Chicago Dermatological Society

Monthly Educational Conference

Case Presentations
and
Continuing Medical Education Certification

Wednesday, October 10, 2007

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

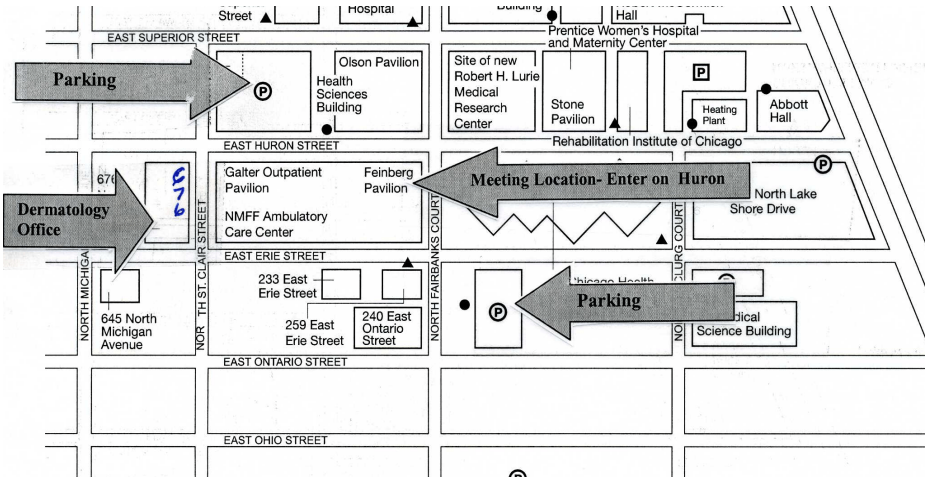
Program

Committees & Registration

8:00 a.m. - 9:00 a.m.	IDS Board of Directors Feinberg B
8:00 a.m. - 9:00 a.m.	CDS Finance Committee Feinberg C
9:00 a.m. - 10:00 a.m.	CDS Plans & Policies Committee Feinberg D

Program Activities

8:00 a.m.	Registration opens & continental breakfast *Feinberg A Foyer*
9:00 a.m. - 10:00 a.m.	Resident Lecture – *Feinberg A* GREAT BLISTERING CASES FROM USC AND NORTHWESTERN David T. Woodley, MD
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. - 12:15 p.m.	General Session - *Feinberg A*
11:00 a.m.	CDS Business Meeting
11:15 a.m.	Guest Lecture – POTENTIAL THERAPIES FOR EPIDERMOLYSIS BULLOSA AND NON-HEALING SKIN WOUNDS David T. Woodley, MD
12:15 p.m. - 1:00 p.m.	Luncheon – *Feinberg Pavilion - Atrium*
1:00 p.m. - 2:30 p.m.	Case Discussions – *Pritzker Auditorium*
2:30 p.m.	Meeting adjourns



CME Information

This activity is jointly sponsored by the Chicago Medical 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. Several companies have paid a fee to be present as exhibitors. The program content is free from any commercial or corporate influence.

Guest Speaker

David T. Woodley, MD is the founding chair of the Department of Dermatology at the Keck School of Medicine, University of Southern California. His research interests are in autoimmune bullous diseases of the skin, wound healing, and gene therapy for hereditary skin diseases. He earned his medical degree at the University of Missouri in 1973 and completed residencies at the University of Nebraska Medical Center, Omaha (1976); and the University of North Carolina Medical Center, Chapel Hill (1978). He is board certified in Internal Medicine and Dermatology.

Speaker CME Disclosure of Financial Interests

Dr. Woodley has no financial interests 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 sign-in sheet located at the Chicago Dermatological Society registration desk. Do so before you leave the conference! If you have any questions about your credits, please contact the Chicago Dermatological Society at 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 Joaquin Brieva, MD, Brandi Kenner-Bell, MD, and Anjeli Krishnan, MD
Department of Dermatology, Feinberg School of Medicine, Northwestern University

HISTORY OF PRESENT ILLNESS

The patient is a 19 year-old African-American man with a history of possible Crohn's colitis and cholestatic hepatitis who presented with a bullous eruption of his arms and legs. Approximately 2-3 days prior to transfer to our hospital, the patient began to develop extremely painful blisters of his right arm, which then spread to his left arm and legs. The patient was empirically started on acyclovir at an outside hospital for presumptive varicella versus disseminated zoster. He had been on multiple other antibiotics for persistently high fevers with nausea, vomiting, and diarrhea. The patient reported a similar bullous eruption on his arms upon his last discharge from the outside hospital one month prior. He was on multiple antibiotics during that hospitalization, including vancomycin. The patient reported having a skin biopsy of a bullous lesion at that time, which showed "chicken pox". He was treated with acyclovir, and that particular eruption resolved after a few days.

PAST MEDICAL HISTORY

Likely Crohn's disease, cholestatic hepatitis, pulmonary embolism and alveolar hemorrhage, pericardial and pleural effusions, episcleritis and peripheral ulcerative keratitis of right eye

MEDICATIONS

Vancomycin, linezolid, imipenem-cilastatin, acyclovir, ursodiol, ferrous sulfate, alprazolam, escitalopram, clonazepam, pantoprazole, prednisolone ophthalmic solution

ALLERGIES: No Known Drug Allergies

LABS

P-ANCA 1:1280 (<1:40), C-ANCA 1:2560 (<1:40), antiproteinase-3 Ab >100 (<3.5), anti-myeloperoxidase Ab 15 (<9.0), ANA 1:640 speckled, anti-histone Ab 2.5 units (<1.0), anti-smooth muscle Ab 1:160, quantitative IgG 2440 (750-1700), CH50 205 (63-145), lupus anticoagulant and anti-cardiolipin IgG positive
The following were normal: RPR, anti-mitochondrial Ab, anti-DNA Ab, anti-smith Ab, anti-RNP Ab, anti-SSa Ab, anti-SSb Ab, anti-Scl 70 Ab, anti-Jo-1 Ab, Herpes Simplex 1 and 2 Ab, G6PD, Hepatitis A, B, and C serologies, quantitative IgA, IgM, C3, C4, HIV 1&2 Ab, Beta-2 glycoprotein Ab

SOCIAL HISTORY

Lives with mother and 3 sisters. Denied tobacco or illicit drug use, social EtOH

PHYSICAL EXAM

Arms and legs with multiple clear fluid-filled vesicles and tense bullae, up to 5 centimeters in diameter, including the dorsal hands and feet, some with yellowish and hemorrhagic crust. Erythematous morbilliform macules on the lower legs with 2+ bilateral pitting edema. No facial or truncal lesions. Ocular and oral mucosa, palms and soles clear.

HISTOPATHOLOGY

Right dorsal forearm: a subepidermal bulla, with numerous neutrophils and few scattered eosinophils. In the adjacent epidermis, there are neutrophils lining up along the dermal-epidermal junction.
DIF, Right dorsal forearm: IgA demonstrates linear deposits at the dermal-epidermal junction (3+). IgG1, IgG4, C3, IgM, and fibrinogen were negative. The intercellular epidermal space is free of deposits.

DIAGNOSIS

Linear IgA bullous dermatosis in association with Crohn's disease

TREATMENT AND COURSE

Vancomycin was discontinued 5/28 and the patient received pulse methylprednisolone 125mg IV for three days, which was subsequently changed to oral prednisone 80 mg daily, to be tapered. He was started on dapsone 25 mg daily, but due to an acute elevation in his bilirubin, the drug was stopped after only 1 dose. The patient improved on prednisone alone and was discharged. Upon follow-up in clinic 1 week later, he had a few new small vesicles, but almost all of the lesions had healed. One week later he was readmitted to the hospital with fever, tachycardia, nausea, vomiting, diarrhea, and new pulmonary nodules. He had continued to develop new vesicles on the extremities while off of vancomycin. A Tzanck smear was negative, and DFAs for HSV and VZV were inconclusive. The patient's prednisone had been tapered to 40 mg daily, but he admitted to having been noncompliant with his medications. He was then started on tetracycline and nicotinamide for recurrent LABD. It is unclear whether the patient improved on the above regimen as it was discontinued secondary to concern for drug reaction causing his liver disease. One month later he returned to clinic with an extensive eruption of annular blistering lesions. At that time, he was started on mycophenolate mofetil 2 grams daily, with which he saw some initial improvement, but after 3 weeks began to develop new blisters, so doxycycline and niacinamide were added.

DISCUSSION

Linear IgA bullous dermatosis (LABD) is a rare subepidermal, autoimmune blistering disease characterized by linear deposition of IgA at the dermoepidermal junction. It is most often idiopathic, but has been reported in association with infections, medications, malignancies, autoimmune and inflammatory bowel diseases (IBD). LABD is mediated by IgA autoantibodies against various antigenic structures of the basement membrane zone and appears to represent a common reaction pattern to various stimuli. The occurrence of LABD secondary to vancomycin has been well established and this was what was initially believed to be the inciting factor in our patient. With vancomycin induced LABD, there is cessation of new lesions formation 24-72 hours after drug withdrawal with resolution of old lesions within 2-7 weeks. However, our patient continued to develop new lesions months after his last dose of vancomycin, making drug-induced LABD highly unlikely.

There have been several reports of LABD in association with IBD, particularly ulcerative colitis (UC), but also with Crohn's and lymphocytic colitis. There is also a frequently described association with gluten-sensitive enteropathy and one report of LABD in association with primary sclerosing cholangitis. A study in the United Kingdom found the prevalence of UC in LABD patients to be 7.1% compared with 0.05% in the normal population. In most of the reported cases the IBD preceded the development of skin disease by anywhere from a few months to several years, though there have been reports of skin lesions preceding the IBD. The reason for these associations is unclear, but suggestions have included: 1) an abnormal permeability of the mucosa causing increased antigenic stimulation or 2) abnormalities in mucosal B cells and mucosal IgA_1 production. All of the reported cases responded rapidly to dapsone therapy. We present this case to highlight the association of LABD and diseases of the bowel and encourage the clinician to consider screening of the gastrointestinal tract for all cases of LABD with no other association or precipitating factors.

REFERENCES

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2. Nanda A, Dvorak, et al. Association of linear IgA bullous disease of childhood with Crohn's disease. *Int J Dermatol*. 2006;45:1184-86.

CHICAGO DERMATOLOGICAL SOCIETY **CASE # 2**

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 is a 69 year-old male with erythematous papules and nodules over his face, neck, scalp, and back for the last 6 years. He has been evaluated by many dermatologists and biopsied multiple times during this period with possible diagnoses of actinic reticuloid, lupus erythematosus, leishmaniasis, but all tests and biopsies have been inconclusive. The lesions have also been injected with corticosteroids, which did not help. He reports that the lesions are pruritic and have been worsening over the last several months. He has since noticed development of enlarging masses in his left groin and neck. Patient denies fevers, chills, weight loss, or malaise.

PAST MEDICAL/SURGICAL HISTORY

Osteoarthritis in elbows
Peptic ulcer disease
Herniated disc (status post back surgery 2003)

MEDICATIONS

Hydroxyzine, fexofenadine, ranitidine, ibuprofen as needed for back pain

ALLERGIES

No known drug allergies

FAMILY HISTORY

No head/neck cancer, lymphoma, or thyroid cancer
Diabetes mellitus

SOCIAL HISTORY

Smokes 3-4 cigarettes per day x 5 years, denies alcohol use
Denies alcohol use

PHYSICAL EXAM

There are multiple, infiltrative, erythematous papules, some coalescing into nodules on the face, ears, scalp, neck, upper back. There are multiple, palpable, nontender cervical lymph nodes and a palpable, nontender lymph node in the left groin.

LABS

The following were negative or within normal limits:
CBC with differential, comprehensive chemistry panel, lactic dehydrogenase, Sezary cell count, hepatitis B antigen, hepatitis C antibody, anti-nuclear antibody, lyme disease antibodies, leishmania IgG, interlukin-6, tuberculin skin test
The following were abnormal:
Helicobacter pylori IgG antibodies reactive, serum protein electrophoresis: serum beta 0.9 (nl: 0.55-0.82 gm/dL), serum gamma 1.4 (0.74-1.3 gm/dL), urine protein electrophoresis: urine total protein 15 (0 mg/dL), urine albumin 4 (0 mg/dL), urine alpha1 2 (0 mg/dL), urine alpha2 3 (0 mg/dL), urine beta 4 (0 mg/dL), urine gamma 3 (0 mg/dL)
Monoclonal T-cell receptor rearrangement: unable to amplify from tissue sample

IMAGING

8/16/2007 CT scan of the neck with contrast: nodular skin and subcutaneous thickening involving the face, upper neck and nasal region. Multiple enlarged cervical lymph nodes, measuring from 1 cm to 1.9 cm.

8/16/2007 CT scan of the chest, abdomen, and pelvis: large enhancing lymph node in the left groin.

HISTOPATHOLOGY

Mid-forehead: The epidermis shows hyperkeratosis with some acanthosis and spongiosis. There is a dense dermal infiltrate composed primarily of plasma cells and scattered small round lymphocytes. Numerous eosinophils and some macrophages are also noted. Immunohistochemistry was performed on deparaffinized section. The infiltrating cells did not stain for CD20. Kappa and lambda demonstrate a ratio of light chains of 4:1. Kappa and lambda in-situ hybridization also demonstrate a normal ratio of light changes of 4:1.

Right Lower Back: Dermis shows dense superficial and deep lymphoid infiltrate with scattered irregular germinal centers. Infiltrate is composed of centrocytes and centroblasts with tangible body macrophages and variable mitotic activity. An interstitial lymphoplasmacytic infiltrate with numerous histiocytes is noted. Many plasma cells are seen.

DIAGNOSIS

Cutaneous/systemic plasmacytosis

TREATMENT AND COURSE

The patient was referred to Otolaryngology and received a parotid lymph node biopsy on 9/28/2007. Results are pending.

