Chicago Dermatological Society

May 2009
Monthly Educational Conference

Program Information
Continuing Medical Education Certification
and
Case Presentations

Wednesday, May 20, 2009

Conference Host:
Department of Dermatology
Rush University Medical Center
Chicago, Illinois

Program

Committees & Registration

8:00 a.m. - 9:00 a.m.	IDS Board of Directors *Game Room (5th Floor)*
9:00 a.m. - 10:00 a.m.	CDS Plans & Policies Committee *Room 541 (Gunn)*

Program Activities

9:00 a.m. - 10:00 a.m.	RESIDENT LECTURE "Disparities in Skin Cancer Diagnosis and Outcomes" Robert Kirsner, MD, PhD *Room 542 Brainard*
9:30 a.m. - 11:00 a.m.	Clinical Rounds – Patient Viewing *Room 264 Professional Building (Elevator III)*
	Slide Viewing *Room 538 (Fenger)*
11:00 a.m. - 12:15 p.m.	General Sessions *Room 542 (Brainard)*
11:00 a.m.	CDS Business Meeting
11:15 a.m.	FREDERICK MALKINSON LECTURE "Advances in Wound Care: What Dermatologists Should Know" Robert Kirsner, MD, PhD
12:15 p.m. - 1:00 p.m.	Awards Luncheon & President's Address *Garden area of Room 500*
1:00 p.m. - 2:30 p.m.	Case Discussions *Room 542 (Brainard)*
2:30 p.m.	Meeting adjourns

Mark the Date!

Next CDS monthly meeting – Wednesday, June 10, 2009
Loyola University Medical Center; Maywood
Watch for details on the CDS website: www.ChicagoDerm.org

CME Information

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

Accreditation Statement: This activity has been planned and implemented in accordance with the Essential Areas and policies of the Accreditation Council for Continuing Medical Education (ACCME) through 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.

Designation Statement: The Chicago Medical Society designates this educational activity for a maximum of 4 AMA PRA Category 1 Credits™. Physicians should only claim credit commensurate with the extent of their participation in the activity.

Commercial Support: There is no commercial support associated with this meeting.

Guest Speaker

Robert Kirsner, MD, PhD – Federick Malkinson Lecture

Dr. Kirsner is the Stiefel Laboratories Professor and vice Chairman of the Department of Dermatology, Univeristy of Miama - Jackson Memorial Medical Center. He earned his undergraduate degree at Texas A&M University, College Station, TX. His medical degree was received at the University of Miami School of Medicine. Dr. Kirsner completed his dermatology residency and also completed a fellowship at the University of Miami, Jackson Memorial Hospital. He also earned a PhD at the University of Miami School of Medicine. Dr. Kirsner's clinical interest is in wound healing, leg ulcers, skin cancer, medical dermatology and cutaneous surgery. His research interests include wound healing, health care policy, dermatoepidemiology, inpatient dermatology, and cancer control and prevention.

Speaker CME Disclosure of Financial Interests

Dr. Kirsner's financial disclosure will be made at the meeting.

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 Lauren Campbell, MD, and Warren Piette, MD
Department of Dermatology, RUSH University Medical Center

HISTORY OF PRESENT ILLNESS

This patient is a 32 year-old white male with a history of diffuse nodules and scarring of the skin for approximately 15 years. The lesions first appeared on his head and neck and have since spread to involve his trunk and extremities. Until 5 years ago the patient states his disease was stable, but recently the lesions on his face have left increasingly extensive scarring. Over the past ten years the patient has developed painful contractures of his hands and ulcerations of the joints of his hands and feet. He has had several episodes of osteomyelitis of the hands and feet, resulting in amputation of the right 5th toe. The patient has been evaluated extensively, including at the University of Iowa where he has been followed for ten years. Currently, he continues to get new lesions. He denies recent weight change, fatigue, dizziness, frequent headaches, nausea, vomiting, fevers, chills, diarrhea or night sweats. He complains of constant severe hand and foot pain and severe difficulty using his hands to perform any task.

PAST MEDICAL HISTORY

Cerebral palsy-noted when the patient first started walking
Recent history of acute stroke
History of lymphopenia with elevated IgE and low IgM, unspecified immunodeficiency
Atopic dermatitis as a child
Nephrolithiasis
Raynaud's phenomenon
Deviation of the nasal septum with resulting perforation
Unspecified polyarticular arthritis
Multiple reconstructive surgeries of the joints of the hands
Chronic osteomyelitis of the hands and feet, with multiple debridements
Amputation of the right 5th toe
Appendectomy

MEDICATIONS

Prednisone 20 mg daily
Levofloxacin 750 mg every other day
Cephalexin 500 mg three times daily
Plaquenil 200 mg twice daily
Dapsone 200 mg daily
Morphine sulfate 150 mg q 4 hours as needed
Quinacrine- recently discontinued

ALLERGIES

Clarithromycin

FAMILY HISTORY

There is a possible history of systemic lupus in the patient's paternal great aunt.

SOCIAL HISTORY

The patient quit smoking one month ago; he has a 10 pack year history of smoking. He drinks alcohol occasionally and does not use illicit drugs. The patient was formerly employed as an office worker, but has been unemployed for the past 10 years because of his illness.

PHYSICAL EXAM

A thin white male in no acute distress, sitting in a wheelchair. On the face, neck, arms, and trunk, there are too numerous to count indurated small firm pink nodules and annular plaques separated with atrophic scarring overlying a reticulated pattern of erythema with minimal scale. The face is most notably involved with focal areas of loss of nasal alar and auricular cartilage. There is obvious perforation of the nasal septum. There is significant perioral vermiculate scarring. There is significant contracture formation of the hands with chalk-like nodules overlying the metacarpo-phalangeal and proximal inter-phalangeal joints of the hands and feet, some ulcerated. The skin of the patient's extensor legs is somewhat bound down, and there is absence of the right 5th great toe. There is no lymphadenopathy or hepatosplenomegaly. The oral and ocular mucosae and nails are unremarkable.

HISTOPATHOLOGY

Punch biopsy forehead, 1999: Superficial and deep perivascular lymphocytic infiltrate. Focal fat necrosis is seen. There is focal vacuolar alteration at the dermal-epidermal junction with dermal mucin deposition. These histologic findings are of a lobular sclerosing panniculitis most consistent with lupus profundus.

Skin, left elbow, punch biopsy, 2005: Superficial ad deep perivascular and perifollicular lymphocytic infiltrate with fat necrosis and hyalinization. The dermis is thickened with fibrosis and eccrine structures are absent. These histologic findings are of a lobular sclerosing panniculitis with fibrosing dermatitis.

LABORATORY RESULTS

Within normal limits

Electrolytes, blood urea nitrogen, creatinine, calcium, liver function tests, complete blood count, erythrocyte sedimentation rate, urinalysis, anti-nuclear antibody (ANA), rheumatoid factor, C3, c-ANCA, p-ANCA, anti-cyclic citrullinated peptide, creatine kinase

Abnormal

C-reactive protein (CRP): 4.67 mg/dL (normal is less than or equal to 3 mg/dL)
C4: 40.4 mg/dL (normal 10-40 mg/dL)
2006: ANA 1:40 titer with speckled pattern, p-ANCA 1:40 titer

RADIOLOGY

Plain film, left elbow 2/09: There is subtle ill-defined lucency at the lateral epicondyle/capitellum and radial head, probably demineralization. There is no joint effusion. There is no cortical disruption or periosteal reaction. There is no evidence of fracture or dislocation. Soft tissues are within normal limits without calcifications. Overall, these findings are most suggestive diffuse osteoporosis. An underlying osseous lesion cannot be entirely excluded.

