Chicago Dermatological Society

Monthly Educational Conference

Program Information
Continuing Medical Education Certification
and
Case Presentations

Wednesday, October 15, 2008

Conference Location:
Feinberg School of Medicine
Northwestern University
Chicago, Illinois

Chicago Dermatological Society

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CDS Monthly Conference Program
October 2008 -- Northwestern University

October 15, 2008

8:30 a.m.	**REGISTRATION, EXHIBITORS & CONTINENTAL BREAKFAST** *Robert H. Lurie Medical Research Center* *Atrium Lobby outside the Hughes Auditorium*
9:00 a.m. - 10:00 a.m.	**RESIDENT LECTURE** Understanding Uncommon Types of Hair Loss *GEORGE COTSARELIS, MD* *Dermatology Lecture Hall, 676 N. St. Clair, Suite 1600*
9:30 a.m. - 11:00 a.m.	**CLINICAL ROUNDS** Patient & Slide Viewing *Dermatology Clinic, 676 N. St. Clair Street, Suite 1600*
11:00 a.m. - 12:00 p.m.	**GENERAL SESSION** *Hughes Auditorium, Lurie Building*
11:00 a.m.	CDS Business Meeting
11:15 a.m.	Hair Follicle Stem Cells and Skin Regeneration in Wound Healing *GEORGE COTSARELIS, MD*
12:15 p.m. - 1:00 p.m.	**LUNCHEON** *Hughes Auditorium, Lurie Building & atrium area*
1:00 p.m. - 2:30 p.m.	**AFTERNOON GENERAL SESSION** Hughes Auditorium, Lurie Building Discussion of cases observed during morning clinical rounds *WARREN PIETTE, MD, MODERATOR*

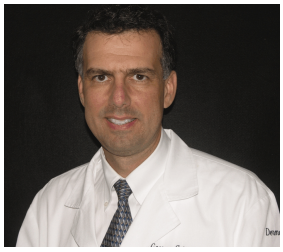
CME Information

This activity is jointly sponsored by the Chicago Medical Society and the Chicago Dermatological Society.

This activity has been planned and implemented in accordance with the Essentials Areas and Policies of the Accreditation Council for Continuing Medical Education (ACCME) through the joint sponsorship of the Chicago Medical Society and the Chicago Dermatological Society. The Chicago Medical Society is accredited by the ACCME to provide continuing medical education for physicians. The Chicago Medical Society designates this educational activity for a maximum of four (4) *AMA PRA category 1 credits*™. Each physician should claim only those hours of credit that he/she actually spent in the educational activity.

Commercial Support: There are no educational grants associated with this meeting. One or more companies may pay a fee to be present as exhibitors. The program content is free from any commercial or corporate influence.

Guest Speaker



George Cotsarelis, MD is the Albert M. Kligman Associate Professor in the Department of Dermatology at the University of Pennsylvania Medical School in Philadelphia where he is the Director of the Hair and Scalp Clinic. Dr. Cotsarelis is a graduate of the University of Pennsylvania School of Medicine (MD, 1987). He completed his residency there in the Geisinger Medical Center, as well as a fellowship also at the University of Pennsylvania. Dr. Cotsarelis was board certified in dermatology in 1992. His research areas of interest include epithelial stem cells, hair follicle biology, cutaneous gene therapy, epithelial carcinogenesis and wound healing.

Speaker CME Disclosure of Financial Interests

Dr. Cotsarelis has no significant financial relationships to disclose.

CME Credit Documentation

Following the meeting, the Chicago Medical Society will send you a certificate documenting your attendance at this conference and the number of Category 1 CME credits you earned. It is essential that you sign the CME attendance sheet at the CDS registration desk before you leave the confernce. If you have any questions about your credits, please contact the Chicago Dermatological Society by phone: 847/680-1666; or by email: RichardPaul@DLS.net

Evaluation Forms

Please complete and return your meeting evaluation form. This feedback is an important part of the CME process and helps us to design programs in the future that better meet the needs of our members. Note that the form will be scanned by computer; keep your responses within the spaces provided, and avoid making any extraneous marks on the sheet. Thank you!

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CHICAGO DERMATOLOGICAL SOCIETY **CASE #1**

Presented by Anthony J. Mancini, MD, Annette Wagner, MD, and Brandi Kenner-Bell, MD
Department of Dermatology, Feinberg School of Medicine, Northwestern University

HISTORY OF PRESENT ILLNESS

Patient A (AF)

The patient is a 6 month old girl with a right-sided segmental facial, retrobulbar, and subglottic hemangioma with associated hypoplasia of the left internal carotid and left vertebral arteries, circle of Willis and right side of the cerebellum consistent with a diagnosis of PHACE(S) syndrome (Posterior Fossa malformations, Hemangioma, Arterial abnormalities, Cardiac and aortic arch anomalies, Eye abnormalities, Sternal/midline development defects). Her hemangioma had been complicated by painful ulcerations of the ear and lip with resultant involution of the helix. At 4 months of age, the patient was on 3mg/kg/day of prednisolone which caused irritability, gastroesophageal reflux and poor feeding. Despite high-dose oral corticosteroids there was continued growth of her hemangioma, especially of the subglottic portion causing increasing respiratory distress. On June 16, 2008, the patient was admitted to the hospital under the care of Cardiology for initiation of oral propranolol at 2mg/kg/day. Within 48 hours there was noted improvement in the color and thickness of the hemangioma. Since that time she has had healing of her ulceration, thinning of the chin and continued improvement in thickness and color.

Patient B (HS)

The patient is a 3 month old girl with a left-sided periorbital and orbital hemangioma causing displacement of the globe inferiorly, ptosis and hypotropia. At 7 weeks of age she was on 3.5mg/kg/day of prednisolone causing hypertension, gastroesophageal reflux and irritability. Because of sight threatening potential of this patient's hemangioma she was admitted to the hospital on July 25, 2008 and started oral propranolol (2mg/kg/day). Again, within 48 hours there was improvement in the color and bulk of the hemangioma. Since that time, the displacement of her globe has resolved and her ophthalmologic exam continues to improve.

Patient C (CR)

The patient is a 15 month old girl with a multifocal large segmental hemangioma of the right cheek, neck and chin followed by an outside physician until she was referred at 14 months of age. She had been on no treatment for her hemangioma which had been complicated by recurrent otitis media and constant otorrhea. At the time of referral, she was outside the window of opportunity for oral steroid therapy, and the risk:benefit ratio of vincristine and interferon was not justified. Because of the large and potentially disfiguring nature of her hemangioma, she was started on oral propranolol (2mg/kg/day) and brain/neck MRI/MRI, ophthalmologic referral and cardiology referral were initiated to evaluate for PHACES syndrome. Three weeks into the therapy, her hemangioma was noted to be softer and slightly smaller compared to baseline.

Patient D (AW)

The patient is a 21 month old girl with a large hemangioma involving the bilateral cheeks, mandibular and parotid regions, lips and chin extending onto the upper chest. She also had hypoplasia of the right anterior cerebral artery and irregularities of her posterior cerebral and communicating arteries, establishing a diagnosis of PHACES syndrome. Her hemangioma was causing obstruction of her external auditory canals and was complicated by recurrent herpes simplex virus infection often necessitating hospitalization. The growth of the hemangioma remained stable on oral prednisolone from age 2 months to 14 months and she was successfully weaned off at 14 months. However, at 21 months the hemangioma had shown no signs of involution and due to concerns about the potentially disfiguring nature of the hemangioma as

well as the social implications, the patient was admitted to the hospital on September 2, 2008 and started on oral propranolol (2mg/kg/day).

Patient E (MP)
The patient is a 4 month old girl with a large left-sided segmental facial and periorbital hemangioma causing complete obstruction of the left eye. She was on oral prednisolone at 3mg/kg/day and had developed hypertension with no improvement in her hemangioma. She was admitted to the hospital and started on oral propranolol (2mg/kg/day). Within 8 days the eye was 50% open and approximately 2 weeks after starting propranolol the eye was almost completely open, she was tapered off of oral steroids 1 week later with no rebound in the growth of the hemangioma. Since that time, the eye has completely opened and the remainder of the segmental hemangioma is flat and some of it has completely disappeared leaving normal skin.

Patient F (ES)
The patient is an 11 month old twin girl with a left-sided hemi-facial segmental hemangioma in a beard distribution with significant involvement of the larynx. Her hemangioma was complicated by ulcerations and required several treatments with pulse dye laser. The hemangiomas continued to grow on over 3mgkg/day of oral prednisolone and as the patient's work of breathing increased she was changed to dexamethasone every other day and started on weekly vincristine. Pt was unable to be weaned off oral steroids and despite 8 courses of vincristine her subglottic hemangioma progressed and was ultimately resected. She was continued on oral prednisolone for the cutaneous and parotid portion of her hemangioma and weaned at six months of age, at which time she had significant rebound growth and new ulceration. At 9 months she was placed back on oral prednisolone with improvement but was developing a cushingoid appearance and had developmental delay. On September 17, 2008 she was started on oral propranolol (2mg/kg/day) and within two days there was 50% improvement that has continued.

Patient G (LSC)
The patient is a 2 year old girl with a small but persistent hemangioma of the left lower lip. She was started on propranolol (2mg/kg/day) and at two weeks the hemangioma was approximately 20% smaller with improvement in the color as well.

DIAGNOSIS
Infantile Hemangiomas (IH)

DISCUSSION
Infantile hemangiomas are the most common tumors of infancy. The incidence is 10% to 12% in Caucasian infants. They are present in approximately 2% to 3% of newborns and in 10% of all infants by one year of age. IH are more common in girls, Caucasians, premature and low birth weight infants, and multiple gestations. One study reported the presence of IH in 20% of premature infants with a birth weight of less than 1000 grams. Maternal risk factors include advanced maternal age, pre-eclampsia and placental abnormalities, notably placenta previa.

IH represent a distinct subset of vascular tumors which have a unique biologic profile and a characteristic clinical history. They only develop in infancy and are usually absent at birth or only present as a precursor lesion ("red dot" or telangietatic patch). During the first few weeks to months of life, there is a rapid proliferation followed by a gradual involution over the first several years of life. A recent study by the Hemangioma Investigator Group revealed that most IH growth is completed by five months of age. And in those lesions that grew beyond six months of age, the most dramatic growth still occurred in the first few months of life. They found that

during the first two months of life nearly all IH double in size, with no difference in the growth rates of localized versus larger, deeper segmental lesions. They noted that deep hemangiomas have a ~1 month delay in onset of growth compared with superficial hemangiomas and have sustained growth of ~1 month beyond superficial hemangiomas. These patterns are important when considering when to refer as well as the risks, benefits and optimal timing of any treatments.

The majority of IH follow a benign course, without the need for any intervention. However, between 10% and 20% of IH are more severe with the potential to be life- or vital-function threatening, and/or permanently disfiguring. High-risk IH include those that can cause ocular compromise, respiratory distress, congestive heart failure, or gastrointestinal bleeding. Large, segmental IH often have associated structural abnormalities and have a significant risk for disfigurement. The most common complication of IH is ulceration which can lead to complications such as pain, scarring, disfigurement, and less commonly infection and anemia. The mainstay of IH treatment is oral corticosteroids. Though the precise mechanism of action is poorly understood, they have affects on the vasculature, including vasoconstriction, decreased angiogenesis, and decreased permeability. They are also anti-neoplastic. The recommended starting dose is 2 to 5 mg/kg/day of prednisolone given in a single morning dose. This dose is titrated based on response and maintained for several weeks to months, followed by a gradual taper. Unfortunately the response rate is variable and the myriad of side effects often limits their usefulness. Other second-line therapies include vincristine and interferon-alfa, both of which have significant side effects, the most concerning being the potential neurotoxicity and irreversible spastic diplegia that can result from interferon.

In June of 2008 a French group reported on the use of propranolol in two infants on oral corticosteroids with IH being treated for cardiac conditions. Within a few days the hemangiomas were noted to lighten in color and soften. The improvement continued even after the discontinuation of oral corticosteroids. Based on these observations, they treated nine additional children who had severe or disfiguring IH with oral propranolol. They reported significant improvement in all nine patients, until all were nearly flat, with only residual skin telangiectasias. Whereas the mechanism of action is not known, they hypothesize that the effects of propranolol, a non-selective beta-blocker, on IH may involve vasoconstriction, decreased expression of *VEGF(vascular endothelial growth factor)* and *bFGF (basic fibroblast growth factor)*, and the triggering of apoptosis of capillary endothelial cells. *VEGF* and *bFGF* are two major angiogenic factors involved during the growth phase of IH. We present these cases to highlight the novel use of propranolol for the treatment of hemangiomas of infancy. Although propranolol is at this time clearly not a first-line therapy for hemangiomas, it may play an increasingly prominent role in the future management of infants with complicated courses or steroid-resistant lesions.

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CHICAGO DERMATOLOGICAL SOCIETY **CASE # 2**

Presented by Anne Laumann MBChB, MRCP, Pedram Gerami, MD, and Elizabeth Grossman, MD
Department of Dermatology, Feinberg School of Medicine, Northwestern University

HISTORY OF PRESENT ILLNESS

This is a 34 year old woman who presented to the emergency department with a 7 day history of bullous eruption over her trunk and limbs. Past medical history is significant for Systemic Lupus Erythematosus (SLE). She had the following history:

07/14: Active SLE. Labs: C3 35 C4 1 DsDNA 17.9. Strongly advised to avoid sun. Patient refused oral prednisone. Started on azathioprine 50 mg daily, to be increased to 100 mg daily after 3 days. She did not increase her dose.
08/10: Traveled to Mexico. Noted a fever and small boil on right flank that enlarged. Presented to hospital. Meds: Tigecycline. R flank abscess was incised and drained. Labs: AST 65, WBC 21.5
08/11: Meds: Tigecycline, amikacin, clarithromycin. Labs: AST 90, ALT wnl, WBC 27.2
08/12: Meds: Tigecycline. Would culture: Streptococcus pyogenes, sensitive to clindamycin.
08/13: Meds: Clindamycin. Bullae develop. Labs: AST 144, GGTP 68, Alk phos 313.
08/14: Meds: Clindamycin, tigecycline, IVIG 2g/kg. WBC 24.9
08/15 - 08/18: Meds: Clindamycin, IVIG. Labs 8/18: AST 100, GGTP 201, Alk phos 292.
08/19: Northwestern Emergency department. Labs: AST 35, ALT 35, WBC 16.6, dsDNA (+), C4 1, C3 43, Ab to SSA (+), Ab to SSB (-), Ab to cardiolipin (+),U/A + protein.

PAST MEDICAL HISTORY

SLE, Raynaud's phenomenon, idiopathic thrombocytopenic purpura, arthritis, alopecia areata, cellulitis. S/p splenectomy.