DISCUSSION

Cutaneous/systemic plasmacytosis is a rare entity arising primarily in patients of Asian descent. This condition is characterized by a peculiar cutaneous eruption of polyclonal plasma cell infiltrates accompanied by polyclonal hypergammaglobulinemia. Approximately 80 cases have been reported, mainly in Japan. There is a slight male predominance and onset ages ranged from 20 to 62 years. Clinically, patients with cutaneous/systemic plasmacytosis present with multiple red-brown macules, plaques, and nodules on the trunk. On histology, the skin lesions are characterized by a moderately dense superficial and deep perivascular infiltrate composed predominantly of mature plasma cells without atypia or light chain restriction. Extracutaneous involvement with infiltration of lymph nodes can occur. However, even in the absence of lymphadenopathy, lymph nodes frequently show infiltrates of mature plasma cells in an interfollicular distribution. Systemic plasmacytosis is defined as infiltration of mature plasma cells into more than two organs, including the skin and lymph nodes, accompanied by polyclonal hypergammaglobulinemia. Most patients are asymptomatic, although some with systemic involvement may present with fatigue and weight loss. The course is chronic without spontaneous remission. Overall, the prognosis of the condition is favorable, although there have been rare reported cases with a more aggressive clinical course. Treatment with immunosuppressive agents of variable potency, including topical tacrolimus, pimecrolimus, photodynamic therapy, topical PUVA, intralesional steroid therapy, and systemic cyclophosphamide/prednisone combination have all been reported in the literature with some success. Asymptomatic cases are usually not treated. Though the pathogenesis is unknown, many cases have been associated with increased serum levels of interleukin-6 (IL-6), a cytokine involved in inducing the differentiation of activated B cells to immunoglobulin-producing plasma cells.

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CHICAGO DERMATOLOGICAL SOCIETY ***CASE # 3***

Presented by Joaquin Brieva, MD, Bethanee Schlosser, MD, Mark Gendleman, MD, David Lorber, MD, and Katherine Brown, MD
Department of Dermatology, Feinberg School of Medicine, Northwestern University

Patient A

HISTORY OF PRESENT ILLNESS

This 34 year-old G3P3 female presented 5 weeks post-partum for an intensely pruritic cutaneous eruption that began at 39 weeks gestation as pruritic patches on her abdomen, with notable involvement of the striae and umbilicus, and gradually generalized with concomitant development of tense blisters on the extremities. Fever sometimes preceded new blisters. The baby was delivered at term, was of normal birth weight, and lacked any skin lesions.

Initial biopsies done at post-partum weeks 1 and 2 showed spongiotic dermatitis and marked eosinophilic infiltrate. Direct immunofluorescence was negative for IgG and C3. These data suggested a diagnosis of polymorphous eruption of pregnancy. Prednisone was initiated at a dose of 20 mg daily but was subsequently increased to 60 mg daily as eruption progressed. At post-partum week 4, a 3rd biopsy showed papular erythema with eosinophiilic infiltrate again consistent with polymorphous eruption of pregnancy. The patient then developed breast tenderness and fever to 103.7° F. and she was treated empirically with cephalexin for mastitis. The patient continued to develop new blisters when the prednisone dose was tapered. As such, a 4th biopsy was performed to rule out bullous erythema multiforme or pemphigoid gestationis.

PAST MEDICAL HISTORY

Two prior uncomplicated pregnancies, atopic dermatitis, allergic rhinitis, urticaria

MEDICATIONS

Prednisone, clobetasol propionate 0.05% ointment, cephalexin, hydroxyzine

ALLERGIES Penicillin

FAMILY HISTORY Hypertension

SOCIAL HISTORY

The patient is married and works as a registered nurse. She drinks occasional wine.

PHYSICAL EXAM

Exam was remarkable for confluent, edematous, erythematous papules, and plaques involving the face, neck, back, and extremities. Feet and soles demonstrated edematous, erythematous plaques. Intact vesicles and tense bullae noted on right forearm. The back and abdomen, including umbilicus, exhibited thin hyperpigmented scaly patches. Oral mucosa was normal.

LABS

Blood chemistries, CBC, ESR, and a liver function panel were within normal limits. Antinuclear antibody was negative. A bacterial culture of lesion was negative for organisms.

HISTOPATHOLOGY

H&E, right arm: supepidermal separation is visualized with an adjacent fragment of residual intact epidermis without acantholysis. A superficial perivascular infiltrate of lymphocytes and numerous eosinophils is present in the dermis.
Direct immunofluorescence: linear basement zone staining for C3. No staining for IgG or IgA.

DIAGNOSIS
Pemphigoid gestationis (formerly herpes gestationis)

TREATMENT AND COURSE
At initial evaluation at our clinic 5 weeks post-partum, 80% body surface area remained involved, and new blisters continued developing on prednisone 25 mg daily. Prednisone was increased to 60 mg daily for 2 weeks, followed by a gradual taper. The patient rapidly improved by week 6 post-partum. At that time, nicotinamide 500 mg 3 times daily and doxycycline 100 mg twice daily were added as steroid-sparing agents. Clobetasol propionate 0.05% ointment and oral antihistamines were continued. The patient has continued to do well on this regimen without developing any new blisters and has tolerated tapering prednisone dose to 5 mg. She attempted to discontinue prednisone but experienced a flare of pruritus within 2 days.

Patient B
HISTORY OF PRESENT ILLNESS
This 36 year-old G1P2 female presented 2 days post-partum from Cesarean delivery of fraternal twins with a mildly pruritic eruption for 10 days that began on the dorsal feet and abdomen, and spread to the thighs. Subsequently, she developed blistering within the eruption on the lower extremities after delivery. She stated, "It seems to be in places that were the most swollen or stretched." She did not endorse any significant outdoor exposure or contact with new shoes or products prior to the onset. The patient denied pain, fever, chills, malaise, dysphagia, fatigue, oral lesions, eye symptoms, or arthralgias. The twins were delivered at term and were of normal birth weight and lacked any skin lesions.

PAST MEDICAL/SURGICAL HISTORY
Allergic rhinitis, no prior pregnancies

MEDICATIONS
Diphenhydramine 1% cream, twice daily, acetaminophen as needed

ALLERGIES Sulfamethoxazole

FAMILY HISTORY Negative

SOCIAL HISTORY
The patient is married and works in publishing. She drinks alcohol 1-2 times weekly.

PHYSICAL EXAM
Well-appearing Caucasian female, with abdomen, thighs, and buttocks notable for erythematous, edematous papules coalescing into plaques with microvesiculation and a zone of sparing around umbilicus. Dorsa of both feet showed erythematous papules and plaques with tense bullae and serous drainage that extended to involve insteps of plantar surface. Face and palms were clear. Ocular and oral mucosa appeared normal.

HISTOPATHOLOGY
H&E, right thigh: Spongiosis of the overlying epidermis is seen. The dermis has variable edema with a superficial, deep, & interstitial infiltrate of lymphohistiocytic cells & numerous eosinophils.
Direct Immunofluorescence: Negative staining for IgA, IgG, IgM, or C3.

DIAGNOSIS
Bullous polymorphous eruption of pregnancy (PEP)

TREATMENT AND COURSE

The patient was initially treated with triamcinolone 0.1% ointment twice daily and antihistamines including loratadine daily and hydroxyzine nightly. At a follow-up visit 1 week post-partum, she had increased affected body surface area, pronounced palmoplantar involvement, and numerous lesions with new targetoid morphology. Prior bullous lesions on feet had crusted and no active bullae were seen. Her face remained spared. A course of oral prednisone was offered, however, the patient preferred to avoid oral steroids due to interim development of post-partum hypertension requiring labetolol. Mid-potency topical corticosteroids and antihistamines were continued and Aveeno oatmeal baths were added for symptomatic relief.

DISCUSSION

Differentiating between pemphigoid gestationis and polymorphic eruption of pregnancy can be challenging. This difficulty is enhanced when pemphigoid gestationis presents early in the course in a pre-bullous phase and when polymorphic eruption of pregnancy presents with an atypical vesicular and bullous morphology. The distinction has prognostic implications as pemphigoid gestationis carries an increased risk of prematurity, small-for-gestational age newborns, and higher rates of reoccurrence in subsequent pregnancies. These cases are presented in comparison to review the key differentiating elements among these disorders.

Polymorphic eruption of pregnancy, synonymous with pruritic urticarial papules and plaques of pregnancy, is the most common of the pregnancy-related dermatoses, occurring in 1 in 160 deliveries. The term "polymorphic eruption of pregnancy" was proposed by Holmes & Black to encompass the variability of clinical manifestations this self-limited entity may exhibit, including urticarial papules, plaques, polycyclic erythematous wheals, vesicles, targetoid lesions, and rarely, bullae. The typical course is a pruritic eruption which arises late in the 3rd trimester of a 1st pregnancy as urticarial papules and plaques, accentuated in the abdominal striae that may spread over days to involve thighs, buttocks, and extremities, and resolves spontaneously within 1 week of delivery. Periumbilical sparing is a hallmark and involvement of the face, palms or soles is only rarely seen. The etiology remains unknown, making it a diagnosis of exclusion in the setting of a typical clinical presentation, normal laboratory tests, and negative direct immunofluorescence. The association with multiple gestations, rapid excessive weight gain, and the predilection of accentuation in the *striae distensae* suggest that late stretching of abdominal skin may be contributory.

In contrast, pemphigoid gestationis, synonymous with herpes gestationis, is a rare autoimmune supepidermal blistering disorder with a reported incidence of 1 per 50,000 deliveries. It typically begins in the 3rd trimester as an intensely pruritic, urticarial eruption on the trunk and extremities that progresses to a vesiculobullous morphology. As in polymorphic eruption of pregnancy, the earliest lesions are often on the abdomen; however, in pemphigoid gestationis they do not spare the umbilicus, nor accentuate in striae. Face and mucosal involvement is rare.

Our case of pemphigoid gestationis demonstrates that, both clinically and histopathologically, pre-bullous pemphigoid gestationis may be indistinguishable from polymorphic eruption of pregnancy. Histopathology of pemphigoid gestationis shows a subepidermal vesicle, spongiosis, marked papillary dermal edema, and an abundant infiltrate of eosinophils, either as a linear pattern along the dermoepidermal junction, or more commonly, as a non-specific mixed infiltrate with lymphocytes and histiocytes. In early pemphigoid gestationis, eosinophilic spongiosis without fully formed blisters may be present. In polymorphic eruption of pregnancy, epidermal spongiosis, papillary dermal edema, and a superficial perivascular lymphocytic and eosinophilic infiltrate may be present, but findings are often nonspecific. Neutrophils and eosinophils may be seen in the infiltrate, but both are more abundant in pemphigoid gestationis.

Direct immunofluorescence is the gold standard for distinguishing between these entities. Staining for C3, with or without IgG, in a linear band along the basement membrane zone of

perilesional skin must be seen to diagnose pemphigoid gestationis. Direct immunofluorescence in polymorphic eruption of pregnancy is usually negative, but rarely a nonspecific granular pattern of IgM, IgA, or C3 deposition is visualized at the dermoepidermal junction.

Treatment for polymorphic eruption of pregnancy is conservative and includes symptomatic relief of pruritus with emollients, moderate to high potency topical corticosteroids, and systemic antihistamines. For severe cases with intractable pruritus, a short course of oral corticosteroids may be considered. Due to its rarity, there are not sufficient therapeutic trials evaluating the treatment options for pemphigoid gestationis. Systemic corticosteroids are typically the mainstay of treatment in doses up to 60 mg daily. The use of steroid-sparing agents, such as dapsone or the combination of doxycycline and nicotinamide, after delivery has been reported for resistant disease.

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CHICAGO DERMATOLOGICAL SOCIETY **CASE # 4**

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

HISTORY OF PRESENT ILLNESS
This is a 46 year-old African-American female with a past medical history of diabetes and psoriatic arthritis who presents with leg swelling, worsening arthritis and rash for several weeks. Her psoriatic arthritis was recently diagnosed and she had been on efalizumab and methotrexate for 3 months. She complained of increasing pruritus and ulcerations within the healed psoriatic plaques on her abdomen and legs. She used clobetasol 0.05% ointment daily with minimal improvement of her skin lesions and takes naproxen for her joint aches. She has not been taking folic acid supplementation.

PAST MEDICAL HISTORY
Diabetes mellitus, Psoriatic arthritis, Multiple pulmonary embolisms, Sickle cell trait

MEDICATIONS
Efalizumab 125mg weekly
Methotrexate 37.5mg weekly
Clobetasol 0.05%ointment
Metformin
Glipizide
Fenofibrate
Naproxen

ALLERGIES
No known drug allergies

FAMILY HISTORY
Diabetes, psoriasis in an aunt, sickle cell disease in a half-sister

SOCIAL HISTORY
Smokes ½ pack per day since 15 years of age, denies alcohol intake

PHYSICAL EXAM
Well-developed obese African American female in no acute distress, scratching at her skin during the examination.
Numerous hyperpigmented, round, erythematous macules and patches with central dusky pigmentation on the legs, arms, trunk, and chest. Several of these patches with shallow central ulcerations. Fine desquamating scale on the arms, legs, chest, and back. Thick keratotic desquamation on the palms and soles. No oral or ocular erosions. No bullae or vesicles.

LABS
CBC significant for a WBC of 3.2 k/ul, Hb 10.7 gm/dl, absolute neutrophil count 600/ul
Folate 2.7ng/ml (nl 4.4-18.6)
Erythrocyte sedimentation rate 39 mm/hr (nl 2-25)
C-reactive protein 3.2 mg/dl (nl <0.8)
Urinalysis – normal

HISTOPATHOLOGY
Right lower leg: Chronic papulosquamous dermatitis with prominent melanoderma

DIAGNOSIS

Skin ulcerations within psoriatic plaques as an early sign of methotrexate toxicity

TREATMENT AND COURSE

The patient was given three doses of leucovorin and started on Folic acid supplementation. The erosions and exfoliation of her skin as well as her laboratory abnormalities normalized after a few days. Methotrexate and efalizumab were stopped and she was started on Remicade for treatment of her psoriatic arthritis.

DISCUSSION

Methotrexate competitively and reversibly inhibits dihydrofolate reductase, an important enzyme in folate metabolism, which in turn is necessary in DNA synthesis. Well-known toxicities of methotrexate administration include bone marrow suppression, oral/GI ulcerations and hepatic toxicity. Supplementation with folic acid can reduce the occurrence of such events without reducing efficacy. In addition, low serum folate levels and low erythrocyte folate levels can serve as a predictor of methotrexate toxicity.