DIAGNOSIS

Chronic lupus profundus possibly evolving into disabling pansclerotic morphea

TREATMENT AND COURSE

The patient initially presented to the University of Iowa Hospitals Department of Dermatology in July of 1999 with a 5-6 year history of diffuse migratory subcutaneous nodules healing with depressed scars and significant cosmetic disfigurement. Before that he was being followed by a community dermatologist. The patient has been treated with various modalities. He has a history of significant non-compliance with medications and often self-discontinues medications because he feels they are ineffective. Prednisone has been used consistently at doses varying between 20 mg and 60 mg daily. He has been treated with dapsone, though he has experienced difficulty with gastrointestinal symptoms. He experienced some improvement and

decreased development of lesions with the addition of quinacrine to hydroxychloroquine, but recently the family has had difficulty obtaining quinacrine. Numerous (approximately 9) cycles of IVIG were administered per the Allergy and Immunology Department at the University of Iowa. The patient elected to discontinue therapy because of lack of efficacy. Cyclosporine was attempted and the patient discontinued therapy due to blurry vision. Methotrexate was tried for a trial of two months and was self-discontinued due to perceived lack of efficacy. One week prior to presentation at Rush, the patient was evaluated at a community hospital for acute onset right-sided weakness, numbness, and tingling. MRI revealed a focal 5 mm acute infarct within the medulla and pons. This patient is extremely depressed and frustrated regarding his disease and the resulting significant cosmetic disfigurement that has resulted, and presented back to Dr. Piette at Rush for a consultation in February, 2009. We present him for discussion regarding a definitive diagnosis and additional treatment options.

DISCUSSION

This patient is presented for discussion regarding a cohesive diagnosis that best fits his clinical and pathologic presentation, and for possible treatment options given his progressive and disabling course. He has carried a diagnosis of lupus panniculitis for many years, though this diagnosis does not fully explain the patient's clinical findings and disease course. Lupus erythematosus panniculitis, or lupus profundus, is a clinical variant of lupus erythematosus that involves the deep dermis and subcutaneous fat. The most commonly affected areas include the face and proximal extremities, and it manifests clinically as indurated plaques that evolve into disfiguring, depressed areas. Many patients have lesions of discoid lupus overlying the panniculitis. Histopathologic findings of lupus panniculitis include hyaline necrosis of fat lobules, a lymphocytic inflammatory infiltrate and nodules at the lobule periphery, variable mucin deposition, and sometimes a lymphocytic vasculitis or vascuolopathy. It may be associated with systemic lupus erythematosus, but most often occurs in the absence of systemic disease. Although our patient has histopathologic findings consistent with lupus panniculitis, such as widespread hyalinization of fat lobules, the degree of scarring and widespread fibrosis is not characteristic of this disease process. This patient's bound down extremities, calcifications, and contractures of his hands and feet are also inconsistent with lupus panniculitis.

Disabling pansclerotic morphea (DPM) is rare form of morphea that involves all layers of the skin, extending through the dermis and subcutaneous tissues to involve muscle, tendon, and bone. It is distinguished from scleroderma by its lack of systemic involvement. Unlike other, more benign forms of morphea, DPM has an aggressive, mutilating course that results in severe functional and physiologic impairment. Similar to lesions seen in this patient, patients with DPM may develop painful ulcerations and contracture deformities. The onset of disabling pansclerotic morphea is usually before the age of 14, around the time this patient began to have his first symptoms. There have been reported cases of adult-onset disease that occurred suddenly with an explosive disabling course. Autoantibody profiles are often negative, as seen in this patient. Interestingly, there has been one case report of childhood DPM with associated hypogammaglobulinemia.

Treatment of DPM is a therapeutic dilemma. The usual course is relentless progression despite aggressive therapy. There has been limited success reported with penicillamine, antimalarials, corticosteroids, and cytotoxic agents, including methotrexate, cyclophosphamide, and azathioprine. Used together these agents appear to have much better efficacy in this disease. There have been some reports of limited improvement with UVA-1 phototherapy. One case report described softening of sclerotic plaques and healing of ulcerations with intravenous immunoglobulin infusion. In this patient, compliance has been an issue, and the use of numerous immunosuppressant medications has not slowed the disease progression.

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Presented by Jason Litak, MD, and Michael Tharp, MD
Department of Dermatology, RUSH University Medical Center

HISTORY OF PRESENT ILLNESS

This is a 57 year old woman with a history of familial common variable immunodeficiency (CVID). She was diagnosed when she was six years old, as her father and his offspring were the subject of the case report "Familial Hypogammaglobulinemia, Splenomegaly, and Leukopenia" (Kushner et al). Notably, her father suffered from superficial, punched-out neutrophilic leg ulcers as part of his disease.

Approximately five years ago our patient began developing nodules on her legs. Initially the nodules were asymptomatic, but over the past two years, lesions on her left leg became ulcerated and painful. In 12/06 cultures were positive for *Serratia marcescens* and *Pseudomonas aeruginosa*. She was treated with multiple courses of intravenous antibiotics, a wound vacuum assisted closure, and surgical debridement without resolution of the ulcers.

Biopsy of an ulcer on the left leg revealed a granulomatous lesion, and she developed granulomatous uveitis. The patient was initially diagnosed as having diffuse granulomatous disease associated with CVID. From 12/06 to 3/08 she received infliximab infusions, which were discontinued due to lack of efficacy.

The patient was referred to Rush for diagnostic considerations. The course and morphology of her ulcers strongly suggested pyoderma gangrenosum.

PAST MEDICAL HISTORY

Familial CVID
Non-Hodgkins Large Cell Lymphoma (1985)
Granulomatous Uveitis

MEDICATIONS

Intravenous immunoglobulin infusions:
20 gm per week
ertapenem
moxifloxacin
risedronate
acetaminophen/hydrocodone
eye drops

ALLERGIES

Sulfa, codeine, penicillin

FAMILY HISTORY

Father: CVID with recurrent superficial, punched-out neutrophilic leg ulcers. Fatal pneumonia at 42 years old.
Brother: CVID, died at 38 years old
Twin Sister: CVID

SOCIAL HISTORY

Patient is employed as a teacher and lives alone. She has no history of tobacco or alcohol abuse.

PHYSICAL EXAM
Well nourished, well developed woman in no acute distress.
Left leg with lateral (60x45mm) and posterolateral (115x90mm) punched-out ulcerations with fibrinous base. 2+ left dorsalis pedis pulse. Physical examination otherwise unremarkable.

HISTOPATHOLOGY
10/08 (edge of ulcer): Acanthotic epidermis with underlying fibrosing dermatitis with focal, dense, perivascular lymphoplasmacytic infiltrate and underlying focal fat necrosis. There are sparse neutrophils surrounding some of the deeper blood vessels. Gram, GMS, Fite, PAS stains were negative. The presence of a lymphoplasmacytic infiltrate with surrounding dermal fibrosis represents chronic inflammation in a longstanding ulcer. These histologic findings are not specific for, but may be seen in pyoderma gangrenosum.

LABORATORY RESULTS
The following were abnormal:
1/09: hematocrit 29.2 (35.0-45.0), absolute lymphocytes 442 (850-3900)

The following were within normal limits:
1/09: white blood cell count 6.4 (3.8-10.8), complete metabolic panel
IgG maintained at 1000 mg/dl (normal: 700-1600) over 40 years
1/09: Tissue culture (aerobic, anaerobic, mycobacteria, fungi): negative
3/09: Lower extremity ultrasound: negative for deep vein thrombosis or venous insufficiency.

DIAGNOSIS
Pyoderma Gangrenosum associated with familial combined variable immunodeficiency.

TREATMENT AND COURSE
In 12/08 the patient was started on dapsone 100 mg daily and prednisone 20mg daily. She noted less pain and healing of her ulcers, but two months after starting dapsone it was discontinued secondary to anemia. At that time mycophenolate mofetil was started and titrated up to 1000 mg BID and prednisone was continued at 20 mg daily. Alternative medications that have been considered include methotrexate and azathioprine, but given the neutropenia associated with her CVID, avoidance of bone marrow suppression was favored.

Two months after starting mycophenolate mofetil, the dose was decreased to 1500 mg daily due to worsening anemia. At that time the patient's primary care physician stopped prednisone and started moxifloxacin for presumed skin infection. The patient's ulcers have remained painful and non-healing. Future treatment with higher doses of intravenous immunoglobulin (2 gm/kg per month) is being considered.