MEDICATIONS

Pantoprazole, Nicotinamide, Amlodipine, Azathioprine

ALLERGIES

Penicillin, dapsone, colchicine, minocycline, hydroxychloroquine, quinacrine (swelling and urticaria)

FAMILY HISTORY

Noncontributory

SOCIAL HISTORY

No history of tobacco or alcohol abuse.

PHYSICAL EXAM

Arms and dorsum of hands bilaterally: tense vesicles and large bullae, filled with clear fluid. Nikolsky and Asboe-Hansen signs negative. Palms and soles clear. Lower extremities: multiple annular coalescing annular and targetoid plaques, most with dusky center, many with bullae in the center of the lesion. Inner thighs with large, coalescing indurated dusky pink plaques. Helices of ears and tip of nose: ill-defined partially eroded papules and plaques, some hemorrhagic, some with crust. Face: ill defined erythematous indurated annular plaques with minimal scale. No oral mucosal, conjunctival, or genital involvement

HISTOPATHOLOGY

Right knee: Subepidermal bullae surmounted by largely unremarkable epithelium with some spongiosis. No acantholysis. Within blister there are numerous neutrophils and some histiocytes.

Dermis with perivascular lymphohistiocytic infiltrate with edema and interstitial neutrophils. Focal interface dermatitis noted at the dermal epidermal junction (DEJ).
Direct immunofluorescence staining: IgM and C3 granular deposits along the DEJ.

DIAGNOSIS

Streptococcal infection in an asplenic patient with Systemic Lupus Erythematosus complicated by a drug reaction and leading to a bullous associated lupus erythematosus

TREATMENT AND COURSE

The patient was started on solumedrol 80 mg IV Q6 and vancomycin 1 gm Q12. Steroids were weaned, and on 8/22/08, she was transitioned to oral prednisone 30 mg BID and azathioprine 50 mg BID and discharged. The patient remained afebrile, and her WBC continued to trend down, while her liver enzymes normalized.

DISCUSSION

Our differential for this interesting patient includes Bullous Systemic Lupus Erythematosus (BSLE) vs. bullous drug eruption, or an overlap of the two processes. Supporting a diagnosis of BSLE is both clinical and pathological evidence. Histopathologic features of bullous lesions of lupus erythematous were seen on H&E: a subepidermal blister with abundant neutrophils, dermal edema and a moderate perivascular infiltrate present in the superficial and mid dermis.

The clinical presentation is consistent with BSLE as well. BSLE presents in patients with active SLE flares as an acute, generalized vesiculobullous eruption that is more severe in sun exposed areas. The bullae are tense and contain clear or hemorrhagic fluid. The lesions may mimic erythema multiforme.

However, on direct immunofluorescence (DIF), a linear deposition of antibody was not seen to support the diagnosis of BSLE. The expectation would be that the DIF would demonstrate linear deposition of IgG without IgM or IgA. The antigen is typically type VII collagen, though other components of the basement membrane zone (BMZ) have been described, including BPAg1, laminin-5 and laminin-6.

The five diagnostic criteria for BSLE as proposed by Camisa and Sharma are: 1)a diagnosis of SLE based upon the American College of Rheumatology criteria, 2) an acquired vesiculobullous eruption, 3) histopathologic evidence of a subepidermal blister and predominantly neutrophilic dermal infiltrate, 4) negative or positive indirect immunofluorescence for circulating BMZ antibodies using salt split skin, 5)direct immunofluorescence microscopy demonstrating linear or granular IgG and/or IgM and often IgA at the BMZ.

Supporting a diagnosis of bullous drug eruption or erythema multiforme is the clinical appearance of the targetoid lesions on the lower extremities, as well as the transaminitis on laboratory evaluation. Non-specific DIF findings of granular deposits of IgM and C3 may be seen. Tigacycline is a glycylcycline, which is structurally similar to tetracycline; the patient has a known allergy to minocycline. Its metabolism is hepatic. Another drug, Clarithromycin, a macrolide, is metabolized using CYP34A. It too can cause hepatitis. However, the histopathology is not suggestive of a drug eruption or erythema multiforme.

REFERENCES

1. Vassileva S. Bullous systemic lupus erythematosus. Clin Dermatol. 2004 Mar-Apr;22(2):129-38.

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CHICAGO DERMATOLOGICAL SOCIETY **CASE #3**

Presented by Joaquin Brieva, MD and Anjeli Krishnan, MD
Department of Dermatology, Feinberg School of Medicine, Northwestern University

HISTORY OF PRESENT ILLNESS

A 32 year old otherwise healthy woman was admitted to the hospital for fevers, headaches, and myalgias. She had returned six days earlier from a trip to Ghana, where she had taken an art class for two weeks. She had refused all vaccines as well as malaria prophylaxis prior to her trip. Based on her history, a thin and thick smear of blood was performed in the emergency room, and the patient was diagnosed with Plasmodium falciparum malaria, with a parasite load of 12%. On hospital day 2, the patient was noted to have cold extremities and a new purpuric eruption.

PAST MEDICAL HISTORY Situs inversus, asplenia

MEDICATIONS None

ALLERGIES None

FAMILY HISTORY None

SOCIAL HISTORY The patient was single and employed as a nurse in a hospital in the city.

PHYSICAL EXAM

The upper and lower extremities, extending from the mid-arms and mid-thighs distally, had retiform purpura with superimposed vesicles and tense bullae, some hemorrhagic, most prominent on the legs. There were scattered retiform purpuric patches on the periumbilical abdomen, chest, and back. The nose, specifically the nasal ala and tip, had a dusky violaceous patch with superimposed bullae. There was marked cyanosis of both hands and feet, most notably in the left hand, which was cold without a palpable radial pulse. All ten digits had dark necrotic patches at the distal tips. There were similar dark necrotic patches of the palms and soles, consistent with dry gangrene.

LABS/STUDIES D-dimers > 40,000; after many transfusions, INR 2.2 and platelets 47

HISTOPATHOLOGY

Right thigh: There is a necrotic epidermis. Within the dermis, there is evidence of edema with occlusion of the superficial and mid-dermal vessels by proteinaceous debris and some neutrophils. The dermis also shows a variable mostly perivascular lymphohistiocytic infiltrate with some neutrophils and extravasated erythrocytes. DPAS, gram, AFB, and giemsa stains negative.

Left forearm: Unremarkable epidermis. Within the dermis, there is evidence of edema with congestion of the superficial and mid dermal vessels by erythrocytes with a suggestion of early thrombi. The dermis also shows a variable mostly perivascular lymphohistiocytic infiltrate with some neutrophils and extravasated erythrocytes. DPAS, gram, AFB, and giemsa stains negative. Consistent with a thrombotic vaso-occlusive process.

DIAGNOSIS

Purpura fulminans secondary to Plasmodium falciparum malaria

TREATMENT AND COURSE

Upon admission to the hospital, the patient was immediately started on quinidine and doxycycline. By day 2 of the hospitalization (only several hours after her symptoms began), the

patient was taken to the intensive care unit for septic shock, massive disseminated intravascular coagulation, acidosis, and evidence of multi-organ system failure. There she received multiple cycles of plasma exchange which reduced her parasite load to <2%. However, she already had evidence of end-organ damage, with dry gangrene of all of her extremities in addition to widespread epidermal necrosis. She was soon thereafter transferred to the University of Chicago burn unit for ongoing care. There she had several successive amputations of all four extremities and continued medical care for several months before being discharged to the Rehabilitation Institute of Chicago. The patient is now at home.

DISCUSSION

Purpura fulminans (PF) is a rare cutaneous disorder related to intravascular thrombosis and hemorrhagic infarction of the skin. It is usually rapidly progressive and accompanied by severe hypotension and disseminated intravascular coagulation. Three forms of the disease exist: 1) neonatal PF, characterized by a hereditary deficiency of proteins C and S and antithrombin III, 2) idiopathic PF, typically heralded by a febrile illness that quickly progresses to purpura and associated with protein S deficiency, and 3) acute infectious PF, most commonly seen with meningococcemia. Physical examination usually reveals diffuse retiform purpuric patches accompanied by hemorrhagic bullae, epidermal necrosis, and distal extremity gangrene.

Malaria is a serious and potentially life-threatening infectious illness caused by the species Plasmodium. It is transmitted by the Anopheles mosquito and is most prevalent in rural tropical areas, particularly sub-Saharan Africa. P. falciparum is the species that typically causes the most severe disease and multi-organ system failure, and it accounts for 90% of all human deaths from malaria. Symptoms include high fevers, rigors, diaphoresis, arthralgias, and myalgias, and a high index of suspicion should be maintained in a patient who has traveled to an endemic area. P. falciparum's ability to adhere to endothelial cell walls and cause vascular obstruction leads to most of its observed complications, including cerebral vessel occlusion, liver and renal failure, pulmonary edema, and cutaneous necrosis. There are several possible treatment regimens available depending upon the particular type of malaria and area from which it was acquired, and consultation with infectious disease is imperative. Parasite load should be monitored throughout therapy to ensure that the parasitemia is resolving. Purpura fulminans associated with malaria should be managed as any widespread epidermal necrosis, with supportive care in a burn unit and amputations as necessary for unviable tissue.

Due to its propensity to cause disseminated coagulation abnormalities and rapid bleeding, P. falciparum malaria can be more broadly classified into the category of hemorrhagic fever syndromes. The differential diagnosis for hemorrhagic fevers is broad and includes West Nile fever, chikungunya fever, yellow fever, dengue fever, Marburg virus disease, Q fever, Lassa fever, and meningococcemia, among others. The cutaneous findings demonstrated in our case may be observed in any of the above entities. To date, there have only been 3 reported cases in the world literature highlighting the finding of purpura fulminans in P. falciparum malaria.

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CHICAGO DERMATOLOGICAL SOCIETY **CASE # 4**

Presented by Stephanie Mehlis, MD and Kimberly Nicholson, MD
Department of Dermatology, Feinberg School of Medicine, Northwestern University

HISTORY OF PRESENT ILLNESS

A 60 year old female with a history of hyperthyroidism presents to the dermatology clinic for evaluation of a blistering disorder for the past seven years. She notes pruritic blisters and erosions over her arms, legs, hands, and feet as well as hair loss, ulcers in the mouth, and burning and itching in the genital region. Her skin is very fragile, and even slight trauma results in lesions. In addition, she notes tightening of the skin over her fingers for 2 years and progressive dysphagia for 4 years; esophagogastroduodenoscopy (EGD) showed diffuse friability, mucosal sloughing, and stricture. At the time of evaluation, she carried a diagnosis of systemic sclerosis and bullous pemphigoid. Prior treatment has included chronic prednisone plus dapsone without improvement, topical steroids, and tetracycline for ten months.

PAST MEDICAL HISTORY Hyperthyroidism, Osteoporosis

MEDICATIONS Omeprazole, Alendronate, Levothyroxine

ALLERGIES No known drug allergies

FAMILY HISTORY Non-contributory

SOCIAL HISTORY Denies smoking or alcohol use and is on disability from her condition.

PHYSICAL EXAM

Scalp noted to have diffuse erythema, mild scale, diffuse milia, and scarring alopecia. Tense 4 cm bullae on left arm and left inner thigh. Fingers with bilateral mitten deformities, scarring and milia formation over knuckles with diffuse nail loss; similar scarring and milia formation with nail loss over feet. Tongue, buccal mucosa, and soft palate with diffuse, large erosive patches. Vulva with diffuse erythema, tense bullae with some scarring and milia formation.

LABS

ANA positive at 1.57 (normal < 0.9, high > 5.0), anti-Sm positive at 192 (normal < 89), anti-SSA positive at 330 (normal < 91), anti-Scl 70 positive at 36 (normal < 32)

HISTOPATHOLOGY

Left forearm: Subepidermal vesicular dermatitis. Extravasated red blood cells and rare lymphoid cells within the bulla, with a superficial perivascular lymphohistiocytic infiltrate. Collagen type IV stain shows localization to the roof of the bulla.

Left forearm (DIF on salt split skin): IgG and C3 produce linear staining of the floor of salt split skin. No evidence of IgA or IgM deposition.

Esophageal ulceration: Esophageal squamous mucosa with extensive ulceration and acute and chronic inflammation. Negative PAS and no evidence of viral inclusions.

DIAGNOSIS

Epidermolysis bullosa acquisita

TREATMENT AND COURSE

Since her diagnosis, she has been started on topical medications(clobetasol ointment for the groin and oral cavity, triamcinolone ointment for the body) and colchicine. Our next step would be rituximab.

DISCUSSION

Epidermolysis bullosa acquisita (EBA) is a chronic autoimmune blistering dermatosis which is acquired in adulthood but clinically appears similar to dystrophic epidermolysis bullosa. The incidence of disease is 0.25 per million in Western Europe.

EBA is often associated with systemic diseases; some reported in the literature include neoplasms (myeloma, lymphoma, leukemia, carcinomas) as well as inflammatory diseases (IBD, SLE, RA, relapsing polychondritis), diabetes, thyroiditis, multiple endocrinopathy syndrome, pulmonary fibrosis, hepatitis C, psoriasis, and amyloidosis. Drugs, including penicillamine, vancomycin and other antibiotics have also been implicated. Most EBA patients form IgG autoantibodies to the non-collagenous terminus of the alpha chain of collagen VII, resulting in decreased anchoring fibrils in the lamina densa.

Clinical features of EBA include lesions consistent with dystrophic EB (skin fragility, trauma-induced blisters, scarring and milia). Scarring blisters are most common on sites of trauma such as the dorsa of hands and feet, elbows, knees, and buttocks. Other features include scarring alopecia, nail dystrophy, and mucus membrane involvement that may mimic cicatricial pemphigoid. Complications of mucus membrane involvement include chronic cicatrizing conjunctivitis, recurrent epistaxis, scarring and obliteration of turbinates, esophageal erosions, casts and stenosis, tracheal stenosis requiring tracheostomy, and anal strictures.

Histologically, patients with EBA show subepidermal blister formation which is often pauci-inflammatory. Staining for collagen IV, which is located in the lamina densa, will be present on the roof of the blister in EBA. On IIF, patients with EBA are more likely to exhibit linear IgG with or without C3 deposition, but may also have IgA or IgM deposition. On DIF of salt-split skin, EBA will have IgG bound to the dermal side of the split, while bullous pemphigoid will have IgG bound to the epidermal side. In EBA, immunoblotting identifies 290-kD and 145-kD proteins corresponding to type VII collagen.

Treatment of EBA can be difficult. Some patients show good responses to systemic steroids alone or in combination with azathioprine or dapsone. Other treatments which have been reported in the literature include mycophenolate mofetil, IVIG, cyclosporine, colchicine monotherapy, gold, plasmapheresis, photophoresis, mesalazine, and daclizumab. More recently, infusions of rituximab, rituximab plus immunoadsorption, and the biologic infliximab have been shown effective in recalcitrant cases of EBA.