Skin ulceration within psoriatic plaques as a consequence of methotrexate toxicity was initially described by Drs. Lawrence and Dahl in 1984. Two patterns of skin ulceration were identified. The type I pattern described skin ulcerations within psoriatic plaques. The type II pattern described ulcerations in skin uninvolved by psoriasis, although injured in other ways.

The ulceration within psoriatic plaques has been described to occur in patients who have recently started the medication, as well as in patients who have been taking methotrexate chronically.

In a review of 17 patients in the literature from 1967 to 1996 by Pearce and Wilson, the most common risk factors identified for cutaneous ulceration were a recent increase in the methotrexate dosage and a concomitant use of non-steroidal anti-inflammatory drugs. Other possible risk factors identified were older age (13 of 17 patients were over 55), renal insufficiency, infection, and a pustular flare of the psoriasis.

In our patient, her methotrexate dosage had been increased from 25 mg to 37.5 mg in the several weeks preceding this eruption and she was also taking naproxen for her arthritis. She did not have renal insufficiency and neither infection nor a pustular flare of her psoriasis was identified. She was at higher risk for developing methotrexate toxicity secondary to coadministration of both naproxen and glipizide. Naproxen is a non-steroidal anti-inflammatory drug which may inhibit renal elimination of methotrexate. Glipizide is a sulfonylurea which can displace methotrexate from its binding sites increasing methotrexate serum levels.

In cases of methotrexate toxicity, treatment with leucovorin can reverse its effects. Leucovorin (folinic acid) bypasses dihydrofolate reductase in folic acid metabolism pathway and allows for DNA synthesis, thus rescuing the cells from the effects of methotrexate.

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CHICAGO DERMATOLOGICAL SOCIETY **CASE # 5**

Presented by Anne Laumann, MBChB, MRCP (UK), and David Reid, MD
Department of Dermatology, Feinberg School of Medicine, Northwestern University

HISTORY OF PRESENT ILLNESS
The patient is a 32 year-old Caucasian man with generalized progressive swelling, tenderness, and tightness of his skin, resulting in widespread restriction of movement since late 2004. The process started in the hands, quickly involved the feet, and continued to extend over his whole body, with associated redness, a 10 pound weight loss, and evening fevers (up to 101°F) over the first 6 months. He had no change in color of the fingers or toes with exposure to cold, and he had no gastrointestinal complaints.

PAST MEDICAL HISTORY
Vitiligo since 1998, alopecia areata, appendectomy 1999

MEDICATIONS
Methotrexate, prednisone, calcipotriene/betamethasone, B12 tablets, folic acid

ALLERGIES
No known drug allergies

FAMILY HISTORY
Father – lung cancer; two children, ages 5 and 1 – healthy

SOCIAL HISTORY
Lithuanian, moved to the US in 1998; truck driver, recently on disability
Smokes ½ pack per day X 10 years; no toxin or drug exposure

PHYSICAL EXAM
Patchy alopecia and poliosis. Joints cannot be extended. The skin is diffusely shiny and bound down. On the trunk, there is near complete depigmentation, with some scattered normally pigmented patches. Hands show a characteristic "prayer sign" with swollen fingers.

HISTOPATHOLOGY

Left leg: dense dermal fibroplasia, extending into the deep subcutaneous tissue. Horizontally arrayed layers composed primarily of plasma cells with some histiocytes. Within the areas of fibroplasia, there are areas suggesting focal necrobiosis. The superficial dermis shows an interstitial lymphohistiocytic infiltrate with telangiectasia and focal homogeneous fibroplasia.

Left forearm: dense dermal fibrosis extending into the subcutaneous septa. There is elevation and entrapment of the eccrine coils within the dermis and a deep lymphoplasmacellular infiltrate.

LABS/STUDIES
The following tests were negative or within normal limits: serum albumin, serum alpha 1, serum alpha 2, DS DNA, U1 RNP/SNRNP IgG, SM (Smith) IgG, SSA IgG, SSB IgG, ScL70 IgG, ribosomal P protein autoantibodies, rheumatoid factor, C3 complement, TSH, HIV, RPR, anti-parietal cell antibody, pulmonary function tests, chest x-ray

The following tests were abnormal: serum gamma 4.0 gm/dl (nl 0.74- 1.3); ANA 8.0 IU/ml (1:40 – 1:80), speckled; C4 15 mg/dl (16-70); ESR 106 mm/hr (3-10); CRP 2.1 mg/dl (<0.5); HB 11.9 g/dl (13-17.5); Hct 35.4% (38-50); vitamin B12 level 152 pg/ml (180-933); intrinsic factor blocking autoantibodies detected

Thyroid peroxidase autoantibody 8/31/2005 15 u/ml (<66); 11/2/2006 66 u/ml

Muscle biopsy: acute fibrinoid necrosis, marked inflammation of the adipose tissue, no eosinophilia, no muscle seen;
Bone marrow biopsy: 1. Mildly hypocellular (30%), no evidence for plasma cell myeloma; 2. Flow cytometry on the aspirate - a small bright CD38+ population (< 1% of total) with polyclonal cytoplasmic immunoglobulin light chain expression;
Right lateral epicondyle upper extremity ultrasound, dermal thickness: 5/31/2007 4.3 mm, 9/5/2007 2.8 mm

DIAGNOSIS

Acute generalized morphea

TREATMENT AND COURSE

Initial therapies included prednisone and methylprednisolone with minimal symptomatic improvement, penicillamine for 6 months, methotrexate, rosiglitazone, hydroxychlorquine, topical pimecrolimus, triamcinolone acetonide 0.1% ointment, and more recently calcipotriene/betamethasone. Narrow band UVB therapy caused burning after one dose of 200 mJ/cm², as did bath PUVA. No improvement with UVA alone. Photophoresis has been considered, but vascular access is a major issue. He has had a 6 week course of rituximab followed by an 8 week course of bortezomib, resulting in further subcutaneous edema and tightness. The current plan is to pursue oral imatinib. FDA and IRB release for an autologous hematopoietic stem cell transplant has been requested.

DISCUSSION

Morphea, or circumscribed scleroderma, is characterized by indurated, smooth-surfaced, whitish plaques giving the appearance of hidebound skin. Unlike systemic sclerosis, morphea does not classically have visceral involvement. The etiology, while unknown, is thought to be immunologic in nature, as morphea can co-exist with other autoimmune diseases such as vitiligo, systemic lupus erythematosus, and primary biliary cirrhosis. Diverse subtypes exist, based on clinical manifestations and level of involvement.

Treatment for morphea remains unsatisfactory. Therapy is directed according to severity and extent of lesions. Localized morphea may be treated with topical agents and often resolves over 3-5 years. Generalized morphea requires aggressive therapy and is frequently recalcitrant. Phototherapy, presumably through modulating cytokines involved in connective tissues remoldeling, has shown some efficacy. Successful treatment has also been reported with systemic steroids in concert with low-dose methotrexate. In other cases, azathioprine, cyclophosphamide, cyclosporine, mycophenolate mofetil, and D-penicillamine have been used. Given evidence that imatinib prevents development of experimental dermal fibrosis, it may prove useful as another potential therapy.

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CHICAGO DERMATOLOGIAL SOCIETY **CASE # 6**

Presented by Mary Martini, MD and Ana Ciurea, MD
Department of Dermatology, Feinberg School of Medicine, Northwestern University

Patient A

HISTORY OF PRESENT ILLNESS

The patient is a 79 year-old man, without prior history of skin cancer or dysplastic nevi, who was admitted for chest pain and shortness of breath 6 weeks after a fall that resulted in a right occipital wound. On admission, he was noted to have a massive "bruise" on his scalp, for unknown duration, for which he had not sought care. An excisional biopsy of the scalp lesion was consistent with a deeply invasive malignant melanoma. Of note, he also developed rapidly enlarging nodules on the arms, trunk and thighs, which were otherwise asymptomatic.
His review of systems was remarkable for increased dyspnea and orthopnea, fatigue, loss of appetite, and headache.

PAST MEDICAL HISTORY

Aortic stenosis, coronary artery disease, diabetes mellitus, hypertension, hyperlipidemia, right pneumothorax

MEDICATIONS

Metoprolol, metformin, fosinopril sodium, rosiglitazone, clopidrogel, simvastatin, aspirin, albuterol, vitamin E, vitamin C, beta carotene, multivitamin

FAMILY HISTORY: Negative for malignant melanoma

SOCIAL HISTORY

Quit tobacco 25 years ago, denies alcohol, lives alone, retired pipeline worker

LABS

Laboratory results were abnormal for low albumin at 1.8 g/dl, total protein 5.1 gm/dl, hemoglobin 10.4 gm/dl, hematocrit 30.4%, glucose 175 mg/dl, LDH 214 U/L (nl 0-200)
MRI of the brain: large scalp/soft tissue lesion overlying the right parietal calvarium with abnormal thickening of the right frontal and occipital calvarium, measuring approximately 7.3 x 2.6 x 12.3 cm. Multiple enlarged lymph nodes in the right neck, right suboccipital and bilateral parotids were noted
CT scans of the chest: multiple micronodules in scattered locations in both lungs
The following were negative or within normal limits:
White blood cell count, blood urea nitrogen, creatinine, electrolytes, CT abdomen and pelvis

PHYSICAL EXAM

Patient is a well-developed, well-nourished male, in no apparent distress.
There is a large confluent, violaceous plaque involving the vast majority of the scalp extending to anterior hairline. There is a 6cm x 5 cm ulcerated plaque with multiple, central, friable nodules on the left temporal-occipital scalp. Numerous brown, 1-2 cm, firm nodules involving the right nasolabial fold, anterior neck, upper chest, thighs and upper arms.

HISTOPATHOLOGY

Right parietal scalp: Deeply invasive melanoma involving the resection margins

DIAGNOSIS

Metastatic malignant melanoma

TREATMENT/COURSE
In view of his age and cardiac insufficiency, patient was not considered a candidate for systemic chemotherapy, immunotherapy, and radiotherapy. A wide scalp excision was not indicated because of the extent of the tumor. Patient expired 4 months after being diagnosed with metastatic malignant melanoma.

Patient B
HISTORY OF PRESENT ILLNESS
The patient is a 98 year-old man, with lifelong history of moderate sun exposure who presented in September 2006 with a malignant melanoma (superficial spreading type, Clark level IV, Breslow depth more than 1.5 mm, with ulceration) on his left cheek, which was initially treated with wide excision. In August 2007, several lesions of metastatic melanoma were noted in the surgical scar and the surrounding areas.
In view of his age and co-morbidities, the patient elected a less aggressive therapy with topical imiquimod 5% cream and tazarotene 0.1% cream topically to the affected area, as it has been successfully reported in the literature. His review of systems was negative for weight loss, night sweats, fatigue, chills or change in appetite.

PAST MEDICAL HISTORY
Hypertension, benign prostate hypertrophy, diabetes mellitus–type II, basal cell carcinoma, squamous cell carcinoma, pacemaker implant, depression

MEDICATIONS
Metoprolol, zolpidem, duloxetine, pregabalin, tamsulosin, vitamin C

FAMILY HISTORY: Negative for malignant melanoma

SOCIAL HISTORY
Denies tobacco, occasional alcohol, lives with wife, retired salesman

LABS
Laboratory results were abnormal for blood urea nitrogen at 40 mg/dl (nl 7-18), creatinine 1.7 mg/dl (0.6-1.3), glucose 211 mg/dl, sodium 133 mmol/l (136-145), hemoglobin 10.1 g/dl, hematocrit 29.9%
The following were negative or within normal limits: electrolytes (except for sodium), liver function test, coagulation profile, chest X-ray

PHYSICAL EXAMINATION
Patient is a thin, elderly man in no distress.
On presentation, patient had multiple new, 8-20 mm skin-colored, brownish red, and dark blue, smooth-surfaced papules and nodules on the left cheek, left medial canthus, and left infraorbital skin. There was a large, 1.5 cm x 1 cm hyperpigmented patch in the center of the scar. No lymphadenopathy.

HISTOPATHOLOGY
Left cheek nodule: Deep dermal aggregates composed of atypical, mostly epithelioid-shaped cells with abundant cytoplasm, pleomorphic nuclei and mitotic figures consistent with metastatic melanoma. Tumor cells stained positively for MART1.

DIAGNOSIS
Metastatic malignant melanoma

TREATMENT/COURSE

The patient applied tazarotene 0.1% cream each morning and imiquimod 5% cream in the evening, 5 days a week with weekend holidays. At 1 month follow-up visit, he presented with significant erythema and crusting of the treated area. The local metastatic nodules decreased in size and the dark brown patch present in the scar completely resolved. No systemic side effects were reported. Patient will continue the treatment for a total of 6 weeks and will return to clinic for re-evaluation.

DISCUSSION

Up to one-third of all patients with a primary cutaneous melanoma will undergo disease progression. Of those patients, 50% will undergo spread to regional lymph nodes, 30% will develop satellite or in-transit metastases and 20% will develop distant metastases as the first manifestation of disease progression.

Patients with a stage IV melanoma typically have a 5-15% five-year survival rate. Of this group, patients with distant metastases to the skin or subcutaneous tissue do have a more favorable prognosis, with median survival times greater than twice those of patients with visceral melanomas.

Metastatic melanoma of the skin is extremely difficult to treat. Despite a variety of available options including surgery, immunotherapy, chemotherapy, treatment is often unsuccessful.

Imiquimod was originally received FDA approval for treatment of genital warts but is currently used to treat a variety of cutaneous cancers, including Bowen's disease, Paget's disease. There have been multiple cases reported where imiquimod was used to treat both lentigo maligna and melanoma in situ as well as metastatic melanoma to the skin. Imiquimod is an immune modulator that has demonstrated both antiviral and antitumor activities. It enhances the immune system by inducing the production of cytokines and activating dendritic cells, macrophages, and other cells via Toll receptor 7 binding. Tretinoin, a retinoid that specifically binds to retinoic acid receptors gamma and beta, reduces the keratinocytes proliferation and decreases the stratum corneum thus improving the penetration of the imiquimod cream. It also produces further antineoplastic effects.