DISCUSSION
Common variable immunodeficiency (CVID) is a heterogeneous group of immunological disorders of unknown etiology, characterized by low levels of serum immunoglobulins and impaired antibody responses. The prevalence is estimated at 1 in 25,000 persons. Most cases are sporadic, but at least 10 percent are familial with a predominance of autosomal dominant inheritance (as in our case). The most frequent clinical manifestation is an increased susceptibility to infections, usually in the respiratory and gastrointestinal tract. Patients with CVID can also develop a variety of autoimmune diseases, hematological malignancies (non-hodgkins lymphoma in this case), and inflammatory bowel disease.

Pyoderma gangrenosum (PG) refers to an ulcerative painful cutaneous eruption which is extremely persistent and resistant to therapy. The etiology of PG is unknown, and its

pathogenesis is poorly understood. Both a lymphocytic and neutrophilic infiltrate may be seen, and it is considered a “diagnosis of exclusion.”

Cutaneous granulomas and pyoderma gangrenosum have rarely been reported in associated with hypogammaglobulinemia and CVID. Both our patient and her father suffered from CVID and PG-like lesions. Given the immune abnormalities in CVID and its association with other autoimmune diseases, it is possible that CVID played a role in the development of PG in our patient and her father.

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CHICAGO DERMATOLOGICAL SOCIETY **CASE # 3**

Presented by William Huang, MD, and Michael Tharp, MD
Department of Dermatology, RUSH University Medical Center

HISTORY OF PRESENT ILLNESS

This 63 year-old white female initially presented for evaluation of “moles” and a total body skin exam after seeing her internist who recommended evaluation by dermatology. The patient’s health was stable and pertinent review of systems was negative. The patient also noted a “rash” on her back for years. Lesions were asymptomatic and she denied pruritus, or gastrointestinal, pulmonary, or cardiac complaints.

PAST MEDICAL HISTORY

Hypothyroidism
Depression
Psoriasis
Rosacea

MEDICATIONS

estradiol
fluoxetine
levothyroxine
fenofibrate
fexofenadine
levocetirizine
ranitidine

ALLERGIES

Trimethoprim/sulfamethoxazole

FAMILY HISTORY

Father – unknown skin cancer

SOCIAL HISTORY

Married
No tobacco, alcohol, or illicit drug use

PHYSICAL EXAM

Back/medial thighs/inframammary/axilla – confluent telangiectatic erythematous macules
Reddish-brown papules on the trunk and proximal extremities
Stroking of lesions produced a mild urticarial flare
Bilateral elbows – few small pink scaly plaques
No liver/spleen enlargement
No palpable lymphadenopathy

HISTOPATHOLOGY

Punch biopsy, right thigh: unremarkable epidermis with superficial perivascular mononuclear infiltrate. The presence of mast cells are found around the superficial vascular plexus. A Giemsa stain highlighted many mast cells.

LABORATORY RESULTS

The following were positive or abnormal:

Tryptase:	60.5	(normal 1.9-13.5)
24-hour urine histamine:	69.9	(normal 4.6-42.4)

D816V positive c-kit mutation

The following tests were negative or normal:
Basic Metabolic Panel
Liver Function Panel
Complete Blood Cell Count with Differential

RADIOLOGY

CT chest and abdomen: normal CT. No lymphadenopathy. No organomegaly or focal lesions seen.

DIAGNOSIS

Mastocytosis: Telangiectasia Macularis Eruptiva Perstans (TMEP)

TREATMENT AND COURSE

A work-up revealed no signs of systemic mastocytosis. She continues to be managed on a regimen of antihistamines and denies any systemic symptoms of mast cell disease. The patient recently underwent molecular studies to evaluate for a mutation in c-kit which was positive for a mutation at codon 816.

DISCUSSION

Mastocytosis represents a spectrum of clinical disorders characterized by the accumulation of mast cells in various tissues. In 1869 Nettleship and Tay first described the condition in a two-year old girl with hyperpigmented papules that spontaneously urticated. Mastocytsis can present at birth or develop at anytime into adulthood, and the disease is typically classified as childhood or adult onset. There is no reported gender or race predilection. Although the skin is most commonly affected, mast cell hyperplasia may occur in multiple organ systems with or without skin lesions. Various presentations of mastocytosis include diffuse cutaneous mastocytosis, mastocytomas, urticaria pigmentosa, telangiectasia macularis eruptiva pestans (TMEP), and systemic mastocytosis.

Telangiectasia macularis eruptiva perstans (TMEP) is rare form of mastocytosis in adults and children characterized by macules and patches of telangiectasias often without hyperpigmentation. Often patients with these lesions will have accompanying macules and papules of mastocytosis as is demonstrated in our patient. The formation of an urticarial wheal (Darier's sign) upon rubbing lesions is often absent in TMEP as compared to other forms of mastocytosis. The histology of TMEP is subtle demonstrating telangiectasias and a slightly increased number of mast cells limited to the upper third of the dermis. Often special stains such as toluidine blue, Giemsa and Leder, and monoclonal antibodies to tryptase can assist in identifying tissue mast cells which are elevated in lesional skin.

Mastocytosis is characterized by mast cell hyperplasia in the skin and other tissues. Mast cells are CD34+ cells derived from the bone marrow, and express the tyrosine kinase KIT (CD117), the protein product of the proto-oncogene c-kit. Activating mutations in the c-kit proto-oncogene leading to activation of KIT and subsequent mast cell development are felt to play a vital role in the pathogenesis of mastocytosis. In particular, mutations in codon 816 have been reported in patients with non-familial mastocytosis. Mutations in codon 560, 820, and 839 have also been reported. More recently, evidence suggests that certain treatments may be effective for some

adult mastocytosis patients depending on the location of the c-kit mutation. For example, imantinib mesylate appears to inhibit the growth of mast cells experiencing a mutation at the 560 locus but not at the 816 locus. In vitro studies from our laboratory suggest that rapamycin inhibits the proliferation of mast cells experiencing a mutation at the 816 locus but not at the 560 locus.

Patients with mastocytosis may be completely asymptomatic or may present with symptoms of mast cell mediator release such as pruritus, flushing, syncope, abdominal pain, diarrhea, and hypotension. No cure for mastocytosis exists, and treatment is directed at symptom control. Therapies include topical corticosteroids, oral antihistamines (H1 and H2), and PUVA. Patients can be followed with serum tryptase levels and/or urinary histamine and histamine metabolite levels to monitor their mast cell burden. Patients should be advised to avoid potential mast cell stimulators such as alcohol, NSAIDs, narcotics, and systemic anesthetics.

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Presented by Lauren Campbell, MD, and Mark Hoffman, MD
Department of Dermatology, RUSH University Medical Center

HISTORY OF PRESENT ILLNESS

This 77 year-old white woman presented with a six week history of a painful ulcer on her right lateral leg. The lesion initially appeared as a "dark spot" that converted into mildly tender erosion which gradually enlarged and became more painful. Three weeks prior to presentation at Rush she had been admitted to an outside hospital where the wound was debrided, after which she experienced an increase in ulcer size and pain. She had been prescribed a ten day course of doxycycline 100 mg BID and mometasone cream 0.1% BID.

She reported no previous history of similar lesions anywhere on her skin. She denied a history of venous or arterial thromboembolic events, or gastrointestinal, hematologic, or rheumatologic disease.

PAST MEDICAL HISTORY

Hypertension
Type II diabetes mellitus
Chronic right lower extremity swelling

MEDICATIONS

Doxycycline
Topical mometasone 0.1% cream
Tramadol
Metformin
Lisinopril
Hydrochlorothiazide

PHYSICAL EXAM

An 8 cm by 7 cm superficial dry hemorrhagic ulceration was present on the lateral distal right leg. Extending from and surrounding the ulcer was retiform purpura associated with minimal blanchable erythema. There were numerous prominent venous varicosities on the bilateral legs and thighs and trace pitting edema.

HISTOPATHOLOGY

Outside hospital 9/2008 (punch biopsy): ulcerated epidermis with underlying dense dermal neutrophilic infiltrate.
Rush 10/2008 punch biopsy: thin epidermis with underlying minimal inflammation with dilated superficial vasculature and abundant extravasated erythrocytes with fibrin deposition around endothelial cells.