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CHICAGO DERMATOLOGICAL SOCIETY **CASE #5**

Presented by Heather Wickless, MD, MPH, Joaquin Brieva, MD, Susan Boone, MD
Department of Dermatology, Feinberg School of Medicine, Northwestern University

HISTORY OF PRESENT ILLNESS

This 51 year old African American woman presented to the emergency room in February 2008 with a 4 year history of a worsening painful and pruritic eruption that started on her hands and feet, then spread to involve her periorificial and anogenital areas. Patient states that she was seen at an outside institution when this started, and was treated with oral antibiotics and topical creams, which did not alleviate the rash. She complained of malaise but denied weight loss, fevers, chills, diarrhea, arthralgias, or worsening of the rash after sun exposure. There were areas on her lower extremities that were eroded and frequently bled, and she had dressed them with toilet paper. During that hospitalization a biopsy was performed, which was consistent with a nutritional or zinc deficiency, necrolytic acral erythema, or necrolytic migratory erythema. Culture of the lesions grew MRSA and she was discharged on oral antibiotics to follow-up in clinic. She was subsequently lost to follow up after many attempts were made to contact her. Eight months later she presented to the hospital again with worsening rash and alopecia.

PAST MEDICAL HISTORY None

MEDICATIONS None

ALLERGIES No known drug allergies

FAMILY HISTORY Mother with unknown type of cancer.

SOCIAL HISTORY Lives with friends, + tobacco with a history of snorting heroin. Denies IVDU.

PHYSICAL EXAM

Well-demarcated thick psoriasiform hyperpigmented plaques on distal extremities, forearms, elbows, knees, and thinner plaques on perioral, perinasal, and anogenital areas. There was impetiginization and pustules around the perioral region and erosions within the plaques on the dorsum of the feet and the ankles.

LABS

2/2008: ANA panel, B2-glycoprotein, CBC, and Chem panel were WNL. Cultures of the pustules and nares were positive for oxacillin resistant Staphylococcus aureus. Blood and urine cultures were negative.
9/2008: CBC, Chem panel, Alpha Fetoprotein WNL; AST 58 and albumin 3.0, otherwise LFTs WNL; Culture of the nares positive for oxacillin resistant Staphylococcus aureus; Ferritin, transferrin, and total iron binding capacity WNL, iron 35 ug/dL; Hepatitis quantitative and qualitative PCR negative, Hepatitis C Abs negative, RPR and HIV 1&2 negative; Glucagon level WNL: <50 pg/mL; Zinc 214 ug/L (nL range: 600-1200), amino acid profile pending.

HISTOPATHOLOGY

Left leg: Skin with pallor and prominent parakeratosis of the upper epidermis. The transition to parakeratosis is acute and the upper epidermis lacks a granular layer and shows numerous pyknotic cells. There is a mild accompanying perivascular infiltrate. Immunohistochemistry was negative for immune deposits.

DIAGNOSIS

Severe acquired zinc deficiency

TREATMENT AND COURSE

The patient was started on high dose oral zinc at 220mg twice a day. She was recently discharged from the hospital in good condition and encouraged to continue zinc and multivitamin supplementation in addition to improving her diet. She has a sister who is attempting to help her social situation. She has established care with a primary care provider through her hospital stay who will monitor her zinc and nutritional status every 3-6 months.

DISCUSSION

Inherited zinc deficiency, or acrodermatitis enteropathica(AE), occurs worldwide with an estimated incidence of 1 per 500,000 children. Dietary zinc deficiency, or acquired AE, affects a third of some populations in developing countries like Southeast Asia and sub-Saharan Africa. In developed countries groups at risk of dietary zinc deficiency include: malnourished (low social economic status, anorexia, alcoholics), vegetarians, and premature infants. The clinical presentation of inherited and acquired AE is similar. Eczematous pink scaly plaques can be vesicular, bullous, pustular or desquamative, and develop over the extremities, anogenital, and periorificial areas. Angular cheilitis, or perleche, is a common early manifestation followed closely by paronychia. Without treatment skin lesions can slowly evolve into erosions and patients develop generalized alopecia and diarrhea. The triad of 1.) alopecia, 2.) dermatitis around body orifices and extremities, and 3.) diarrhea or other gastrointestinal dysfunction was once thought to be essential in making the diagnosis of zinc deficiency. Patients with advanced disease will experience growth delay, mental slowing, poor wound healing, anemia, photophobia, hypogeusia, anorexia, delayed puberty, and hypogonadism in boys and men. Hair shafts have been reported to display alternating dark and bright bands on polarized light microscopy. Secondary infections with bacteria and *Candida albicans* are common. Chronic lesions of AE may appear psoriasiform with accompanying nail dystrophy in some cases. However, accurately assessing the body's zinc status if difficult, as homeostatic regulatory mechanisms can maintain plasma zinc concentrations in AE. However, initial assessment should include serum or plasma zinc concentrations. Before breakfast a blood sample should be drawn in a trace element-free collection tube (royal blue). Results may be falsely elevated if sample is hemolyzed. A serum zinc level of less than 500ug/L is suggestive of AE. The histopathologic features of zinc deficiency are generally indistinguishable from other deficiency dermatitis (including niacin/vitamin B3 deficiency, or pellagra), glucagonoma associated necrolytic migratory erythema, or Hepatitis C associated necrolytic acral erythema. Pathognomonic in the histopathology is presence of fully developed necrolysis, or cytoplasmic pallor, vacuolization, ballooning degeneration, and subsequent confluent necrosis of keratinocytes within the superficial stratum spinosum and granulosum of the epidermis. Affected keratinocytes often have pyknotic nuclei and confluent parakeratosis can be seen with hypogranulosis.

Zinc replacement therapy should be started at 0.5 to 3mg/kg/day of elemental zinc (there is 50 mg of elemental zinc per 220mg zinc sulfate). Serum or plasma levels should be monitored every 3-6 months. Typically, clinical improvement is seen very rapidly, within days to weeks, before a significant change in serum zinc levels. In patients who are malnourished a multi-nutrient replacement approach is warranted.

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CHICAGO DERMATOLOGICAL SOCIETY **CASE # 6A**

Presented by Heather Wickless, MD, MPH and Sandra Han, MD
Department of Dermatology, Feinberg School of Medicine, Northwestern University

PATIENT A

HISTORY OF PRESENT ILLNESS

A 39 year old Caucasian female presents with 6 months of hair loss. She also noticed a rash in the affected area 3 years ago, which has expanded and become pruritic in the past 2 months. The patient has tried two topical corticosteroids for the problem, clobetasol 0.05% foam and fluocinonide 0.05% soln, which have helped with the rash but not with the alopecia.

PAST MEDICAL HISTORY Hyperlipidemia, uterine fibroids

MEDICATIONS Ezetimibe, simvastatin, nortrel 7/7/7 (norethindrone/ethinyl estradiol)

ALLERGIES NKDA

FAMILY HISTORY No known family history of skin diseases or scalp disorders.

SOCIAL HISTORY Administrative assistant at a real estate company. No alcohol or tobacco.

PHYSICAL EXAM

Prominent perifollicular erythema with keratotic plugging on the parietal and occipital surfaces of the scalp. Scarring with loss of follicular units within the involved areas is also present.

LABS

Hemoglobin 13.1, ferritin 21.5

HISTOPATHOLOGY

Scalp: Scarring and inflammatory alopecia. Unremarkable epidermis. Changes of an interface dermatitis or a significant inflammatory infiltrate are not identified. There is prominent fibroplasia of the dermis which focally wraps around the follicular units. Overall a decreased number of follicular units are identified. A patchy lymphohistiocytic infiltrate with numerous plasma cells is noted. Occasional granulomatous foci around hair shafts are seen.

DIAGNOSIS

Lichen planopilaris or pseudopelade of Brocq

TREATMENT AND COURSE

The patient has been seen in our clinic for the past 8 months. She was continued on her corticosteroid solutions and began monthly injections of intralesional triamcinolone 5mg/mL to the affected area. She was also recommended to start minoxidil 5% OTC and noted improvement. She was started on iron supplements for low ferritin. Three months ago, the patient was started on doxycycline 100 mg PO daily. On this regimen, the patient has had moderate improvement of her perifollicular erythema and stabilization of her hair loss.

PATIENT B

HISTORY OF PRESENT ILLNESS

A 54 year old Caucasian female presents for a chronically tender scalp with hair loss. The patient states that the problem began 14 years ago during a time of significant psychosocial stress. Her symptoms have consisted of scalp pain that feels like "hot pokers" diffusely throughout her scalp as well as patchy hair loss. She also reports a history of inflammatory papules and pustules of the

scalp, although these have not been seen on clinical exam. The patient has seen an internist and two other dermatologists for the condition. During the workup, she was found to have anemia and hypothyroidism. The patient was started on appropriate medications, but her scalp symptoms persisted. Treatment for this problem has included intralesional corticosteroid injections, topical steroids, and short courses of oral antibiotics for superinfection.

PAST MEDICAL HISTORY Hypothyroidism

MEDICATIONs Levothyroxine

ALLERGIES NKDA

FAMILY HISTORY No known family history of skin diseases or scalp disorders.

SOCIAL HISTORY The patient has a kitchen and bath remodeling business. No tobacco. Occasional alcohol.

PHYSICAL EXAM
Small patches of scarring with loss of follicular units that have coalesced into a large patch on the vertex of her scalp. Admixed are areas of 2mm scarring patches of alopecia resembling "footprints in the snow." No facial lesions.

HISTOPATHOLOGY
Scalp (1996): A scarring alopecia with linear fibrotic tracts that have replaced the hair follicles. The findings are that of an end stage scarring alopecia with no active inflammation currently seen. This could represent the end stage of a lichen planopilaris. Serial cryostat sections stained by direct immunofluorescence show no staining for C3, IgG, IgM, or IgA.

DIAGNOSIS
Lichen planopilaris or pseudopelade of Brocq

TREATMENT AND COURSE
The patient was started on fluocinonide 0.05% solution and doxycycline 100mg po BID. In the three months since, she has had significant reduction of the draining pustules on her scalp. The alopecia has remained stable. She still has occasional scalp pain, but is much improved.

DISCUSSION
Lichen planopilaris (LPP) and pseudopelade of Brocq (PPB) are both conditions that lead to scarring alopecia. PPB was introduced by Brocq in 1885 and LPP by Pringle a decade later. Notably, Brocq described the appearance of "footprints in the snow," in affected areas, which represents dermal atrophy causing a depression in the skin. In 1930, Photinos presented some of the earliest literature implying that PPB is a distinct entity. This was challenged in the 1950s by Degos who coined the term Etat pseudopeladique to describe PPB as the final endpoint of a variety of scarring dermatoses, including LPP. Since then, the debate whether these two are distinct entities or part of the same spectrum of cicatricial alopecia has continued.

Much of the conflict has been due to a lack of consensus on clinical or histologic criteria that define PPB despite attempts to depict features pathognomonic for PPB. Widely cited classification criteria for PPB were introduced by Braun-Falco in 1986. Based on a combination of histologic examination and direct immunofluorescence (DIF) studies of 41 cases, 26 were deemed to be PPB in the study. Clinical criteria for PPB included the following: 1) irregularly defined and confluent patches of alopecia; 2) moderate atrophy (later stage); 3) mild

perifollicular erythema (early stage); 4) female : male = 3 : 1; 5) long course (at least 2 years); 6) slow progression with spontaneous termination possible. According to Falco, DIF in PPB is either negative or positive only for IgM. Histologic criteria are as follows: 1) absence of marked inflammation; 2) absence of widespread scarring; 3) absence of significant follicular plugging; 4) absence or at least decrease of sebaceous glands; 5) presence of normal epidermis (only occasionally atrophy); 6) fibrotic streams into the subcutis.

Further supporting PPB as a distinct condition, Moretti found different phenotypic patterns of dermal infiltrate in LPP and PPB. The infiltrate of CD3+ cells in LPP had a high CD4+/CD8+ ratio, variable numbers of macrophages, and fewer mast cells and fibroblasts compared to lymphocytes. In contrast, the CD3+ infiltrate found in PPB had a variable ratio and conspicuous macrophages, mast cells and fibroblasts that outnumbered lymphocytes.

These arguments were challenged by several studies thereafter. Amato examined the histopathology of 33 patients who fulfilled Braun-Falco's clinical criteria for PPB and found that 11 specimens displayed findings typical for LPP, whereas 7 showed typical DLE features. The remaining 15 cases were not suggestive of any specific dermatosis. Nayar examined the histopathology of 10 patients. Among these were 3 patients diagnosed clinically as PPB having the classical "footprints in the snow" and 7 patients diagnosed clinically with LPP including 5 who had manifestations of lichen planus in addition to their scarring alopecia. The histologic diagnosis of LPP was made in 4 cases, including one clinically diagnosed as PPB. The histologic findings in the remaining cases were non-specific.

The North American Hair Research Society (NAHRS) recently proposed a classification system for primary cicatricial alopecias based on the predominant inflammatory cellular infiltrate. In this system, classification is divided into predominantly neutrophilic, lymphocytic, and mixed. Mirmirani conducted blinded and prospective histopathologic examination of 20 patients diagnosed with various scarring alopecias, including PPB and LPP. They found that lymphocytic and neutrophilic groups were readily distinguished histologically, but within the two groups clinically distinct primary cicatricial alopecias could not be distinguished using defined, systematic criteria. In this study, PPB and LPP were both found to have predominantly lymphocytic infiltrate in contrast to Moretti's study. In summary, the conflicting clinical and histopathologic interpretations of LPP and PPB by a number of authorities have led to more questions than answers, and thus the controversy extending over a century continues.

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Presented by Joaquin Brieva, MD, and Victoria Wang, MD
Department of Dermatology, Feinberg School of Medicine, Northwestern University

UNKNOWN

CHICAGO DERMATOLOGICAL SOCIETY **CASE #8**

Presented by Anthony J Mancini, MD and Melissa L Abrams, MD
Department of Dermatology, Feinberg School of Medicine, Northwestern University

HISTORY OF PRESENT ILLNESS

The patient is an 11 month old male noted at birth to have fair skin and rapid eye movements. Shortly after birth his hair and eyelashes turned white. His past medical history is otherwise unremarkable, except for easy bruising first noted with the start of crawling. The bruising involves trauma and non-trauma prone areas including his lower legs, knees, forearms and upper/lower back. He has not had episodes of epistaxis or hematochezia, but he does have gum bleeding when he bites down on toys.

PAST MEDICAL HISTORY Negative

MEDICATIONS None

ALLERGIES Amoxicillin- Rash

FAMILY HISTORY No history of albinism or bleeding diatheses, No known consanguinity; Two maternal half siblings and four paternal half siblings are healthy.