Although surgical excision remains the gold standard for treatment of cutaneous melanomas including local metastasis, in a patient who is not a surgical candidate, alternative treatment options should be considered.

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CHICAGO DERMATOLOGICAL SOCIETY **CASE # 7**

Presented by Anne Laumann, MBChB,MRCP (UK) Elizabeth Wolf, BA, and Aimee Smidt, MD
Department of Dermatology, Feinberg School of Medicine, Northwestern University

HISTORY OF PRESENT ILLNESS

This 42 year-old woman with a 14-year history of known systemic lupus erythematosus was seen in April 2006 for exquisitely painful, stellate ulcers with surrounding livedo reticularis on both shins, and acutely flared Raynaud's changes in her fingers. Initial medical management involved: increasing her immunosuppressive regimen (including three boluses of intravenous methylprednisolone), increasing erythropoietin dosage, starting iron supplements and oral antibiotics, and maintaining her on continuous oxygen. We added intensive supervised topical therapy, consisting of compresses (aluminum acetate and later vinegar), followed by polyurethane foam dressings on and triamcinolone ointment around the wounds. However, the ulcers continued to enlarge. By September, the ulcers were still purulent and painful, and hard yellow granules had developed within them.

PAST MEDICAL HISTORY

Systemic lupus erythematosus (SLE) diagnosed in 1992, characterized by previously positive anticardiolipin IgG antibody, Raynaud's phenomenon, small vessel disease, pulmonary fibrosis and pulmonary hypertension.

LABS/STUDIES

July 2006
ANA 50 IU/ml (1:320-1:1280): speckled; ds DNA 7.8 IU/ml (nl <5)
NRNP/SM IgG 7.8 IU/ml (<5); ScL-70 IgG < 5; Smith IgG 114 (<5)
SSA IgG 158 (<5); SSB IgG 167 (<5); C4 25 (16-70); C3 76 (82-235)
Anticardiolipin antibodies IgG, IgM, IgA negative; Anticentromere antibody < 7.5 (<7.5)
Renal function, liver function, urinalysis: normal
Hgb 8.8, HCT 28.3, MCH 25.3, WBC 5000, Plts 295 k/ul

June 2007
DsDNA > 50; C4 12; C3 42; Hgb 10.1, HCT 29.6
October 2007 MRI of the legs was negative for osteomyelitis

MEDICATIONS

Methotrexate 12.5 mg weekly, folic acid, prednisone 5 mg daily, hydroxycholoroquine, pentoxyphilline, coumadin, budesonide and fluticasone inhalers, fexofenadine, erythropoietin, sildenafil, amlodipine, gabapentin, acetaminophen-codeine, tramadol, famciclovir, tolterodine, calcium, vitamin E, alendronate, esomeprazole.

ALLERGIES

Sulfa drugs, penicillin

FAMILY & SOCIAL HISTORY

Noncontributory

PHYSICAL EXAM

Pale, well-nourished, oriented woman in pain and on oxygen. BP 110/80
4cm x 5cm deep well-demarcated ulcer at the right lower leg with dense granulation tissue, an adherent yellow, purulent membrane and underlying hard granular material.
4cm x 4cm ulcer at the left lower leg with pink granulation tissue, less extensive superficial hard granules and purulent material. Sclerodactyly with blue hands and finger tip atrophy.

HISTOPATHOLOGY

Lower leg; center of ulcer: Ulcerated epidermis with dense neutrophilic infiltration; dermis and subcutis show suppurative and granulomatous inflammation, calcification and bone formation with surrounding mixed inflammatory cells and dermal necrosis in the area of the abscess.

DIAGNOSIS

Non-healing leg ulcers with dystrophic calcification

TREATMENT AND COURSE

Manual removal of the hard granules was performed at every in-office dressing change. This was very painful, and new deposits were noted at each subsequent visit. Twice-weekly in-office sodium thiosulfate compresses were then begun, followed by the ongoing foam dressings with surrounding topical corticosteroid. At home she continued daily saline irrigations and vinegar compresses. The granular deposits rapidly resolved and her pain has lessened significantly. Antibiotics have been stopped and the wounds have decreased in size, albeit slowly.

DISCUSSION

Calcinosis cutis, or deposition of calcium salts within the skin and subcutaneous tissue, is associated with several connective tissue diseases, including scleroderma, CREST syndrome, dermatomyositis, mixed connective tissue disease and rarely, SLE. Typically in lupus patients, the disease is limited to the extremities and buttocks and is termed calcinosis cutis circumscripta. Calcification is thought to occur either from elevated alkaline phosphatase activity or by phosphate binding of denatured proteins in areas of inflammation triggering dystrophic calcium deposition. There are four main types of soft tissue calcification: dystrophic (as in this case), metastatic, idiopathic, and calciphylaxis. Dystrophic calcification occurs in the context of normal calcium and phosphorus levels and absent visceral involvement, while metastatic calcification involves increased calcium and/or phosphorus. Calciphylaxis, commonly seen in renal dialysis patients, is thought to represent a hypersensitivity-type reaction beginning with livedo reticularis, in which the media of small to medium blood vessels in the dermis and subcutis become calcified.

As spontaneous resolution of dystrophic calcification generally does not occur, multiple treatment modalities have been attempted, including warfarin, colchicine, osteoclast-inhibitors, carbon dioxide laser, minocycline, salicylates, intralesional steroids and anti-TNF agents, with inconsistent results. Successful surgical excision has been reported. Treatment of calciphylaxis with intravenous sodium thiosulfate (25 gm three times weekly) has been documented recently. The proposed mechanism involves chelation of calcium into more soluble calcium thiosulfate salts. We hypothesized using topical sodium thiosulfate in our patient would result in similar dissolution of the calcium precipitate, and thus aid in pain relief and wound healing. We present this case to document a novel therapy for the dystrophic calcification which can occur in many connective tissue diseases.

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CHICAGO DERMATOLOGICAL SOCIETY **CASE # 8**

Presented by David Lorber, MD and Melissa Abrams, MD
Department of Dermatology, Feinberg School of Medicine, Northwestern University

HISTORY OF PRESENT ILLNESS
The patient is a 74 year old man with an approximately 15 year history of an eruption on his scalp and face. He describes the eruption as "bumps" that are slightly pruritic but not painful. They are most obvious when he combs his hair or towel dries his face, as his skin peels off and leaves denuded, bleeding areas. Individual lesions can last days or weeks before resolution and new lesions always arise. Initially diagnosed as psoriasis, previous treatment has included tar and salicylic acid shampoos and topical steroid ointments. With these treatments he has seen improvement, but he continues to develop new lesions. Recently, he developed similar lesions on his chest, shoulders and abdomen and the scalp lesions have become very thick.

PAST MEDICAL HISTORY
Encephalitis (age 10), sleep apnea, episodic amnesia-1st episode 10 years ago; 2 episodes this past summer, cardiac arrhythmia

MEDICATIONS
Lanoxin

ALLERGIES
No known drug allergies

FAMILY HISTORY
No history of skin disease or autoimmune disease

SOCIAL HISTORY
Currently lives in Evanston with his wife of 50 years. He has one daughter.
Professor of Economics at DePaul, Chicago City College for 37 years, retired 1994

PHYSICAL EXAM
At the vertex and frontal scalp extending onto the anterior forehead, there are discrete, large, thick hyperkeratotic plaques with associated scale and erosions on a pink base.
At the chest, abdomen and back there are scattered well demarcated pink, scaly patches.
No intertriginous involvement, oral lesions, or nail dystrophy.

LABORATORY
ANA screen – normal

HISTOPATHOLOGY
8/10/2007, right pre-auricular: There is acanthosis, spongiosis, parakeratosis and exocytosis of neutrophils within the epidermis, with focal areas of acantholysis in the superficial portion. Within the dermis there is a dense perivascular lymphohistiocytic infiltrate mixed with numerous plasma cells.
8/22/07, forehead: There is a superficial erosion and marked acantholysis within the epidermis involving the hair follicles. This acantholysis produces suprabasilar bullae with tombstoning of the basilar keratinocytes. There is a dermal lymphohistiocytic infiltrate with plasma cells.
Direct immunofluorescence: There are intercellular deposits of IgG, IgA and C3 in the lower layers of the epidermis.
Indirect Immunofluorescence: Negative for IgG, IgM and IgA
Immunoblot studies and/or ELISA: Not performed

DIAGNOSIS
Pemphigus (Vulgaris versus Foliaceous)

TREATMENT AND COURSE
On initial presentation the patient was prescribed fluocinolone acetonide 0.01% oil and Urea 50% in a vehicle containing lactic and salicylic acid. His scalp lesions have become less hyperkeratotic, leaving residual pink, scaly plaques. All of the lesions have improved.

DISCUSSION
Pemphigus is an autoimmune disease characterized by blistering of the skin and mucous membranes most commonly presenting in the fifth and sixth decade of life. Blister formation is mediated by autoantibodies against desmosomal proteins (desmogliens) responsible for direct binding between epithelial cells. Target antigens can be examined using immunoprecipitation and immunoblotting as well as ELISA (enzyme-linked immunosorbent assay). Clinical phenotype is determined by antigen specificity.

Our patient is intriguing in that his clinical presentation is most consistent with pemphigus foliaceus (localized erosions with no oral involvement) while the histopathologic findings and immunofluorescence are consistent with pemphigus vulgaris. Another unique aspect of our patient is that his DIF reveals an intercellular IgA deposition in addition to IgG and C3. Indirect immunofluorescence is negative and neither immunoblot studies nor ELISA were performed to determine the target antigens.

Autoantibodies in pemphigus vulgaris (PV) are most commonly directed against desmoglien 3(Dsg3), specific for mucosal lesions, but can often have antibodies against desmoglien 1(Dsg1), specific for skin lesions if the clinical presentation is consistent with mucocutaneous disease. Autoantibodies in pemphigus foliaceus (PF) are directed against Dsg1. There have been reported cases of pemphigus that clinically resembled pemphigus foliaceus while the histology and antigen specificity were consistent with mucocutaneous PV. It is postulated that these cases could be explained by examining the pathogenic potential of a given antibody, with pathogenicity defined as the quantity and quality of antibodies.

The expression of Dsg3 is much lower in the skin than in the oral mucosa. Thus, low levels of a weak pathogenic anti-Dsg3 acting with high levels of anti-Dsg1 will be potent enough to affect epithelial cell binding in the skin at the parabasal/basal layer which have smaller numbers of desmosomes than the upper layers, but not potent enough to block epithelial binding in the oral mucosa. Other authors suggest that while differences in "antibody potency" may contribute, certainly the quantity of anti-Dsg3 does not explain the absence of oral lesions in patients with cutaneous PV. They propose that we consider an alternate cause such as the involvement of antibodies other than anti-Dsg1 in the pathogenesis of cutaneous PV.

Studies have also shown that occasionally in classic IgG mediated pemphigus, IgA is also present. In the majority of cases, the antigen specificity of IgA follows the antigen specificity of IgG; however IgA can be present against an antigen not recognized by IgG. The antigens reported to have evoked IgA reactions in pemphigus include desmocollin1, Dsg1 and Dsg3. Whether IgA also plays a role in the pathogenesis of pemphigus vulgaris is yet to be elucidated.

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CHICAGO DERMATOLOGICAL SOCIETY **CASE # 9**

Presented by Gerta Janss, MD, Joan Guitart, MD, and Victoria Nguyen, MD
Department of Dermatology, Feinberg School of Medicine, Northwestern University

UNKNOWN

CHICAGO DERMATOLOGICAL SOCIETY **CASE # 10**

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

HISTORY OF PRESENT ILLNESS
This is a 29 year-old man with a fourteen-year history of a nodule on the lower left leg. The nodule was stable in size and solitary until approximately nine months prior to presentation. Three years earlier the patient was diagnosed with rheumatoid arthritis (RA) and after two years of destructive joint changes, a decision was made to initiate etanercept at 50 mg subcutaneously twice weekly. During the period after starting the etanercept, the nodule on the left leg more than tripled in size and multiple large satellite nodules became evident. He presented at our dermatology department for evaluation of these lesions.

PAST MEDICAL HISTORY
Rheumatoid arthritis

MEDICATIONS
CHOP (cyclophosphamide, adriamycin, vincristine, prednisone) every 3 weeks

FAMILY HISTORY
No history of skin malignancies

SOCIAL HISTORY
Married, lives in Wisconsin. Smokes 1 pack per day (recently cut down from 3-4 packs per day x 15 years)

PHYSICAL EXAM
Left lower leg with approximately 7, infiltrated, erythematous papules and tumors (largest measuring 6.5 cm x 4 cm). Minimal peripheral erythema. No popliteal lymphadenopathy.

HISTOPATHOLOGY
Left lower medial leg: Dense sheets of monocytoid lymphocytes, lymphoplasmacytic cells and aggregates of large plasma cells with a Grenz zone sparing the epidermis and extending through the entire dermis and subcutis. Many cells have prominent intranuclear Dutcher and cytoplasmic Russell Bodies. Immunohistochemistry revealed focal aggregates of CD20 positive cells and many aggregates of CD138 positive cells. Lambda light chain restriction throughout. EBER-1 and CD30 negative. MUM1 positive.

LABS/STUDIES
T-cell receptor and immunoglobin gene rearrangement (tissue): positive clonality
Pan CT scans, PET scan, CBC, comprehensive metabolic panel: unremarkable
Bone marrow flow cytometry: normocellular

DIAGNOSIS
Primary cutaneous marginal zone lymphoma

TREATMENT AND COURSE
Based on these results, the patient was started on five weeks of daily radiation therapy with rituximab to the affected areas at an outside hospital. This treatment proved to be minimally effective, so the patient was switched to CVP (cyclophosphamide, vincristine, prednisone) x 3 cycles every three weeks. Once again, the patient failed to respond to therapy, so CHOP was initiated (currently in his second cycle).

DISCUSSION

Primary cutaneous marginal zone lymphoma is considered an indolent lymphoma in the WHO-EORTC classification system. Patients present with slow growing lesions, typically small deep seeded nodules in the skin of the trunk or upper extremities. Dissemination to extracutaneous sites is uncommon and most studies report an excellent outcome with 5-year disease specific survivals of 100%. Treatment options include observation, surgical excision, local radiation, and rituximab systemically or intralesionally.

