukemia cutis and arthropod bites, and therefore corresponds with the patient's other cutaneous lesions of CLL. It has also been described in association with lesions of CLL that clinically mimic rosacea similar to our patient's initial presentation.

Patients with CLL are at increased risk of developing cutaneous infections, a non-specific cutaneous manifestation of CLL. Our patient developed orbital cellulitis and herpes zoster. Development of leukemia cutis in healed zoster scars is a well-documented phenomenon in CLL. Curiously, our patient did not have this is a feature among her numerous cutaneous manifestations of CLL.

Treatment for skin lesions in CLL is limited, though lesions tend to improve with therapy directed toward the underlying hematologic malignancy. Chemotherapeutic regimens typically include a combination of fludarabine, chlorambucil, and rituximab, with newer agents emerging as potential options. Other reported treatments for cutaneous disease include imiquimod, radiation therapy, narrow band UVB, surgical excision, and topical steroids. Oral steroids are frequently prescribed for symptomatic arthropod bites.

Other cutaneous findings seen in patients with CLL include nodules and tumors in Richter's syndrome in which large cell transformation of CLL or development of a new large-cell B-cell lymphoma in patients with CLL heralds a poor prognosis. Other non-specific skin findings in CLL include an eight-fold increased risk of skin cancer and petechial or purpuric lesions secondary to hemorrhage.

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CHICAGO DERMATOLOGICAL SOCIETY **CASE # 4**

Presented by Kimberly Nicholson, MD and Joaquin Brieva, MD
Department of Dermatology, Feinberg School of Medicine, Northwestern University

UNKNOWN

CHICAGO DERMATOLOGICAL SOCIETY **CASE # 5**

Presented by Melissa Abrams, MD and Bethanee J Schlosser, MD, PhD
Department of Dermatology, Feinberg School of Medicine, Northwestern University

HISTORY OF PRESENT ILLNESS

A 72 year old Caucasian female presented for evaluation of erosive lesions involving her vulva, perianal area and buttocks. The patient's vulvar disease began with pruritus in 2000 which was self-treated with topical antifungals, hydrocortisone 1% cream and benzocaine cream. She did not seek medical care until 2002 at which time a vulvar biopsy was performed, and a diagnosis of vulvar lichen planus was rendered. Between 2002 and 2005, treatment with topical corticosteroids, estrogen cream and a low oxalate diet resulted in stabilization, but not resolution, of disease. In 2007, the patient's vulvar symptoms worsened, and she developed blisters and "open sores" on the vulva and perianal area resulting in vulvar pain, hematochezia and pain with defecation. Gastroenterologic evaluation was negative for inflammatory bowel disease. In November 2008, repeat vulvar biopsy was consistent with erosive lichen planus, and treatment with mid- to high-potency topical corticosteroids was reinitiated. In June 2010, progressive blistering and erosions of the vulva and perianal skin precipitated a third vulvar biopsy; pathology was consistent with a vesiculobullous disease. Recent ophthalmologic and dental evaluations had been unremarkable. The patient was referred to the NMFF vulvar mucosal specialty clinic.

PAST MEDICAL HISTORY

Emphysema, fibromyalgia, hyperlipidemia, hypertension, macular degeneration, nephrolithiasis, parathyroid tumor, ulcerative blepharitis (ocular)

MEDICATIONS

Amlodipine/benazepril, hydrochlorothiazide, simvastatin, meloxicam, aspirin, estradiol vaginal cream, tacrolimus 0.1% ointment

ALLERGIES

Vicodin, sulfa, contrast dye

FAMILY HISTORY

Crohn's disease (mother)

SOCIAL HISTORY

Single. Retired. No alcohol use. Quit tobacco in 1985.

PHYSICAL EXAM

Examination of the oral mucosa revealed no erythema, erosions or ulcerations. Vulvar examination demonstrated severe tissue loss of the labia minora with diffuse erosions superiorly. The labia minora were agglutinated to the labia majora and the labia majora were agglutinated at the midline forming a solid vertically oriented band of scar tissue across the majority of the mid introitus. Patent introitus was noted superior to the midline scar tissue but residual eroded labia minora and mid vulvar agglutination/scarring precluded further introital and vaginal evaluation. Inferior to the midline scar tissue, introital patency was less than 5 mm. There was significant narrowing of the introitus with a few mm opening inferiorly. There was complete agglutination of the clitoral hood with burying of the clitoris. Multiple, well-demarcated 2-3 cm erosions and superficial ulcerations of the perianal skin were surrounded by pink to hypopigmented patches consistent with scarring.

LABS

Abnormal: BUN 27 mg/dL [ref 0-20]; GFR 42 mL/min/1.73m^2 [ref >59]
Negative/normal: CBC with differential, urinalysis, creatinine, hepatitis panel, HIV1/2 ELISA, G6PD, TPMT, CXR, intradermal TB test, indirect immunofluorescence on 1M NaCl split skin: IgG negative, IgA negative, ELISA for anti-BP180 IgG, anti-BP230 IgG, anti-Dsg1 IgG, anti-Dsg3: negative

HISTOPATHOLOGY

Right perianal: Submucosal paucicellular blister with prominent subepithelial scarring.
Right perianal,DIF: Linear IgG and C3 deposits at the dermal-epidermal junction.

DIAGNOSIS

Mucous membrane pemphigoid (MMP) limited to anogenital disease

TREATMENT AND COURSE

Given the severity of her anogenital MMP, the patient was started on prednisone 40mg daily after baseline screening studies (CXR, TB skin test) were performed. After 3 weeks, the patient reported great improvement and exam revealed almost complete re-epithelialization of the previous perianal erosions, improvement in vulvar erosions and no new lesions. Azathioprine 75mg daily was added as a steroid-sparing immunosuppressant. Ten days after starting azathioprine, the patient noted improved symptoms (dysuria, vulvar/rectal pain), but examination demonstrated progressive introital narrowing and recurrent perianal erosions. Prednisone was increased to 80mg daily with continuation of azathioprine. Given disease progression on immunosuppressants and the extent of scarring which limited examination, examination under anesthesia (EUA) was performed. EUA revealed the previously noted band of scarring between the agglutinated labia minora and majora extending from approximately 1 cm below apex of confluence of labia minora anteriorly down to perineal body. A 5 mm superficial punctum was present at the posterior introitus, just anterior to perineal body, but this could not be probed with a small Hagar dilator or hysteroscope. Hysteroscopically, patent and uncompromised urethra and vagina (patent 8cm in length x 2.5cm in width based on Hagar dilator insertion) were noted.

DISCUSSION

Mucous membrane pemphigoid (MMP) is a rare, highly variable group of chronic, inflammatory, autoimmune subepithelial blistering diseases that can affect one or all mucous membranes with or without skin involvement. The oral mucosa is most commonly affected followed by the ocular, nasal, nasopharyngeal, anogenital, laryngeal and esophageal mucosa. Skin lesions involve the head and superior trunk. The estimated incidence of this disease is 1 per 1 million in Western Europe.

Patients present with erythematous patches, vesicles, and erosions. Scarring is typical and can lead to airway obstruction, blindness, and urinary/sexual dysfunction. Site-specific findings include symblepharon, ankyloblepharon and entropion in ocular disease and agglutination of labial tissue with architectural distortion in genital disease. Stenosis of the urethral meatus and introitus, as well as clitoral phimosis may also be seen.

Histopathology and immunofluorescence studies help distinguish MMP from other erosive mucocutaneous diseases. In 1999, the First International Conference on Mucous Membrane Pemphigoid concluded that clinical presentation and direct immunofluorescence of perilesional mucosa/skin with linear deposits of one or a combination of IgG, IgA or C3 at the epithelial basement membrane zone (BMZ) were essential for diagnosis. Histopathologic findings of subepithelial blisters with or without a significant leukocyte infiltrate and circulating autoantibodies detected by IIF, seen in 20-30% of patients, can be non-specific and are not required for diagnosis.

The pathogenic mechanism is unclear. Autoantibodies against 10 different BMZ antigens have been identified in MMP patient sera. Autoantibodies to BP230, BP180 and laminin 332 are most common. IIF on

1M NaCl split skin may reveal dermal binding of antibodies in a minority of cases. Autoantibodies in an individual patient can target one or more antigens, most likely due to "epitope spreading". Initial autoantibody titers can correlate with disease activity. Individuals with both IgG and IgA autoantibodies may have more severe and persistent disease. There is a clear correlation between autoantibodies to laminin 332 and increased malignancy risk. Treatment is based on the sites of involvement, disease severity and rate of disease progression. High-risk sites with the greatest risk of scarring include ocular, nasopharyngeal, tracheal/laryngeal and anogenital mucosa. Oral prednisone in combination with either cyclophosphamide or azathioprine is considered first-line treatment for high-risk patients. Dapsone, mycophenolate mofetil, IVIG and etanercept have also been reported to be effective. Low-risk patients can improve with high-potency topical corticosteroids alone or may require systemic agents.

As seen in our patient, the clinical findings of vulvar MMP can mimic more common dermatologic vulvar disorders including erosive lichen planus, lichen sclerosus and pemphigus vulgaris. Our case demonstrates the importance of vulvar biopsy and more specifically DIF to distinguish between these diseases. Distinction is important regarding treatment options and future clinical implications.

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CHICAGO DERMATOLOGICAL SOCIETY **CASE #6**

Presented by Nilanthi Gunawardane, MD and Jonathan Cotliar, MD
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HISTORY OF PRESENT ILLNESS
A 61 year old Caucasian female with a history of metastatic breast cancer on lapatinib and capecitabine presented with a 2-3 week history of painful erosions/ulcerations of her hands and feet. She denied any systemic symptoms. She has had intermittent flares of Hand-Foot Syndrome (grade 1-2) since 2007. Past treatments have included keratolytics and topical steroids. She had also been successfully treated with ciprofloxacin in 12/09 for a pseudomonal skin superinfection.

PAST MEDICAL HISTORY
Stage IV breast cancer – Her2+, ER+ infiltrating mixed ductal and lobular carcinoma of the right breast (diagnosed in 2005) with osseous metastasis. Started on lapatinib and capecitabine in 2007. New left breast invasive ductal carcinoma diagnosed in 2009 and started on fulvestrant. Most recent CT/PET in 02/2010 with stable disease.
Hand-foot syndrome, grades I-2 since 2007
Hypertension

MEDICATIONS
Lapatinib - since 04/2007, capecitabine - since 01/2007, fulvestrant – since 05/2009, pamidronate

SOCIAL HISTORY
Single. Works as a teacher. 1-2 drinks per week.

PHYSICAL EXAM
Well-developed, well-nourished female in no apparent distress. No scleral icterus. Bilateral palms with erythema and fissuring. R thumb and L 3rd digit with extensive, circumferential erosions with underlying beefy red base. Bilateral soles and web spaces with erythema and superficial ulcerations.

LABS
Abnormal: Wound culture: *Pseudomonas aeruginosa*
Abnormal (In Emergency Department): WBC 5.2 k/uL [ref 3.5-10.5], 91% neutrophils, hemoglobin 7.2 gm/dL [ref 11.6-15.4], platelets 83 k/uL [ref 140-390], potassium 6.4 mEq/L [ref 3.5-5.0], creatinine 5.0 mg/dL [ref 0-1.7], bilirubin 12.0 mg/dL [ref 0-1.3]), INR 4.1 [ref 0.8-1.2], fibrinogen 110 mg/dL [ref 221-498], lactic acid 6.0 mMol/L [ref 0-2.4]

DIAGNOSIS
Grade 3 Hand-foot syndrome with pseudomonal superinfection resulting in sepsis and death

TREATMENT AND COURSE
The patient was started on empiric ciprofloxacin in addition to mupirocin and spectazole cream. Her primary oncologist was consulted and capecitabine was discontinued. Two days following clinic visit, the wound culture was noted to grow pan-sensitive pseudomonas aeruginosa. The patient was called at home to discuss culture results. At this time, she reported yellow discoloration of her sclera but denied any other systemic symptoms. She was advised to go to the emergency room for immediate evaluation. Upon presentation to the emergency room, patient was noted to have severe hypotension with accompanying renal and hepatic dysfunction. The patient was admitted to the Medical Intensive Care Unit with septic shock and multi-system organ failure. Her condition deteriorated rapidly and she expired the next day.