SOCIAL HISTORY

He lives at home with both parents and two older maternal half siblings. His mother is of Mexican descent and notably his father is from Puerto Rico.

PHYSICAL EXAM

Well-developed, well-nourished male with complete depigmentation of his skin and hair, including eyelashes and eyebrows. He has blue irides and rapid beating nystagmus with apparent photophobia. Multiple ecchymotic patches are noted on his lower legs, knees, forearms and upper/lower back. He has no appreciable nevi, ephiledes or gingival hemorrhage.
Ophthalmologic exam: Very blond fundi, horizontal nystagmus and almost no pigment of the retinal structures. Optic nerve was not fully visualized.

LABORATORY TESTS:

Molecular genetic testing revealed two mutations in the Hermansky Pudlak Syndrome 1 (HSP1) gene on chromosome 10q23 including a 16-base pair duplication in exon 15 and Q242X:c.724C>T in exon 8.

Wet mount platelet electron microscopy – Absence of platelet dense bodies; Normal PT/PTT

DIAGNOSIS

Hermansky-Pudlak Syndrome 1

TREATMENT AND COURSE

Our patient is currently being followed by dermatology, genetics, hematology and ophthalmology.

DISCUSSION

Hermansky-Pudlak syndrome (HPS) is a group of rare autosomal recessive disorders characterized by oculocutaneous albinism, a bleeding diathesis and systemic complications associated with ceroid lipofuscin deposition within the reticuloendothelial system. HPS is a

genetically heterogeneous disorder that results from mutations in any of eight genes in humans. These genes encode subunits of 4 multi-protein complexes, Adaptor Protein (AP)-3, and Biogenesis of Lysosome-related Organelles Complex (BLOC)-1 through 3 that are involved in the trafficking of proteins to premelanosomes and other lysosome-like organelles or vesicle formation from the trans-Golgi network.

HPS has been classified into seven subtypes. Our patient has HPS-1 the most common variant which occurs with high frequency (1:1800 to 1:400) in northwest Puerto Rico. All affected inhabitants of Puerto Rico are homozygous for a 16-base pair duplication in exon 15 of the HPS1 gene due to a founder effect. Approximately 20 additional HPS1 mutations have been identified in patients outside this genetic isolate resulting in phenotypic variability.

The oculocutaneous albinism results in a variable degree of skin, hair and eye pigmentary dilution, congenital horizontal nystagmus, decreased visual acuity, photophobia, and marked iris transillumination. Hair color ranges from white to light brown while the skin is usually light, however up to 20% of Puerto Rican patients have skin color similar to unaffected family members. Additional dermatologic findings may include eyelash hypertrichosis, trichomegaly of the arms and legs, acanthosis nigricans-like lesions and multiple melanocytic nevi which are rarely atypical. Lesions typical of solar damage including freckles, lentigines, solar keratoses and non-melanoma skin cancer are extremely rare in children and more common in Puerto Rican patients secondary to their increased sun exposure.

The hemorrhagic diathesis typically manifests as easy bruising and epistaxis in childhood, but can be aggravated by the ingestion of aspirin and other prostaglandin blockers as well as dental and surgical procedures. Older female patients may have excessive menstrual and/or postpartum bleeding. The absence of platelet dense bodies (secretory granules) seen on electron microscopy is the most consistent diagnostic feature of Hermansky Pudlak syndrome. Without secretory granules, the secondary platelet aggregation response is impaired.

Ceroid lipofuscin accumulation is associated with the development of granulomatous colitis and pulmonary fibrosis. Average life expectancy is 30 to 50 years of age. Death is secondary to pulmonary fibrosis (70%), hemorrhage (15%) or granulomatous colitis (15%).

The diagnosis of HPS raised by clinical suspicion is confirmed by molecular genetic analysis and platelet electron microscopy. Although there are no specific treatments for a majority of the clinical manifestations, establishing the diagnosis is important to provide supportive care including prenatal/genetic testing and sun education. Medication is available for the late complications.

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CHICAGO DERMATOLOGICAL SOCIETY **CASE #9**

Presented by Neill Peters, MD and David Reid, MD
Department of Dermatology, Feinberg School of Medicine, Northwestern University

HISTORY OF PRESENT ILLNESS

This 57 year old woman originally presented in January 2008 with a new-onset, scaly, red eruption on the face, neck, torso, and extremities. The lesions were pruritic and mildly painful. Initial pathology suggested resolving erythema multiforme, but she progressed despite empiric treatment with prednisone and valacyclovir. She continued to develop new areas of involvement, and the existent lesions became more gyrate and confluent. She had no arthralgias, photosensitivity, or oral lesions.

PAST MEDICAL HISTORY

Sjogren's syndrome, hypothyroidism, osteoporosis, gastroesophageal reflux disease

MEDICATIONS

Ethinyl estradiol/norethindrone acetate, alendronate/cholecalciferol, calcium gluconate, levothyroxine, esomeprazole

ALLERGIES No known drug allergies

FAMILY HISTORY

Mother – breast cancer. No history of rheumatologic or connective tissue disease.

SOCIAL HISTORY

The patient is a former FBI agent who now works in health care fraud.
She is single, drinks alcohol in moderation, and does not use tobacco.

PHYSICAL EXAM

Arcuate erythematous papules and plaques with prominent scale over the face, neck, chest, back, arms, and legs, including the dorsal feet. No acral ulcerations. No oral or vulvar lesions.

LABS/STUDIES

The following tests were negative or within normal limits: complete blood count; comprehensive chemistry panel; urinalysis; dsDNA IgG, nRNP/Sm IgG, Smith IgG, and Scl-70 IgG autoantibodies; cardiolipin IgA, IgG, and IgM autoantibodies; lupus anticoagulant; C3, C4, and CH50 complement; rheumatoid factor, erythrocyte sedimentation rate; C-reactive protein; serum zinc.
The following tests were abnormal: ANA positive (1:320, speckled); SS-A IgG 134.0 U (<5); SS-B IgG 7.0 U (<5); HSV 1 and HSV 2 IgG antibodies positive.

HISTOPATHOLOGY

1/23/08, DP08-1492 (left upper back): Layer of epidermal necrosis and reactive epidermis demonstrating repair changes of keratinocytes. There are many necrotic and mitotic figures. There is also an interface mononuclear cell infiltrate with pigment laden macrophages.

3/5/08, DP08-3815 (left shoulder): Interface lymphocytic infiltrate with focal vacuolar changes of basal cells. There is epidermal hyperkeratosis, dermal edema and telangiectasia, and a perivascular and periadnexal lymphohistiocytic infiltrate.

3/5/08, IF08-38 (left deltoid): lupus band negative for immune deposits.

DIAGNOSIS

Rowell's syndrome

TREATMENT AND COURSE

Disease proved recalcitrant to initial therapy with prednisone 40mg BID, hydroxychloroquine 200mg BID, and clobetasol 0.05% lotion topically BID. In March 2008, mycophenolate mofetil 1g QD was initiated in concert with plaquenil 200mg BID. Though this yielded an excellent response, both medications were discontinued due to persistent leukopenia. Shortly thereafter, she developed recurrent and progressive lesions. In September, she began treatment with methotrexate, and has had some improvement at the current dosage of 10mg weekly.

DISCUSSION

Rowell's syndrome is a rare disease characterized by erythema multiforme-like lesions in association with lupus erythematosus (LE). The relationship between the two has been well-established, dating back to 1922. While some believed the linkage coincidental, in 1963 Rowell et al. declared it a distinct entity when occurring in the appropriate immunological setting. Today, it remains a controversial, evolving, and rare diagnosis.

Rowell's report profiled 4 out of 120 patients with discoid lupus who had erythema multiforme-like lesions and a specific serological profile: speckled antinuclear antibodies, positive rheumatoid factor, and antibodies to saline extract of human tissue (anti-SjT). Classic erythema multiforme, characterized by macules and papules that develop a targetoid configuration, does not produce immunological abnormalities, and none of the other 116 discoid patients had such serological findings, supporting a distinct entity.

Following the original series, similar cases occurring in patients with systemic and subacute lupus were reported. Chilblains, present in all 4 of Rowell's patients, was subsequently proposed as an additional diagnostic criteria. In addition, because anti-SjT antibodies are no longer tested, an updated immunological profile is now recognized as representative of the syndrome.

As revised by Zeitouni et al., the diagnosis currently requires three major and one minor criteria. The former include LE (systemic, discoid, or subacute cutaneous), erythema multiforme like-lesions, and a speckled pattern of antinuclear antibody. Minor criteria include chilblains, anti-Ro or anti-La antibody, and positive rheumatoid factor. To date, fewer than 50 cases of Rowell's syndrome have been reported. Middle-aged women are predominately affected, corresponding to the known epidemiology of lupus. Younger patients and males have more recently been described. Therapeutic options include oral prednisone, azathioprine, and antimalarials such as chloroquine or hydroxychloroquine. In recalcitrant cases, dapsone may induce clearance.

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CHICAGO DERMATOLOGICAL SOCIETY **Case #10**

Presented by Joaquin Brieva, MD and Kavita Menon, MD
Department of Dermatology, Feinberg School of Medicine, Northwestern University

HISTORY OF PRESENT ILLNESS

The patient is a 19 year old man with a history of ankylosing spondylitis (AS), controlled with adalimumab, sulfasalazine and prednisone since October 2007, who presented for evaluation of acral pustular and erosive lesions which had been present for 1 week. The lesions were accompanied by fever, malaise, anorexia and myalgias. The patient had a history of psoriasis, developing psoriatic plaques on his extremities and scalp 1 week after the initiation of adalimumab in October 2007. Prior to the development of pustular lesions, his psoriasis had been well-controlled with topical clobetasol ointment and shampoo.

PAST MEDICAL HISTORY

Ankylosing Spondylitis, Psoriasis, Uveitis

MEDICATIONS

Adalimumab 40 mg SC weekly
Prednisone 12.5 mg daily
Sulfasalazine
Tramadol , Hydrocodone, Loperamide

ALLERGIES

Indomethacin, Vancomycin, Sulfa

FAMILY HISTORY Non-Contributory

SOCIAL HISTORY

The patient is a college student. He smoked approximately 3 packs/week for the last 4 years and quit smoking soon after developing the pustular lesions and the accompanying fevers and myalgias.

PHYSICAL EXAM

There are numerous small, tender, crusted ulcerations with erythematous rims and a few 1-2 mm pustules with a deeply erythematous base and yellow crusting located predominantly on the dorsal fingers, toes and intradigital spaces. The palms and soles contain similar erythematous erosions.

HISTOPATHOLOGY

DP08-11449 (Left Thigh) The epidermis is ulcerated and covered by a fibropurulent crust with extensive neutrophils. There is a large collection of neutrophils with some nuclear debris throughout the dermis and extending along the eccrine coils. Some exocytosis of neutrophils with spongiosis is noted. There is also marked dermal edema and some telangiectasia with margination of neutrophils.

DIAGNOSIS

Pustular psoriasis secondary to tumor necrosis factor-alpha inhibition

TREATMENT AND COURSE

Adalimumab was discontinued and the patient's prednisone dose was increased to 60mg daily. The pustular lesions resolved and the patient's prednisone was tapered. Currently, the patient is treating his AS and psoriasis with methotrexate.

DISCUSSION

Biologic agents that inhibit tumor necrosis factor-alpha (TNF-a), such as etanercept, adalimumab and infliximab, successfully treat several rheumatologic and dermatologic conditions including rheumatoid arthritis, ankylosing spondylitis and psoriasis with fewer side effects than traditional systemic therapies. While overall well-tolerated, notable side-effects of TNF-a inhibitors include increased risks for serious infections, demyelinating disease and lymphoproliferative malignancies. In some patients, TNF-a inhibition paradoxically leads to the development of psoriasis.[1-4]

There are several published reports of patients who developed new-onset psoriasis or worsening of pre-existing psoriasis following the initiation of TNF-a inhibitor therapy with the majority of cases presenting in patients without a history of psoriasis. [1-4] In one clinical study, approximately 3% of patients with spondyloarthropathy treated with TNF- a inhibition developed psoriasis. [1] Most patients present with either plaque, palmoplantar pustular or guttate psoriasis, although many patients develop more than one type of lesion. In patients with spondyloarthropathies, pustular lesions are the most common. [1,2]

The underlying mechanism of TNF-a induced psoriaisis is largely unknown. It has been postulated that the development of psoriatic lesions may involve the upregulation of plasmacytoid dendritic cell precursors (PDCs) and interferon alpha (IFN-a), leading to the activation and expansion of T-lymphocytes and subsequent development of psoriatic plaques. [1-4] TNF-a regulates IFN-a production by inhibiting the maturation of PDCs and the release of IFN-a by PDCs. The inhibition of TNF-a may induce sustained IFN-a production causing plaque formation. Patients receiving TNF-a inhibitor therapy have been shown to have increased IFN-a expression within psoriatic lesions.[1]

Treatment of TNF-a induced psoriasis does not necessarily involve discontinuation of the TNF-a inhibitor. Many patients are treated aggressively with topical agents including superpotent topical corticosteroids, keratolytics, and vitamin D analogs. [1-3] Phototherapy and systemic therapy with methotrexate or cyclosporine are also used. In those patients with recalcitrant psoriasis, TNF-a inhibitors are often discontinued or switched to another TNF-a inhibitor with resolution of symptoms.

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CHICAGO DERMATOLOGICAL SOCIETY **CASE # 11**

Presented by Joaquin Brieva, MD and Diana Leu, MD
Department of Dermatology, Feinberg School of Medicine, Northwestern University

Patient A

HISTORY OF PRESENT ILLNESS

Patient A is a 38 year old previously healthy female who presented with a diffuse rash for 10 days. She was visiting from Italy and arrived in the US the day prior to presentation. She saw several dermatologists in Italy who felt that it would be safe for her to travel and have been treating her with IM betamethasone 4mg injections daily x 8 days. She stopped the injections two days ago because the rash was worsening and she was also not feeling well. She had been taking bupropion and an oral contraceptive pill for ~15 days prior to the onset of the rash, but stopped them both 5 days ago when her rash worsened. Per patient, she was taking bupropion for the purposes of weight loss. She denied any sick contacts or mucosal symptoms.

PAST MEDICAL HISTORY Denies

MEDICATIONS IM Betamethasone, Bupropion, Oral contraceptive pill

ALLERGIES No known drug allergies

FAMILY HISTORY Father with psoriasis

SOCIAL HISTORY Works as a pharmacist in Italy, does not smoke, drinks occasional alcohol

PHYSICAL EXAM

T 99.2 HR 132 RR 22 BP 133/69 SaO2 100% on RA
Numerous erythematous 1-5cm annular plaques, some coalescing and confluent, many with a dusky center with inner rim of scale on the chest, abdomen, back, arms, and legs. Few erythematous plaques with peripheral rim of micropustules. Palms bilaterally with 1-2mm erythematous edematous papules. Soles were clear.