LABORATORY RESULTS

The following studies were performed and were within normal limits or unremarkable:
Tissue cultures for acid-fast bacilli, bacteria, and fungus.
CBC with differential, glucose, sodium, blood urea nitrogen, creatinine, glomerular filtration rate, potassium, chloride, carbon dioxide, calcium. liver function tests, PT, PTT, antinuclear antibody (ANA), rheumatoid factor, C3/C4/CH50, cryoglobulins, immunofixation electrophoresis, anticardiolipin antibodies, anti B2GP1, lupus anticoagulant, protein S activity, antithrombin III, proteinase 3, myeloperoxidase, hepatitis A, B, and C serologies, thyroid stimulating hormone, urinalysis, glucose-6-pyruvate dehydrogenase level

The following studies were performed and were abnormal:
Erythrocyte sedimentation rate 37 (0-16 mm/hr)
C-reactive protein 4.3 (0-1 mg/dL)
Albumin 3.0 (3.5-5.5 gm/dL)

RADIOLOGY
Ankle to Brachial Index (ABI) studies: right = 1.20 with biphasic waveforms, left = 1.16 with biphasic waveforms. Right lower extremity greater saphenous and lesser saphenous vein reflux was identified.

DIAGNOSIS
Ulcerative retiform purpura consistent with possible atypical pyoderma gangrenosum versus vasculitic or vasculopathic process

TREATMENT AND COURSE
The patient was seen in consultation with Dr. Robert Kirsner at the University of Miami and was started on cyclosporine 100 mg TID (~ 4 mg / kg / day) and prednisone 60 mg daily. Her hypertension became more difficult to control, so cyclosporine was discontinued after three weeks and dapsone 50 mg daily was initiated. Within one month after initial consultation at Rush, the patient's ulcer had more than doubled in size and her pain had increased. Due to worsening of the clinical findings combined with a significant drop in hemoglobin levels over one month, dapsone was discontinued and the patient started mycophenolate mofetil 1 gram BID and trimethoprim/sulfamethoxasole one single strength tablet daily. Within one month the ulcer decreased in size and pain by approximately 25%. The prednisone has been tapered and discontinued and the mycophenolate mofetil dose has also been decreased. Her ulcer has continued to heal and become much less painful over the past month, with islands of re-epithelialization appearing throughout the lesion.

DISCUSSION
Chronic leg ulcers are open wounds, usually occurring below the knee, which do not heal within a period of 6 weeks. When evaluating a painful ulcer with a sudden onset in the context of retiform changes, the differential diagnosis can be extensive. Infectious causes of ulceration must be ruled out with tissue biopsy for special stains and culture. The differential diagnosis may be quite broad and includes vaso-occlusive disorders, vasculitic diseases, and pyoderma gangrenosum.

Pure occlusion usually occurs in the absence of early inflammation, and therefore erythema is often minimal or absent. Differential diagnostic possibilities that arise when considering occlusion include antiphospholipid antibodies, anti-coagulant necrosis, myeloproliferative diseases with thrombocytosis, cryoglobuinemia, infection with invasive organisms, livedoid vasculopathy, embolic phenomenon, and numerous other causes.

Inflammatory disorders that may result in mixed retiform and inflammatory purpura include including IgA vasculitis, the ANCA associated pauci-immune vasculitides, polyarteritis nodosa (PAN), and pyoderma gangrenosum (PG). Although PG can be associated with surrounding retiform change, this presentation is relatively uncommon. Early erythema (noted within the first 72 hours) is often a sign that the underlying process is inflammatory and not occlusive. This may be elucidated by using diascopy.

The most important and most interesting clinical question is, did the lesion's central necrosis and resultant ulceration occur from mounting initial inflammation, or conversely, did an early

occlusion lead to ischemia that induced an inflammatory response? The clues to discerning between these divergent pathophysiologic processes are usually found early on in a lesion's natural history, or during periods of dynamic disease activity or progression. It may be difficult to elucidate an etiology when examining a patient several weeks or months after a lesion develops and especially when the lesion appears clinically inert. This patient's ulcer has almost completely healed, due to either pharmacologic intervention or resolution of the occlusive event or inflammatory process.

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Presented by Melinda Simon, MD, and Victoria Barbosa, MD
Department of Dermatology, RUSH University Medical Center

HISTORY OF PRESENT ILLNESS

A 58-year-old white female presented with a one day history of painful red papules and vesicles on the right flank and abdomen in a T10/T11 dermatomal distribution. The eruption was preceded by five days of pain in the same area. The patient was diagnosed with herpes zoster. She was started on valacyclovir 1000 mg by mouth three times a day and gabapentin 100 mg by mouth twice daily. When the patient returned for follow up three weeks later, she presented with a right flank and abdominal protrusion that had been increasing in size for one week. The protrusion was not symptomatic and her pain secondary to the herpes zoster had resolved. The protuberance was mobile, nontender, soft and not indurated. Pink patches and thin scaling plaques were noted in the area affected, which were consistent with the resolving zoster.

PAST MEDICAL HISTORY

Achalasia status post laparoscopic correction
Incisional hernia status post laparoscopic correction
Tonsillectomy

MEDICATIONS

Multivitamin
Caltrate
Folic acid

ALLERGIES

NKDA

FAMILY HISTORY

Non-contributory

SOCIAL HISTORY

Alcohol occasionally. The patient works in advertising.

PHYSICAL EXAM

The patient had a right flank and abdominal protrusion. The protuberance was soft, mobile, nontender, and not indurated. Pink patches and thin scaling plaques were noted in the area affected, which were consistent with the resolving herpes zoster.

DIAGNOSIS

Pseudohernia secondary to herpes zoster

TREATMENT AND COURSE

The patient received valacyclovir 1000 mg three times daily for seven days with resolution of the herpes zoster. Gabapentin was started at 100 mg twice daily and increased to 300 mg three times daily for the associated pain. The total duration of gabapentin was two months. No treatment was needed for the pseudoherniation, which resolved completely 1.5 months after onset, with no residual protrusion or symptoms.

DISCUSSION

Herpes zoster is caused by reactivation of the varicella zoster virus, usually several decades after the initial infection. The virus remains dormant in the dorsal root ganglia, and upon reactivation leads to the classic cutaneous manifestations of a vesicular eruption and pain. Involvement of the anterior horn and nerve may also occur, and in this instance motor involvement in the form of segmental paresis and pseudoherniation may be noted[1, 2]. Thus, corresponding dermatomes and myotomes are involved[3, 4].

Pseudoherniation is a rare complication that may occur more frequently in elderly patients with a hematological malignancy. Clinical paresis is seen in 0.3% of zoster cases when they occur between T2 and LI segments[3]. Visceral neuropathy may also occur and symptoms can include urinary retention as well as constipation or obstipation[5].

Although the exact etiology of the pseudoherniation is unknown, it is characterized by degeneration and neuritis of the affected motor and sensory nerve roots[6]. It is thought that the virus spreads from the dorsal root ganglion to the anterior horn, leading to inflammation of the peripheral nerve or plexus, the root, or the medullary[3]. This inflammation then results in paresis from denervation, which can be seen with an electroneuromyography[3].

With each of the cases reported, a favorable prognosis has been seen with complete resolution in the patients within three months to one year[3]. It is important to recognize this condition in order to avoid unnecessary work up.

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CHICAGO DERMATOLOGICAL SOCIETY **CASE # 6**

Presented by William Huang, MD, and Arthur Rhodes, MD
Department of Dermatology, RUSH University Medical Center

HISTORY OF PRESENT ILLNESS

This 15 year-old Hispanic female initially presented for evaluation of a lesion of her left foot. She has a history of multiple vascular lesions of her gastrointestinal tract and skin, and had been seen elsewhere by pediatric gastroenterology and dermatology. This condition was noted first at age 4 years, and she continues to develop new lesions on her skin. Currently, she denies black or bloody stools, chest pain, headaches, seizures, fatigue, or shortness of breath. Review of systems was otherwise unremarkable.

PAST MEDICAL HISTORY

Anemia
Multiple vascular lesions of GI tract and skin
Gastrointestinal bleeding

MEDICATIONS

Iron supplements, famotidine, acetaminophen

ALLERGIES

None known

FAMILY HISTORY

Negative for skin cancer, vascular lesions, or other skin conditions

SOCIAL HISTORY

Lives with parents and four siblings.
No tobacco, ethanol, or illicit drug use.