DISCUSSION

Hand-foot syndrome (HFS), also known as palmar plantar erythrodysesthesia or acral erythema, was first described by Zuehlke in 1974. It is an adverse cutaneous reaction to chemotherapy agents, most commonly capecitabine, cytarabine, doxorubicin, 5FU and taxanes. Recently, there has been controversy regarding the use of the term "hand-foot skin reaction" to describe the common occurrence of similar symptoms (somewhat more localized) in patients receiving multiple tyrosine kinase inhibitors such as Sumatinib and Sorafenib. Furthermore, others have recommended the use of the term "toxic erythema of chemotherapy" to encompass the multitude of clinical entities associated with the toxic cutaneous effects of chemotherapy. The incidence of HFS in patients treated with capecitabine ranges from 28-74%.

HFS is characterized by painful, symmetric edema and erythema of the palms, digits and soles that may evolve to blisters and erosions. Hands are more commonly affected than the feet and most patients have a prodrome of dysesthesia. The time of onset following exposure to the chemotherapeutic agent may range from 24 hours to 10 months. The severity and rapidity of onset may depend on peak drug concentration, cumulative dose, and schedule of administration. Two classifications, WHO (grades I-4) and NCI (1-3), are used to categorize disease severity. Most patients with HFS present with less severe (WHO 1-2) symptoms. Superinfections with Staphylococcus and gram-negative organisms have been observed, but there are no published reports of any patients developing sepsis as a result of these superinfections.

The exact pathophysiology of HFS is yet to be elucidated, however direct toxic injury is the most commonly accepted theory of pathogenesis. This is supported by the histological findings of dyskeratotic keratinocytes and cell-poor interface dermatitis. High turn-over rates, high occurrence of eccrine glands, low levels of dihyropyrimidine dehydrogenase, and increased pressure resulting in capillary rupture have all been proposed to explain the preferential impact on the palms and soles.

The only therapy that has been shown to be effective for the treatment of HFS is dose reduction or withdrawal of the causative chemotherapeutic agent. General measures such as wound care, cold compresses and emollients are commonly utilized. Successful treatment of HFS with pyridoxine has been reported. Case reports of treatment with topical steroids, systemic steroids, keratolytics, and topical 99% dimethyl-sulfoxide have also been noted.

Given the high incidence of HFS with certain chemotherapeutic agents and given the morbidity associated with HFS, various preventive strategies have been investigated. Systemic corticosteroids, pyridoxine, COX-2 inhibitors, and vascoconstrictive therapies with regional cooling or use of nicotine patches have all been attempted with no definitive results.

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CHICAGO DERMATOLOGICAL SOCIETY **CASE # 7**

Presented by Annie Goldsberry, MD, MBA and Joaquin Brieva, MD
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HISTORY OF PRESENT ILLNESS
A 64 year old Caucasian male presented with a one year history of progressive skin erythema, thickening and hand swelling. He reported his symptoms started as subtle hand swelling, lip swelling, and facial erythema. Initial biopsy was consistent with granuloma annulare. However, the patient's erythema progressed to involve his trunk, upper extremities, and lower extremities; he also developed raised bumps on his skin and edema of both his hands. He was treated with a five day course of systemic corticosteroids with only mild and transient improvement. He subsequently presented to the rheumatology department who referred him to dermatology.

PAST MEDICAL HISTORY
Benign thoracic mass, hernia, nephrolithiasis, peptic ulcer disease

MEDICATIONS
Prednisone 10 mg BID

SOCIAL HISTORY
15 pack year history of tobacco, quit 30 years prior; occasional alcohol

PHYSICAL EXAM
Trunk, arms, face with erythematous, shiny indurated plaques. Widespread superimposed monomorphic firm waxy papules over the head and neck, chest and upper back. Skin stiff with sclerodactyly and decreased finger motility.

LABS
Abnormal: WBC 11.9 k/UL [ref 3.5-10.5], neutrophils: 8.7 k/uL [ref 1.5-8]; serum immunofixation IgG lambda monoclonal band seen; kappa light chain: 481 mg/dL [ref 629-1350]; kappa/lambda ratio: 1 [ref 1.5-3]; IgG quantitative: 675 mg/dL [ref 750-1700]
Negative/normal: Chem-10, LFTs, TSH, ESR, urinalysis, C-Reactive Protein, Beta-2-Glycoprotein, ANA, anticentromere, anti-dsDNA, anti-Smith, Anti-SS-A/SS-B, thyroid peroxidase, C3 and C4, complement, rheumatoid factor, serum protein electrophoresis

HISTOPATHOLOGY
Right neck: Unremarkable epidermis. Reticular dermis with proliferation of haphazardly arranged prominent fibroblasts in a myxoid stroma. Dermis with a variable perivascular lymphohistiocytic infiltrate. Colloidal iron stain demonstrated dermal deposits of acid mucopolysaccharides. Immunohistochemistry showed prominent fibroblasts which were factor XIIIa positive and CD34, CD68 negative suggesting fixed tissue fibroblast origin.

DIAGNOSIS
Scleromyxedema

TREATMENT AND COURSE
After workup for hematologic malignancy, the patient was found to have a monoclonal paraproteinemia. Bone marrow biopsy demonstrated a mildly hypercellular but no definitive morphologic evidence of plasma cell myeloma or malignancy. The patient was treated with Prednisone 10 mg BID with improvement in skin thickening; however his improvement plateaued after one month. He subsequently enrolled in a clinical trial at Johns Hopkins and received his first dose of IVIG in May

2010. Within one week, he noticed significant clinical improvement. Improvement was also evident on biopsy. A second dose of IVIG was given in August 2010.

DISCUSSION

Scleromyxedema is a primary cutaneous mucinoisis associated with monoclonal gammopathy and systemic manifestations. The disease is characterixed by dermal depostion of mucin with an increase in dermal collagen. It is quite rare and classically affects middle aged adults of both sexes.

Clinically, patients present with firm, waxy papules and indurated plaques. Skin findings are localized to the hands, forearms, head and neck, upper trunk and thighs. Patients may develop deep furrowing over the glabella, simulating leoinine facies. Because of the increase in dermal collagen, many patients develop sclerodactyly and decreased motility. Skin thickening over the proximal interphalangeal joints results in a central depression surrounded by elevated rim recognized as the "doughnut sign."

In nearly all cases, scleromyxedema is associated with an IgG lambda monoclonal gammopathy the significance of which is not known. Less than 10% of individuals progress to multiple myeloma. Extracutaneous manifestations include dysphagia, proximal myositis, peripheral neuropathy, arthropathy, carpal tunnel syndrome, restrictive or obstructive lung disease, scleroderma-like renal disease and coma.

Histopathology reveals diffuse mucin deposition in the upper and mid reticular dermis, increased collagen deposition and fibroblast proliferation with fibrosis. Diagnosis is not based solely on histopathology, and requires the clinical findings of a generalized popular eruption, the serologic findings of a monoclonal gammopathy as well as the absence of thyroid disorder.

The historic therapy of choice, melphalan is no longer used due to the potential development of hematologic malignancy. Other chemotherapy regimens may have a similar side effect profile. Systemic corticosteroids may be effective but improvements, as with our patient, are often temporary. Isolated case reports have discussed topical hyaluronidase, PUVA, UVA1, systemic retinoids, IVIG, plasmapheresis, extra corporeal phototherapy, G-CSF, and cyclosporine. Case reports have also shown complete remission after an autologous stem cell transplant. Finally, spontaneous improvement and clinical resolution has been observed after 15 years.

Differential diagnosis includes scleroderma, scleredema, nephrogenic systemic fibrosis, and localized variants of lichen myxedematosus.

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CHICAGO DERMATOLOGICAL SOCIETY **CASE # 8**

Presented by Sapna Patel, MD and Joaquin Brieva, MD
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UNKNOWN

CHICAGO DERMATOLOGICAL SOCIETY **CASE # 9**

Presented by Sonal Shah, MD and Amy Paller, MD
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HISTORY OF PRESENT ILLNESS

The patient is a 7 month old male who presented for evaluation of a rash in his diaper region, which began at 5 days of life. Originally, he was treated by his PCP for diaper dermatitis and secondary candidal infection with nystatin and zinc oxide without improvement. He was seen by a pediatric dermatologist at 2 months of age, and routine biopsy and immunofluorescence were performed which revealed suprabasilar acantholysis. Bacterial culture revealed MRSA that was sensitive to trimethoprim-sulfamethoxazole (TMP-SMZ). Zinc levels were found to be low, as well. He was started on zinc sulfate, Vusion cream, Tetrix cream, mupirocin, and TMP-SMZ for the MRSA infection. He was also started on prednisolone and bleach baths. Repeat zinc level was normal, and supplementation was discontinued. He then presented to Mayo Clinic for evaluation and was admitted to the hospital for acetic acid wet dressing therapy and topical steroids. Upon presentation to our clinic, his topical regimen consisted of bleach baths twice weekly, hydrocortisone 2.5% ointment twice daily, and Triple Paste. Despite all of these interventions he has never had healing.

PAST MEDICAL HISTORY

Born at 39 weeks via Cesarean section secondary to vaginal Group B Streptococcal infection; H1N1 infection in first month of life; MRSA infection of diaper area

MEDICATIONS

Hydrocortisone 2.5% ointment; hydroxyzine

ALLERGIES

NKDA

FAMILY HISTORY

No family history of Darier Disease or Hailey-Hailey. No family history of other congenital skin disorders.

SOCIAL HISTORY

Lives at home with family

PHYSICAL EXAM

On the left upper and mid upper back are two 1 cm erythematous patches, each with a central vesiculopustule. The axillary vaults show one (right) to two (left) 4 mm slightly scaly, inflammatory papules. The skin superior to the gluteal cleft has an erythematous eroded plaque, bilaterally symmetric. The perianal skin has moderate hyperkeratosis with erosions, surrounded by a wide zone of resolving erythema. The scrotum is brightly erythematous with scaling and superficial erosions. The penis has mild erythema and a small erosion at the base. The neck fold shows post inflammatory hyperpigmentation.

HISTOPATHOLOGY

Perineum: Suprabasilar acantholysis and dyskeratosis. No evidence of immune complex deposition on immunofluorescence. Differential diagnosis includes Hailey-Hailey, Darier disease, or an undescribed acantholytic disorder.

DIAGNOSIS

Neonatal acantholytic dermatosis, awaiting further studies

TREATMENT AND COURSE

The patient was prescribed a 10 day course of TMP-SMZ 40/200mg twice daily. Mupirocin ointment twice daily was continued to the diaper area as well as in the nares for all family members twice daily for 5 sequential days each month. Bleach baths were continued daily. The patient has had intermittent improvement, but despite these interventions, still develops flares with new acantholytic patches in the diaper area. He also gets new discrete pustules, particularly on his trunk, which may be due to MRSA. Genetic testing for the ATP2A2 gene was performed and was negative.