LABS

Normal or negative: complete blood count except for WBC of 12.4, 75% neutrophils, basic metabolic panel, liver panel, magnesium, phosphorous, hepatitis panel, HIV, urine pregnancy

HISTOPATHOLOGY

Left arm: Prominent neutrophilic exocytosis with spongiosis and focal subcorneal collections of neutrophils in the epidermis. Areas with confluent parakeratosis and neutrophils suggestive of conventional psoriasis in the adjacent epidermis. Edema with margination of neutrophils and a perivascular lymphohistiocytic infiltrate with some red blood cell extravasation suggestive of an acuteprocess.
DIF : Immunofluorescence is negative

DIAGNOSIS

Generalized pustular psoriasis –Annular pattern associated with Bupropion

TREATMENT AND COURSE

Given that the patient was leaving for Italy in a few days, cyclosporine was started in addition to warm compresses with aclometasone. As she is a reproductive female, she is not a candidate

for acitretin. Infliximab was not an option given the uncertainty of the availability in her country. After several weeks on cyclosporine, her lesions completely resolved.

Patient B

HISTORY OF PRESENT ILLNESS

Patient B is a 52 year old Caucasian female with steroid-dependent asthma/chronic obstructive pulmonary disease, diabetes, and hypertension who presented with a new painful, progressive rash x 5 days. Patient states that the rash initially started on her abdomen and inner thighs, and then generalized to the arms and legs.

She started taking bupropion six weeks ago for smoking cessation and discontinued it 10 days prior to presentation because she felt "strange." She is chronically on steroids for her asthma/COPD and was weaning down from Prednisone 50mg daily to 10mg daily over the past several weeks. She has never been diagnosed with psoriasis although she complains of scaly plaques on her elbows for many years. She denies any family history of psoriasis. She denies sick contacts.

PAST MEDICAL HISTORY

Asthma/COPD, hypertension, obesity, diabetes, gastroesophageal reflux disease

PAST SURGICAL HISTORY Hysterectomy

MEDICATIONS

Prednisone 10mg, theophylline 300mg BID, tiotropium inhalation, Advair discus (fluticasone-salmeterol) inhalation, home oxygen, lisinopril, metformin, simvastatin

ALLERGIES Zafirlukast

FAMILY HISTORY

Denies any family history of psoriasis
Mother died of heart disease at age 45, Sister died of complications related to asthma at age 30

SOCIAL HISTORY

Denies alcohol use, smokes ½ packs per day currently, has smoked for 30 years

PHYSICAL EXAM

T 97.4 HR 98 BP 121/67 RR 18 SaO2: 92% on 2L O2 via nasal cannula
Numerous erythematous indurated papules, some coalescing to plaques with overlying scale on the arms and legs; Elbows and knees with confluent thick silvery scaly plaques, Abdomen with confluent erythema and overlying pustules. No nail changes were noted.

LABS

Normal or negative: complete blood count except for WBC of 17.3, consisting 79% of neutrophils, basic metabolic panel, liver panel, lipid panel

HISTOPATHOLOGY

Abdomen (9/3/2008): Marked spongiosis with exocytosis of neutrophils and subcorneal abscess formation in the epidermis. Dermal edema with margination and with an interstitial mononuclear infiltrate with many neutrophils and eosinophils.

DIAGNOSIS

Generalized pustular psoriasis –von Zumbusch pattern associated with Bupropion

TREATMENT AND COURSE

Given that the patient had had a hysterectomy, she was started on acitretin 25mg daily with triamcinolone wet wraps. She slowly improved over the next several days and was discharged from the hospital. Several days later, she developed fevers and was admitted to an outside hospital where infectious work-up was negative and fevers attributed to the von Zumbusch type of generalized pustular psoriasis. Currently, her pustular psoriasis has mostly resolved on Acitretin and she feels systemically well.

DISCUSSION

Bupropion is a dopamine-norepinephrine reuptake inhibitor. It is marketed in the United States for treatment of depression (Wellbutrin) and smoking cessation (Zyban). Generalized pustular psoriasis secondary to bupropion was described in the British Journal of Dermatology in 2002. [1] In the three cases presented, the patients all had a personal history of prior psoriasis. In addition, flaring of their psoriasis occurred within 3-5 weeks from the onset of the medication. All three patients required admission to the hospital, 2 with mild fever to 37.1C and leukocytosis. For both our patients, the pustular psoriatic flare occurred several weeks following onset of bupropion. When encouraging smoking cessation in patients with psoriasis, patients should avoid using bupropion and discuss with their primary care physician regarding other options.

Generalized pustular psoriasis (GPP) is a variant of psoriasis with sterile neutrophilic pustules as its primary presentation. [2] Baker and Ryan observed four clinical patterns: von Zumbusch, annular, exanthematic, and localized. [3] Development of generalized pustular psoriasis has been observed with infection, pregnancy, topical irritants (i.e. Dovonex), and rapid tapering of oral steroids or systemic psoriatic therapies. The von Zumbusch pattern of GPP is the most concerning with generalized erythema and extensive pustulosis. The pustules coalesce to form "lakes of pus" which eventually rupture leading to superficial desquamation. The patient is systemically ill with signs of fever, plaque tenderness, arthropathy, hypocalcemia, leukocytosis, and an elevated ESR. Occasionally, their course may be complicated by congestive heart failure or infections. Rarely, this condition may be fatal. [4] The annular pattern of GPP consists of numerous annular lesions with sterile pustules at the periphery along with central healing and desquamation. This can be associated with fever, malaise, and plaque tenderness. The exanthematic pattern of GPP abruptly appears and resolves within a few days. It is typically associated with infection or drugs. The localized pattern of GPP consists of pustules appearing within preexisting psoriatic plaques during flares or following topical irritants.

Successful therapies for generalized pustular psoriasis reported in the literature include cyclosporine, infliximab, etanercept, acitretin, and adalimumab.

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CHICAGO DERMATOLOGICAL SOCIETY **CASE # 12**

Presented by Joan Guitart MD, Amy Paller, MD and Katherine Brown, MD
Department of Dermatology, Feinberg School of Medicine, Northwestern University

HISTORY OF PRESENT ILLNESS

The patient is a 38 year old woman with a history of diabetes insipidus (DI) for 3 years with a pruritic, tender scalp eruption for 2 months accompanied by enlarged lymph nodes of occipital scalp. She has also had an eruption under her breasts for 1 year that failed to improve with miconazole/zinc oxide/petrolatum barrier ointment or 1% iodoquinol/2% hydrocortisone. She has no history of childhood skin eruptions. Review of systems was significant for fatigue and weight gain, and negative for ocular symptoms. Since the onset of DI, a diagnosis of Langerhans cell histiocytosis (LCH) had been suspected by her previous providers. An outside bone scan was suggestive of histiocytosis in the rib region, however a follow-up bone survey did not show any lytic lesions. A bone marrow biopsy and chest CT were unremarkable. A brain MRI was reportedly suggestive of an infiltrative process in the pituitary such as histiocytosis or sarcoidosis. She declined a pituitary biopsy and has since been receiving an MRI every 6 months to monitor changes. She is followed in endocrinology for DI and PCOS and is s/p bromocriptine treatment for galactorrhea and hyperprolactinemia.

PAST MEDICAL HISTORY

Central diabetes insipidus, (diagnosed in 2005), iron deficiency anemia, polycystic ovarian syndrome, asthma, hypertension, osteopenia, anxiety, depression, irritable bowel syndrome, gastroesophageal reflux disease, s/p cholecystectomy, hyperprolactinemia

MEDICATIONS

DDAVP (antidiuretic hormone replacement), metformin, paroxetine, lorazepam, quetiapine, metroprolol, montelukast, fexofenadine, trimethobenzamide, tiagabine, lansoprazole, dicyclomine, lisinopril, guaifenesin, levalbuterol, mometasone nasal spray

FAMILY HISTORY Diabetes mellitus (grandmother), hypertension (both parents), polycystic kidney disease (maternal grandmother)

SOCIAL HISTORY Teacher; 7 year history of smoking, quit in 2001. Denies alcohol or drug use.

PHYSICAL EXAM

Well-appearing woman in no distress. There are pink follicular and non-follicular based papules on the scalp and in intertriginous regions of breast and groin. Several of these papules are excoriated, slightly hemorrhagic, and crusted.

LABS/STUDIES

Normal: TSH, LDH, CBC with differential, peripheral smear, bone marrow biopsy.
Abnormal: ALT 67 (30-65 U/L), elevated total protein 8.7 (6.4-8.2 g/dl), remainder of metabolic panel unremarkable. Serum electrophoresis: mild elevations in beta (1.0, normal range 0.55-0.82 GM/DL) and gamma fractions (1.4, range (0.74-1.3 GM/DL). Kappa light chain fraction was elevated at 1670 (range 629-1350 mg/dl), lamba light chain and K/L ratio was normal. Quantitative immunoglobulins showed elevated IgG 1720 (range 750-1700 MG/DL) and IgA fractions 427 (range 82-400 mg/dl).

- Brain/neck MRI: thickened, homogeneously enhancing base of the pituitary infundibulum consistent with histiocytic involvement. Diffuse, scattered cervical lymph nodes suggestive of LCH vs. reactive lymphadenopathy.

- Nuclear medicine bone scan, bone survey, high resolution chest CT, and panoramic Xray of jaw and craniofacial bone negative for neoplastic involvement.
- CT, abdomen & pelvis: No evidence of histiocytic involvement of the abdomen or pelvis. Remarkable for hepatomegaly with hepatic steatosis.

HISTOPATHOLOGY

Scalp, left: Epithelium with serohemorrhagic crust. The lower epidermis is infiltrated with histiocytic appearing cells with abundant pink cytoplasm and reniform nuclei. There are numerous eosinophils and neutrophils associated with the infiltrate. Immunohistochemistry for CD1a and S100 positively labeled the histiocytic infiltrate.

DIAGNOSIS

Langerhans Cell Histiocytosis, adult-onset.

TREATMENT AND COURSE

We recommended continued treatment with the miconazole/zinc/petrolatum barrier ointment to intertriginous areas and referred the patient to oncology at Northwestern. Based on her pituitary involvement and progressing cutaneous involvement, they have recommended initiation of vinblastine.

DISCUSSION

Langerhans cell histiocytosis (LCH) is a spectrum of clinical disorders characterized by a clonal proliferation and infiltration of organs by pathologic Langerhans cells. Skin, bone, liver, lung, lymph nodes, and hypothalamus may be involved. The four clinical syndromes grouped under Langerhans cell histiocytosis are Letterer-Siwe disease, Hand-Schuller-Christian disease, eosinophilic granuloma, and Hashimoto-Pritzker disease. The clinical manifestations range from asymptomatic or mild single organ involvement to progressive multisystem disease. The etiology and pathogenesis remains poorly understood. A familial association has been suggested, with another affected relative seen in nearly 1% of cases.

Although LCH most commonly develops in children ages 1-3, it may occur at any age. The incidence in adults is estimated at 1-2 cases per 1 million adults. In the largest case series of adult onset LCH in 274 patients, there was a slight male predominance (52%) and mean age at diagnosis was 35. Skin involvement was present in 37%, but isolated skin findings was only noted in 7% which stresses the need for a thorough workup after biopsy proven cutaneous involvement to look for multiorgan disease. Diabetes insipidus occurred in 30% of patients and in 43% of those with multisystem disease. In this series, 60% of patients with multisystem disease were treated with chemotherapy; vinblastine being the most common agent. Five year event-free survival was 100% for single-system disease and 92% for multisystem disease.

Therapeutic interventions for adults with LCH is based on degree and pattern of organ involvement and have largely been based on multicenter trials in children (LCH-1, LCH-II, LCH-III). Options include watchful waiting, local treatment, immunomodulation, irradiation, chemotherapy, and allogeneic stem cell transplant. For isolated skin disease, there are reports of effective treatment with topical corticosteroids, topical antibacterial agents, PUVA, or topical nitrogen mustard. For refractory cutaneous disease or disseminated disease, systemic therapy is usually beneficial and vinblastine with or without prednisone is the most common initial chemotherapy regimen. The first international study of treatment of LCH in adults (LCH-A1), launched in 2004 by the Histiocyte Society, aims to inform a more evidence-based approach to therapeutic intervention in adult-onset LCH.

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CHICAGO DERMATOLOGICAL SOCIETY **CASE #13**

Presented by Joan Guitart, MD, Pedram Gerami, MD, and Susan Boone, MD
Department of Dermatology, Feinberg School of Medicine, Northwestern University

HISTORY OF PRESENT ILLNESS

This 65 year old man presented to our clinic in 12/2007 with a biopsy proven diagnosis of cutaneous T-cell lymphoma (CTCL). In 10/2006, he noticed a red lesion on his left chest and was treated for Lyme disease. When the lesion did not resolve, a biopsy showed subcutaneous lupus per patient. He was treated with low dose methotrexate and topical steroids. By 6/2007, his disease had progressed, and a repeat biopsy showed CTCL. Despite some improvement with cyclophosphamide, doxorubicin, vincristine, and prednisone (CHOP) and prednisone tapers, results were not long-lasting. A subsequent biopsy showed persistent aggressive disease. In addition, the patient reported feeling "knots on the back of the tongue" and difficulty breathing through his nose with nasal bleeding. He had an otolaryngology evaluation and found to have a deviated septum without other abnormalities. There was no improvement of his nasal symptoms despite multiple nasal cultures and antibiotics.

PAST MEDICAL HISTORY

CTCL, diabetes mellitus, hyperlipidemia, coronary artery disease status post three stents, varicose vein removal, melanoma in-situ in 1/1999 treated by wide local excision, basal cell carcinoma

MEDICATIONS

Prednisone 30mg daily (taper), Vitamin B12 and antioxidants, insulin lispro

ALLERGIES

No known drug allergies

FAMILY HISTORY

Sister with immunodeficiency

SOCIAL HISTORY

Married, retired automotive worker, history of smoking but quit 30 years ago, social alcohol

PHYSICAL EXAM

On the arms, back, and left chest, there were numerous edematous erythematous to dark gray-brown plaques and tumors of variable sizes, up to 8cm. There were hyperpigmented patches on the medial right ankle. No plaques or tumors were ulcerated. Mucosal exam did not reveal any significant lesions. Total body surface area was 12%. No lymphadenopathy was noted.