PHYSICAL EXAM

Left medial plantar foot – 6 x 6 mm round blue plaque, 2 mm height, blanchable and compressible (excised 8/21/08)
Left plantar metatarsal-phalyngeal joint – 3 x 3 mm blue subcutaneous papule
Left third toe – 6 x 6 mm blue subcutaneous mass
Left forearm – 25 x 20 mm subcutaneous mass
Left neck – 10 x 10 mm subcutaneous mass
Right shoulder – 6 x 2 mm blue macule
Right upper abdomen - 2 x 2 mm blue macule

No liver/spleen enlargement
No palpable lymphadenopathy

HISTOPATHOLOGY

Excision, left medial plantar foot lesion: biopsy reveals a group of proliferating enlarged vascular spaces lined by thin endothelial cells

Jejunum – muscosa and muscularis show large ectatic vascular channels. Some areas show thickened vessel walls and phleboliths. The lesion is consistent with a vascular malformation.

LABORATORY RESULTS

The following were positive or abnormal:

Ferritin:	9	(normal 12-260)

The following tests were negative or normal:

RBC:	5.15	(normal 4.00-5.20)
HGB:	14.7	(normal 12.0-16.0)
HCT:	43.6	(normal 37.0-47.0)
PLT:	248	(normal 150-399)
WBC:	7.66	(normal 4.00-10.00)

RADIOLOGY

MRI left ankle – 13 x 3 x 4 cm multilobulated mass consistent with a vascular lesion
CT head, non-contrast – depression within left frontal lobe with soft tissue component, consistent with a vascular malformation
Tagged RBC scan – abnormal accumulation at multiple sites consistent with vascular lesions
Double ballon enteroscopy with fluoroscopy – multiple hemangiomas vs. vascular malformations in proximal jejunum and ileum
MRI left shoulder – multiple enhancing masses suggestive of "hemangiomas" (largest measuring 2.0 x 2.7 cm)
MRI left lower extremity – multiple enhancing masses suggestive of "hemangiomas" (largest 9.5 x 2.5 x 3.1 cm)

DIAGNOSIS

Blue Rubber Bleb Nevus Syndrome (Bean Syndrome)

TREATMENT AND COURSE

The patient had the lesion of her left medial plantar foot excised. The pathology of this lesion is consistent with a vascular malformation. She continues to be followed by pediatric gastroenterology for the ongoing issue gastrointestinal bleeding from these lesions.

DISCUSSION

Blue rubber bleb nevus syndrome, or Bean syndrome, is a rare sporadic disorder of venous malformations of the skin and internal viscera originally described by Gascoyen in 1860. Presenting at birth to early childhood, the disease is characterized by widely distributed cutaneous soft deep blue compressible masses that may or may not be associated with pain and sweating. Internal venous malformations may be present. These lesions number from a few to hundreds. Males and females are equally affected. Approximately 150 cases have been reported in the literature. The differential diagnosis includes familial cutaneous and mucosal venous malformation syndrome, familial glomangiomatosis, diffuse neonatal hemangiomatosis, and Maffuci syndrome.

The most common site of visceral involvement is the gastrointestinal tract, most commonly the small intestine, documented by upper endoscopy, colonoscopy, and magnetic resonance imaging (MRI). Case reports of other organ system involvement include the central nervous system, liver, kidney, bladder, heart, thyroid, and spleen. However, these latter sites of involvement are far less common than the gastrointestinal tract. The initial evaluation of blue rubber bleb nevus syndrome includes a full history and physical examination, complete blood cell count, stool for blood, and appropriate investigations of involved organ systems.

Patients with blue rubber bleb nevus syndrome are at risk for gastrointestinal hemorrhage and subsequent iron deficiency anemia, and should receive close surveillance by gastroenterology.

Patients require regular stool blood testing, and should be treated with iron supplementation, transfusions, endoscopic cauterization, or bowel resection as necessary. Significant complications of gastrointestinal involvement include intersucception, volvulus, internal hemorrhage, and infarction.

Cutaneous lesions of blue rubber bleb nevus syndrome can be treated for cosmesis or for pain, sweating, or functional impairment. Although CO2 and pulsed dye lasers have been described for the treatment of superficial venous malformations, surgical excision is often needed. Patients should be warned that lesions will often recur after surgical excision.

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CHICAGO DERMATOLOGICAL SOCIETY **CASE # 7**

Presented by Reshma Nair Haugen, MD, Clarence Brown, MD and Arthur Rhodes, MD
Department of Dermatology, RUSH University Medical Center

HISTORY OF PRESENT ILLNESS

A 13 year-old boy presented to our clinic for evaluation of lesions on his trunk and forehead initially noticed by his parents at 2 month of age, as well as three patches on his scalp with abnormal or no overlying hair. A nevus spilus on the patient's right arm was noted at age 12 years. There were no neurologic symptoms or overlying hyperhidrosis. He denied musculoskeletal, auditory, or visual difficulties.

PAST MEDICAL HISTORY

Growth hormone deficiency
Delayed bone age

MEDICATIONS

Somatropin

ALLERGIES

No known drug allergies

FAMILY HISTORY

Non-contributory

PHYSICAL EXAM

Left arm, chest, and back: light brown slightly raised papules coalescing into minimally raised linear and whorled plaques

Right temple extending onto eyebrow: yellow/tan linear minimally raised plaque

Left posterior auricular scalp and occipital scalp: faint yellow plaque with overlying sparse but wiry hair

Right extensor forearm: very light brown patch with numerous scattered medium brown macules

HISTOPATHOLOGY

Right back and right forehead: consistent with epidermal nevus

Left parietal scalp, anterior and posterior: consistent with nevus sebaceous of Jadassohn

LABORATORY RESULTS

Calcium 9.6 (8.5-10.3), Phosphorus 4.9 (2.4-4.7)

RADIOLOGY

MRI of the brain (4/06): No significant. Normal pituitary.
Hand and wrist for bone age (2/07): Bone age is greater than two standard deviations below chronological age.

DIAGNOSIS

Phacomatosis pigmentokeratotica

DISCUSSION

Phacomatosis pigmentokeratotica (PPK) is a rare syndrome characterized by organoid (epidermal) nevus with sebaceous differentiation, nevus spilus, and occasional extracutaneous abnormalities[1]. PPK has been grouped with the other epidermal nevus syndromes which differ in genetic origin but share the common feature of mosaicism[2]. There have been six different epidermal nevus syndromes described: Proteus syndrome, CHILD (congenital hemidysplasia with ichthyosiform erythroderma and limb defects) syndrome, nevus comedonicus syndrome, Becker nevus syndrome, Schimmelpenning syndrome and PPK[3,6]. The most important differential diagnosis is Schimmelpenning syndrome, a disorder that shares the organoid nevus with sebaceous differentiation, but includes eye abnormalities such as coloboma and lipodermoid of the conjunctivae that are absent in PPK[2,7].

Since Dr. Rudolf Happle first described PPK in 1996, there have been 32 reported cases. All of the cases observed thus far have been sporadic[6]. Of these 32 cases, there have been 5 cases without extracutaneous findings[1]. The most frequently associated extracutaneous alterations are neurologic (hemiatrophy with variable muscle weakness, dyesthesia, and hyperhidrosis in the region of the nevus spilus); ophthalmologic (internal strabismus and ptosis); and skeletal disorders (kyphosis and scoliosis)[4]. Associated growth hormone deficiency has not been described. At least six of the reported PPK cases have been associated with hypophosphatemic vitamin D-resistant rickets[5]. It is important to monitor patients for possible malignancies arising in the organoid nevi or nevi spili. To date, there have been 6 PPK patients who have developed basal cell carcinoma in a nevus sebaceous, and two cases of melanoma arising in the nevus spilus[1].