DISCUSSION

Darier disease is an autosomal dominant disorder caused by mutations in the *ATP2A2* gene, which encodes an intracellular Ca^{2+}ATPase pump. Ca^{2+} signaling pathways play an important role in epidermal cohesion, and dysfunction leads to loss of suprabasilar keratinocyte adhesion and induction of apoptosis. Men and women are equally affected, and the average age of onset is between 6 to 20 years with peak onset during puberty. Clinically, multiple reddish brown, greasy, keratotic papules are noted in a seborrheic distribution symmetrically, particularly on the trunk, scalp, face, and lateral neck. These lesions may be pruritic and are frequently exacerbated by sun exposure and perspiration. Superinfection with yeast, bacteria, and dermatophytes can lead to worsening of disease. In half of all patients, small 2-4 mm skin–colored to tan, flat topped papules may be seen on the dorsal hands and feet. Localized lesions of Darier Disease are typically unilateral and follows the lines of Blaschko, which are segmental regions of skin thought to represent migration of cell lines during embryogenesis and is considered to be a form of mosaicism. Localized lesions are categorized into Type I and Type II based on distribution and underlying disease expression. Type I disease is segmental and follows the lines of Blaschko. Type II disease is generalized with few linear areas of increased severity. Type II disease is thought to be due to loss of heterozygosity of a normal somatic allele in a segmental area.

Hailey Hailey disease is also an acantholytic dermatosis, which is autosomal dominant and results from mutation in the *ATP2C1* gene. This defect leads to interference with intracellular calcium signaling. Clinically, flaccid vesicles and erosions are seen on the neck and intertriginous areas. The axillae and groin are frequently involved, and foul smelling vegetations and fissures often develop. Symptoms usually develop after the second or third decade of life. Pathology reveals widespread acantholysis within the epidermis, in contrast to Darier disease, which shows more focal acantholysis. Necrotic keratinocytes are less commonly seen. Type I and Type II variants of this disease may develop.

There has been one case report each of Darier disease and Hailey Hailey with a congenital presentation. In our patient, the distribution of skin lesions does not fit with that of classic Darier disease, and his lesions are more erosive than would be expected in Darier disease. Moreover, he is negative for the *ATP2A2* mutation. In the previously described case of congenital Hailey Hailey, the patient had erosions in the groin and axillae with a known family history of the disease. In our patient no such history is present. We have requested genetic testing for Hailey Hailey; if this is also negative, we propose that our patient may have a previously undescribed neonatal acantholytic dermatosis with the etiology to be determined.

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CHICAGO DERMATOLOGICAL SOCIETY **CASE # 10**

Presented by Bryan Gammon, MD and Joan Guitart, MD
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HISTORY OF PRESENT ILLNESS

The patient is a 49 year old male with a past medical history of common variable immunodeficiency (CVID) who presents for one-year history of eruption of asymptomatic red papules and firm nodules on his extremities. These initially began on his proximal upper extremities, and have since progressed. He was biopsied and diagnosed with cutaneous T cell lymphoma at an outside facility. He was initiated on oral bexarotene up to a dose of 300mg daily. He noted limited progression while on bexarotene but not resolution of existing lesions. He subsequently also developed an oral lesion of the soft palate as well as destructive arthritis of the bilateral hands, largely affecting the metacarpophalangeal joints, over the last year. He was diagnosed with rheumatoid arthritis for which he was started on hydroxychloroquine, methotrexate and prednisone with some relief of symptoms. He has had concomitant worsening of his CVID with recurrent upper respiratory infections and increasing lung parenchymal involvement despite escalation of his immunoglobulin replacement regimen. His review of systems is positive for fatigue, chronic cough, but is otherwise negative

PAST MEDICAL HISTORY

Rheumatoid arthritis, Common Variable Immune Deficiency, diagnosed in 1966, on IVIG since 1991, hypothyroidism

MEDICATIONS

Methotrexate 20 mg weekly, hydroxychloroquine 200 mg twice daily, prednisone 50 mg daily, 50g IVIG per month, bexarotene 225mg daily, clobetasol 0.05% ointment daily, levothyroxine

ALLERGIES

NKDA

FAMILY HISTORY

No family history of lymphoma or carcinoma

SOCIAL HISTORY

Six alcoholic beverages per week, denies tobacco use

PHYSICAL EXAM

On exam, shotty supraclavicular lymphadenopathy was noted. A 1 cm sharply demarcated, round, well-granulated ulcer with rim of erythema was noted on the soft palate. Indurated erythematous dome shaped papules, nodules and plaques without surface change or necrosis, ranging from 0.5 - 2.0 cm in size, were noted on the upper and lower extremities.

LABS

Abnormal:

7/2010: tissue T cell receptor rearrangement by PCR positive for clonal T cell population
5/2010: LDH 271 IU/L [ref 120-240]
4/2010: cholesterol 298 mg/dL [ref <200]; triglycerides 286 mg/dL [ref <150]; free T4 0.75 ng/dL [ref 0.78-2.19]
12/2009: IgA, IgM undetectable

Negative/normal: SPEP, UPEP, SSA, SSB, Sm, RNP, C3, C4, ANA, RF, CBC, CMP, urinalysis, viral hepatitis panel, ACE level, serum IgG, peripheral blood smear

Total body FDG-PET 1/2010: patchy nodular and ground glass opacities with moderate FDG avidity in both lungs, as well as small scattered cutaneous foci of FDG avidity
Bilateral hand X-ray 12/2009: erosions of multiple bilateral MCPs and carpal bones with joint space narrowing
CT chest 12/2009: enlarged bilateral hilar and mediastinal lymph nodes and multifocal bilateral pulmonary nodular infiltrates with patchy consolidation

HISTOPATHOLOGY
7/1/2009 Left elbow: Atypical CD8+ lymphohistiocytic infiltrate. CD2, CD3, and CD5 positive with some reduced expression of CD7. The CD4:CD8 ratio is extremely aberrant with the majority of T-cells marking with CD8. Lymphoid cells are positive for TIA-1, but negative for CD56 and EBER in situ.
12/23/2009 Hard palate: The submucosa contains a dense lymphohistiocytic infiltrate with cytologic atypia. Immunohistochemical stains demonstrate a predominance of CD3+ T cells which are primarily CD8+ with a CD4:CD8 ratio of 1:10.
7/2010 Right upper arm: The epidermis shows slight hyperkeratosis. There are numerous dermal aggregates composed of epithelioid histiocytes with occasional multinucleated giant cells. A dense lymphocytic infiltrate composed of intermediate elongated atypical cells is also noted. Focal angiocentric features with hemorrhage are also noted. The remaining dermis shows some fibroplasia with a variable mostly perivascular lymphohistiocytic infiltrate. The process extends into the mid reticular dermis. Immunohistochemistry was performed on deparaffinized sections. All controls stained simultaneously were reviewed and appeared adequate. The infiltrate is composed of primarily T cells (CD3 positive) with rare B cells (CD20 positive). The atypical cells are mostly CD8, BF1, TIA-1 and granzyme B positive. The CD4:CD8 ratio of the T cell infiltrate is approximately 1:4. CD56, gamma-M1 are negative. EBER-1 in situ hybridization is negative for Epstein-Barr mRNA. Special stain (DPAS, Gram and acid fast bacilli) are negative for microorganisms.

DIAGNOSIS
CD8+ granulomatous lymphoma in the setting of common variable immunodeficiency

TREATMENT AND COURSE
The patient is currently tapering bexarotene therapy and considering other systemic agents for his lymphoma including gemcitabine single agent chemotherapy or a stem cell transplant.

DISCUSSION
Common variable immunodeficiency (CVID) is a rare immunodeficiency with an incidence of 1 per 25,000 in the Caucasian population. Patients with CVID have low serum levels of immunoglobulin A, G and/or M, and an impaired immunoglobulin response. It is commonly diagnosed in young adults aged 20-40, but can be seen in any age group. Several different genetic loci have been linked to the phenotype, but mutations in the TNF superfamily receptor transmembrane activator and calcium-modulating ligand interactor (TACI) occur most frequently. Recurrent infections are the major cause of morbidity and mortality in this population, as they can result in complications such as bronchiectasis, pulmonary hypertension and cor pulmonale. CVID is also often complicated by lymphoproliferative disorders and granulomatous disease. These complications represent a management conundrum, as they may require further immunosuppression to control. Granulomatous disease occurs in 8-22% of CVID patients and confers a much higher risk for autoimmunity. Fifty-four percent of patients with granulomas in the setting of CVID suffer from at least one autoimmune condition, most commonly autoimmune hemolytic anemia or idiopathic thrombocytopenic purpura. In contrast only 18% of CVID patients without granulomas were diagnosed with autoimmune conditions.

T cell lymphoproliferations have been previously described in the setting of CVID, and have been reported to be both polyclonal and monoclonal. Most interestingly, the previous report of a monoclonal T cell proliferation of the skin had a strikingly similar phenotype. The infiltrate was CD8+, TIA-1+, and was

histopathologically granulomatous in nature. The clinical presentation was also similar; the patient presented with indurated erythematous papulonodules on the trunk and extremities. In the previous case, the lesions resolved with immunoglobulin replacement, leading the investigators to suggest that this was a peculiar prelymphoma in the setting of CVID. Lymphomas in the setting of CVID are predominantly extranodal B cell lymphomas that respond to standard chemotherapy and rituximab protocols. Given the rarity of T cell lymphomas in CVID, treatment has yet to be standardized. However, given the reports of improvement of granulomatous lung disease as well as granulomatous lymphoma on high doses of immunoglobulin, it may be prudent to initially treat with higher doses of replacement IVIG.

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CHICAGO DERMATOLOGICAL SOCIETY **CASE # 11**

Presented by Lisa Arkin, MD and Peter Lio, MD
Department of Dermatology, Feinberg School of Medicine, Northwestern University

HISTORY OF PRESENT ILLNESS
The patient is a 35 year old female of Pakistani descent with no significant past medical history who presented to an outside dermatology clinic in December 2009 with hair loss and an erythematous, papular rash. Four months prior to presentation, she developed red acuminate papules that began on her back and spread to her trunk, neck, ears, and scalp over 3-4 days. The scalp was highly pruritic and tender. Within a week, she developed multiple patches of alopecia. She had no known chemical exposures, recent travel, or sick contacts. There were no new medications. She had received the hepatitis B vaccine in September 2007. She was initially treated with a course of prednisone and topical betamethasone with no improvement. A biopsy of her scalp demonstrated mild vacuolar change at the dermal-epidermal junction with pigment incontinence. She was referred to Northwestern for further evaluation and management.

PAST MEDICAL HISTORY
Depression

MEDICATIONS
Escitalopram

ALLERGIES
NKDA

FAMILY HISTORY
Sister with hypothyroidism
No history of cutaneous disease or other autoimmune diseases

SOCIAL HISTORY
Housewife. Denies, alcohol, smoking, or drug use

PHYSICAL EXAM
The patient was noted to have keratotic erythematous spinules on the back, axilla and torso. Moderate alopecia of the scalp was observed with accentuation over the vertex and occiput, with peri-follicular scaling and scarring of follicular ostia. In addition, mild non-scarring alopecia of the axilla was seen.

LABS
Negative/Normal: urinalysis, complete metabolic profile, complete blood count, PPD

HISTOPATHOLOGY
Scalp: Sections of skin show focal hypergranulosis and focal basal vacuolar changes. The papillary dermis contains a mild superficial perivascular lymphocytic infiltrate with prominent pigment incontinence. Within the reticular dermis, there is a follicular structure surrounded by a mild perifollicular lymphocytic infiltrate and fibroplasias. PAS is negative for fungi.
Arm: Perifollicular and intrafollicular inflammation showing features consistent with folliculitis.