This patient's clinical presentation with rapidly growing, large multinodular lesions on the leg was clinically more suggestive of primary cutaneous large B cell lymphoma of the leg type (an aggressive lymphoma). However, the histology was clearly that of a marginal zone lymphoma.

Our patient was placed on etanercept because of his RA and destructive joint changes. RA itself is a well-recognized condition predisposing to malignant lymphoma, usually B-cell non-Hodgkin's lymphoma (NHL), particularly diffuse large B-cell lymphoma (DLBCL). These increases have been attributed to persistent inflammatory disease activity, and there is a higher incidence of lymphoma seen with the increasing severity of disease.

There is debate regarding whether TNF-alpha blockade also increases one's risk for lymphoma. It is speculated that TNF-alpha promotes a T-cell cytotoxic response against B-cell malignancies. Also, binding of TNF-alpha to its cell surface receptors (TNFR1 & 2) has been shown to trigger multiple intracellular signaling pathways, some of which are linked to programmed cell death. It is therefore possible that this blockade of apoptosis enables growth of lymphoma cells. Additionally, this blockade may inhibit both innate and acquired immunity, so that normal immunosurveillance for malignancy is compromised.

In cases where a lymphoma develops after initiation of a TNF-alpha inhibitor, it is often unclear whether the lymphoma was a direct consequence of the TNF-alpha inhibitor, was part of a disease entity or blossomed and became clinically evident as a direct result of the medication. There have been multiple cases postulating all three examples, while other reports report no increased risk. Unfortunately, there have been no large studies yet in this area and so it is not proven that TNF-alpha inhibitors are directly involved.

This case serves as an important in-vivo example of a normally indolent process showing rapid growth under the influence of TNF-alpha inhibitor. By documented history we know that the primary lesion had been there and was behaving indolently for years and only began rapidly growing after initiation of etanercept. It can be speculated that this tumor was kept in check by cellular immunity, and that is was through TNF-alpha blockade, that this tumor began to grow. While the debate continues about increased lymphoma risk or unmasking a pre-existing lymphoma with TNF-alpha antagonists, this is a significant observation that calls for more research in this area.

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CHICAGO DERMATOLOGICAL SOCIETY **CASE # 11**

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

Patient A

HISTORY OF PRESENT ILLNESS

This 63 year-old man with a history of psoriasis on adalimumab (stopped 3/07) was admitted for three weeks of lymphadenopathy and two weeks of a pruritic eruption on extremities and buttocks. The patient reported low grade fevers, chills, night sweats, fatigue, and 50-pound weight loss since 3/07. He had joint pain but no recent infections.

PAST MEDICAL HISTORY

Psoriasis, coronary artery disease, hypertension, hyperlipidemia, aortic dissection s/p repair, bleeding peptic ulcers, fatty liver with grade I steatohepatitis, esophageal varices, hypothyroidism, osteoarthritis, benign prostatic hypertrophy, nephrolithiasis, chronic sinusitis

MEDICATIONS

Tolterodine tartate, lisinopril, psyllium, simvastatin, metoprolol succinate, levothyroxine

ALLERGIES

No known drug allergies

FAMILY HISTORY

noncontributory

SOCIAL HISTORY

The patient is married and smokes one cigar a month. He quit cigarettes 25 years ago. He has a history of alcohol abuse but quit 11 years ago

PHYSICAL EXAM

Palpable annular and arcuate, purpuric plaques and papules on arms, dorsum of hands, palms, buttocks, thighs, knees, feet, and soles without mucosal involvement

LABS

The following were negative or within normal limits:
Liver panel, hepatitis panel, complement C3, rheumatoid factor, ANA panel, C-ANCA, P-ANCA
The following were abnormal:
White blood cell count 15.2, hemoglobin 8.4, hematocrit 24.9, platelet 89, sedimentation rate 137, urinalysis trace protein, blood urea nitrogen 26, creatinine 1.5, direct bilirubin 1.3, LDH 284 (nl 100-190), complement c4 10 (14-43), c-reactive protein 6.3 (<0.8), cardiolipin IgA autoantibodies 14 (<13), T-cell gene receptor rearrangement positive for clonal T-cell receptor gene rearrangement, serum immunofixation electrophoresis IgG Kappa, serum protein electrophoresis accentuated alpha 2 band observed and restricted band 0.5 G/DL seen in the gamma region

HISTOPATHOLOGY

Left arm: superficial vascular plexus with fibrinoid necrosis with extravasation of erythrocytes and neutrophils. Nuclear debris (karyorrhexis) also noted.

Right cervical lymph node: 1. Malignant lymphoma most features consistent with angioimmunoblastic peripheral T-cell lymphoma, EBER positive. 2. Flow cytometric immunophenotypic studies performed on the right cervical lymph node demonstrate a population of T-cells that are dim CD3+, CD7-, CD2+, CD5+, CD4+, CD8-, CD25-, and dim CD10+

Bone Marrow: 1. Previously diagnosed angioimmunoblastic T-cell lymphoma involving approximately 30% of a hypercellular (80% cellular) bone marrow. 2. Flow cytometric immunophenotypic studies performed on the bone marrow aspirate reveal an immunophenotypically abnormal T-cell population, which is CD3+, CD5+, CD2+ but CD7- as well as CD4+, CD8-, and CD10+, which represents approximately 6% of the T-cell population. Special Stains: Reticulin stain shows mild-to-moderately increased reticulin fibrosis. Immunohistochemistry: lymphoid infiltrate composed predominantly of CD3 positive lymphocytes with occasional CD20 positive cells

DIAGNOSIS
Leukocytoclastic vasculitis and angioimmunoblastic T-cell lymphoma post adalimumab

TREATMENT AND COURSE
The patient is currently being treated with intrathecal methotrexate (started on 7/26/07) and proMACE and cytaBOM (started on 7/27/07)

Patient B
HISTORY OF PRESENT ILLNESS
This 55 year-old man with psoriatic arthritis previously on etanercept 2002-12/06 and adalimumab 12/06 presented with a growing asymptomatic lesion on his scalp for six months.

PAST MEDICAL HISTORY
Psoriatic arthritis, hyperlipidemia, nephrolithiasis

MEDICATIONS
Ciclopirox cream and gel, atorvastatin, aspirin, ezetimibe, calcipotriene 0.005% cream, halobetasol 0.1% cream

ALLERGIES
meperidine

FAMILY HISTORY
Mother-breast cancer, hyperlipidemia, psoriasis; sister-breast cancer

SOCIAL HISTORY
The patient is married and has never smoked. Drinks 3 beers a week

PHYSICAL EXAM
The patient had a 5cmx5cm, well-defined, violaceous smooth plaque on the right frontal scalp

LABS
The following were negative or within normal limits:
Epstein Barr virus PCR
The following were abnormal:
LDH 197 (100-190)

HISTOPATHOLOGY
DP07-2009 (right forehead): The sections reveal a dense deep dermal infiltrate composed of sheets of atypical large lymphocytes. Numerous necrotic cells and some mitotic figures are noted. The process is diffuse and there is no significant epidermotropism or adnexotropism. Germinal centers are not identified. Immunohistochemistry was performed on deparaffinized sections. All controls stained simultaneously were reviewed and appeared adequate. Tumor cells are positive for CD20 and negative for CD3 and CD30. Bcl2 is positive for about 30% of the cells in a similar pattern as CD3 (inconclusive). Bcl6 was positive for the large B cells. MUM-1 was

negative. Kappa and lambda immunohistochemistry demonstrate a ratio of light chains within the normal limits. Light chain restriction was not demonstrated.

DIAGNOSIS
Follicular center cell lymphoma post etanercept and adalimumab

TREATMENT AND COURSE
CT and PET staging negative. Bone marrow biopsy negative. The patient is s/p radiation 3/07 and is in complete remission.

DISCUSSION
There is some controversy to whether TNF alpha inhibitors increase the risk of lymphoma. Some groups advocate screening for hematologic malignancies or premalignancies with at least blood counts prior to starting TNF alpha inhibitor therapy.

In a Food and Drug Administration Medwatch postmarket surveillance system, 26 cases of lymphoproliferative disorders following treatment with etanercept and infliximab were identified. 81% were non-Hodgkin's lymphoma. The median time between start of therapy and development of lymphoma was 8 weeks. This can range up to 20 weeks. Other reported associated hematologic malignancies include acute myeloid leukemia, Hodgkin's disease, B cell lymphoma, T cell lymphoma, central nervous system lymphoma, and mucosa associated lymphoid tissue lymphoma. In the SEER (Surveillance, Epidemiology End Results) database of 18,572 patients with rheumatoid arthritis, the relative risk of lymphoma was 2.6 or 3.8 for patients receiving infliximab or etanercept, respectively, compared with rheumatoid arthritis controls. A metaanalysis by Bongartz et al. calculated a malignancy odds ratio of 7.91 for rheumatoid arthritis patients receiving TNF alpha inhibitors compared to rheumatoid arthritis controls who only received methotrexate +/- placebo. Proponents of hematologic screening believe that the possible mechanism of development of lymphoma lies in the evidence that TNF alpha is proapoptotic to tumor growth.

However, many specialists do not believe TNF alpha inhibitors are associated with the development of lymphoma. The diseases themselves that are treated with TNF alpha inhibitors, such as rheumatoid arthritis, Crohn's disease, and even psoriasis, actually carry their own increased risk for lymphoma. In fact, compared to the general population patients with rheumatoid arthritis have been shown to have a threefold risk for lymphoma. The risk of lymphoma seems to be increased with the increased severity of the rheumatoid arthritis disease up to 5-25 fold. This severe disease group is probably the group that is more likely to be treated with the TNF alpha inhibitors. When compared with rheumatoid arthritis patients treated with methotrexate, those treated with TNF alpha inhibitors showed no increase in the relative risk of lymphoma. In adalimumab clinical trials, the standardized incidence ratio for lymphoma in adalimumab treated patients was 3.19, which is similar to what would be expected in rheumatoid patients without exposure to TNF alpha inhibitors. In Crohn's patients the odds ratio for hematologic malignancies is 2.04. For psoriasis, the odds ratio is 7.95. In addition to the inherent risk of these diseases, another confounding factor is that the concomitant treatments with azathioprine, methotrexate, and cyclosporine have been associated with lymphoproliferative disorders. Another possibility is that perhaps in the cases in which lymphoma developed in association with TNF alpha inhibitor therapy, these patients may already have had a premalignancy that was simply accelerated with the TNF alpha inhibitors. There have been 165 reports of lymphoma associated with etanercept and infliximab in postmarketing surveillance among 780,000 patient-years of exposure. This is similar to the rate in the normal population of 0.03 per 100 patient years.

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CHICAGO DERMATOLOGICAL SOCIETY **CASE # 12**

Presented by Ginat W. Mirowski, DMD, MD, and Aimee Smidt, MD
Department of Dermatology, Feinberg School of Medicine, Northwestern University

HISTORY OF PRESENT ILLNESS
The patient is a 43 year-old African-American woman who presents with intense, chronic vulvar inflammation, swelling, pain and pruritus for over one year's duration. She initially presented to an outside institution, where, by report she underwent a biopsy and was diagnosed with Zoon's vulvitis. She improved with a course of intravenous steroids, but her symptoms subsequently recurred. She had since seen multiple gynecologists who treated her with cephalexin, valcyclovir, prednisone, misoprostol, and clobetasol ointment without improvement.

PAST MEDICAL HISTORY
Crohn's disease, diagnosed in adolescence, status post total colectomy with end ileostomy in 1978
Hepatitis C, diagnosed in the late 1990s
Depression

MEDICATIONS
Mirtazapine, quetiapine fumarate, topical clobetasol, misoprostol

ALLERGIES
No known drug allergies

FAMILY HISTORY
Noncontributory

SOCIAL HISTORY
Single, heavy tobacco user

PHYSICAL EXAM
Obese woman who appears extremely uncomfortable and in pain.
Oral exam is normal with exception of buccal mucosa leukoedema.
Mons pubis and clitoris are markedly edematous, with extensive, erythematous, tender, macerated fissures between the labia majora and minora and at the posterior fourchette. At the medial left labia majora, there is a bright red, ulcerated 3 cm plaque, and there are tender fissures perianally extending both anteriorly and posteriorly. There is bilateral inguinal adenopathy.

DIAGNOSIS
Metastatic Crohn's disease

TREATMENT AND COURSE
The patient refused biopsy in our clinic due to severe pain. Gastroenterology was consulted and she was admitted to confirm diagnosis, address pain control and expedite treatment. MRI of the abdomen/pelvis was without evidence of fistulas. Ileoscopy was macroscopically normal, and ileal biopsy showed normal mucosa. CT enterography did not show evidence of fistula, inflammation or strictures, indicating the diagnosis of metastatic (not contiguous) Crohn's disease. She was started on IV methylprednisolone 60 mg daily, and later, ciprofloxacin was added. The patient did not agree to vulvar biopsy until one week later, which was performed under sedation and confirmed the diagnosis. She was discharged to home on prednisone and ciprofloxacin, and has since been followed by gastroenterology. Prednisone has been tapered

off and ciprofloxacin was discontinued. A trial of 6-mercaptopurine was not tolerated due to nausea and vomiting. She is currently beginning a three-dose induction cycle of infliximab.

DISCUSSION

Crohn's disease, first described in 1932, is a chronic granulomatous inflammatory disease of unknown etiology which can occur at any age. It may affect any segment of the gastrointestinal tract, but most commonly involves the ileocecal component. Mucocutaneous findings are associated in 22-75% of patients, and have been classified into four categories: 1) granulomatous skin disease with sinus tract and fistula formation, 2) oral changes such as aphthous ulcers and mucosal cobblestoning, 3) nutritional changes including acquired zinc deficiency and 4) miscellaneous cutaneous markers including pyoderma gangrenosum, erythema nodosum, erythema multiforme, epidermolysis bullosa acquisita and necrotizing vasculitis. Of these, contiguous perianal skin lesions are by far the most common, and up to 25% of all patients will present with these findings. Of note, women with Crohn's disease frequently report gynecological symptoms. Genital manifestations can include pain, tenderness, ulcerations, fissures, skin tags, induration and edema. Thus variability of clinical presentation has probably led to underestimation of the true incidence.