The genetic concept of twin spotting is thought to explain the combination of skin lesions seen in patients with PPK[1,3,5]. Twin spots consist of two genetically different clones of neighboring cells in a background of normal cells[8]. It is presumed that the organoid nevus and the nevus spilus are caused by recessive mutations in two genes that reside at different sites on the same chromosome[5]. If an embryo is a double heterozygote, somatic crossing-over can result in two populations of cells, each homozygous for one of two recessive mutations[5]. The two distinct mosaic spots are by the nature of the process always in close proximity to each other and thus are called 'twin spots'[6,8]. Different cell lines may migrate to different body segments during development and thus may have clinical presentations in different areas of the body[6].

There is no specific therapy for PPK. Potential methods for symptomatic improvement of the lesions include dermabrasion, excision or laser therapy[7]. Supportive care is required for associated neurologic, ophthalmologic, or auditory problems.

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CHICAGO DERMATOLOGICAL SOCIETY **CASE # 8**

Presented by Reshma Nair Haugen, MD, and Michael D. Tharp, MD
Department of Dermatology, RUSH University Medical Center

HISTORY OF PRESENT ILLNESS

This is a 59 year-old white male who has suffered from chronic urticaria since 2001. Individual hives last less than 24 hours and resolve without a bruise. There is associated pruritus and occasional burning. He has had episodes of angioedema. He denies significant arthralgias with the exception of some pain in his knees and hands.

PAST MEDICAL HISTORY

Hypertension, prostate cancer status post radical prostatectomy and Paget's disease of the left iliac crest

MEDICATIONS

See treatment and course

ALLERGIES

Sulfa, penicillin

FAMILY HISTORY

Non-contributory

SOCIAL HISTORY

The patient is a retired fireman.

PHYSICAL EXAM

Numerous urticarial wheals on the trunk, extremities, palms and feet

HISTOPATHOLOGY

7/02: polymorphonuclear predominant urticaria
3/04: lymphocyte predominant urticaria
10/07: lymphocyte predominant urticaria
1/09: lymphocyte predominant urticaria

LABORATORY RESULTS

The following were abnormal: serum IgE 507 (0-125), serum IgM 32 (35-213)

The following were within normal limits: comprehensive metabolic panel, complete blood count, ANA (<1:40), CRP, ESR,TSH, T4, thyroid peroxidase antibodies, thyroglobulin antibodies, G6PD, serum IgG and IgA, urinalysis, serum protein electrophoresis, C3, C4

DIAGNOSIS

Recalcitrant chronic idiopathic urticaria

TREATMENT AND COURSE

Prior to presentation at Rush, the patient tried individual courses of cetirizine, montelukast, ranitidine, doxepin and hydroxyzine without improvement. Systemic prednisone at doses of 30 mg or higher cleared his hives. Initially, the patient was started on combination antihistamines

including fexofenadine 180-360 mg daily and cetirizine 10-20 mg nightly. A 3 month trial gave the patient no relief.

A biopsy of lesional skin showed polymorphonuclear rich urticaria, and thus dapsone 50 mg was added to his antihistamine regimen. The dose of dapsone was steadily increased by 25 mg every 1-2 weeks until 125 mg. Dapsone provided the patient significant relief within 1 month of initiating therapy and continued to do so for 7 months. However, the patient began complaining of tingling in his palms and soles resulting in a decrease of the dapsone. Colchicine was added to dapsone and antihistamines without benefit. The dose of dapsone was increased again to 100 mg, but was discontinued because of increasing fatigue. The patient discontinued all medications and sought therapy with acupuncture. After a flare of hives, the patient was started again on dapsone 100 mg daily, colchicine 0.6 mg twice daily, and zileutin 600 mg four times daily. With this regimen, he was controlled with only pressure hives and was free of spontaneous urticaria for 5 months.

However, his hives returned and a repeat biopsy showed lymphocyte predominant urticaria. Cyclosporine was then added to his regimen of antihistamines, dapsone, and colchicine. After 7 months with no significant relief, azathioprine was added and cyclosporine was discontinued. Azathioprine, dapsone, colchicine and combined antihistamines provided the patient some relief for several months. Unfortunately, the patient was diagnosed with prostate cancer in August 2005 necessitating the discontinuation of azathioprine.

After his prostatectomy, trials of NB-UVB (1 month), plaquenil 200 mg BID (2 months), methotrexate 20 mg weekly (5 months), pentoxyfylline 400 mg TID (6 weeks) and sulfasalazine 400 mg QID (6 weeks) were tried in addition to antihistamines without success. A repeat biopsy again demonstrated a lymphocyte predominant urticaria. A 12 week course of etanercept 25 mg twice weekly in addition to dapsone, colchicine, and combination antihistamines also did not help. IVIG was considered, but not approved by the patient's insurance company. The patient is currently on montelukast, fexofenadine and diphenhydramine. We are awaiting approval from the patient's insurance company for a trial of omalizumab. Omalizumab, marketed under the trade name Xolair, is a recombinant monoclonal antibody that selectively binds to IgE and inhibits its binding to the high-affinity IgE receptor on mast cells and basophils.

DISCUSSION

Urticaria is quite common, affecting as many as 25% of all people at some time during their lives[1,2]. While the origin of acute urticaria is usually detectable, the etiology of chronic urticaria often remains elusive[1,2].

Approximately one-third of chronic urticaria patients have evidence of circulating IgG antibodies directed against either IgE or IgE receptors. These patients have been labeled as "autoimmune urticaria" [5,6]. They may have a greater likelihood of other autoimmune diseases. However, autoimmune and nonautoimmune urticaria are indistinguishable clinically and histologically, and their initial management often remains the same[6].

The management of chronic urticaria is often unsatisfactory, resulting in patient and physician frustration[3]. Some of the difficulty in treating urticaria stems from the confusion that surrounds the etiology of the disease[3]. The dermal mast cell and its mediators play a central role; however, lymphocytes and polymorphonuclear cells have also been implicated[1].

The ideal treatment for urticaria is identification and removal of its cause[1,2]. While this is often not possible, it is important to eliminate exacerbating factors such as alcohol, aspirin, opiates, heat and stress[1,2,6].

We believe that the optimal treatment of chronic idiopathic urticaria is best guided by the identification of the predominant cell type histologically. Urticaria in which a lymphocyte-predominant infiltrate is seen often responds to one or more H_1 antihistamines[1]. However, in polymorphonuclear predominate urticaria, the addition of agents that alter polymorphonuclear function, such as colchicine or dapsone, is often required[1]. Colchicine is an anti-inflammatory agent that has proven effective in treating a number of neutrophils related diseases. Its mechanism of action is multifaceted; it appears to limit the chemotactic and phagocytic activity of polymorphonuclear neutrophils and also suppresses leukocyte function[4]. Dapsone is a sulfone derivative with anti-neutrophils effects. It is postulated that dapsone impairs neutrophil chemotaxis and inhibits the function of neutrophils at the site of inflammation[4]. Because of numerous side effects, long-term use of systemic corticosteroids should be avoided; however, short-term corticosteroid therapy can be effective in controlling active disease while additional therapeutic agents are instituted[1].

We are presenting this patient with recalcitrant chronic urticaria for treatment suggestions. Interestingly, throughout his course, histologic examination has demonstrated both polymorphonuclear and lymphocyte predominant urticaria. Because of this, various treatment regimens have been tried. Unfortunately he continues to have daily hives.

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Unknown Case

Case # 9

Presented by Jason Litak, MD, and Vassilios Dimitropoulos, MD

CHICAGO DERMATOLOGICAL SOCIETY **CASE # 10**

Presented by Jason Litak, MD, and Vassilios Dimitropoulos, MD
Department of Dermatology, RUSH University Medical Center

HISTORY OF PRESENT ILLNESS

This patient is a 22 year-old Caucasian male who had a history of Leishmaniasis after a trip to Costa Rica in the summer of 2006. He was initially treated with IV pentivalent antimony for 3-4 weeks in the winter of 2006. Two years later (12/08) he presented to our clinic for routine skin exam, at which time activity in his old lesions was incidentally noted.

PAST MEDICAL HISTORY

Leishmaniasis (2006) treated with pentivalent antimony

ALLERGIES

clarithromycin

PHYSICAL EXAM

Over the right posterior-lateral and anterior-medial leg are approximately six sclerotic, slightly hyperpigmented plaques ranging in size from one to six centimeters. The largest plaque contained focal, slightly erythematous areas and one pustule. One of the smaller lesions was also erythematous.