DIAGNOSIS
Graham Little-Piccardi-Lassueur syndrome

TREATMENT AND COURSE

The patient was started on cyclosporine A (4 mg/kg/day), with decreased hair loss and flattening of the hyperkeratotic papules. The treatment was subsequently discontinued when she developed severe flank pain and tingling in her distal extremities. Several months ago, she was started on oral tacrolimus, which appears to have induced complete remission of her disease.

DISCUSSION

Graham Little-Piccardi-Lassueur syndrome (GLPS) is a rare lichenoid dermatosis marked by the triad of cicatricial scalp alopecia, noncicatricial alopecia in the axilla and groin, and keratotic follicular papules and plaques on the body. It was first described by Piccardi in 1914 and later documented by the British dermatologist Sir Graham-Little in a patient referred by his Swedish colleague, Lassueur. The disorder now bears the names of all four dermatologists. To date, there are fewer than 45 cases documented in the literature.

Both clinically and histologically, the etiology is linked to lichen planus. The keratotic papules and plaques resemble follicular lichen planus, while the scalp alopecia is similar to lichen planopilaris. Up to 50% of patients report one episode of associated oral lichen planus. There is no known association with systemic underlying disease or malignancy. GLPS typically develops in healthy, middle-aged women.

The pathophysiology remains purely speculative but is presumed to involve a cytotoxic T cell mediated response that targets specific antigen-presenting lymphocytes. HLA-DR1 is one of several HLA subtypes that have been associated with GLPS. These HLA subtypes may facilitate the presentation of particular cutaneous epitopes that subsequently trigger autoimmunity.

GLPS is most likely a sporadic disorder that does not follow Mendelian genetics. Only one familial case has been reported, in a 47 year old woman and her 19 year old daughter, both of whom were found to share the HLA subtype DR1. In addition, there is one case report of GLPS following HBV vaccination, which suggests a possible association.

The diagnosis is predominantly a clinical one, which may be confirmed with histology. On scalp biopsy, an early inflammatory peri-follicular lichenoid infiltrate can be observed, which is often associated with the bulge of the hair follicle. The bulb region is typically spared. End stage disease may show an atrophic dermis with fibrotic, empty hair shafts, sometimes with scattered keratinous follicular plugs and loss of sebaceous glands. Biopsies from the follicular papules typically show a lichenoid lymphocytic infiltrate in the upper dermis, with hyperkeratosis, acanthosis, and the presence of Civatte bodies (dyskeratotic keratinocytes). Treatment is largely anecdotal. Systemic, intralesional, and topical steroids, PUVA, metronizadole, and retinoids have been tried with variable success. Cyclosporine A (4 mg/kg/day) and thalidomide were beneficial in several case reports. In our center's experience, oral tacrolimus has showed promising results for disease stabilization and remission.

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CHICAGO DERMATOLOGICAL SOCIETY **CASE # 12**

Presented by Benjamin Marks, MD, PhD, Joaquin Brieva, MD, and Anne Laumann, MBChB,MRCP(UK)
Department of Dermatology, Feinberg School of Medicine, Northwestern University

HISTORY OF PRESENT ILLINESS
The patient is a 48 year-old healthy African American male who presents with a 3-4 month history of extensive, asymptomatic hypopigmented lesions on his extremities, back and shoulders. He attributed them to an environmental exposure while mowing the lawn. The lesions have been slowly enlarging over the past few months. Review of systems was negative for dysphagia, Raynaud's phenomenon, fevers, or arthralgias.

PAST MEDICAL HISTORY
None

MEDICATIONS
None

ALLERGIES
No known drug allergies

FAMILY HISTORY
Hypertension

SOCIAL HISTORY
He is married with two healthy children. He works in an office at a warehouse. He is not aware of any chemical contactants.

PHYSICAL EXAM
On the trunk and proximal extremities, sparing the face, there are diffuse hypopigmented, shiny, wrinkled patches over the shoulders and dark patches on the rest of the arms. Many of the truncal lesions appear atrophic with a shiny, cigarette paper-like surface.

LABS
Abnormal: AST 50 U/L [1-40 U/L], ALT 62 U/L [1-48 U/L]
Negative/normal: CBC, ESR Chem-7, C3, C4, alkaline phosphatase, bilirubin; Scl-70, anti-nuclear, snRNP, Smith, SS-A, SS-B, cardiolipin autoantibodies

HISTOPATHOLOGY
Left shoulder: Sections demonstrate a square shaped punch of dermis with dense fibrosis of dermal collagen. There is elevation and entrapment of the eccrine coils within the dermis.

DIAGNOSIS
Generalized morphea

TREATMENT AND COURSE
The patient has been started on calcipotriene 0.005%/betamethasone diproprionate 0.064% ointment topically.

DISCUSSION
Morphea is a rare condition consisting of inflammation and subsequent sclerosis of the dermis and subcutaneous fat in the absence of systemic involvement. This disorder is subdivided into plaque, linear, generalized, and deep morphea based on the extent and depth of tissue involvement. Generalized

morphea represents about 10% of all morphea cases. Often, these patients undergo extensive evaluation for internal organ involvement but only rarely progress to develop systemic sclerosis. In contrast to the typical gradual progression of generalized morphea, our patient presented with rapid onset of diffuse sclerotic lesions over the course of a few months.

The etiology of morphea is poorly understood. However, dysregulation of the vasculature, the immune system, and tissue fibroblasts are thought to play a significant role in disease development. Disruption of capillaries and small arterioles occur secondary to endothelial swelling and thickened vascular basement membranes. Various cytokines such as transforming growth factor β, interleukin 1 (IL-1), IL-2, IL-4, IL-6, IL-8, and IL-13 are thought to play important roles in pathogenesis by promoting enhanced collagen production by tissue fibroblasts. Morphea is often seen in association with other autoimmune conditions such as Hashimoto's thyroiditis, vitiligo, systemic lupus erythematosus, and type 1 diabetes mellitus, further implicating the role of immune dysregulation as an underlying disease mechanism.

On histology, morphea typically displays a sparse lymphoplasmacytic perivascular infiltrate involving the deeper dermis and subcutaneous fat. Collagen bundles in the reticular dermis appear thickened and closely packed with a paucity of adnexal structures and diminished peri-eccrine adipose tissue. The subcutaneous septae are widened and replaced by thick hypocellular hyalinized collagen. Histologic changes alone cannot differentiate between morphea (i.e. localized scleroderma) and systemic scleroderma; the latter should be suspected in the presence visceral symptoms, Raynaud's phenomenon or sclerodacty. These diseases are likely two distinct entities with shared pathophysiologic aberrations leading to a similar cutaneous phenotype.

Various laboratory abnormalities may be seen in the setting of morphea including peripheral eosinophilia, hypergammaglobulinemia and an increased erythrocyte sedimentation rate. Circulating autoantibodies have been associated with morphea including antinuclear antibodies in 46% to 80% of cases, anti–single-stranded DNA antibodies in 50% of cases, and anti-histone antibodies in 47% to 87% of cases. Antibody titers may correlate with the burden of skin disease. Uniquely, patients with generalized morphea often display elevations of anti-topoisomerase IIa antibodies in up to 76% of cases and rheumatoid factor in up to 82% of cases. The presence of rheumatoid factor may predict articular involvement in patients with generalized morphea.

The natural history of morphea is variable; however, the long-term prognosis is generally good. Lesions tend to be active for 3 to 5 years, often leaving residual dyschromia or atrophy in their wake. Treatment of generalized morphea is challenging, and no definitive guidelines have been established. High-potency topical glucocorticoids may be beneficial, often in conjunction with topical calcipotriene. Systemic glucocorticoids, antimalarials, colchicine, cyclophosphamide and azathioprine are usually ineffective. Methotrexate may provide some benefit to a subset of patients, as may mycophenolate mofetil. D-penicillamine has been shown to halt the formation of new lesions and induce the softening of the older lesions. Oral calcitriol may improve joint mobility and skin extensibility in adult patients with generalized morphea. In addition, UVA phototherapy and extracorporeal photochemotherapy have been reported to provide benefit for generalized morphea. Narrowband UVB therapy, although less potent owing to its limited dermal penetration, may also be helpful.

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CHICAGO DERMATOLOGICAL SOCIETY **CASE # 13**

Presented by Kavita Menon, MD, Bethanee J. Schlosser, MD, PhD, and Joan Guitart, MD
Department of Dermatology, Feinberg School of Medicine, Northwestern University

HISTORY OF PRESENT ILLNESS

This 63 year old Caucasian female with a history of cutaneous T-cell lymphoma presented for evaluation of erythematous plaques and ulcers of the vulva of 5 months duration. She was initially diagnosed with mycosis fungoides in 1993 with patches and plaques on her trunk and extremities. By1999, her disease evolved to tumors, and she developed vulvar pruritus for which she intermittently used clobetasol ointment. In 2006, she developed papules and plaques on her vulva and perineum. In August 2009, the patient noted progression of her skin and mucosal disease, with the development of infiltrative plaques and punched out ulcers involving her vulva and perineum. She had minimal response to interferon. Treatment with pulsed dexamethasone resulted in partial improvement, but she continued to have significant vulvar ulcers and infiltrative plaques. Her review of systems was notable for fatigue, weight loss, decreased appetite and vulvar pruritus. She had no fevers, chills or recent infections.

The patient's mycosis fungoides, both vulvar and cutaneous, has been refractory to numerous therapies including oral and topical bexarotene, topical nitrogen mustard, topical corticosteroids, phototherapy (psoralen and ultraviolet A, narrow band ultraviolet B) and interferon. In the past, an ulcerated tumor on the right posterior thigh was successfully treated with external beam radiation.

PAST MEDICAL HISTORY

Cutaneous T-Cell lymphoma, hypothyroidism

MEDICATIONS

Levothyroxine, hydroxyzine, estradiol, interferon
Triamcinolone 0.1% ointment, clobetasol 0.05% ointment, lidocaine 5% ointment

ALLERGIES

NKDA

SOCIAL HISTORY

The patient is married. She does not smoke and drinks 5 alcoholic beverages weekly.

PHYSICAL EXAM

The patient had coalescing well-demarcated, erythematous infiltrative plaques on her right and left labium majus and interlabial creases extending to the perineal body. She had scattered punched out ulcers on her right labium majus and interlabial crease and scattered scalloped ulcerations on her right labium minus. She had several erythematous patches and plaques overlying her trunk and extremities, including a 7.5 cm well-demarcated erythematous plaque in her left axilla.

HISTOPATHOLOGY

Vulva : There is a dense superficial and interstitial lymphoid infiltrate with small and medium cells some of which form lacuna. The dermis shows abundant eosinophils. The epidermis is hyperplastic with focal ulceration. Immunohistochemistry was performed and revealed cells which are CD3 positive with a predominance of CD4. The CD4:CD8 ratio is 6:1. The CD20, HSV CMV, and DPAS stains are negative. Biopsy for pan-tissue culture (bacterial, fungal, AFB) was also performed and was negative. Viral swab cultures for HSV were also negative.

DIAGNOSIS

Vulvar mycosis fungoides

TREATMENT AND COURSE

Interferon was discontinued. The patient received 2 additional cycles of pulsed dexamethasone with additional mild improvement in lesions and symptoms. She was then treated with external beam radiation to her left axilla, vulva and perineum. Within 1 month, her symptoms have improved rapidly, with near resolution of lesions on her vulva, perineum and left axilla.