LABS/STUDIES

9/2007: ANA panel was normal
12/2007: CBC significant for WBC 5.4 but otherwise normal, LDH 207, HIV-1&2 non-reactive, HTLV IgG negative, flow cytometry negative for phenotype abnormality or clonality of both T and B cells, Sezary count was 19, TCR rearrangement negative, Epstein-Barr Virus (EBV) DNA detected

IMAGING

- 9/2007 CT chest, abdomen, and pelvis: 2mm pulmonary nodule, mild splenomegaly, punctuate calcification in the liver and
- 12/2007 PET: extensive cutaneous lymphomatous involvement and extensive focal soft tissue masses noted in the region of the left lower neck and thoracic inlet, consistent with lymphomatous involvement, hepatosplenomegaly.
- 1/2008 CT sinus: interval increase in the right maxillary sinus mucosal thickening and fluid, increased middle meatal opacification, no gross neoplasm

- 1/2008 CT chest, abdomen, and pelvis: without significant change

HISTOPATHOLOGY

12/2707 (mid-back): Dense deep dermal infiltrate composed of sheets of atypical large lymphocytes extending from the superficial to deep dermis. The infiltrate tracks down the adnexal structures. Tumor cells are large with irregularly shaped nuclear membranes and one or several identifiable nucleoli. There are prominent mitoses. The process is diffuse and there is no significant epidermotropism or epidermal necrosis. No germinal centers were identified. Tumor cells are positive for CD3, TIA-1, CD56, but negative for CD4, CD8, CD45RA, CD30, CD20, and ßF-1. Occasional cells are Granzyme B positive; EBER is also positive. Impression: large T cell lymphoma with cytotoxic features most consistent with nasal/ nasal-type NK/T cell lymphoma.

DIAGNOSIS

Nasal-type NK/T-cell lymphoma with cutaneous involvement

TREATMENT AND COURSE

The patient completed one cycle of etoposide, methylprednisolone, cytarabine, and cisplatin (ESHAP) and underwent consultation for a hematopoietic stem cell transplant (HSCT). However, while HLA typing of his siblings and a matched unrelated donor search was ongoing, he developed new lesions. The patient underwent a second course of ESHAP. Unfortunately, prior to HSCT, the patient developed complications from his lymphoma and passed away.

DISCUSSION

Nasal lymphomas expressing a T- or NK-cell phenotype are rare in the United States and Europe but more common in Asia and Central/South America. Clinical presentation of NK-cell lymphomas (NKL) includes red to purple papules, plaques, nodules, or tumors of the nasal/nasopharyngeal regions, the skin, bone marrow, and lymph nodes. Histologically, these lymphomas are characterized by a diffuse infiltration of pleomorphic medium-sized to large tumor cells. Neoplastic cells will show positivity for CD2, cytoplasmic CD3ε, CD56, granzyme B, CD45RO, and EBER1/2 (in-situ hybridization using EBV markers), whereas ßF1, surface CD3, CD4, CD5, CD7, and CD8 are frequently negative. In general, clonal T-cell receptor by gene rearrangement is not found. Reported treatments include radiation, polychemotherapeutic agents including CHOP, DeVIC (dexamethasone, VP16, ifosfamide, carboplatin) with radiotherapy, CMED (cyclophosphamide, methotrexate, etoposide, and dexamethasone), and SMILE (methotrexate, ifosfamide, etoposide, steroid and L-asparaginase). NKL shows a poorer response to chemotherapeutic agents than other lymphomas due to the expression of p-glycoprotein. Despite initial responses to treatment, disease course is very aggressive. Compared with peripheral T-cell lymphoma, NKL is associated with significantly inferior rates of complete remission and decreased survival. HSCT is the only curative strategy for advanced stage patients.

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CHICAGO DERMATOLOGICAL SOCIETY **CASE # 14**

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

HISTORY OF PRESENT ILLNESS

This 61 year old Caucasian female with a history of hypertension and hypothyroidism presented for evaluation of a generalized, erythematous eruption with associated burning sensation of six weeks duration. The patient had been diagnosed with a drug reaction to newly started antihypertensive medications (carvedeliol and irbesartan-hydrochlorothiazide). The patient was started on prednisone and triamcinolone 0.1% cream and ointment without significant improvement. She reported no fevers, chills, unexplained weight loss, recent infections, or pruritus.

PAST MEDICAL HISTORY

Hypertension, hyperlipidemia, hypothyroidism

MEDICATIONS

Nadolol, levothyroxine, triamcinolone 0.1% cream and ointment, prednisone

ALLERGIES

No known drug allergies

FAMILY HISTORY

Noncontributory

SOCIAL HISTORY

Married, two adult daughters, no tobacco, rare alcohol

PHYSICAL EXAM

The patient had generalized erythema with scaling and well-defined islands of non-erythematous skin characterized by pinpoint erythematous follicular-based papules. Her palms and soles showed diffuse waxy, yellow keratoderma without fissuring. Exam of the scalp showed diffuse erythema and scaling; focal alopecia with intact follicular ostia was noted at the left vertex. Hair pull test was positive. No vesicles, pustules, or ulceration were noted. The patient did not exhibit ectropion. There were no ocular, nasal, or oral mucosal lesions.

HISTOPATHOLOGY

6/7/08 (right abdomen): The epidermis reveals marked thickening of the stratum corneum with alternating areas of hyperkeratosis and parakeratosis. The granular cell layer is mostly present. The dermis also shows a variable mostly perivascular lymphohistiocytic infiltrate. Mild telangiectasia is noted. Follicular plugging is focally seen. Papulosquamous dermatitis consistent with pityriasis rubra pilaris.

DIAGNOSIS

Pityriasis Rubra Pilaris

TREATMENT AND COURSE

Prednisone was discontinued. The patient began full-body triamcinolone 0.1% ointment wraps three times a day with fluocinonide 0.05% ointment under occlusion to her palms and soles twice daily. Emollients (Aquaphor healing ointment, petroleum jelly) were applied liberally and frequently. The patient recently discontinued topical corticosteroids due to concerns regarding elevated blood pressure. Topical PUVA therapy was started for the hand/foot keratoderma. The

patient's erythema and scaling has decreased significantly. Hyperkeratosis of the palms and soles with occasional painful fissuring continues to be significant. Acitretin was considered as a therapeutic option, but the patient deferred this treatment given her history of hyperlipidemia and prior inability to tolerate several lipid-lowering medications.

DISCUSSION

Pityriasis rubra pilaris (PRP) is a rare, hyperkeratotic, papulosquamous skin disease of unknown etiology. First described in 1828 by Claudius Tarral as a variant of psoriasis, PRP is classified into six distinct subtypes, with Type I, classical adult PRP, presenting as the most common form. PRP affects men and women equally and has a bimodal incidence, with peaks during the first and second decades and later during the sixth decade. The prognosis varies according to subtype; patients with Type I PRP have the best prognosis, with 80% achieving clearance within 3 years. For some patients, PRP is a life-long debilitating disease associated with substantial impairments in quality of life.

Clinically, lesions of PRP are characterized by symmetric, small, follicular, hyperkeratotic papules that evolve into large, scaly, orange-red plaques. Lesions typically start on the head and neck and progress caudally. Palmoplantar keratoderma and islands of skin sparing within generalized erythroderma are also characteristic features. Patients may also develop nail changes consisting of nail plate thickening, subungual debris, and yellow-brown discoloration. In patients with severe disease, ectropion may also be present.

Clinical and histopathologic correlation is necessary to diagnose PRP, which is often misdiagnosed as psoriasis. Histologically, PRP is characterized by alternating orthokeratosis and parakeratosis, follicular plugging, parakeratotic mounds at follicular ostia (shoulder parakeratosis), and elongated and thickened rete ridges. Superficial perivascular lymphocytic inflammation is also seen.

Treatment of PRP is challenging, and many therapeutic regimens have had variable success. Historically, PRP had been treated with oral vitamin A. However, toxic doses were required for effective treatment, limiting its use. Today, synthetic oral retinoids, acitretin and isotretinoin, are a mainstay of treatment for adult PRP and can result in clearance within three months of initiation. Methotrexate, with or without oral retinoids, is considered a second-line therapy. Other therapies include topical corticosteroids and vitamin D analogs, phototherapy, hydroxychloroquine, and systemic immunosuppressants such as cyclosporine and azothioprine. Tumor necrosis factor- alpha (TNF-alpha) inhibition may be a potential therapy for this disease. A few published cases report improvement of PRP following the initiation of TNF-alpha inhibitor therapy, and TNF- alpha may have a role in disease pathogenesis. Further research in understanding the pathophysiology of PRP and potential treatments is needed.

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CHICAGO DERMATOLOGICAL SOCIETY **CASE # 15**

Presented by Anthony J. Mancini, MD and Katherine Brown, MD
Department of Dermatology, Feinberg School of Medicine, Northwestern University

HISTORY OF PRESENT ILLNESS

This 10 month old male presented at five months of age with changes in his nails. He was born full term with abnormal brittle fingernails and toenails that had not required trimming. His mother was instructed to call when his teeth erupted if they were abnormal in appearance. Three months later, his first primary teeth erupted and were noted by his mother to be "pointed", at which point she contacted pediatric dermatology. The patient sweats normally and has had no problems with overheating. He is otherwise healthy and developing normally.

PAST MEDICAL HISTORY

None

MEDICATIONS

None

FAMILY HISTORY

No family members affected by nail, tooth, skin, or hair abnormalities. No known history of consanguinity.

SOCIAL HISTORY

Lives at home with parents

PHYSICAL EXAM

The patient has marked concavity (koilonychia) noted of the nails of the first three digits bilaterally and all toenails. There is no subungual debris, thickening, or discoloration. He has conical primary teeth. Facial features and hair appear normal. No patches of alopecia are present.

HISTOPATHOLOGY

None

LABS/STUDIES

CBC, TSH, and T4 are normal.

DIAGNOSIS

Tooth and nail syndrome

TREATMENT AND COURSE

The patient is currently being followed by pediatric dentistry and genetics. To evaluate for X-linked hypohydrotic ectodermal dysplasia, genetic testing for EDA1 mutation was performed and was negative. Further MSX1 gene sequencing was negative for the known mutation that has been associated in one family with Witkop syndrome. Based on these results, this patient either has a novel mutation for Witkop tooth and nail syndrome or may represent the autosomal recessive form of hidrotic ectodermal dysplasia with similar features, Fried syndrome, for which a mutation has not yet been identified.

DISCUSSION

Tooth and nail syndrome is an autosomal dominant hidrotic ectodermal dysplasia characterized by hypodontia and dysplastic nails with normal hair and normal sweating ability. Described in 1965 by Witkop, the incidence of this rare autosomal dominant disorder is estimated at 1-2:10,000. Genetic linkage analysis in affected and unaffected members of a three generational family showed an association with a nonsense mutation in the MSX1 protein involved in regulation of a tooth and nail development. MSX1 knockout mice have phenotypes with features of the tooth and nail syndrome. An autosomal recessive form of tooth and nail syndrome was described by Fried in two cousins with similar clinical features, however no genetic testing is available.

Published reports reveals wide variability in the severity of tooth abnormalities, ranging from one or two missing teeth to severe absence of up to 20 teeth. The most common missing teeth are maxillary incisors, secondary molars, and maxillary canines. Tooth shape is also distinctive, described as peg-shaped or conical and may be most notable in primary teeth. However, primary teeth may be only mildly affected and hypodontia or anodontia is not noted until permanent teeth fail to erupt. Hypodontia in a mildly affected adult may manifest only as widely spaced dentition. Therapeutic interventions for these patients focuses on management of dental anomalies, including early and frequent dental exams and utilization of dental prosthetics to maintain cosmesis and optimize alveolar bone growth.

Koilonychia may be present at birth with toenails classically being more severely affected than fingernails. Thin small friable nails are prone to breakage and rarely, if ever, require trimming. Nail findings often improve with age. Hair is typically normal in texture and distribution, although fine, thin, slow-growing hair has also been reported in some case series.

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CHICAGO DERMATOLOGICAL SOCIETY **CASE # 16**

Presented by Joaquin Brieva, MD and Anjeli Krishnan Isaac, MD
Department of Dermatology, Feinberg School of Medicine, Northwestern University

HISTORY OF PRESENT ILLNESS

This 38 year old woman with a history of hidradenitis suppurativa and keloids was referred from plastic surgery to dermatology for ongoing treatment of the same. The patient reports that she has been getting keloid formation since childhood. While the patient does not know what has instigated some of the keloids, she states that others have developed after a variety of cutaneous insults, including "little white bumps" that she has picked, cat scratches, a match falling on her, and boils, most recently in her groin. She does report manipulating these boils, more specifically, placing potatoes on the lesions and then picking and squeezing at them. The patient has had a variety of treatments in the past, including surgery and radiation, but the keloids either did not respond or recurred.

PAST MEDICAL HISTORY

Hidradenitis suppuritiva

MEDICATIONS

None

ALLERGIES

None

FAMILY HISTORY

Noncontributory

SOCIAL HISTORY

Single, sales specialist, smokes 5-10 cigarettes per day

PHYSICAL EXAM

There were large hyperpigmented firm keloidal plaques encompassing the entire jawline, upper neck, right breast, left chest, axillae, mons pubis, and groin. Other scattered keloidal papules and plaques were present on the back, right shoulder, and thighs. There was one draining nodule in the right groin.

HISTOPATHOLOGY

None

DIAGNOSIS

Extensive keloids

TREATMENT AND COURSE

The patient was started on doxycycline and chlorhexidine topical washes twice a day for the hidradenitis suppuritiva. Unfortunately, she has missed several appointments, and we have been unable to follow up with her since her first visit.

DISCUSSION

It is generally accepted that keloids develop after cutaneous injury or inflammation, but the underlying pathogenesis has not yet been elucidated. Both genetic and environmental factors are thought to play a role. While there has been no specific genetic link to the development of keloids, a positive family history is not unusual. In addition to surgery, lacerations, and earlobe

piercing, many inflammatory skin conditions can lead to keloids, including acne vulgaris, folliculitis, varicella infection, or vaccinations, especially the BCG vaccination. Multiple keloids have even been reported to be the presenting complaint in scleroderma. In addition, several familial syndromes have been associated with keloidal scarring including Rubinstein-Taybi, Goeminne syndrome, and conjunctivo-corneal dystrophy.

Keloids usually develop from a few weeks to many months after the inciting trauma. Reported in the literature, "spontaneous" keloids may occur after an inflammatory process that was initially unrecognized by the patient. In addition, there have been case reports of a series of Jamaican patients with "aggressive" keloids, in which the patients showed severe scarring after minor trauma with a family history of the same. These cases had an unusual extent and severity, with the formation of keloids resembling a neoplastic process.