HISTOPATHOLOGY

Necrotizing palisading granulomatous dermatitis.
A Giemsa stain failed to reveal any microorganisms.

LABORATORY RESULTS

Specimen was sent to Center for Disease Control for testing:
Microscopic exam of smear and cultures using fetal calf serum were negative.
PCR was positive for *Leishmania Panamensis*

DIAGNOSIS

Leishmaniasis recidiva cutis: recurrent leishmania after treatment with pentivalent antimony.

TREATMENT AND COURSE

The patient was referred to the Infectious Disease Department at Rush University Hospital for treatment.

DISCUSSION

Leishmaniasis is a disease caused by the protozoa of the *Leishmania* species, which is transmitted by the bite of a female sandfly (subfamily Phlebotominae). The Centers for Disease Control and Prevention (CDC) estimates that approximately 1.5 million new cases of cutaneous leishmaniasis and 500,000 cases of visceral leishmaniasis occur worldwide each year. Mucocutaneous leishmaniasis is less common. The estimated worldwide prevalence is 12 million with an annual incidence of 2 million cases. Incidence is highest in tropical and subtropical regions where conditions are favorable for sandflies. Leishmaniasis is found in some parts of 88 countries within Central America, South America, Africa, India, the Middle East, Asia, southern Europe, and the Mediterranean.

Infection with many different *Leishmania* species can lead to disease, and the clinical spectrum can be quite broad, from insignificant pustules to fatal systemic disease. Each case can be classified as being cutaneous, mucocutaneous, or visceral leishmaniasis. Cutaneous leishmaniasis constitutes 50 to 75 percent of all incident cases, and is the mildest form of the disease. Cutaneous leishmaniasis can further be classified as either Old World or New World depending on the geographic region of origin, with different subsets of Leishmania species responsible for each.

Localized cutaneous leishmaniasis typically begins as an inflammatory papule, which later progresses to an ulcer several weeks to months after sandfly bite inoculation on exposed skin. Lesions may have sporotrichotic lymphatic spread and usually heal spontaneously. Diagnosis of cutaneous leishmaniasis can be a challenge. Skin scrapings can be obtained from the base of an active ulcer, or a 4-mm biopsy specimen can be obtained from the edge of a suggestive lesion or ulcer. Direct visualization of the organism is diagnostic, but can be difficult in tissue sections. Giemsa, Brown-Hopps, Gram, or Leishman stains are all used to enhance *Leishmania* organisms. In vitro cultures of tissue are regularly obtained to aid in diagnosis and to help identify difficult *Leishmania* species. In vivo diagnosis of *Leishmania* organisms can also be achieved by inoculating clinical specimens into golden hamsters or certain highly susceptible mouse strains. Even when smear, histology, and culture results are combined, in 10 to 20 percent of cases, the parasite may not be detected. Polymerase chain reaction (PCR) is now routinely used in experienced laboratories as a rapid diagnostic technique. Species-specific PCR probes allow for rapid speciation in confirmed cases of leishmaniasis. Difficult cases should be referred to reference laboratories in the United States for rapid diagnosis and speciation, such as the Walter Reed Army Institute of Research Leishmania Diagnostic Laboratory or the Leishmania Diagnostic Laboratory at the US Centers for Disease Control and Prevention (CDC).

Treatment of cutaneous leishmaniasis differs according to the etiology and geographic location of the infection. For certain types of cutaneous leishmaniasis where the potential for mucosal spread is low, topical paromycin can be used. For more invasive lesions (eg, those failing to respond to topical treatment; metastatic spread to the lymph nodes; or large, disfiguring, and multiple skin lesions, especially those on the face, near mucosal surfaces, or near joints), sodium stibogluconate, meglumine antimonate, or pentamidine can be used. Infectious disease consultation can offer the most effective antiprotozoal regimen. Early lesions can also be treated with physical measures, such as local cryotherapy, heat therapy, electrocoagulation, or surgical removal.

Rare recurrence of previously cured cutaneous leishmaniasis lesions is known as leishmaniasis recidiva cutis (LRC). LRC appears after a variable period of time (months or years) in the same place, or very near the old scar, of a previous acute lesion that has appeared clinically healed. The pathogenesis of the reactivation of the disease is not clear, but retreatment is necessary.

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CHICAGO DERMATOLOGICAL SOCIETY **CASE # 11**

Presented by Melinda Simon, MD, and Vassilios Dimitropoulos, MD
Department of Dermatology, RUSH University Medical Center

HISTORY OF PRESENT ILLNESS

A 66-year-old African American male presented to our office with right buccal trichosis of one and half years duration. The patient originally noted a red sore on his buccal cheek that gradually grew in size over three months. He was evaluated and the lesion was biopsied, revealing a mucosal squamous cell carcinoma. He subsequently underwent excision and reconstruction per otolaryngology with a pedicle flap rotated from the right neck. Three days post-operative, the patient noticed a "hairy cheek." The density of hair continued to increase and disturbed his eating.

PAST MEDICAL HISTORY

Squamous cell carcinoma of buccal mucosa status post resection and repair
Hypertension
Atrial fibrillation
Hypercholesterolemia

MEDICATIONS

Diltiazem
Hydrochlorothiazide
Simvastatin
Atenolol
Coumadin
Enalapril

ALLERGIES

No known drug allergies

FAMILY HISTORY

Non-contributory

SOCIAL HISTORY

Seventy pack year history of tobacco use, with cessation for nine years
Thirty-five year history of alcohol abuse, with cessation for nine years
Retired factory worker

PHYSICAL EXAM

Right buccal mucosa revealed a medium brown patch with overlying trichosis

DIAGNOSIS

Buccal trichosis status post pedicle flap from the neck after excision of a mucosal squamous cell carcinoma

TREATMENT AND COURSE

Due to the fact that the patient's buccal trichosis interfered with his eating, it was decided a trial of laser treatment would be an appropriate therapeutic option. The patient received the alexandrite 755 nm laser for a total of five sessions over one and a half years with a greater than 80% reduction in the hair density. The fluence used was 20-25 J/cm^2 with spot sizes of

8mm and 15 mm. The energy was increased with subsequent sessions to reach the desire results. A total of 50-100 pulses were used for each session. The patient denied any pain with the procedure and is extremely satisfied with his results.

DISCUSSION

The alexandrite (755 nm) laser targets melanin and tattoo pigment. The Q-switched alexandrite 755 nm has thus been used to treat pigmented lesions such as nevi and lentigines as well as black, blue, green and brown tattoos. The laser can also be used to treat venulectasias and telangiectasias. Additionally, as demonstrated in our patient, the long-pulsed alexandrite 755 nm laser can be used for epilation with good success. Hair density reductions of 70-80% have been noted after an average of 3-5 treatments with fluences between 20-40 J/cm^2 [1-3].

Studies evaluating the efficacy of hair removal systems treating back or thigh hair showed no statistical difference between the alexandrite 755 nm, intense pulsed light with a red filter or a yellow filter, and the 810 nm diode laser[4]. When comparing the alexandrite 755 nm to the Nd-YAG 1064 nm, to a combination therapy of both lasers, there was no difference in hair reduction in the treatment of leg hair of 15 patients[5]. However, other studies have shown greater efficacy of the alexandrite 755 nm when compared to the Nd-YAG 1064 nm[6].

An extensive review of the literature revealed no data in the treatment of mucosal trichosis with laser therapy. One of the major complexities of this case, in addition to the surgical history and location, is the fact that the patient is Fitzpatrick skin type 5. Because of this, the patient is growing dark hair on a dark background. He also has grey and white hair dispersed throughout the patch. These factors make the procedure more difficult with decreased efficacy. Despite this, the patient had very good success in treating the trichosis. Electrolysis using an electric needle to the white hair was offered to the patient. The patient deferred this treatment stating he was extremely satisfied with his results thus far and was not interested in a perfectly hairless oral mucosa. Therefore, we report this case of successfully treating a patient with buccal trichosis with an alexandrite 755 nm laser status post resection and repair of squamous cell carcinoma.