DISCUSSION

Mycosis fungoides (MF) is an indolent form of cutaneous T-cell lymphoma (CTCL), a rare group of Non-Hodgkin lymphomas, characterized by the infiltration of malignant T-cells into the skin. CTCL accounts for approximately 4% of the Non-Hodgkin lymphomas in the U.S. Of the different subtypes of CTCL, MF and its leukemic variant, Sezary Syndrome, are the most common.

Clinically, lesions of MF present as pruritic, often scaly, erythematous patches and plaques that may infrequently evolve into tumors or generalized erythroderma. Lesions most frequently involve the cutaneous skin, preferentially in double-covered skin, and mucosal involvement is uncommon. Vulvar MF is a rare manifestation of CTCL, and there are few published cases. Presenting complaints include vulvar fissure, vulvar pruritus and dyspareunia. Vulvar MF may also present with infiltrative plaques or ulcers. In many cases, patients will also have cutaneous MF, and vulvar MF should be strongly considered in these patients with known disease who then present with new vulvar lesions, pruritus or pain.

The diagnosis of vulvar MF is challenging. The differential diagnosis for vulvar fissures and ulcers include infection (candidiasis, group B streptococcus, herpes simplex virus, cytomegalovirus, chancroid), eczematous disease (lichen simplex chronicus, atopic dermatitis, allergic or irritant contact dermatitis), lichen sclerosus, metastatic Crohn's disease or malignancy (vulvar intraepithelial neoplasia, extramammary Paget's disease, squamous cell carcinoma). Histopathology and immunochemistry of MF reveal a dense dermal infiltrate composed of predominantly CD4-positive atypical T-cells. T-gamma polymerase chain reaction analysis will demonstrate clonal T-cell rearrangement.

Treatment of vulvar MF initially involves the use of potent topical corticosteroids and topical anesthetics such as topical lidocaine 5% ointment. Systemic therapies including interferon, high-dose systemic corticosteroids, oral bexarotene and radiation have a role in the treatment of more refractory disease. External beam radiation has long been employed for the palliation and treatment of cutaneous MF tumors, ulcerations and fissures. The malignant CD4 cells of MF are among the most radiosensitive cells, and radiation can provide effective therapy and improve quality of life. In our patient, external beam radiation treatment resulted in dramatic resolution of MF plaques and ulcers with concomitant improvement in vulvar pruritus, dysuria and vulvar pain.

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CHICAGO DERMATOLOGICAL SOCIETY **CASE # 14**

Presented by Bryan Gammon, MD and Roopal Kundu, MD
Department of Dermatology, Feinberg School of Medicine, Northwestern University

HISTORY OF PRESENT ILLNESS
The patient is a 70 year old African American female with past medical history significant for hypertension who presents with a one-year history of a pruritic rash consisting of solitary and occasionally grouped pustules on the trunk and proximal extremities. She was diagnosed by an outside provider as having disseminated varicella zoster, and was treated with antivirals without relief. A biopsy performed at an outside facility was suggestive of impetiginized dermatitis. Direct immunofluorescence and anti-desmoglein antibodies were negative. She was started empirically on dapsone 100 mg BID, but could not tolerate it due to GI distress. She presented to our department for consultation.

PAST MEDICAL HISTORY
Hypertension

MEDICATIONS
Atenolol, hydrochlorothiazide, lansoprazole, alprazolam

FAMILY HISTORY
Non-contributory

ALLERGIES
Penicillin -- rash; codeine – vomiting; ampicillin

SOCIAL HISTORY
Smokes one half pack per day of tobacco and occasional alcohol use

PHYSICAL EXAM
The patient has flaccid pustules, scale crusts, and hyperpigmented patches on the chest, abdomen and back. Her mucous membranes, palms and soles were spared.

LABS
Abnormal: Wound culture, neck: rare coagulase negative *Staphylococcus aureus*
Negative/normal: CBC with differential, AST, ALT, creatinine, SPEP, G6-PD level, Varicella zoster IgM, anti-desmoglein 1 and anti-desmoglein 3 antibodies, glucagon level

HISTOPATHOLOGY
Left breast: There is subcorneal and intracorneal acantholysis with focal collections of neutrophils and nuclear debris. The upper dermis shows mixed inflammation with some exocytosis of neutrophils. Vasculitis was not identified.
DIF left breast: no evidence of immune deposits

DIAGNOSIS
Subcorneal pustular dermatosis

TREATMENT AND COURSE
The patient was initiated on dapsone 25 mg PO BID, and cleared completely without hematologic abnormalities or gastrointestinal distress.

DISCUSSION

Subcorneal pustular dermatosis (SCPD) is a rare, sterile pustular eruption that occurs most frequently in middle-aged women and follows a relapsing and remitting course. The classic lesion is a flaccid pustule that coalesces to form bullae in annular or serpiginous patterns. The trunk and intertriginous skin is most commonly affected, and mucous membranes are invariably spared.

The lesions may clinically resemble pemphigus foliaceus, subcorneal IgA pemphigus, acute generalized exanthematous pustulosis (AGEP), or pustular psoriasis. Distinction from AGEP or pemphigus is usually straightforward. However, distinguishing SCPD from classic pustular psoriasis may be challenging. In fact, some suggest that SCPD and pustular psoriasis are variants of the same disease process. In one report of a cohort of 23 patients with SCPD, 10 subsequently developed classic psoriatic lesions.

The lesions are histopathologically characterized by subcorneal accumulations of neutrophils with acantholysis. Biopsy of a very early lesion may demonstrate only a perivascular mixed inflammatory infiltrate with neutrophils and eosinophils. The exact pathogenesis of the disorder is unknown, but several descriptive studies have implicated certain cytokines in the pathogenesis of SCPD.

Numerous reports of disease associations with SCPD exist in the literature. Most significantly, SCPD is described as being associated with IgA gammopathy, as well as malignant IgA myeloma. As such, it is recommended that all patients diagnosed with SCPD be evaluated for myeloma with serum and urine protein electrophoresis.

Treatment of choice for SCPD is dapsone, with dosing ranging from 50-150mg daily. Clinical resolution occurs rapidly, usually within 4 weeks. For patients either recalcitrant to dapsone, or in those who develop hemolytic anemia or methemoglobinemia, acitretin and ultraviolet light therapy are reportedly efficacious.

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CHICAGO DERMATOLOGICAL SOCIETY **CASE # 15**

Presented by Lisa Arkin, MD; Sarah Chamlin, MD; and Amy Paller, MD
Department of Dermatology, Feinberg School of Medicine, Northwestern University

HISTORY OF PRESENT ILLNESS

This is a 2 year old female who has been followed since infancy for a persistent exfoliative erythroderma, brittle hair, and a history of atopy.

At birth she showed diffuse desquamating erythroderma and her perinatal course was complicated by pneumonia. Initial skin biopsy revealed bacterial colonization within a discohesive, parakeratotic epithelium; direct and indirect immunofluorescence studies were negative. When blood, skin, and respiratory cultures grew methicillin-sensitive S. aureus, the diagnosis of staphylococcal scalded skin syndrome (SSSS) was entertained and she was treated with IV antibiotics. Within weeks of discharge, she was readmitted with recurrent fever and erythroderma. A second skin biopsy, again in the setting of staphylococcal bacteremia, suggested recurrent SSSS. An extensive immunodeficiency work-up was negative.

Multiple courses of antibiotics, along with topical steroids, did not improve the cutaneous erythroderma. As her hair grew in, it appeared fine, sparse and lusterless, with scant eyebrows and lashes. At 2 months of age, light microscopic evaluation confirmed trichorrhexis invaginata of multiple hair shafts. During the next year, she developed multiple food allergies to egg, milk and peanuts, and chronic otitis externa requiring serial drainage by ENT. She remains below the 5th% for weight and height.

PAST MEDICAL HISTORY

Ex 37.5 weeker born via spontaneous vaginal delivery to a 17 yo G2P0→1 GBS+ mother with otherwise normal prenatal labs. Delivery was complicated by maternal chorioamnionitis and prolonged rupture of membranes. At birth, she required intubation for bradycardia and respiratory distress.

MEDICATIONS

Hydrocortisone 2.5% ointment, fluocinolone 0.1% oil, tacrolimus 0.03% ointment, acetic acid 2% drops

ALLERGIES

NKDA
Egg - angioedema, RAST + for peanut and milk

FAMILY HISTORY

There is no family history of ichthyosis or early childhood death. Older sibling has atopic dermatitis. Parents are not consanguineous.

PHYSICAL EXAM

Diffuse erythroderma with adherent scale throughout, most pronounced on her scalp, face, and trunk, with areas of desquamation of her hands and feet. Scalp with fine, sparse, brittle hair. Sparse eyebrows and eyelashes, normal conjunctiva. Normal nails. Ears impacted with cerumen bilaterally. No lymphadenopathy or hepatosplenomegaly. No mucous membrane involvement.

LABS

Abnormal: IgA 135 mg/dl [ref 14-122]; IgE 175 mg/dl [ref <52]
Negative/normal: CBC with differential, mitogen studies, T cell flow cytometry, IgG & IgM

HISTOPATHOLOGY

Back, right lower – Prominent parakeratosis, with split dyscohesion throughout, which also involves the superficial granular layer. There is a mild perivascular mononuclear cell infiltrate with bacterial colonization in the fragments of dyshesive parakeratotic epithelium. Gram stain +gram positive cocci, culture + MSSA. Direct immunoflourescence is negative.

Back, right lower – Chronic spongiotic dermatitis with icthyosiform changes and superficial acantholysis. Gram stain shows gram positive cocci within the stratum corneum. DPAS is negative. Direct immunoflourescence is negative.

Hair mount – Trichorrhexis invaginata

DIAGNOSIS

Netherton Syndrome

TREATMENT AND COURSE

Various topical therapies have been prescribed, including low potency topical steroids (used sparingly due to concern for systemic absorption), antiseptic baths, and emollients, which remain the mainstay of her therapy. Most recently, her mother has been applying topical tacrolimus to limited areas of her face and arm, with some improvement in erythema and scaling.

DISCUSSION

Netherton syndrome is an autosomal recessive disorder characterized by congenital erythroderma and ichthyosis, hair shaft abnormalities, and an atopic diathesis. The disease was first described by Comel in 1949 and subsequently documented by Netherton in 1958. Although it is rare with an estimated prevalence of 1 in 200,000, Netherton syndrome may account for as many as 20% of individuals with congenital erythroderma.

The disease typically presents in the neonatal period with generalized erythroderma and scaling, which may be associated with bacterial superinfection and secondary sepsis. Histologic and ultrastructural studies are nonspecific but may reveal abnormal cornification with incomplete keratinization of the epidermis. Life-threatening complications include dehydration, severe hypernatremia, and hypothermia. Patients who survive the neonatal period often fail to thrive due to compromised barrier function, increased metabolic requirements, and recurrent infections.

The cutaneous phenotype can be quite variable over time. In some, the exfoliative erythroderma persists, while others develop erythematous, serpiginous and circinate hyperkeratotic plaques with double-edged scale, termed icthyosis linearis circumflexa. Immune dysregulation produces a Th2 skewed response with severe atopy (including angioedema and anaphylaxis), elevated IgE levels, and eosinophilia. Atopic dermatitis may complicate the cutaneous picture and can be difficult to treat. Finally, the pathognomonic hair shaft abnormality, trichorrhexia invaginata or "bamboo hair," typically develops in early childhood and is due to swelling and invagination of the distal part of the hair shaft to its proximal part. Several hairs should be examined for this clinical sign, and eyebrows often show the trichorrhexis invaginata most easily. A host of other structural hair abnormalities, including pili torti, trichorrhexis nodosa, and trichoclasis, generally co-exist.