Metastatic Crohn's disease refers to granulomatous inflammation within skin noncontiguous to the gastrointestinal tract. Most patients have known colonic involvement, though there have been reports of patients with skin disease preceding bowel symptoms. As is also evident from our case, the severity of skin disease does not necessarily parallel internal involvement. Histopathology characteristically shows a non-caseating granulomatous infiltrate within the dermis, sometimes extending to the subcutaneous tissue. The granulomas are comprised of epithelioid and multinucleated giant cells and lymphohistiocytic inflammation, similar to the findings in bowel lesions. The cause of metastatic Crohn's has not been elucidated, but some have proposed a T-lymphocyte-mediated type IV reaction to an unknown antigen within the skin. While immune complexes were also thought to play a role, this has not been a consistent finding.

Genital metastatic Crohn's disease tends to be recalcitrant to many therapies, as opposed to cutaneous involvement in other locations, which may resolve spontaneously. Proposed treatments include topical, intralesional and systemic corticosteroids, dapsone, sulfasalazine, azathioprine, metronidazole, tetracycline, 6-mercatopurine, zinc supplementation, hyperbaric oxygen and surgical debridement or reconstruction. As is evident from our patient's chronic history and previous ineffective management, mucocutaneous Crohn's disease can present in many ways, often delaying both diagnosis and treatment. Thus metastatic Crohn's should be considered when dealing with chronic genital fissures, ulcers, pain or swelling, and evaluation for occult bowel disease should be pursued.

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CHICAGO DERMATOLOGICAL SOCIETY **CASE # 13**

Presented by Amy Paller, MD, Anne Laumann, MBChB (UK), and James Collyer, MD
Department of Dermatology, Feinberg School of Medicine, Northwestern University

HISTORY OF PRESENT ILLNESS
This is a 31 year-old male who started having swallowing difficulties around four years of age. At age eight his nails became brittle and thin with pterygium formation. Over the next few years, white plaques developed on his buccal mucosa and tongue, his eyes began to tear constantly, his urinary stream became increasingly narrow, and he experienced intermittent dysesthesias of his fingertips. His easily irritated and sensitive skin showed redness of the cheeks, upper extremities, eyes and upper body with axillary discoloration. There is no history of developmental delay.

PAST MEDICAL & SURGICAL HISTORY
Born to non-consanguineous parents, delivered at 37 weeks, nail evulsion x 3, lacrimal duct dilation (1999), urethral meatotomy (2007)

ALLERGIES
Penicillin

FAMILY HISTORY
29 year-old brother: geographic tongue, otherwise healthy
Paternal uncle: intermittent tearing and smokes cigarettes
No known birth defects, genetic disorders, multiple miscarriages, still births, infant deaths, developmental delay, mental retardation, or psychiatric conditions.

SOCIAL HISTORY
Married and is a banker. Smokes 1-3 cigarettes/day

PHYSICAL EXAM
Injected conjunctivae
Well-defined, white plaques on his buccal mucosae, hard palate, and tongue with some scarring on the left, lateral tongue
Reticulated grey-brown hyperpigmentation with surrounding hypopigmented, atrophic erythematous, telangiectatic patches over the face, neck, upper trunk, upper and lower extremities
Most nails are absent, the remaining are thin and dystrophic, with full pterygium formation.
Erythema and swelling over the proximal fold areas

LABS
Normal (4/19/07): Complete blood count with differential, PT, PTT, INR, comprehensive metabolic panel, urinalysis, urine culture

DIAGNOSIS
Dyskeratosis congenital, X-linked recessive type

TREATMENT AND COURSE
He is being followed by ENT for the leukoplakia, ophthalmology for his eyes and urology for his urinary difficulties. So far, he has developed no hematologic abnormalities. He has been encouraged to stop smoking and practice strict sun protection. The patient and his wife are also interested in having children in the near future and requested genetic counseling. They were referred to genetics specialists at Children's Memorial Hospital and testing was performed,

resulting in the diagnosis of the X-linked recessive form of DC. Genetic testing was also performed on his mother, revealing no genetic mutations.

DISCUSSION

Dyskeratosis congenita (DC) is a rare syndrome primarily affecting the skin, nails, mucosa and bone marrow. Reticulated skin hyperpigmentation and dystrophic nails occur in approximately 90%, leukoplakia occurs in approximately 80% and over 90% eventually develop bone marrow failure (severe aplastic anemia, splenomegaly, neutropenia) leading to death in the 20s or 30s. Squamous cell carcinoma, gastrointestinal hemorrhage, and opportunistic infections may also develop.

In all individuals telomeres shorten over time, contributing to the aging process. In those with DC, telomere shortening occurs very fast, especially in tissues with rapid cell turnover such as the skin, mucosa and bone marrow.

At least three genes have been implicated in DC. The most common form of DC, as seen in our patient, is the X-linked recessive type. It results from a mutution in the *DKC1* gene, which encodes for the protein dyskerin. Dyskerin is an RNA component of telomerase (which adds sequence repeats to chromosome ends using an internal region of its RNA as a template). A second gene is *TERC*, which encodes for a component of the enzyme responsible for maintaining telomere length, and is inherited in an autosomal dominant fashion. An autosomal recessive form of DC also exists, though the specific gene responsible has not been elucidated.

Management of patients with DC consists of excision of leukoplakia of the oral and anal mucosae, treatment of esophageal stenosis, and regular medical follow up for monitoring of mucosal or cutaneous carcinomas. Bone marrow failure is initially treated with systemic corticosteroids and androgens, although bone marrow transplantation is the treatment of choice. The development of graft-versus-host disease may be accompanied by fatal pulmonary fibrosis.

Because the causative mutation was identified in our patient, prenatal and preimplantation testing is available to him and his wife in future pregnancies. Chorionic villus sampling can be performed around 10 to 12 weeks gestation, and amniocentesis is an option at 15 weeks gestation. In-vitro fertilization with preimplantation genetic diagnosis is also available.

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CHICAGO DERMATOLOGICAL SOCIETY **CASE # 14**

Presented by Mario Lacouture, MD[1], Vesna Petronic-Rosic, MD, MSc[2], and David Reid, MD[1]
1. Department of Dermatology, Feinberg School of Medicine, Northwestern University
2. University of Chicago Section of Dermatology

HISTORY OF PRESENT ILLNESS
This 83 year-old Caucasian, Fitzpatrick type I man first developed an erythematous, nontender, pruritic eruption over his left lower extremity in September 2006. He did not improve with multiple courses of antibiotics for presumed cellulitis, and new lesions appeared over his right leg, chest, back, and arms. Biopsies at outside institutions were read as superficially invasive and well-differentiated squamous cell carcinoma (SCC), as well as inflamed seborrheic keratoses. Evaluation for internal malignancy, including colonoscopy and PSA screening, had been negative. He had no history of HIV or other syndromes associated with immunodeficiency.

Many of the lesions had been surgically excised, but given progression with new lesions, he presented to our clinic for medical management options.

PAST MEDICAL HISTORY
Hypothyroidism, hypertension, hypercholesterolemia, basal cell carcinoma of the left leg

MEDICATIONS
Amlodipine, rosuvastatin, levothyroxine, hydroxyzine

ALLERGIES
Neosporin

FAMILY HISTORY
Daughter - melanoma

SOCIAL HISTORY
Lives with his wife; retired engineer; no tobacco, alcohol, or illicit drugs

PHYSICAL EXAM
Over his bilateral arms, chest, and back, there are multiple skin-colored to erythematous papules and nodules, with central keratotic plugging and overlying scale.

HISTOPATHOLOGY
Left lower leg, right lower leg: At the center of the specimens there is symmetrical epithelial hyperplasia with a craterlike formation. There is an inward proliferation of the epithelium with broad lobules of keratinocytes infiltrating into the dermis. The keratinocytes show abrupt keratinization with abundant glossy cytoplasm. At the periphery the keratinocytes show some hyperchromasia but no frank atypia. At the center of the crater there is some papillomatosis with large parakeratotic cells. At the periphery of the lobules there is a polymorphous inflammatory infiltrate with some exocystosis. Telangiectasia and some fibroplasia are also noted in the surrounding stroma.

DIAGNOSIS
Eruptive keratoacanthomas (KAs)

TREATMENT AND COURSE
Given the extent of his disease, medical therapy was recommended. The patient declined therapy with acitretin due to concern about adverse effects. In late August 2007, he started

erlotinib at a dose of 150mg daily, and continues on this regimen today.

DISCUSSION

Keratoacanthomas are rapidly growing cutaneous tumors of controversial biologic behavior. Four types – solitary, multiple, eruptive, and keratoacanthoma centrifugum marginatum – have been described. Sun exposure, human papilloma virus (HPV), and chemical carcinogens have been identified as possible causative factors. On histopatholgoic examination, early lesions demonstrate an invaginating epidermis and keratogenous, crateriform plugging. While lesions spontaneously involute over a period of 4-6 months, they can cause significant destruction and scarring.

First described in 1950, generalized eruptive keratoacanthomas of Gryzbowksi is a disorder in which numerous, 2-7mm, dome-shaped papules appear diffusely. Papules commonly have a keratatotic center and exhibit identical microscopic features to keratoacanthomas. Lesions may number in the hundreds or thousands, and are often intensely pruritic. It mostly commonly affects patients aged 50-80.

The etiology of eruptive KAs remains unknown. Gryzbowski originally postulated a viral pathogenesis, but evidence linking HPV and KAs has been inconclusive. Although sun-exposed areas are most commonly affected, studies have failed to reproduce lesions with UV radiation. Other proposed associations include internal malignancy, immunodeficiency, dysregulation in tumor suppressor genes (p53) and cellular oncogenes, and carcinogens such as tar and turf paper. Muir-Torre Syndrome is a distinct entity in which KAs and sebaceous tumors arise in association with internal malignancies.

Effective therapies of solitary KAs include surgical excision, cryotherapy, radiotherapy, and intralesional injections of 5-FU, bleomycin, and methotrexate. Multiple keratoacanthomas are more challenging; the number of lesions makes surgical or destructive techniques impractical, and the disease is frequently chronic. Systemic therapy with retinoids (isotretinoin and etretinate) has been used, but with little benefit in the Gryzbowksi-type.

Given the considerable overlap between SCC and KA, therapies directed against SCC may prove effective for generalized KAs. It is known that SCC, like many other malignancies, features overexpression of epidermal growth factor receptor (EGFR). Consequently, erlotinib, an EGFR inhibitor, may provide a novel and effective therapeutic option for eruptive KAs.

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CHICAGO DERMATOLOGIAL SOCIETY **CASE # 15**

Presented by Scott Wickless, DO and Ana Ciurea, MD
Department of Dermatology, Feinberg School of Medicine, Northwestern University

HISTORY OF PRESENT ILLNESS
The patient is a 21year-old woman from Liberia, who presented with a 2-week history of tender, enlarging lesions on the face, ears, trunk and extremities that started after a febrile episode. The patient denied any significant past medical history, however, upon further questioning, admitted that she was diagnosed with HIV and hepatitis B when she came from Liberia. Patient was on no treatment for her disease. She denied any sick contacts. She immigrated to the United States in 2004 and has not traveled abroad in the past year.
Her review of systems was negative for weight loss, night sweats, fatigue, chills, loss of appetite, headache, dyspnea, and diarrhea.

PAST MEDICAL HISTORY
AIDS, hepatitis B, toxoplasmosis, cervical intraepithelial neoplasia grade III

MEDICATIONS: None at presentation

ALLERGIES: No known drug allergies

SOCIAL HISTORY: Denies alcohol, tobacco, and intravenous drug use, married, 1 child – healthy

PHYSICAL EXAM
On presentation, the patient has numerous large, 1- 8 cm reddish-brown, indurated, scaly papules and plaques on the face including the nose, cheeks, earlobes and many scattered similar smaller plaques on the trunk and extremities. No lymphadenopathy.

LABS
The following were abnormal:
Blood urea nitrogen 4 mg/dl (nl 0-20), total protein 8.4 g/dl (6.0-8.0), albumin 2.6 g/dl (3.5-5.0), AST 43 U/L (0-40), ACE 196 U (15-60), WBC 3.4 K/UL (3.5-10.5), MCV 75 FL (80-99), CD4+ 317 mm^3 (340-1568)
CXR: multiple small bilateral axillary and subpectoral lymph nodes, negative for granulomas
CT sinuses: mild patchy thickening of the paranasal sinuses
Tissue culture: rapidly growing mycobacteria, the species unable to be identified based on the rRNA gene sequence analysis

The following were negative or within normal limits:
Electrolytes, creatinine, liver function tests (except AST, albumin and total protein), hemoglobin, hematocrit, platelets, coagulation profile, urine analysis, RPR, blood cultures

HISTOPATHOLOGY
Glabella: The epidermis showed slight hyperkeratosis. There were numerous confluent dermal aggregated composed of epithelioid histiocytes with numerous Langhans' multinucleated giant cells. AFB stain reveals numerous intracellular aggregates of mycobacteria with globi formation. DPAS and Giemsa were negative.

DIAGNOSIS
Rapid growing atypical mycobacterium infection in an AIDS patient

TREATMENT/COURSE

The patient was started empirically on isoniazid 5 mg/kg, rifampin 10mg/kg, ethambutol 15 mg/kg daily and clarythromycin 500 mg twice a day, under the direct supervision of infectious disease service with significant improvement of the skin lesions. Concomitantly, she was started on highly active retroviral therapy (HAART). The patient has not returned for follow-up in dermatology clinic since her initial presentation.

DISCUSSION

Nontuberculous mycobacteria (NTM) or atypical mycobacteria are important environmental pathogens that seldom cause clinical diseases in immunocompetent hosts.

Distribution of atypical mycobacterial infection is worldwide and affects both sexes equally. They exist in a wide variety of natural sources such as soil, water, vegetables, and animals and are classified based on their growth rates. Rapidly growing mycobacterium of the M. fortuitum and M. chelonae/abscessus groups are usually associated with localized post-traumatic wound infection. In addition to skin disease, pulmonary infections, osteomyelitis and and disseminated infections are usually associated with HIV infection. Between 25 to 50% of AIDS patients in Europe and USA are infected with NTM.