Keloid-derived fibroblasts show abnormalities in the expression of various growth factors and their receptors, including TGF-β1, TGF-β2, VEGF, CTGF, and PDGF-a receptor, with TGF-β1 being the best studied factor in the pathogenesis of abnormal scarring. It is unclear whether these factors cause keloid formation or simply increase in response to the scarring process. Fibroblasts derived from keloids demonstrate increased production of collagen and matrix metalloproteinases when compared with normal dermal fibroblasts. Keloid fibroblasts also exhibit higher proliferation rates than those derived from hypertrophic scars. In addition, while normal scars appear to have a negative feedback mechanism where fibroblast activity is reduced to prevent excessive repair, this mechanism may be defective in keloids, leading to excessive scar formation.

There are many therapeutic options for keloids, including intralesional steroid injection, surgical excision, cryotherapy, laser therapy, radiation therapy, and the application of silicone gel sheets. In addition, variable success rates have been reported with bleomycin, imiquimod, 5-fluorouracil, retinoids, calcium channel blockers, mitomycin C, and interferon-alpha 2b. While all of these agents have shown some efficacy in limited keloid formation, there have been very few reports of successful treatment for such an extensive presentation of keloids.

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CHICAGO DERMATOLOGICAL SOCIETY **CASE # 17**

Presented by Joaquin Brieva, MD and Sandra Han, MD
Department of Dermatology, Feinberg School of Medicine, Northwestern University

HISTORY OF PRESENT ILLNESS

This 82 year old Caucasian male with a history of Grover's disease that resolved with triamcinolone 0.1% cream and selenium sulfide 2.5% presented for evaluation of a new eruption of scaly bumps on the back for the past six months. The bumps were asymptomatic, and the patient had not used any topical treatments for the lesions. This new eruption was distinctly different from the papules of his previous Grover's disease.

PAST MEDICAL HISTORY

Amyloidisis with secondary cardiomyopathy and pacemaker placement, IgA nephropathy, gout, hypothyroidism

PAST SURGICAL HISTORY

tricuspid valve replacement 1/2008

MEDICATIONS

Metoprolol, losartan, torsamide, warfarin, allopurinol, levothyroxine

ALLERGIES

No known drug allergies

FAMILY HISTORY

No family history of skin disease

SOCIAL HISTORY

Entrepreneur and businessman, no tobacco or alcohol

PHYSICAL EXAM

The patient has numerous**,** monomorphous 1-6mm gritty firm papules with an erythematous base and central keratinous plug distributed over the back.

HISTOPATHOLOGY

7/15/08 (back): At the center of the specimen one identifies elongation of the rete ridges with suprabasal acantholysis and dyskeratosis. Atypical changes are not noted. The dermis shows a variable inflammatory infiltrate. Impression is warty dyskeratoma.

DIAGNOSIS

Eruptive warty dyskeratoma. Less likely, an atypical re-presentation of Grover's disease.

TREATMENT AND COURSE

The largest lesions were treated with two freeze-thaw cycles of liquid nitrogen. The patient was also started on tazarotene 0.1% cream daily to the lesions.

DISCUSSION

Warty dyskeratoma (WD) is found in middle-aged to older individuals. It was initially described in 1954 by Helwig as "isolated Darier's disease," which reflects the typical solitary nature of the lesion and the characteristic histologic findings. We describe here the eruptive development of numerous warty dyskeratomas in a patient.

WD characteristically appears as a solitary flesh-colored papule with a rolled, smooth edge and a central hyperkeratotic plug. It measures less than 1cm and is usually located on the scalp, face, or neck. The lesions grow slowly and are typically asymptomatic. In most cases, they have been present for a period of several months to several years before presentation to a dermatologist. The diagnosis of WD is rarely made before microscopic examination is done, and clinical diagnoses at the time of biopsy have included basal cell carcinoma, squamous cell carcinoma, epidermal cyst, keratoacanthoma, verruca vulgaris, and dermatofibroma, among others. Biologically, WD acts in a benign manner, with no reports of malignant transformation, local invasion, or metastasis.

Microscopic examination of these lesions reveals a cup-shaped pilosebaceous follicle extending into the dermis with variable hyperkeratosis and acanthosis. Suprabasal acantholysis results in narrow clefts and Darier-like lacunae that separate the basal cells from the overlying epidermis. These basal cells cover dermal papilla that project into the lacunae. The overlying epidermis contains dyskeratotic keratinocytes, and free-floating corps ronds and grains are evident.

Only four reports exist in the English literature of multiple WD. Of these cases, the greatest number of papules on an individual patient was 25, and these were all localized to the scalp. There have been no documented cases of numerous WD on the trunk as seen in our patient.

The pathogenesis of WD is largely unknown. Factors proposed to be involved in the pathogenesis of WD have included viral infection, chronic actinic damage, and smoking. A study specifically investigating the role of human papillomavirus (HPV) as a possible etiologic agent failed to demonstrate HPV DNA in any of the WD specimens examined. Thus, despite its name, any relationship to verruca, or "warts," is unlikely. Another study demonstrated the presence of HKN-6 and HKN-7, specific for human hair cortex and inner root sheath, respectively, in WD thus supporting a follicular origin of these lesions.

Treatment for WD has largely been surgical excision. In rare instances at the site of excision, recurrence has occurred, requiring re-excision. In one recent report, topical tazarotene was used successfully to treat agminated WD papules localized to the intertriginous region.

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CHICAGO DERMATOLOGICAL SOCIETY **CASE#18**

Presented by Amy Paller, MD and Melissa Abrams, MD
Department of Dermatology, Feinberg School of Medicine, Northwestern University

HISTORY OF PRESENT ILLNESS

The patient is a 2 year-old girl followed at Children's Memorial Hospital since 22 days of life for thick, scaly skin. She was born as a collodion baby at 35-weeks gestational age with generalized skin thickening and shininess, and associated mild ectropion and ear deformity. No blistering was noted. She spent ten days in a humidified incubator. By two weeks of age her collodion membrane had largely peeled and by three months of age her skin clearly showed the thick brown scaling of lamellar ichthyosis, but localized to her trunk and scalp with sparing of the extremities.

PAST MEDICAL HISTORY

Schizencephaly; diagnosed at one year of age, mild developmental delay (gross/fine motor), tricuspid aortic valve, delayed tooth eruption

MEDICATIONS

Tazarotene 0.1% cream, aquaglycolic shampoo, Baker's psoriasis and seborrhea liquid or plain mineral oil

FAMILY HISTORY

No history of collodion membrane at birth or ichthyosis
Mom and two healthy sisters had infantile hemangiomas

PHYSICAL EXAM

At her most recent visit, she showed no evidence of scaling other than a small patch of mild lamellar scale on the upper right side of the chest and on her scalp. Her extremities remain clear without application of the tazarotene.

DIAGNOSIS

Lamellar ichthyosis, bathing suit distribution

TREATMENT AND COURSE

Since birth she has been treated with bland emollient application, Aquaphor 4-5 times per day. She is bathed daily with mild soaps (largely Cetaphil liquid cleanser), and bleach baths (two teaspoons of bleach to a full bath) have been used rarely to eliminate any odor associated with her thickened skin. Tazarotene 0.1% cream was added to her Aquaphor at 15 months of age with almost complete resolution of her ichthyosis. Currently, she continues to have a fair amount of scaling on her scalp, despite the use of aquaglycolic shampoo and mineral oil/ Baker's psoriasis and seborrhea shampoo. At her last visit, we suggested intermittent application of tazarotene to the scalp as well, which she did not tolerate.

While she has had dramatic improvement in her ichthyosis from using the tazarotene, the patient continues to have mild hypohidrosis, but this has not caused any problems.

DISCUSSION

Bathing suit ichthyosis (BSI) is a unique clinical phenotype of autosomal recessive lamellar ichthyosis. It was originally reported in the 1970's in South Africa but has been shown to affect patients from Europe as well. Individuals with BSI are born with a collodion membrane and then during the first or second month of life they develop large dark grey/brown scaling limited to the

trunk, with complete healing of the face and extremities. The palms and soles may be mildly hyperkeratotic.

Similar to more generalized lamellar ichthyosis, BSI is caused by a mutation in *TGM1* (14q11.2). Thirteen different mutations leading to this specific phenotype have been identified. Each of these mutations leads to a deficiency of keratinocyte transglutaminase (TGase 1), a calcium dependent enzyme which plays a vital role in the formation of the cornified cell envelope (CCE) by crosslinking several precursor proteins (including involucrin). With a defective CCE**,** the lipid barrier of the stratum corneum is impaired. Of note, missense mutations which are present on at least one allele in all BSI patients tend to produce a functionally active, but functionally diminished TGase 1 protein.

Regarding the striking clinical presentation, it has been shown that TGase 1enzyme activity is differentially expressed in unaffected and affected BSI skin. In unaffected skin, there is almost normal membranous TGase 1 activity. In contrast, affected skin only shows a residual cytoplasmic activity.

Oji et al suggest that BSI can be explained as a temperature-sensitive phenomenon. The gene mutations resulting in BSI directly or indirectly render the TGase 1 enzyme sensitive to differences in body temperature. In vivo testing has provided evidence that increased temperature can have a direct effect on the TGase 1 protein through protein destabilization. Additionally, it is hypothesized that temperature can also cause a change in pH or activity of proteolytic enzymes thereby affecting epidermal homeostasis. TGase 1 activity is reduced under higher temperatures, and skin temperatures greater than 33 degrees Centrigrade predispose to ichthyosis. Clinically, warmer body areas correspond to affected skin whereas colder areas appear normal. A characteristic clinical skin finding is sparing of the suprarenal skin of the trunk, as this skin is 2-3^{o} cooler than the surrounding skin.

Treatment of these patients includes emollients for dry skin, topical keratolytic agents, and topical or systemic administration of retinoids. Typical of many patients with milder forms of lamellar ichthyosis, our patient responded very well to topical tazarotene. Given the poor cutaneous barrier of these patients and potential toxicity, the use of keratolytic agents and retinoids should not be started until at least six months of age. Nevertheless, Nguyen et al recently showed that there is little systemic absorption in patients with lamellar ichthyosis using tazarotene for more than 12 months. Cutaneous infections (especially folliculitis and impetigo) may occur, and an odor can develop secondary to scale accumulation. Antibacterial soaps and bleach baths are helpful in this regard, and sometimes systemic antimicrobial therapy is required. Patients are also at increased risk of dermatophyte infections, which can be masked by the chronic ichthyotic scale.

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CHICAGO DERMATOLOGICAL SOCIETY **CASE # 19**

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

HISTORY OF PRESENT ILLNESS

This 49 year-old woman with a history of hidradenitis suppurativa of the axillae, inframammary, and groin areas since age 17 presented for evaluation of very painful sores on her calves that developed approximately 5 months ago. These sores initially began as pustules but subsequently enlarged. She has received intralesional triamcinolone injections and silver-coated antimicrobial dressings for these lesions as well as fentanyl and tylenol/hydrocodone for pain management. The patient also complained of a non-radiating left hip pain aggravated by movement that started the week before her office visit; this was not related to trauma.

PAST MEDICAL HISTORY

Hidradenitis suppurativa, morbid obesity, diabetes mellitus, hypertension, mild anemia, elevated C-reactive protein

MEDICATIONS

Trimethoprim/sulfamethoxazole, metformin, lisinopril, spironolactone, sertraline, metoclopramide, tylenol/hydrocodone, fentanyl

ALLERGIES None

FAMILY HISTORY

Father with possible hidradenitis suppuritiva, aunt and cousin with inflammatory bowel disease

SOCIAL HISTORY

The patient is on disability and is married. She smokes 1 pack of cigarettes per day.

PHYSICAL EXAM

On the medial calves bilaterally, there were two 2-3 centimeter erythematous plaques with undermined borders and central ulcerations. Both of the lower legs had erythematous and violaceous edematous papules and pustules. The axillae, inframammary region, and groin had numerous erythematous papules, large open draining cysts and sinuses, and scars.

LABS/STUDIES

White blood cell (WBC) count 14.5 (high), erythrocyte sedimentation rate (ESR) 100 (high), IgA 510 (high), IgM 31 (low), rheumatoid factor negative

HISTOPATHOLOGY

11/30/2007 (left calf): At the center of the specimen, there is a collection of neutrophils and some granulomatous inflammation surrounding follicular epithelium. The adjacent dermis shows reactive changes with fibroplasia, a lymphohistiocytic infiltrate and plasma cells. Atypia was not identified. The epidermis shows some spongiosis and a serous crust. DPAS, gram, and AFB stains were negative. Consistent with a deep dermal perifollicular abscess and reactive changes, compatible with pyoderma gangrenosum.

11/30/2007, left shin - Changes as above; in addition, neutrophilic infiltration of the interstitium, and several deep blood vessels have fibrinoid necrosis and neutrophilic debris in the walls near the center of the neutrophilic infiltration. Consistent with a dermal perifollicular and interstitial abscess and reactive changes.

DIAGNOSIS

SAPHO syndrome associated with hidradenitis suppurativa with concomitant pyoderma gangrenosum and neutrophilic vasculitis

TREATMENT AND COURSE

The pyoderma gangrenosum of the legs cleared completely soon after starting dapsone 100mg daily and infliximab 5mg/kg, infused every 6 weeks. However, after an initial improvement, her hidradenitis suppurativa flared. The infliximab frequency was increased to every 5 weeks, while an attempt was made to wean her dapsone dose to 50mg daily. However, the flare persisted, and the patient's dose of infliximab was increased to 10mg/kg, and the dapsone dose was increased back to 100mg daily. The patient continues to have ongoing lesions of hidradenitis. On the other hand, since beginning dapsone and infliximab, the patient has had no recurrence of joint pain or pyoderma gangrenosum. The patient is currently not a surgical candidate for excision of her sinus tracts due to morbid obesity.

DISCUSSION

Synovitis-acne-pustulosis-hyperostosis-osteitis (SAPHO) syndrome is a chronic and relapsing condition that was first described in 1987 by Chamot et al. There are four subtypes of this heterogeneous disease: 1) rheumatologic manifestations associated with acne conglobata or acne fulminans or hidradenitis suppurativa, 2) rheumatologic manifestations associated with palmoplantar pustulosis, 3) axial or appendicular hyperostosis with or without dermatosis, 4) chronic recurrent multifocal osteomyelitis involving the axial or appendicular skeleton with or without dermatosis.

A variety of skin manifestations have been associated with the syndrome, including palmoplantar pustulosis, hidradenitis suppurativa, acne fulminans, acne conglobata, pustular psoriasis, dissecting cellulitis of the scalp, Sweet's syndrome, and Sneddon-Wilkinson disease. Skin findings may also be minimal or absent. Musculoskeletal manifestations include acute or chronic synovitis, sacroiliitis, sclerosing bone lesions, sterile osteomyelitis, synovitis, and osteitis. Joint involvement is classically seen in the sternoclavicular region.