The disease is caused by pathogenic mutations in the SPINK5 gene on chromosome 5q32, which encodes a serine protease inhibitor termed LEKTI (Lymphoepithelial Kazal-Type related Inhibitor). LEKTI is strongly expressed in epithelial and lymphoid tissue and localizes to the most mature, differentiated cells, including those in the stratum corneum. Loss of function has been shown to result in unchecked proteolytic activity with consequent destruction of corneocytes. Accelerated proteolysis, particularly because of increased expression of elastase 2, impairs both filaggrin and lipid processing, contributing to the formation of an abnormal cornified envelope. This defective epidermal barrier may also facilitate exposure to allergens with resultant development of an IgE-mediated response. Kallikrein 5, a proteolytic

enzyme that is markedly increased in activity in Netherton syndrome, has also been shown to activate protease activated receptor 2 (PAR2) and increase thymic stromal lymphopoietin (TSLP) expression in skin. Given that PAR2 and TSLP have been implicated as important drivers of atopic dermatitis, they may contribute to the cutaneous inflammation of Netherton Syndrome. Finally, LEKTI is thought to contribute to the anti-inflammatory and anti-microbial properties of epithelial cells, with loss of function increasing the risk of recurrent infections.

Treatment is conservative and largely supportive. Emollients remain the mainstay of therapy. Topical steroids can be helpful when used sparingly due to the risk of increased transcutaneous absorption. Topical tacrolimus may be useful but also carries a risk of systemic absorption and requires close monitoring of serum levels. In our personal experience, tacrolimus levels can be undetectable, despite application of tacrolimus to large areas of the body surface, stressing that this therapy should not be ignored when levels to check for possible toxicity can be checked. The administration of systemic or topical retinoids is controversial.

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CHICAGO DERMATOLOGICAL SOCIETY **CASE # 16**

Presented by Benjamin Marks, MD, PhD, Joaquin Brieva, MD, and Anne Laumann, MBChB,MRCP(UK)
Department of Dermatology, Feinberg School of Medicine, Northwestern University

HISTORY OF PRESENT ILLINESS
This 48 year old Caucasian female with a history of interstitial lung disease, bronchiolitis obliterans with organizing pneumonia (BOOP), currently managed with prednisone presented to a rheumatologist in early 2008 for new onset of arthralgias, myalgias and Reynaud's phenomenon. At that time her rheumatologist suspected a collagen vascular disease and she was started on methotrexate with the goal of weaning prednisone. As the prednisone was tapered down, the patient developed an erythematous eruption on her posterior legs and buttock in addition to thickening of the skin on her palms. The patient was thus referred to dermatology for further evaluation.

PAST MEDICAL HISTORY
Hypothyroidism

MEDICATIONS
Prednisone, tacrolimus(oral), tacrolimus 0.1% ointment , urea 20% cream, levothyroxine, naproxen, vitamin D

FAMILY HISTORY
Arthritis, heart disease and hypertension

SOCIAL HISTORY
The patient is married and works as a teacher. She does not use alcohol or tobacco.

PHYSICAL EXAM
The palmar and lateral hands are hyperkeratotic with a thick scale. The fingers are tapered and show prominent capillary loops at the paronychial folds. The buttocks, posterior legs and posterior medial arms have large tan patches with geographic borders. Strength is preserved throughout the upper extremities, but her legs show proximal muscle weakness and pain with movement.

LABS
Abnormal: WBC: 12.4 K/UL [ref 3.5-10.5]; platelet count: 702 K/UL [ref 140-390]; AST: 160 U/L [ref 0-40]; ALT: 170 U/L [ref 0-48]; Albumin: 3.0 G/DL [ref 2.5-5.0]; Aldolase: 50 U/L [ref <8]; CPK: 2598 U/L [ref 0-125]; ESR: 35 mm/hr [ref 2-25]; Jo-1 quantitative: 166 U [ref <20]
Negative/normal: Hgb, Chem-7, ANA, anti-RNP, SS-A, SS-B, Smith, Scl-70, RF, CCP, C3, C4, bilirubin, alkaline phosphatase

DIAGNOSIS
Anti-synthetase syndrome

TREATMENT AND COURSE
The patient was initially treated with prednisone and methotrexate, however the methotrexate was later replaced by tacrolimus due to gastrointestinal upset. As the prednisone was subsequently tapered, the patient experienced progressive joint pain and weakness. Laboratory evaluation revealed drastically increased serum creatine phosphokinase. The patient was thus restarted on high dose prednisone.

DISCUSSION
Polymyositis and dermatomyositis are idiopathic inflammatory myopathies characterized by circulating autoantibodies in the setting of symmetric proximal muscle weakness. A distinct subset of dermatomyositis is the anti-synthetase syndrome. This subset of patients present with one or more of the

following clinical symptoms: myositis, interstitial lung disease, polyarthritis, Raynaud's phenomenon, mechanic's hands and fever. There is a female to male ratio of 2:1. It is evenly distributed among all age groups.

Laboratory data consists of anti-synthetase autoantibodies with the most common being anti-Jo-1 (15-20%) followed by PL-7 (5-10%), EJ (5-10%) OJ (5%) PL-12 (<5%), KS (<5%), Zo (<1%) and YRS (<1%). These antibodies are directed against enzymes that acetylate tRNAs. Several viruses, such as the picornavirus family (which includes the Coxsackie viruses), use these enzymes during replication within host cells. Viral RNA and histidyl-tRNA synthetase form a complex within myocytes during this process which may facilitate immune activation to self-antigen resulting in autoantibody production.

Treatment of the inflammatory myositis and idiopathic pulmonary fibrosis is of primary concern. Glucocorticoids have proven to be effective for articular, muscular and constitutional symptoms, as well as some forms of pulmonary disease. Other treatment options include cyclophosphamide, tacrolimus and cyclosporine A. One study has shown that methotrexate and azathioprine are not effective for anti-synthetase syndrome.

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CHICAGO DERMATOLOGICAL SOCIETY **CASE # 17**

Presented by Annie Goldsberry, MD, MBA and Amy Paller, MD
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HISTORY OF PRESENT ILLNESS
A six month old Mediterranean female presents for evaluation of slightly thickened skin on her toes and a history of her hands and feet "turning white" in the water. She also develops fissures on her fingers when she sucks on them. Her mother notes that she has malodorous hands and feet on occasion. The patient's parents denied any skin thickening on other parts of the body.

PAST MEDICAL HISTORY
Born at full term by spontaneous vaginal delivery; no perinatal or subsequent medical problems

MEDICATIONS
None

ALLERGIES
NKDA

FAMILY HISTORY
Father has a history of palmoplantar hyperkeratosis since the age of 3. He was diagnosed with Mal de Meleda based on genetic analysis of a SLURP-1 mutation by Dr. Daniel Hohl in Switzerland. The patient's parents are of Middle Eastern descent and are noted to be third cousins. Her father's parents are also related. There is no other family history of palmoplantar keratoderma.

PHYSICAL EXAM
The patient is a well-appearing, well-nourished female in no apparent distress. On the tips of the toes there is mild thickening with a slightly white appearance. There are increased skin markings on the palmar surface of fingers without overt hyperkeratosis or erythema. The remainder of the cutaneous examination was within normal limits.

Her father had diffuse palmoplantar hyperkeratosis on both hands and feet with transgredient spread to the dorsal aspect of the distal tips. The hyperkeratosis is sharply demarcated and there is mild erythema. No other hyperkeratotic plaques on rest of body. The teeth and hair are normal.

DIAGNOSIS
Congenital palmer hyperkeratosis, likely Mal de Meleda

TREATMENT AND COURSE
In general, autosomal recessive disorders are not passed to offspring, except in the unusual situation of an affected individual marrying a carrier (in which case there is a 50% chance of transmission). In SE's case, the family history of Mal de Meleda sensitized the parents to consider the possibility of Mal de Meleda PPK. The mild hyperkeratosis would otherwise surely have been considered a normal variant. We have been in touch with Dr. Hohl to confirm the causative SLURP-1 mutation, and he has agreed to analyze the genomic DNA in SE. Given that patient's age and mild presentation, she was advised to use moisturizers for the hyperkeratosis.

Her father has responded well to the application of tazarotene 0.1% cream daily.

DISCUSSION

Mal de Meleda is a rare autosomal recessive congenital palmoplantar keratoderma. It is also referred to as Meleda disease, Mljet disease, Keratosis palmoplantaris, Transgradiens of Siemens, Mutilating palmoplantar keratoderma of the Gamborg-Nielsen Type, Palmoplantar ectodermal dysplasia type VIII, Palmoplantar keratoderma of the Norrbotten type, and Acral keratoderma. Mal de Meleda was first described in 1826 by L. Stulli. Although affected individuals have been described worldwide, a founder effect is responsible for the high concentration of individuals on the island of Mljet, off the Dalmatian coast where the disease occurs in 1 in 200 individuals. In contrast, Mal de Meleda occurs at a frequency of only 1 in 100,000 individuals of the general population. The gene defect responsible for the clinical manifestations of Mal de Meleda is a mutation in the ARS Component B gene which encodes SLURP-1 (secreted Ly-6/uPAR related protein 1), which is located at chromosome 8q24.3. SLURP-1 regulates keratinocyte differentiation by potentiating the action of acetylcholine. It has been linked to transmembrane signal transduction, cell activation, and cell apoptosis.

Clinically there is hyperkeratosis of the palms and soles that occurs in a transgredient (extending to the dorsal surface) pattern. Affected individuals may also have hyperhidrosis, deep fissuring and secondary bacterial or fungal infections, leading to a malodorous maceration. In addition, perioral erythema, brachydactyly (short, cone shaped fingers), and nail abnormalities (koilonychia, subungual hyperkeratosis, or parchyonychia) are also seen. Severe cases can have constricting bands around the digits which can lead to spontaneous amputation (pseudoainhum).

The diagnosis is made through DNA sequencing to identify the gene mutation. The Ly-6/uPAR related protein 1 is secreted in biological fluids such as sweat, saliva, tears, and urine. As the protein is present in fluids, Favre et al postulated that immunologic testing for the protein could be used for rapid screening, and these tests are currently in development.

Histopathology of lesional skin from patients with Mal de Meleda shows acanthosis, pseudospongiosis, small papillary bodies, enlarged sweat glands with a perivascular lymphohistiocytic infiltrate.

As in other types of hereditary and nonhereditary palmoplantar keratodermas, patients can achieve symptomatic improvement with saltwater soaks, paring, topical keratolytics, and topical retinoids. Patients treated with acitretin experience improvement in hyperkeratosis and reduction in contractures of the hands but continue to have erythema. Patients require long term treatment, experiencing relapse with cessation of medication.

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CHICAGO DERMATOLOGICAL SOCIETY **CASE # 18**

Presented by Sarah Baker, MD and Murad Alam, MD, MSCI
Department of Dermatology, Feinberg School of Medicine, Northwestern University

HISTORY OF PRESENT ILLNESS
The patient is a 76 year old African American female who presents for evaluation of a large mass on her right upper back. She describes that it started as a small "pimple," which was present for many months. However, over the course of 2 months, the lesion grew rapidly to the size of a "golf ball." The patient was initially seen by an outside dermatologist who performed an incisional biopsy. Pathology showed an incompletely excised sebaceous carcinoma, and she was subsequently referred to our institution for further evaluation and treatment options.