Host immunity seems to play a major role because a low $CD4^+$ lymphocyte count (fewer than 100cells/$mm^{3)}$ is associated with an increased frequency of NTM. Some cytokines such as interleukin IL-1 and IL-6 enhance extracelullar growth of the organism.
Infections are often misdiagnosed because of their nonspecific or subtle clinical presentation and should be suspected in patients with indolent plaques, nodules and ulcers with draining sinuses that are not responsive to standard treatment.

Identification of fast growing Mycobacterium species in cultures is gold standard. M. fortuitum and M. chelonae/abscessus organisms grow at 30 to 33°C on selective mycobacterial media, such as a Lowenstein-Jensen. Nucleic acid hybridization probes using target sequences or ribosomal RNA are available for rapid identification of clinical isolates.

The optimal regimen for treatment of rapid growing mycobacteria has not been defined. Excision and debridement may be required for abscesses and ulcers. The disease is often resistant to systemic antimicrobials, including those used for tuberculosis. Initial therapy is amikacin plus cefoxitin intravenously, followed by erythromycin, clarithromycin, doxycycline, or ciprofloxacin orally. Clarythromycin 500 mg twice daily for 4 to 9 months is effective and well tolerated in many patients treated with disseminated cutaneous infection caused by M. chelonae. Surgical debridement and prolonged antibiotic therapy may be necessary for patients with osteomyelitis.

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CHICAGO DERMATOLOGICAL SOCIETY **CASE# 16**

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 25 year-old woman with ataxia-telangiectasia (A-T) who has been followed at Children's Memorial Hospital since 9 years of age for cutaneous granulomas on her arm which have responded to intermittent triamcinolone injections and oral antibiotic therapy for secondary infection. She was last seen more than 5 years ago, prior to the development of an ovarian dysgerminoma. She presented again in January 2007. Although the granulomas were quiescent, she had the progressive development of cysts, pustules, and widespread comedones that first appeared after chemotherapy. Bacterial cultures once revealed methicillin-sensitive *S. aureus*, but she failed to respond to several courses of cephalexin.

PAST MEDICAL HISTORY
Ataxia-telangiectasia including extensive telangiectasias, premature graying of hair, seborrheic dermatitis, chronic non-infectious granulomas, immunodeficiency, and progressive neurologic changes (ataxia, dysarthric, choreoathetosis, mask-like facies)
Ovarian dysgerminoma (May 2002; treated with oophorectomy and Cisplatin/VP16, no recurrence with negative tumor markers)
Partial hearing loss (after chemotherapy)
Depression

MEDICATIONS
IVIG injections monthly
Amitriptyline 10mg twice daily

FAMILY HISTORY
Younger brother-ataxia-telangiectasia

PHYSICAL EXAM
Hundreds of 1-to 6-mm cysts cover the neck, trunk, abdomen, and lower extremities; larger, more inflamed draining cysts are noted at the suprapubic, inguinal, and inframammary areas with residual scarring. Her breasts, trunk, abdomen and groin are studded with open and closed comedonal lesions. Her face shows no evidence of acne. She has telangiectasias on the bulbar conjunctivae, cheeks, ears and tongue. She has a violaceous, scarred plaque with underlying soft tissue atrophy on the posterior aspect of the right upper arm, and prematurely gray hairs on the scalp and pubic areas. She shows generalized sparsity of scalp hair with fine white scaling unaccompanied by erythema.

DIAGNOSIS
Ataxia-telangiectasia and severe hidradenitis suppurativa

TREATMENT AND COURSE
A course of doxycycline 100mg was initiated and clindamycin 1% lotion was applied twice daily to the inframammary and inguinal areas. No improvement was noted after two months and a course of isotretinoin was slowly initiated in April 2007. During the initial month of therapy, she was concurrently treated with low-dose prednisone to prevent an inflammatory flare. Although the plan was to gradually increase to 1mg/kg/day, her cutaneous granulomatous plaque became eroded after 6 weeks of therapy at a dose of 20mg daily. She remained at this dose and by July 2007 she experienced significantly less inflammation, fewer cysts and a marked reduction in comedonal lesions; however the ulceration on her arm had not responded to concomitant administration of intralesional triamcinolone, topical gentamicin ointment, and oral

cephalexin. She had experienced no other side effects. Given the potential effects of isotretinoin on wound healing, the isotretinoin was stopped in August 2007. Off isotretinoin, the granulomatous plaque is healing with cephalexin 500mg twice daily and monthly intralesional triamcinolone injections. She restarted doxycycline 100mg twice daily for the hidradenitis suppurativa, but it has progressively worsened.

DISCUSSION

Ataxia-telangiectasia(A-T) is an autosomal recessive disorder that results from a mutation in ATM (Ataxia telangiectasia mutated) which plays a critical role in cell-cycle and apoptotic responses after DNA damage. The classic cutaneous features include telangiectasias and non-infectious cutaneous granulomas. Telangiectasias develop by six years of age, initially affecting the bulbar conjunctivae and subsequently involving other areas of the face, neck and chest. Granulomas are persistent and ulceration is common. Other cutaneous manifestations include loss of subcutaneous fat; large, irregular café-au-lait lesions; vitiligo, and seborrheic dermatitis. Premature graying of the hair may occur before adolescence, and during adolescence the facial skin can become sclerotic and atrophic: which coupled with the neurologic deterioration, presents as mask-like facies. Non-cutaneous features include cerebellar ataxia, combined immunodeficiency, endocrine abnormalities, and an increased risk of malignancy.

Hidradenitis suppurativa(HS) is a chronic, recurrent, inflammatory disorder that usually affects the axillae and perineum. The pathogenesis is unclear; however occlusion and subsequent rupture of the hair follicle promotes an inflammatory state. Individuals develop painful abscesses, malodorous discharge, sinus tract formation and scarring. Currently there is no reported association between hidradenitis suppurativa and immunodeficiency.

There are many treatment options for HS, ranging from topical and oral antibiotics, antiandrogens, systemic and intralesional steroids, and surgical modalities, of which the latter is most effective yet has associated risks. More recently, treatment with isotretinoin, infliximab or etanercept has been evaluated. Isotretinoin appears to be moderately effective and response is inversely proportional to disease severity. Early case reports on the efficacy of infliximab were promising; however a recent retrospective review of 7 patients concluded that the efficacy of infliximab is transient and associated with significant toxicity, including neoplastic and severe neurologic disease. Etanercept appears to be effective for patients with severe HS with limited side effects. Initial responses were observed at a mean of 2 weeks after commencing therapy with reduced tenderness, induration, and sinus drainage. Potential adverse effects included delayed hypersensitivity reactions, lymphoproliferative diseases, increased infection rates and demyelination. Discoid lupus and cryoglobulinemic vasculitis have also been reported. Further studies are needed to evaluate the efficacy and safety of these treatments.

Given the side effect profiles of potential treatments and our patient's medical history, she presents a therapeutic challenge. Once her cutaneous granuloma is stable, the goal would be to restart isotretinoin at a lower dose given her earlier response. Another consideration given her associated discomfort would be a trial of etanercept.

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CHICAGO DERMATOLOGICAL SOCIETY **CASE # 17**

Presented by Joaquin Brieva, MD and Katherine Brown, MD
Department of Dermatology, Feinberg School of Medicine, Northwestern University

HISTORY OF PRESENT ILLNESS
This is a 25 year-old African American man with a history of epilepsy, controlled with phenytoin, presented for evaluation of scarring alopecia on vertex and parietal scalp for 1 year. He complains of pruritus, but denies pain associated with lesions. He has not experienced any trauma to his scalp and has never shaved his scalp. Treatment for this problem has included over the counter Neutrogena T-gel, with minor improvement in discomfort.

PAST MEDICAL HISTORY
Epilepsy

MEDICATIONS
Phenytoin, for 9 years

ALLERGIES
None

FAMILY HISTORY
Seizure disorder

SOCIAL HISTORY
The patient is single, has a military background and is currently working in sales.

PHYSICAL EXAM
Well developed, well appearing African American male. Normal oral mucosa without significant gingival hyperplasia. Exam of vertex, parietal, and frontal scalp revealed symmetric areas of scarring alopecia and firm erythematous fibrous papules coalescing into keloid-like plaques. Tufted hairs visualized exiting papules. No pustules or scaling observed. Nail units are normal.

HISTOPATHOLOGY
Frontal parietal scalp: horizontal and vertical sections both revealed disrupted follicular units with hair shaft granulomas and dense dermal fibroplasias. Multinucleated foreign body giant cells, numerous histiocytes, and a lymphoplasmacytic infiltrated were seen. DPAS was negative. These findings were consistent with a scarring alopecia with suppurative and plasma cell rich perifollicular infiltrate.

DIAGNOSIS
Acne keloidalis, associated with phenytoin use

TREATMENT AND COURSE
The patient has been encouraged to discuss alternative anti-epileptic medications with his neurologist and to consider a trial of phenytoin discontinuation.

DISCUSSION
We present this case to illustrate a unique fronto-parietal distribution of acne keloidalis, which occurred during treatment with phenytoin. Acne keloidalis first named by Bazin in 1872, is a form of primary scarring alopecia. The presentation is classically numerous smooth firm papules and occasionally pustules distributed along the nape of the neck of young African American males. Lesions may be mildly symptomatic of pruritus and often progress to indurated fibrous keloidal nodules. The male to female ratio of this disorder is 20:1, and it is 10 times more common in

blacks than in whites. The etiology of acne keloidalis remains unclear. Although not a prominent feature of our patient's history, repetitive trauma, for example, from helmets or very short haircuts, is the most frequent cause proposed in the literature.

There are reported cases of acne keloidalis with an atypical distribution on the vertex of the scalp. Grunwald et. al. reported one such case in 1990 associated with the use of antiepileptic drugs. They described a Caucasian male treated for epilepsy with diphenylhydantoin (synonymous with phenytoin) and carbamazepine for 6 months and 1 year respectively, prior to onset of acne keloidalis. He had a history of a prior one-year course of diphenylhydantoin two years preceding the scalp eruption. In vitro tests for drug hypersensitivity were positive for both drugs. Withdrawal of carbamazepine with continuation of diphenylhydantoin for one year resulted in worsening of his skin despite treatment; however, improvement was noted when diphenylhydantoin was discontinued, and no worsening was noted when carbamazepine was restarted.

As in our case, histopathology of acne keloidalis shows a disruption of follicular units with a foreign-body reaction around hair sheaths and a perifollicular infiltrate, composed of neutrophils in early lesions, and plasma cells, lymphoid cells, and fibroblasts in areas of chronic inflammation. Dense dermal fibrosis and absence of sebaceous glands are seen in older lesions.

Treatment remains difficult; regimens often include combination of potent topical steroids, prolonged use of topical and/or oral antibiotics, and intralesional corticosteroid injections for early popular lesions. Surgical removal of larger keloidal lesions may be considered. In our case, discontinuation of phenytoin was considered.

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CHICAGO DERMATOLOGICAL SOCIETY **CASE # 18**

Presented by Pedram Gerami, MD and Diana Leu, MD
Department of Dermatology, Feinberg School of Medicine, Northwestern University

HISTORY OF PRESENT ILLNESS
A previously healthy 42 year-old African American female presented to us with a 9-month history of a recurrent nodular eruption with outside diagnosis of erythema nodosum. She developed lesions every 3-4 days, primarily distributed on the thighs, buttocks and upper arms in areas of high fat content. The lesions were suppurative with yellow oily material and were exacerbated by activity. She failed treatment with super saturated potassium iodide and had recurrence of lesions after tapering prednisone.

PAST MEDICAL HISTORY
None

MEDICATIONS
Naproxen

ALLERGIES
No known drug allergies

FAMILY HISTORY
No family history of similar nodules

SOCIAL HISTORY
Denies smoking or drinking alcohol

PHYSICAL EXAM
Well-developed, well-nourished African American female in no acute distress
Soft erythematous subcutaneous 2-4 cm nodules on the right dorsal foot, left shin, and right shoulder
Hyperpigmented ill-defined patches on the posterior thighs and upper arms

LABS/STUDIES
Normal: CT Chest/Abd/Pelvis, CT Sinus, Bartonella henselae screen, Bartonella quintana screen, Blastomyces antibody, Histoplasma antigen, TSH, T3, T4, ANA, RF, Myeloperoxidase antibody, Proteinase-3, RPR, urinalysis, Hepatitis A, B, C, bacterial culture, G6PD
Serum alpha-1 antitrypsin – 108 (nl 83-199)

Abnormal:
CBC is normal except for plt of 517 k/ul
Complete metabolic panel is normal except for Calcium of 10.6 mg/dl
Erythrocyte sedimentation rate -55 mm/hr
Alpha-antitrypsin phenotype: PI-MZ

HISTOPATHOLOGY
Right dorsal foot: Neutrophilic-rich lobular panniculitis with necrobiosis of the reticular dermis. DPAS, Gram, and AFB stains were negative. Bacterial, fungal, and mycobacterial cultures were also negative

DIAGNOSIS
Alpha-1-antitrypsin associated panniculitis

TREATMENT AND COURSE

She was started on doxycycline initially without much change in her symptoms. Following a normal G6PD level, dapsone was initiated with significant improvement with the development of fewer lesions as well as a shorter duration for lesions which did occur. She was counseled as to the increased risk for development of liver disease particularly with increased alcohol use and the development of COPD with smoking.

DISCUSSION

Alpha-1-antitrypsin is the most abundant serine protease inhibitor in humans and is involved in regulation of various serine proteinases including trypsin, elastase, chymotrypsin, and cathepsin G. Deficiency in alpha-1-antitrypsin is associated with COPD, cirrhosis of the liver, and panniculitis.

There are over 90 genetic variants of AAT which are categorized based on their movement on acid starch gel including F (fast), M (medium), S (slow), and Z (very slow). The Z allele produces the least amount of effective enzyme while the S allele produces more functional enzyme. The M allele produces normal levels of functional enzyme.