The pathogenesis of SAPHO syndrome is unknown, and it is likely multifactorial. A mutation in a gene that encodes CD2 binding protein 1 is responsible for the autoinflammatory PAPA syndrome (pyogenic sterile arthritis, pyoderma gangrenosum, and acne). Mutations in CD2BP1 are thought to alter T cell activity and precipitate the observed influx of neutrophils seen in an inflammatory site. Additionally, a mutation in the MEFV gene which encodes pyrin has been found to be the cause of familial mediterranean fever, another autoinflammatory condition. Pyrin mutations may induce a prolonged inflammatory response, which could also play a role in SAPHO. Finally, nuclear factor kappa beta (NF-kB) which is highly activated at sites of inflammation and caspases, enzymes involved in cytokine maturation, have also been postulated to contribute to the clinical manifestations seen in SAPHO syndrome.

The usual treatments for SAPHO syndrome include NSAIDs, corticosteroids,and sulfasalazine. Anti-tumor necrosis factor–alpha agents, particularly infliximab, may be useful, as well as methotrexate, smoking cessation, and weight reduction.

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CHICAGO DERMATOLOGICAL SOCIETY **CASE #20**

Presented by Anthony J. Mancini, MD and Kimberly Nicholson, MD
Department of Dermatology, Feinberg School of Medicine, Northwestern University

HISTORY OF PRESENT ILLNESS

This 3 year-old female with a history of atopic dermatitis initially presented to clinic at 13 months of age for episodic erythema of her cheeks. The erythema was noted at 6 months of age around the time of introduction of solid foods. It consistently occurred within seconds of ingesting solid foods and then resolved over 30 to 60 minutes. She was evaluated by multiple allergists for potential food allergy with RAST testing which had been negative. Her diet was nonetheless modified to formula and oatmeal only, with only a modest decrease in her erythema episodes. She had no history of lesions elsewhere.

Ten months after the patient's initial presentation to our clinic, her mother inquired about a similar eruption on the cheeks of her younger sister, then 6 months of age.

PAST MEDICAL HISTORY

Normal vaginal delivery (no forceps or vacuum assistance)
Atopic dermatitis
Multiple congenital nevi

MEDICATIONS Cetirizine, hydrocortisone 1% cream

ALLERGIES None

FAMILY HISTORY

Mother with "sensitive skin" and thyroid disease and father with corn syrup allergy

SOCIAL HISTORY

The patient lives at home with her parents, younger sister, and two dogs.

PHYSICAL EXAM

Cutaneous findings on the face were initially absent. Within minutes of ingesting fruit snacks in the clinic, she developed intense erythema of the bilateral cheeks in a linear distribution extending from the oral commissures diagonally across the cheeks and up to the temporal scalp. There was no urticaria, angioedema, or respiratory distress. The findings resolved over 20 minutes.

Photographs of her younger sibling (forwarded to AJM via e-mail from her mother) showed a similar pattern of erythema.

HISTOPATHOLOGY None

DIAGNOSIS

Bilateral, familial auriculotemporal nerve (Frey) syndrome in two sisters

TREATMENT AND COURSE

The parents were educated about the disorder and watchful waiting was recommended. No further allergy testing was recommended, and liberalization of the diet was encouraged. Both patients continue to develop the asymptomatic cutaneous reaction upon ingestion of certain foods.

DISCUSSION

Auriculotemporal nerve (Frey) syndrome was first described by Duphenix in 1757 and publicized by Lucja Frey in 1923. It is characterized by unilateral or rarely bilateral flushing and hyperhidrosis in the distribution of the auriculotemporal nerve in response to gustatory stimuli. In adults, it typically occurs as a complication of surgery, cerebellopontine angle tumors, parotid gland disease, radical neck dissection, or cervical sympathectomy. The condition is rare in children and forceps-assisted delivery is implicated as an etiology in around half of reported cases. Inflammation, such as viral or suppurative parotiditis and herpes virus infection, has also been implicated in children.

In adults the predominant feature of Frey syndrome is unilateral sweating. In infants and children, flushing is more common and hyperhidrosis is often absent. The flushing is typically noticed around 2 to 6 months of age with the initiation of solid foods. When trauma is implicated in older children and adults, symptoms usually begin 3 to 6 months following the incident. Clinically, flushing begins a few seconds after the onset of mastication and resolves 30 to 60 minutes later. The disorder is often confused with food allergy, and patients typically have undergone extensive RAST testing, trials of anti-histamines, and special diets without improvement before the diagnosis is made.

The auriculotemporal nerve is a branch of the mandibular nerve and provides sensory, sympathetic, and parasympathetic fibers to the preauricular and temporal areas. The parasympathetic secretory fibers course to the parotid gland while sympathetic fibers supply the subcutaneous arterioles and eccrine sweat glands. The mechanism of injury is thought to be disruption of parasympathetic fibers with subsequent misdirection along sympathetic pathways during regeneration of the nerve. Therefore, with mastication, patients experience flushing and sweating rather than normal saliva production. For children without any preceding injury, the explanation for disease may be congenitally aberrant nerve crossing, subclinical viral infection of the parotid, or subclinical intrauterine infection. Bilateral Frey syndrome has never been described in siblings prior to this case.

Treatment in adults has included anticholinergic agents (topical and oral), botulinum toxin, cervical sympathetic block, aluminum chloride, or anti-perspirant. These treatments are typically not recommended in children, and symptoms tend to diminish with increasing age. Spontaneous remission has been described, and few children undergo any intervention. It is thus important to recognize this benign and often self-limited disease in children to avoid unnecessary testing for food allergy and elimination diets.

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CHICAGO DERMATOLOGICAL SOCIETY **CASE #21**

Presented by Joaquin Brieva, MD, Bethanee Schlosser MD, and Victoria Wang, MD
Department of Dermatology, Feinberg School of Medicine, Northwestern University

HISTORY OF PRESENT ILLNESS

This 67 year-old woman with a history of Sjogren's syndrome presented for evaluation of a one year history of a pruritic eruption, which started on her arm. On review of systems, the patient also noted dry eyes and a dry mouth. The patient denied malar rash, Raynaud-type symptomatology, alopecia, renal disease, central nervous system disease, arthritis, or pleuritic pain.

PAST MEDICAL HISTORY

Sjogren's syndrome

MEDICATIONS

Chloroquine 250mg daily

ALLERGIES

Sulfamethaxazole

FAMILY HISTORY

Father with coronary heart disease and mother with rheumatoid arthritis

SOCIAL HISTORY

The patient is single and is employed as a hostess. She drinks two glasses of alcohol a day. She has a five pack-year tobacco history.

PHYSICAL EXAM

There were annular and arcuate erythematous plaques on her back and arms with trailing scale and crust and telangiectasia at the active border. Central clearing was present in several plaques. The parotid glands were normal in size.

LABS

4/2008 - Abnormal:
Complete blood count significant for WBC 2.8
ANA 1:80-1:320, speckled pattern; dsDNA 7.9 (<5.0 normal), anti-Smith IgG 7.0 (<5.0 normal), SS-A IgG 158 (<5.0 normal), SS-B IgG 178 (<5.0 normal)
4/2008 – Normal:
Urinalysis, complete metabolic panel, Scl-70 IgG, nRNP/Sm IgG, C3, C4, cardiolipin IgG, cardiolipin IgM, cardiolipin IgA

HISTOPATHOLOGY

4/4/2008 **(**left forearm): The epidermis reveals atrophy and an interface lymphocytic infiltrate with vacuolar changes and scattered and focally coalescing necrotic keratinocytes. There is marked edema of the papillary dermis with telangiectasia and inflammation. Hair follicles are not markedly involved. Consistent with an interface dermatitis.

DIAGNOSIS

Annular erythema of Sjogren's syndrome

TREATMENT AND COURSE

The patient initially used mometasone ointment, clobetasol ointment, and hydroxychloroquine 400mg daily. However, she had to stop hydroxychloroquine in 4/2008 due to hives after just two doses. Currently, the patient is using clobetasol ointment, halobetasol ointment, tacrolimus ointment, and chloroquine 250mg daily. Rheumatology is also following the patient. Strict sun protection was advised in addition to regular dental and ophthalmologic care.

DISCUSSION

Annular erythema is a cutaneous manifestation of Sjogren's syndrome. Other manifestations include eyelid dermatitis, cutaneous vasculitis, xerosis, and angular cheilitis. Annular erythema is seen more often in primary Sjogren's syndrome (6.45%) compared to secondary (3.2%). Some consider annular erythema of Sjogren's to be a subset of subacute cutaneous lupus erythematosus, and some even consider it to be the Asian counterpart of subacute cutaneous lupus erythematosus in Caucasians.

Clinically, patients present with annular erythematous indurated plaques with central clearing on the face, back and arms. There are many diagnostic tests that may confirm Sjogren's syndrome, including 1) positive antibodies against Ro/SS-A and La/SS-B, 2) Schirmer's test (blotting paper placed under the eyelid to measure tear production), 3) lip biopsy (to assess for salivary gland inflammation), 4) MRI sialography (to assess for ectasia of parotid ducts), and 5) rose bengal test (dye placed on the surface of the eye to evaluate how effective tear glands are). 75% of patient with annular erythema of Sjogren's have positive Ro/SS-A and La/SS-B. On cutaneous histology, a perivascular and periappendigeal lymphocytic infiltrate is seen.

Treatment options include hydroxychloroquine 200mg twice a day and/or quinacrine 100mg daily, tacrolimus 0.1% ointment twice a day for facial involvement, mid-potency topical steroids, and prednisolone 10-20mg daily. If there are any symptoms or signs of thyroid disease, thyroid function tests should be checked given the association of autoimmune thyroid disease and Sjogren's syndrome. Lesions clear without scarring.

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CHICAGO DERMATOLOGICAL SOCIETY **CASE #22**

Presented by Simon Yoo, MD, Pedram Gerami, MD, and David Reid, MD
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HISTORY OF PRESENT ILLNESS

In December 2004, this 56 year-old man developed a large, red, pruritic lesion on the left aspect of his scrotum and inner thigh. It failed to resolve with topical steroids and soon developed into a bleeding, nonhealing sore with extension to the penis and left groin. He had a history of basal cell carcinoma (BCC) of the nose and scalp, treated with excision 4 years prior, but was otherwise feeling well. Biopsy of the left groin revealed an ulcerated, invasive BCC. He underwent wide excision (20x15 centimeters), with resection down to the penile shaft, left scrotal area, and left medial thigh, and repair with scrotal and abdominal flap reconstruction. In June 2007, he developed recurrence that was treated with left groin dissection from the superior pubic area down to the level of the testicle and spermatic cord. Frozen section analysis confirmed BCC with positive deep margin involvement and invasion into 2 regional lymph nodes. Review of systems is positive for a 30 pound weight loss over the past 4 months, night sweats, and fatigue.

PAST MEDICAL HISTORY Hypertension, benign prostatic hypertrophy

MEDICATIONS Terazosin, lisinopril-hydrochlorothiazide, oxycodone

ALLERGIES None

FAMILY HISTORY Mother and 2 sisters – basal cell carcinoma

SOCIAL HISTORY

The patient is employed as a customer service leader. He is single and lives with his girlfriend. He smoked less than 1 pack per day for 30 years, and he quit in 2007.

PHYSICAL EXAM

The left inguinal area revealed a large scar with nodularity near the scrotal tissue. There were no epidermal changes or evidence of basal cell carcinoma at the skin surface.

LABS/STUDIES

Whole body PET/CT-Scan (6/5/08) - Hypermetabolic uptake in the left inguinal region medial to the surgical clips, and in the left iliac lymph node and right inguinal lymph node.
Complete blood count (CBC) - within normal limits.

HISTOPATHOLOGY

Left shoulder - The dermis is infiltrated by nests of atypical basaloid cells which show peripheral palisading and are associated with fibromyxoid stroma from which they are separated by clefts. Some necrotic cells are indentified in several nests. A few of these islands show keratinization near the central portion. The tumor is deeply infiltrative and has foci with small jagged tumor islands infiltrating a desmoplastic stroma invading into the subcutis as well as surrounding and invading the smooth muscle. Consistent with a basal cell carcinoma, infiltrating and metatypical types. Tumor extends to the margin.

DIAGNOSIS

Metastatic metatypical basal cell carcinoma

TREATMENT AND COURSE

He was treated with external beam irradiation, 5000 centrigray, 200 centigray per fraction, over five weeks duration, to a generous field including the left groin and lower pelvis. Four months after completing therapy, he again developed recurrence, this time at the left tunica vaginalis, which was excised with a positive margin. In June 2008, a whole body PET/CT-Scan showed uptake in the left inguinal region, the left iliac lymph node, and the right inguinal lymph node. He has noted increased swelling and nodularity in the region since that time. Additional radiotherapy has not been recommended given concern for soft tissue fibrosis, ulceration, and erectile dysfunction. Currently, he is being considered for a planned clinical trial at Northwestern examining the effectiveness of cyclopamine for advanced BCC.

DISCUSSION

Basal cell carcinoma (BCC), the most common cutaneous malignancy, is typically characterized by slow growth, local destruction, and confinement to the skin. Metastases from BCC are exceedingly rare, occurring in only 0.0028% to 0.5% of cases. Most patients are Caucasian males; the male to female ratio is 2-3:1. Median time from appearance of primary tumor to development of metastatic disease is 9 years. Well-established risk factors for metastatic disease include long-standing lesions, large single or multiple primary tumors, and localization to the head and neck. In particular, BCC of the scrotum, while rare, has a relatively high rate of metastasic spread, estimated at 13%. In addition to localization of primary tumor, histologic subtype may influence spread; morpheaform, metatypical, and basosquamous types have been noted to be particularly aggressive.

Criteria for metastatic BCC, as established by Lattes and Kessler, include a neoplasm of cutaneous origin (rather than glandular or mucosal), matching histologic subtypes of primary and metastatic tumor, and metastases at a distant, noncontiguous site. Most commonly, metastatic disease involves the local lymph nodes (70%) through regional spread, but hematogenous dissemination to the lungs, bone, and skin may occur. If metastasis occurs, the median survival time is 8 months, and the 5-year survival is approximately 10%.

The traditional treatment options for metastatic BCC are chemotherapy, radiotherapy, and surgery. Chemotherapeutic agents, including cisplatin, bleomycin, cyclophosphamide, 5-fluorouracil, and vinblastine, are generally ineffective at altering prognosis. Radiation therapy, on the other hand, is more successful, and cure rates can approach 94-98%. Recently, electrochemotherapy, which employs electrical pulses to augment cytotoxic drug penetration, has been reported as an effective option. Cyclopamine, a steroidal alkaloid isolated from the plant *Veratrum californicum*, may be effective in the treatment of advanced BCC through inhibition of the hedgehog signaling pathway.

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