PAST MEDICAL HISTORY
Congestive heart failure, hyperlipidemia, hypertension, obesity

MEDICATIONS
Aspirin, tramadol, furosemide, spironolactone, digoxin, lisinopril, lovastatin, metoprolol

PAST SURGICAL HISTORY
Normal colonoscopy 2007, sigmoidectomy for bowel perforation and colovaginal fistula 1998 (not associated with malignancy), left axillary cyst removal, total abdominal hysterectomy

FAMILY HISTORY
Papillary thyroid carcinoma (daughter); No colon, breast, ovarian, uterine, or genitourinary cancer

PHYSICAL EXAM
On the right upper back, there is a 3 cm firm, poorly defined reddish brown nodule with overlying yellow oily papules. No cervical, supraclavicular, axillary or inguinal lymphadenopathy is noted.

LABS
CT chest/abdomen/pelvis: negative for metastatic disease

HISTOPATHOLOGY
Back: Sections reveal a large multilobular tumor with superficial ulceration. Focal pagetoid changes and scattered necrotic areas with a comedo-like appearance are noted. There is cellular pleomorphism with a high nuclear cytoplasmic ratio and numerous mitotic figures. Some cells display squamoid changes and vacuolated cytoplasm. The stroma shows variable fibroplasia with a lymphohistiocytic infiltrate. MLH1 and MSH2 show normal expression within the tumor.

DIAGNOSIS
Extra-ocular sebaceous carcinoma

TREATMENT AND COURSE
Mohs micrographic surgery was used to clear the peripheral margins of the tumor. A total of seven stages were performed, leaving a 15 x 20 cm defect extending to muscle. Peripheral margins were clear of tumor; however the deep margin remained positive. As per institutional protocol for removal of large, uncommon, deeply penetrating nonmelanoma skin cancers, the patient was referred to surgical oncology for clearance of the residual deep margin in the operating room and repair of the resulting defect by plastic surgery. At the time of resection of the deep margin under general anesthesia, the margin was assessed intraoperatively by surgical pathology, and the wound was closed by plastic surgery with a split thickness skin graft. Subsequent permanent section analysis of the excised tumor

revealed focal residual tumor at the deep margin. After a lengthy discussion between the patient, her family and the surgical and medical oncology teams, the decision was made to monitor the patient carefully with serial physical examinations and imaging.

DISCUSSION

Sebaceous carcinoma is a rare, aggressive cutaneous neoplasm which has the propensity to metastasize to lymph nodes and distant organs in up to 25% of cases. These tumors most commonly arise from the sebaceous glands in the periocular region, and 75% of all sebaceous carcinomas are located on the head and neck. While large truncal lesions such as the case presented are uncommon, they have been reported in the literature. Risk factors for the development of sebaceous carcinoma include increased age, ethnicity (Caucasian, South Asian and East Asian), previous radiation therapy, genetic disorders such as Muir-Torre syndrome, immunosuppresion, and pre-existing nevus sebaceous.

Clinically, sebaceous carcinomas may present as non-specific yellow papules, nodules or subcutaneous thickening. When near the eye, they are sometimes mistaken for benign lesions such as chalazia. Given the diverse presentation, histopathological evaluation is crucial for the diagnosis of sebaceous carcinoma. Microscopically, these tumors typically exhibit an irregular lobular growth pattern with atypical sebocytes containing bizarrely configured hyperchromatic nuclei and numerous mitotic figures. Frothy eosinophilic cytoplasm laden with lipid globules may also be seen, and tumor cells may involve adjacent epithelium, displaying pagetoid spread.

In all patients with sebaceous carcinoma, it is important to consider the potential association with Muir-Torre syndrome, an autosomal dominant condition characterized by cutaneous tumors (sebaceous adenomas, carcinomas and epitheliomas; keratoacanthomas) as well as internal malignancies (colon, genitourinary, hematologic and breast malignancies). Muir-Torre is due to mutations in the DNA mismatch repair genes MLH1 and MSH2, and was excluded in our patient based on the normal expression of these markers on histopathology. Interestingly, sebaceous carcinomas associated with Muir-Torre syndrome are thought to be less aggressive, less likely to metastasize, and more likely to occur in extraocular locations.

A multidisciplinary surgical and pathological approach is often appropriate for the treatment of medium to large sebaceous carcinomas. At our institution, Mohs micrographic surgery is utilized to clear the peripheral margins of the tumor, and the final stage is sent for permanent sections. The deep tumor margins are subsequently removed by surgical oncology, and frozen sections are evaluated intraoperatively. Once tumor clearance is confirmed, the resulting defect may be repaired by plastic surgery with the necessary flaps or grafts.

While surgery remains the first-line approach in the treatment of sebaceous carcinoma, radiation and chemotherapy have been used to treat inoperable, metastatic or recurrent cases, especially those involving the orbit. Radiation may also be used as adjuvant therapy for tumors that cannot be completely resected. Sentinel lymph node biopsies have been performed in a small number of cases; however, there is limited evidence to suggest their utility, and their interpretability is limited due to the lack of sufficient reference cases. Poor prognostic factors for sebaceous carcinoma include lymphovascular or perineural invasion, poor differentiation, pagetoid spread, and tumor diameter greater than 10mm. Sebaceous carcinomas are associated with overall survival rates of approximately 91.9% at 5 years and 79.2% at 10 years, but some reports note a 5 year mortality rate nearing 20%.

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CHICAGO DERMATOLOGICAL SOCIETY **CASE # 19**

Presented by Sonal Shah, MD and Anthony J. Mancini, MD
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PATIENT A

HISTORY OF PRESENT ILLNESS
A 6 week old female presented for evaluation of greater than 35 2-20 mm infantile hemangiomas. Per her parents, these lesions began to develop within the first week of life. They were first noted on her face and trunk but had since spread to her extremities. They appeared to be asymptomatic and the family denied any history of bleeding or ulceration.

PAST MEDICAL HISTORY
Otherwise healthy

MEDICATIONS
None

ALLERGIES
No known drug allergies

FAMILY HISTORY
Noncontributory

SOCIAL HISTORY
Lives at home with parents.

PHYSICAL EXAM
On the scalp, face, ears, trunk, buttocks, and extremities, there were approximately 35-40 red/purple vascular papules and small plaques, ranging in size from 2 - 20 mm. No lesions appreciated on lips, oral mucosa, or perianal areas. Few small vascular papules on right upper eyelid. Mild hepatomegaly was present.

DIAGNOSIS
Diffuse neonatal hemangiomatosis

TREATMENT AND COURSE
Abdominal ultrasound revealed multiple liver hemangiomas. Her hepatomegaly increased over the course of two weeks, so oral propranolol 1.5 mg/kg/day was started and later increased to 2.0 mg/kg/day. Abnormal thyroid studies were identified with a TSH of 9.47 mIU/L and a normal free thyroxine, for which she was placed on thyroid replacement. After two months her thyroid function normalized and medication was discontinued. After four months of propranolol therapy, the cutaneous infantile hemangiomas were partially involuted and repeat abdominal ultrasound revealed a decrease in the size of the hepatic hemangiomas as well as complete resolution of one of the lesions. No features of high-output cardiac failure were noted throughout the course of therapy.

PATIENT B

HISTORY OF PRESENT ILLNESS
An 8 week old female was admitted to the hospital for evaluation of a new cardiac murmur. She had been in her usual state of health until two days prior to admission when she developed cough,

decreased oral intake, and diaphoresis. She had multiple 1-3 mm vascular papules on her trunk, extremities, and scalp. Ultrasound and CT examination of the abdomen showed several multifocal vascular hepatic lesions and increased hepatic vasculature. She was diagnosed with high-output cardiac failure secondary to diffuse neonatal hemangiomatosis. She was started on oral corticosteroids at 2 mg/kg/day as well as propranolol 1.5 mg/kg/day. Additionally, she was also started on spironolactone, digoxin, and ranitidine.

PAST MEDICAL HISTORY
Infantile hemangiomas, high-output cardiac failure

MEDICATIONS
Prednisolone, digoxin, furosemide, propranolol, ranitidine, spironolactone

ALLERGIES
No known drug allergies

FAMILY HISTORY
Non-contributory

SOCIAL HISTORY
Lives at home with mother.

PHYSICAL EXAM
Skin exam revealed numerous 1-3 mm bright red vascular papules scattered on her trunk, extremities, and scalp. No ulcerations or bleeding noted. Her liver exam revealed a palpable liver edge approximately 2 cm below the right costal margin. On cardiac examination she had a 2/6 systolic ejection murmur along the left sternal border. She had 2+ peripheral pulses bilaterally.

DIAGNOSIS
Diffuse neonatal hemangiomatosis with high-output cardiac failure.

TREATMENT AND COURSE
On propranolol, furosemide, and digoxin her cardiac function continued to improve and she was tapered off of the prednisolone in 4 months. On propranolol there was continued improvement in the size of the cutaneous lesions. Abdominal CT after 2 months showed a decrease in size of the hepatic hemangiomas, and 16 months later revealed complete regression of the lesions. After 20 months of propranolol therapy the medication was discontinued with complete resolution of both hepatic and cutaneous hemangiomas.

PATIENT C

HISTORY OF PRESENT ILLNESS
A 3 month old male presented for evaluation of multiple cutaneous hemangiomas. Shortly after birth he was noted to have 8 cutaneous vascular papules, the largest of which were on his scalp and the left dorsal hand. A routine echocardiogram performed for a patent ductus arteriosus revealed multiple liver hemangiomas, which were later confirmed by Doppler ultrasound. At 3 months of age a follow-up echocardiogram showed a dilated left ventricle (with no clinical signs of heart failure) and he was admitted for further management. He was also noted to have an elevated TSH with normal T4 on laboratory evaluation. He was started on thyroid replacement, digoxin, furosemide, and propranolol 1.0 mg/kg/day for presumed hemangiomatosis with early cardiac failure.

PAST MEDICAL HISTORY
Patent ductus arteriosus, diffuse neonatal hemangiomatosis, hypothyroidism

MEDICATIONS
Digoxin, furosemide, propranolol, levothyroxine

ALLERGIES
No known drug allergies

FAMILY
Non-contributory

SOCIAL HISTORY
Lives at home with parents and sibling.

PHYSICAL EXAM
He was a well-developed, well-nourished male in no apparent distress. His skin and mucosal examinations revealed multiple small cutaneous vascular papules and plaques on trunk and extremities. Of note, left dorsal hand had a 7 mm vascular papule, and his left plantar foot had a pinpoint vascular macule. There was no ulceration or bleeding. No hepatomegaly was noted. On cardiac examination he had a 2/6 systolic ejection murmur at the upper left sternal border that radiated throughout the entire precordium.

DIAGNOSIS
Diffuse neonatal hemangiomatosis

TREATMENT AND COURSE
The patient's dose of propranol was increased to 1.5 mg/kg/day. Echocardiogram revealed resolution of left ventricular dilation so digoxin and furosemide were discontinued. His TSH continued to trend downward and his dose of levothyroxine was also decreased. After 4 months of propranol therapy the majority of his cutaneous hemangiomas had resolved, and abdominal ultrasound showed regression in his hepatic lesions.

DISCUSSION
Infantile hemangiomas (IH) are the most common benign tumors in infancy. They occur in up to 5-10% of all infants, and in 30% of premature infants. Up to 90% of IH will resolve spontaneously, however in certain circumstances, either location or complications associated with these lesions may warrant treatment. IH can be limited to the skin, or can have visceral involvement as well. Diffuse neonatal hemangiomatosis refers to multiple cutaneous hemangiomas as well as diffuse visceral involvement. The most common site for visceral hemangiomas is the liver, called infantile hepatic hemangiomas (IHH). IHH are classified into 3 categories based on their pattern of involvement: focal, multifocal, or diffuse. The diffuse pattern of IHH carries a risk of high output cardiac failure due to high volume of vascular shunting. In addition, hypothyroidism can also occur due to overproduction within the hemangioma tissue of iodothyronine deiodinase, an enzyme that deactives thyroid hormone. A variety of treatments have been employed for IH (both cutaneous and hepatic), most notably systemic corticosteroids, vincristine, cyclophosphamide, interferon, and laser therapy. These treatments had variable response rates and carried with them a high side effect profile, which often outweighed the benefits of the medication.