Most patients with significant pulmonary or liver disease from alpha-1-antitrypsin deficiency have the ZZ phenotype with low alpha-1-antitrypsin levels. However, AAT panniculitis may also be seen in patients with the SS, MS and MZ phenotype and they may have "normal" serum alpha-1-antitrypsin levels and still develop clinically significant disease.

Environment plays a role in the development of disease in patients with alpha-1-antitrypsin deficiency. The MS or MZ alone is insufficient to produce pulmonary or liver disease. However, MZ patients who smoke or drink alcohol are at higher risk than the general population of developing lung or liver disease.

Alpha-1-antitrypsin panniculitis was first described in 1972. It is one of a few panniculitides with ulceration and suppuration of lesions with oily material. The histology of alpha-1-antitrypsin panniculitis shows a neutrophil rich panniculitis with septal and lobular fat necrosis. DPAS, AFB, and Gram stains are helpful to rule out an infectious cause of a neutrophilic rich panniculitis. If diagnosis of alpha-1-antitrypsin panniculitis is suspected, a phenotype and serum level can be obtained for confirmation.

Treatment options include tetracyclines, non-steroidal anti-inflammatory drugs, plaquenil, colchicine and dapsone.

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CHICAGO DERMATOLOGICAL SOCIETY **CASE # 19**

Presented by Anne Laumann MBChB, MRCP, Joaquin Brieva, MD, and Brandi Kenner-Bell, MD
Department of Dermatology, Feinberg School of Medicine, Northwestern University

Patient A

HISTORY OF PRESENT ILLNESS

The patient is a 52 year-old female presented in early March with a several week history of an intensely pruritic eruption unresponsive to oral diphenhydramine. The eruption had started on her face and spread to involve her face, entire trunk, extremities, fingers and soles. She had been on oral terbinafine 250mg daily for onychomycosis and had had a one week's course of penicillin in February 2007 related to a titanium tooth implant. Following a skin biopsy, two separate ten day courses of prednisone together with topical applications of fluocinonide 0.05% cream 1:1 with sarna ultra resulted in some fading, but not complete resolution, of the problem. A second biopsy was performed.

PAST MEDICAL HISTORY

Obesity s/p Roux en Y Gastric bypass surgery in 2000 (>100 lbs weight loss), Hashimoto's thyroiditis with hypothyroidism, chronic fatigue syndrome, depression

MEDICATIONS

Terbinafine 250mg daily (12/11/06 to 2/17/07), oral contraceptives, mometasone nasal spray, calcium carbonate-vitamin D, levothyroxine, prenatal B vitamin and B12 vitamin, acidophilus, milk thistle.

ALLERGIES Sulfa drugs (rash), macrolides (rash), sertraline HCl (rash)

FAMILY HISTORY Father with brain cancer

PHYSICAL EXAM

Multiple coalescing erythematous annular plaques with pale centers on the back and chest. Palms with violaceous mottling and paronychial erythema as well as violaceous patches on the dorsum of toes when dependent.

LABS

4/4/07: ANA, speckled 1:40 – 1:80, C4 complement 14 (nl 16-70), SS-A IgG 127 (<5), Anti cardiolipin IgM Ab 65 (<10); Scl-70, anti-dsDNA, anti-nRNP, anti-Smith, C3, SS-B IgG, anticardiolipin IgG, IgM and IgA were within normal limits.
4/17/07: Urinalysis – trace ketones and LE, 6-10 WBCs/HPF, 2+ bacteria, 2+ calcium oxalate crystals. CMP – potassium 3.1 (3.5-5.0), CBC within normal limits.

HISTOPATHOLOGY

3/5/07; L leg: Subacute spongiotic dermatitis. Epidermis shows spongiosis, acanthosis and mild parakeratosis. There is some edema of the upper dermis with a perivascular mononuclear cell infiltrate without atypia. DPAS negative.
4/4/07; Back: Interface dermatitis. Skin with apoptotic keratinocytes at multiple levels of the epidermis and basal vacuolization. Occasional melanophages and lymphocytes at the DEJ. There is an underlying superficial and deeper perivascular inflammatory infiltrate as well. Colloidal iron stain weakly positive. DIF with no evidence of immune deposits.

Patient B

HISTORY OF PRESENT ILLNESS

The patient is a 24 year-old woman who presented in June 2007 with a pruritic rash of six weeks duration which initially began on her stomach. She had flu-like symptoms several days before the appearance of the rash. She had started taking oral contraceptives in December 2006 and took terbinafine in January and February of 2007. She was seen by a dermatologist in May and received a triamcinolone 40 mg intramuscular injection and started using triamcinolone topically. A biopsy done at that time was read as consistent with pityriasis lichenoides. She was then given minocycline which made her nauseous so it was changed to doxycycline. A subsequent course of oral prednisone was unhelpful.

PAST MEDICAL HISTORY

None

MEDICATIONS

Terbinafine (January to February 2007), doxycycline

ALLERGIES

NKDA

FAMILY HISTORY

Negative

PHYSICAL EXAM

Numerous annular confluent erythematous to dusky plaques with central clearing, photodistributed, most pronounced on the arms. Mostly annular hyperpigmentation on the abdomen, back, and legs. Erythema of malar region of face and dorsum of hands.

HISTOPATHOLOGY

5/22/07; R abdomen *(outside read):* Epidermis with layered parakeratosis and small amount of serous. Scattered necrotic keratinocytes present throughout the epidermis. Dermis shows moderate lymphocytic infiltrate.
(internal read): Epidermis reveals atrophy and an interface lymphocytic infiltrate with vacuolar changes, scattered and focally coalescing necrotic keratinocytes. The is marked edema of the papillary dermis with telangiectasia and inflammation. Hair follicles are not markedly involved.

LABS

5/07: ANA screen 5.41 (positive), ESR 27 (<20), C2 58 (25-47); CMP, CBC, TSH, RPR, ASO all within normal limits
6/15/07: ANA 75 (<7.5) speckled, SS-A IgG 141 (<5), SS-B IgG 130 (<5); Scl-70, dsDNA, anti-Smith, anti-nRNP, C3, C4, anti-cardiolipin IgG, IgM, and IgA all within normal limits

DIAGNOSIS

Subacute cutaneous lupus erythematosus (SCLE) secondary to terbinafine

TREATMENT AND COURSE

Patient A continued to have active disease. Prednisone was increased to 30 mg daily and hydroxychloroquine was started with significant improvement. She did have an episode of facial swelling accompanied by hand and foot numbness after sun exposure. Pt subsequently failed prednisone taper past 25 mg daily and developed joint aches in elbow and thumbs with a flare of her skin disease. Pimecrolimus cream was added to her topical regimen and over the next two weeks the patient's skin lesions cleared. She continues on a slow prednisone taper.

Patient B was started on prednisone 30mg daily, tapering by 10mg every 10 days, as well as hydroxychloroquine 200mg BID and strict sun protection with desonide lotion topically. Within one month she was almost clear. Her prednisone was stopped and she was changed to tacrolimus 0.1% ointment on which she has continued to improve.

DISCUSSION

Drug-induced SCLE is most commonly reported with thiazide diuretics, as well as calcium channel blockers and angiotensin-converting enzyme inhibitors. The most common cutaneous adverse effects associated with oral terbinafine therapy are rash (6% incidence), pruritus (3%), and urticaria (1%). Most reactions are mild and do not require discontinuation of the drug. However, there are reports of more serious cutaneous adverse effects including erythema multiforme, toxic epidermal necrolysis, acute generalized exanthematous pustulosis, psoriasis flare, hypersensitivity syndrome and serum sickness-like reaction.

Terbinafine-induced SCLE was first reported by Murphy and Barnes in 1998 and there have been several additional reports which have solidified the link as more than coincidental. In addition to those patients in which terbinafine therapy was associated with the onset of SCLE, many reports include patients with a history of SCLE, systemic lupus erythematosus, or other autoimmune symptoms or conditions who experienced an exacerbation of their disease after starting oral terbinafine therapy.

Of the patients reported in the literature, all developed skin disease within four to eight weeks of beginning therapy. In many patients, like our cases, the eruption continued to spread despite discontinuation of terbinafine. This may be explained by the prolonged tissue retention of terbinafine, which has measurable plasma levels and tissue concentrations for up to three months after a four week oral course. Fortunately, with therapy (including topical corticosteroids, alone or in combination with hydroxychloroquine, oral corticosteroids, dapsone and/or strict sun protection) all patients experienced a complete remission within a few months of stopping the drug. There is also a fairly consistent autoantibody profile among reported patients with most having a positive ANA and anti-Ro antibody, with a slightly less frequently positive anti-La antibody. Though many of the cases do not report long term follow up, the few that have show a decrease in ANA titers over time with occasional persistence of anti-Ro and/or anti-La antibodies. Though the mechanism by which terbinafine may trigger SCLE is not known, some have postulated that due to the highly lipophilic and keratophilic nature of terbinafine, it may, in susceptible persons, deposit in keratinocytes and alter nuclear antigen structure, inducing autoantibody formation.

We present these cases as a reminder of potentially serious adverse effects of a commonly prescribed drug and caution its use in patients with a history positive or even suspicious for autoimmune connective tissue disease.

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CHICAGO DERMATOLOGICAL SOCIETY **CASE # 20**

Presented by Joan Guitart, MD, Pedram Gerami, MD, Susan Boone, MD
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HISTORY OF PRESENT ILLNESS
This 31 year-old man presented with a 2-year history of patches, plaques, and tumors, many of which were necrotic and ulcerated, on his back, chest, and extremities. He was originally diagnosed in October 2005 with mycosis fungoides with lymphomatoid papulosis at an outside institution and started on bexarotene with improvement within three months. Since then, the dose has been maximally increased but then discontinued due to increased cholesterol and triglycerides. He has also had four sessions of PUVA but stopped because he developed blisters. He was seen in the Emergency Room in May 2007 for increasing pain in his ear and oral skin lesions, and was subsequently referred to our Multidisciplinary Lymphoma Clinic. Over the last six months, he reported worsening with explosive growth of the fungating necrotic tumors.

PAST MEDICAL HISTORY
Asthma

MEDICATIONS
Bexarotene, clindamycin, nystatin

ALLERGIES
No known drug allergies

FAMILY HISTORY
Patient has father with myocardial infarction at age 46 and an aunt with breast cancer.

SOCIAL HISTORY
Married with 4 children, ex-pawn shop owner but has stopped working because of cosmetic disfigurement of his disease. Smokes a pack a day x 10 years.
No alcohol use or use of illicit drugs. He has multiple tattoos.

PHYSICAL EXAM
There are multiple circinate and arcuate erythematous scaly and crusted papules and plaques, many with ulceration and necrosis, diffusely involving the scalp (with patchy alopecia), face, tongue, palate, neck, chest, abdomen, back, buttocks, penis, extremities, hands, and feet. There are many tender lesions with foul-smelling serosanguinous drainage. Lesions were not classic mycosis fungoides lesions in a bathing suit distribution. There was palpable cervical and axillary lymphadenopathy.

LABS
Platelet count slightly elevated at 433 K/UL. Otherwise, complete blood count with differential, complete metabolic panel, and T & B cell quantitation were all within normal limits.
Negative for monoclonal T-cell receptor rearrangement
No significant number of Sezary cells in peripheral blood

IMAGING
5/8/2007 CT scan of the chest, abdomen, and pelvis demonstrate a small anterior mediastinal mass suspicious for adenopathy, enlarged axillary lymph nodes, bilateral inguinal adenopathy, and multiple pulmonary nodules.
5/11/2007 PET shows widespread cutaneous lesions in the head, neck, chest, abdomen, pelvis and proximal lower extremities. Focal areas of lymphadenopathy are demonstrated in the

axillary, cervical, and inguinal regions bilaterally. There are no other definite sites of lymphomatous involvement demonstrated elsewhere.

HISTOPATHOLOGY

Mid-Back and Left Back: Acanthotic epidermis with prominent parakeratosis and a serous exudate. There is a dense mostly intraepidermal atypical lymphoid infiltrate with prominent pagetoid features. The cells are irregular, intermediate to large and pleomorphic with hyperchromasia. The upper dermis shows also some of the atypical lymphocytes, edema and some reticular fibroplasia. Significant adnexotropism (follicular and eccrine is noted). Immunohistochemistry on Mid-Back was performed on deparaffinized section. Tumor cells are positive for CD3, CD8, CD45RA, TIA-1, CD7. The cells are negative for CD4, CD30, CD20, CD45RO, BF1, CD56.

DIAGNOSIS

Cutaneous CD8-Positive Cytotoxic T-Cell Lymphoma, Berti's Variant

TREATMENT AND COURSE

The patient completed three cycles with HyperCVAD (combination of cyclophosphamide, vincristine, doxorubicin, and dexamethasone, alternated with high doses of methotrexate and cytarabine), and prophylactic intrathecal methotrexate x four doses. He initially showed good improvement but three days after the third cycle of HyperCVAD new lesions began to erupt. He was started on gemcitabine and pegfilgrastim, but only had minimal response. He has since been admitted to the hospital three times for spiking fevers and pain control. During the last hospital stay, he received ICE (ifosfamide, carboplatin, and etoposide) along with dexamethasone and intrathecal MTX and tolerated well. He has undergone radiation therapy and recently received an allogeneic stem cell transplant on September 21, 2007.

DISCUSSION

Cutaneous T-Cell Lymphoma expressing a CD8+ T cell phenotype is a rare primary cutaneous lymphoma exhibiting extremely aggressive clinical behavior, first officially described by Berti in 1999. Only approximately twenty cases have been described. Clinical presentation includes generalized patches, plaques, nodules, and tumors, and metastatic spread to the lungs, testis, CNS, and oral cavity. Histologically, these lymphomas are characterized by band-like infiltrates consisting of pleomorphic T cells, with an acanthotic epidermis and necrosis. Neoplastic cells will show high Ki-67 proliferation index and expression of CD3, CD8, CD7, CD45RA, βF1 (negative in our patient), and TIA-1 markers, whereas CD2 and CD5 are frequently negative. Reported treatments include PUVA, polychemotherapeutic agents including CHOP, radiotherapy, interferon, etretinate. However, despite initial responses to treatment, disease course is very aggressive, with rapid extracutaneous spread and death within several years (median survival reported to be 22.5 to 32 months).

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