A recent major development in IH management has been the use of the non-selective beta blocker, propranolol. The effects of propranolol on hemangiomas were discovered incidentally and it is has evolved to become the first line therapy in the treatment of most of these vascular lesions, primarily

related to the excellent clinical response and safety profile. Propranolol is a non-selective β adrenergic antagonist which inhibits both β1 and β2 receptors. Proposed mechanisms of action include the ability of propranolol to induce vasoconstriction, inhibit angiogenesis, and the induce apoptosis in capillary endothelial cells of hemangiomas. It has been used extensively for cutaneous hemangiomas with reduction in size and cessation of growth as well as more rapid involution. There have also been reports in the literature of successful treatment of a subglottic hemangioma that was obstructing the airways.

Less described in the literature is the treatment of diffuse neonatal hemangiomatosis with liver involvement with propranolol. A recent case series in the Journal of Pediatrics described 8 cases of patients with IHH, 3 of which were in clinical heart failure, all treated with propranol with good outcomes. All 8 of the patients experienced clinical and or radiographic improvement in their lesions.

In our patient series, all of the patients had complications secondary to their diffuse neonatal hemangiomatosis including hypothyroidism or high-output cardiac failure. Within a short duration of time after starting propranolol therapy, not only did their hemangiomas improve, but their associated complications improved or reversed as well. In all of the patients described, the medication was well tolerated without any significant toxicities noted. Given our experience with treating hemangiomas, we propose that propranolol be considered a first line agent in the treatment of IHH. However, randomized prospective studies are needed to support this recommendation.

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CHICAGO DERMATOLOGICAL SOCIETY **CASE # 20**

Presented by Nilanthi Gunawardane, MD, Jonathan Cotliar, MD, and Joan Guitart, MD
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HISTORY OF PRESENT ILLNESS
A 60 year old Caucasian male with cutaneous T-Cell lymphoma/Sezary Syndrome presented with a two day history of a diffuse erythematous eruption, associated fevers, and fatigue. Three days prior to presentation, the patient had been discharged after a short hospitalization for MRSA cellulitis associated with a chronic leg ulcer. He had been discharged on intravenous vancomycin therapy.

PAST MEDICAL HISTORY
Cutaneous T-Cell Lymphoma/Sezary Syndrome

MEDICATIONS
Doxorubicin, vancomycin

ALLERGIES
NKDA

FAMILY HISTORY
Non-contributory

SOCIAL HISTORY
Nonsmoker. Occasional EtOH.

PHYSICAL EXAM
Upon examination, the patient appeared toxic and was erythrodermic with over 90% BSA involved. His intertriginous skin displayed prominent desquamation. A Nikolsky sign was positive. Mucous membranes were uninvolved.

LABS
Abnormal: WBC 11.2 K/uL [ref 3.5-10.5], Neutrophils 92%
Blood cultures: negative
Tissue culture: *Staphylococcus aureus* (oxacillin resistant)
Negative/normal: Chem-7

HISTOPATHOLOGY
Axilla: Subcorneal vesicle formation at the level of the granular cell layer with prominent acantholysis and scattered neutrophils and nuclear debris. Upper dermis shows edema and a mixed inflammatory infiltrate. DPAS, Gram and acid fast bacilli stains were negative for microorganisms.

DIAGNOSIS
Adult MRSA-induced Staphylococcal Scalded Skin Syndrome without renal disease

TREATMENT AND COURSE
The patient was briefly treated with IV corticosteroids given concern for a hypersensitivity eruption to vancomycin. Upon admission, patient had a higher creatinine level when compared to his baseline, likely due to dehydration. This resolved with IV fluids within the subsequent 24 hours. After a frozen section confirmed the diagnosis of SSSS, the steroids were discontinued, and the patient was transitioned to daptomycin and clindamycin. His symptoms gradually abated, and he was discharged home in his usual state of health.

DISCUSSION

Staphylococcal Scalded Skin Syndrome (SSSS) was first described by Baron Gotfried Ritter von Rittershain in 1878. It is usually seen in infants and children under the age of 5 yrs. Adult SSSS is rare and was first reported in 1972. There are now more than 50 reported cases of adult SSSS in the literature.

The onset of SSSS is preceded by a localized staphylococcal infection, frequently conjunctivitis or an upper respiratory infection. Subsequently, patients develop fever accompanied by diffuse erythematous, tender patches and flaccid bullae in the flexural areas. These bullae rupture revealing a red, beefy base with a scalded appearance. The diagnosis of SSSS is established based on the clinical and histopathologic pattern in the setting of infection with exfoliative toxin-producing strains of S. aureus. Given the histologic similarity, direct immunofluorescence may sometimes be needed to exclude pemphigus foliaceous.

SSSS occurs rarely in healthy adults, likely a result of the presence of antibodies against the exotoxins and rapid renal excretion. Approximately 91% of adults have been found to have antibodies against ETA. Most cases of adult SSSS occur in the setting of chronic renal failure or immunosuppression. The exotoxin responsible for SSSS is renally excreted and impaired renal function can increase the exotoxin burden, precipitating the disease. Individuals who are immunosuppressed as a result of malignancy, immunosuppressive drugs, HIV or alcohol abuse have a higher incidence of SSSS. This is thought to be a result of increased proliferation of S. aureus with resulting higher exotoxin burden.

SSSS is a result of cleavage of Desmoglein 1 by exfoliative toxins (ETA and ETB) produced by Staph aureus strains. Although phage II strains are most common, especially in children, phage I and III strains have also been isolated in adults. SSSS due to MRSA is less common and only a few cases of SSSS due to MRSA have been reported in adults.

SSSS in adults and children differ in a few ways. Adults with SSSS are more likely to develop extensive blistering complicated by hypotension, electrolyte disturbances and hypothermia when compared to children or infants. S. aureus can also be cultured from the blood in most adults with SSSS as opposed to less than 3% of children with SSSS. Moreover, the mortality rates in adults have been reported to be close to 60%, much higher than in children, likely due to comorbid disease.

Management of patients with SSSS includes prompt initiation of parenteral antibiotics as well as wound care, pain management, fluid management and nutritional support.

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CHICAGO DERMATOLOGICAL SOCIETY **CASE # 21**

Presented by Sapna Patel Vaghani, MD and Anthony J. Mancini, MD
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HISTORY OF PRESENT ILLNESS

The patient is a 16 year old healthy female who presented with a growing lesion on her right index finger. Three weeks prior to presentation, she was at a petting zoo and was bitten by a goat, with some initial bleeding. Over the next few days, she developed a hemorrhagic papule at the site. She was seen by her PCP who attempted incision and drainage, but no fluid was expressed. The lesion continued to enlarge and started draining purulent fluid, which was sent for bacterial and viral culture by the PCP. She was also started on valcyclovir, amoxicillin/clavulanic acid, and mupirocin ointment. At the time of presentation in our clinic, the swelling had improved, and she felt the lesion was stable. She reported intermittent pruritus and only mild discomfort and denied any fevers or other symptoms.

PAST MEDICAL HISTORY

Depression. No surgeries.

MEDICATIONS

Valcyclovir, amoxicillin/clavulanic acid, mupirocin ointment.

SOCIAL HISTORY

12th grade student

PHYSICAL EXAM

Right index finger - 2.5 x 2cm erythematous to violaceous nodule with an overlying purulent bulla over the distal, dorsal aspect (between the PIP and DIP joint) extending to proximal nail fold. Mild swelling of the finger, partially limits movement. Non-tender. No active drainage or bleeding.

DIAGNOSIS

Orf (ecthyma contagiosum)

TREATMENT AND COURSE

The patient was continued on mupirocin ointment twice daily and started on hydroxyzine at bedtime for pruritus. She completed the course of valcyclovir and amoxicillin/clavulanic acid. 10 weeks after initial presentation, the lesion had almost completely resolved with minimal scarring.

DISCUSSION

Orf, also known as ecthyma contagiosum, is an infection caused by the orf virus, which belongs to the Parapoxvirus genus of double-stranded DNA viruses. This genus also encompasses the virus that causes milker's nodule. Orf is widespread in sheep and goats, and less frequent in reindeer, and infection causes a scabby, sore mouth. It is transmitted to humans by direct contact with an infected animal or with contaminated carcasses or fomites. Human to human transmission does not occur. Orf is most commonly seen in farming communities and amongst meat handlers, shepherds, and veterinarians, with the highest prevalence found in Europe and New Zealand. The virus is relatively resistant to physical damage and survives the winter on hedges, feeding troughs, and in barns.

Orf infection in humans typically begins as a small papule or less frequently as a few lesions on the dorsal aspect of the fingers, hands, or forearms about one week after exposure. The papule is often reddish-blue and grows to form a hemorrhagic flat-topped pustule or bulla, sometimes with an umbilicated center. The fully developed lesion is usually 2-3 cm in diameter but can be as large as 5 cm. It is often tender and friable. The infection goes through 6 clinical stages, and each lasts about one week.

- Stage 1 (maculopapular) - A red elevated lesion
- Stage 2 (targetoid) - A bulla with an iris-like configuration (nodule with a red center, a white middle ring, and a red periphery)
- Stage 3 (acute) - A weeping nodule
- Stage 4 (regenerative) - A firm nodule covered by a thin crust through which black dots are seen
- Stage 5 (papillomatous) - Small papillomas appearing over the surface
- Stage 6 (regressive) - A thick crust covering the resolving elevation

Low-grade fevers and malaise can occur but these symptoms typically resolve after 3-4 days. Regional lymphadenopathy and lymphangitis may also be seen. Immunocompromised patients and those with atopic dermatitis often develop fungating lesions. In addition, immunocompromised patients can develop progressive, destructive lesions that are refractory to treatment with antiviral therapy and surgical debridement.

The differential diagnosis includes erysipeloid, furuncle, sporotrichosis, milker's nodule, tularemia, anthrax and acute febrile neutrophilic dermatosis. Although orf is typically a clinical diagnosis, confirmation can be obtained via electron microscopy (EM) of the crust of a small biopsy, or of fluid obtained from the lesions. EM cannot, however, distinguish between the orf virus and other parapoxviruses. Polymerase chain reaction (PCR) can definitively identify a parapoxvirus as orf virus. It is ideally performed on frozen tissue specimens, vesicle material, or scab debris from orf lesions.

Histopathology reveals an epidermis with marked pseudoepitheliomatous hyperplasia. Necrosis of the epidermis with ulceration occurs in the center of the lesion. Intranuclear and intracytoplasmic inclusion bodies with vacuolization and acantholysis of keratinocytes is caused by the virus. Pyknosis of individual keratinocytes occurs. A dense inflammatory infiltrate of plasma cells, macrophages, histiocytes, and lymphocytes is also seen.

Orf is a self-limited disease, but symptomatic treatment with moist dressings, local antiseptics, and finger immobilization is helpful. Cryotherapy has been reported to shorten the duration of disease. Successful use of topical imiquimod and cidofovir have been reported. Electrodessication and curettage or shave excision may be used to treat large, exophytic lesions. Secondary bacterial infection from orf is not uncommon and should be treated with topical or systemic antibiotics. Animals should be vaccinated every 6-8 months, which is the best method for prevention. The prognosis is excellent, with most lesions healing with scarring within 4-8 weeks.

REFERENCES

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