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CHICAGO DERMATOLOGICAL SOCIETY **CASE # 12**

Presented by Tracy Campbell, MD, and Julie Moore, MD
Department of Dermatology, RUSH University Medical Center

HISTORY OF PRESENT ILLNESS

A 72 year-old Spanish speaking Hispanic female with a history of pemphigus vulgaris presented in July 2008 with a bleeding oral mucosa, multiple erosions on her back, and a jar containing a long wormlike rubbery tube. The patient had been noncompliant with her medications resulting in a flare of her disease. This severe flare necessitated an emergency room visit where her prednisone was increased to 60 mg daily. The prednisone temporarily alleviated the patient's discomfort until she vomited up a cast like structure.

PAST MEDICAL HISTORY

Diabetes mellitus, osteoporosis

MEDICATIONS

Mycophenolate mofetil
Predisone
Travoprost
Glimepride
Omeprazole
Naphazoline ophthalmic solution
Calcium 1000mg
Vitamin D 1000 units
Alendronate sodium

ALLERGIES

Penicillin

FAMILY HISTORY

Non-contribultory

SOCIAL HISTORY

Often travels to Mexico and stays for an extended period of time

PHYSICAL EXAM

July 2008: Multiple bleeding oral ulcerations on bilateral buccal mucosa, right lateral tongue, and a few erosions on her central back

HISTOPATHOLOGY

2002: Consistent with pemphigus vulgaris

LABORATORY RESULTS

2/04: Indirect immunofluorescence: pemphigus antibodies at titers higher than 1:160

DIAGNOSIS

Esophagitis dissecans superficialis secondary to pemphigus vulgaris

TREATMENT AND COURSE

The patient was diagnosed with pemphigus vulgaris in 2002 with direct and indirect immunoflourence at the University of Chicago. She presented to our clinic in August of 2007. Since that time she has been treated with mycophenolate mofetil 2-3 g daily, intermittent prednisone tapers and calcium and vitamin D supplements. Unfortunately due to the patient's noncompliance and frequent trips to Mexico her treatment has been challenging.

DISCUSSION

Esophagitis dissecans superficialis (EDS) is an exceedingly rare condition in which the patient sloughs the entire mucosal lining of the esophagus. The causes of EDS include trauma, medications (bisphosphonates, NSAIDS, potassium chloride), hot beverages, burns, chemical irritants, nasogastric intubation, and bullous dermatoses[5]. Dermatological diseases include Darier's diease, Hailey-Hailey disease, epidermolysis bullosa, bullous pemphigoid, and pemphigus vulgaris[2]. These bullous dermatoses can cause blistering, stricture, erosion, and sloughing of the esophagus. Esophageal involvement in pemphigus was first documented in 1935; Rosenberg noted EDS occurs predominantly in healthy patients without cutaneous manifestations[1].

Pemphigus vulgaris (PV) is an autoimmune blistering disease with antibodies targeted against desmoglein III (130 Kda component of desmosome)[1]. Desmoglein III is found in the skin and stratified squamous epithelia, oral mucosa and esophagus. Histologically PV exhibits acantholysis in the suprabasilar region with formation of the pathognmonic "tombstoning" of the basal cell layer along. Immunofluorescence of perilesional skin demonstrating IgG deposition in the intercellular spaces of the epidermis confirms the diagnosis[1,2]. Indirect immunofluorescence generally reveals circulating IgG auto-anti-intercellular space antibodies; titers tend to correlate with disease activity[1,2].

Oral involvement in PV is extremely common. It is the only manifestation in 50% patients, and in 70% of cases it is the first site to be involved[1]. Usually the patient complains dysphagia and odynophagia when esophageal involvement is present[2]. In a study of the upper gastrointestinal tract in 40 PV patients by esophago-gastro-duodenoscopy (EGD) significant involvement of oral (87%), esophageal (76%), gastric (52%), and duodenal mucosa (20%) was observed[6].

The esophageal cast is grossly normal-appearing and free of necrotic foci or ulcerations[2]. Since the separation is suprabasilar, the cast itself consists only of mucosal epithelium. Speculation suggests that the cast is sloughed from distal to proximal end so that gradual re-epithelialization of the esophageal lining may be completed before the cast is extruded[1,2]. This is hypothesized because of the patient's rapid and complete recovery. Treatment for this entity is full bowel rest, steroids if needed, and immunosuppressive agents[1,2].

In conclusion, it is important to recognize that EDS occurs predominantly in healthy patients without cutaneous disease. Although oral and esophageal involvement is a known complication of PV, this is only the fourth case recorded in the medical literature of pemphigus vulgaris associated with esophagitis dissecans superficialis.

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CHICAGO DERMATOLOGICAL SOCIETY **CASE # 13**

Presented by William Huang, MD, Victoria Barbosa, MD, and Clarence Brown, MD
Department of Dermatology, RUSH University Medical Center

HISTORY OF PRESENT ILLNESS

This 61 year-old female initially presented approximately one and a half years ago with a new bleeding lesion on her left lower leg which histologically was consistent with a pyogenic granuloma. She presented about a year later with a new "growth" on her right lateral lower leg clinically resembling another pyogenic granuloma. The lesion was biopsied; however, the pathology was consistent with Kaposi's sarcoma with positive immunostaining for human herpesvirus 8 (HHV-8). The patient and her primary care physician were immediately notified, and per her primary care physician, the patient has had known Kaposi's sarcoma for the past three years treated with radiation and chemotherapy. The patient had several violaceous nodules on her bilateral lower legs. The patient was advised to follow-up with her oncologist.

More recently the patient presented with a several week history of a rapidly growing lesion on her right posterior lower leg with a base on erythema. The lesion bled occasionally but was not painful or pruritic. She was placed on ciprofloxacin, and biopsied at her follow-up appointment. The patient denied any constitutional symptoms and review of systems was unremarkable.

PAST MEDICAL HISTORY

Diabetes mellitus
Gastroesophageal reflux disease
Pyogenic granuloma
Kaposi's sarcoma

MEDICATIONS

Ibuprofen, rosiglitazone

ALLERGIES

No known drug allergies

FAMILY HISTORY

Negative for skin cancer, melanoma, or chronic skin disease

SOCIAL HISTORY

Married
No tobacco, alcohol, or illicit drug use

PHYSICAL EXAM

Right posterior leg ~ 30 mm diameter erythematous, bleeding tumor with surrounding erythema

HISTOPATHOLOGY

Right posterior leg – multifocal areas of hemorrhage in the dermis. At higher magnification the dermal proliferation consists of spindle cells with surrounding lymphocytes and plasma cells. HHV-8 staining was ordered and is currently pending.

LABORATORY RESULTS

The following tests were negative or normal:
Complete blood cell count

Comprehensive metabolic panel
Human Immunodeficiency Virus screen

DIAGNOSIS
Classic Type Kaposi's Sarcoma

TREATMENT AND COURSE
The patient underwent an excision of her lesion which was consistent with Kaposi's sarcoma. HHV-8 staining was ordered and is currently pending. The patient is to follow-up in the dermatology clinic and also with her oncologist.

DISCUSSION
Kaposi's sarcoma (KS) is a common neoplasm of endothelial cells associated with human herpesvirus 8 (HHV-8). First described in 1872 by Moritz Kaposi in five men with an unusual cutaneous sarcoma, Kaposi's sarcoma received very little attention until it became epidemic among HIV positive patients and recognized as a sign of AIDS. The four clinical variants of Kaposi's sarcoma include classic KS, African endemic KS, KS in iatrogenically immunosuppressed patients, and AIDS related epidemic KS.

Kaposi's sarcoma typically affects the skin and variably presents with pink patches, blue-violet to black nodules, and polyps depending on the clinical type or stage. Human herpesvirus 8 (HHV-8) is considered the inductive agent of all clinical variants of Kaposi's sarcoma. Patients with Kaposi's sarcoma frequently have involvement of internal viscera especially the gastrointestinal tract, lymph nodes, and lung. Any patient with KS should be evaluated for systemic disease.

The differential diagnosis of Kaposi's sarcoma depends on the presentation of the lesion. Diagnosis is confirmed by biopsies demonstrating characteristic small angulated vessels lined by endothelial cells separating collagen bundles in a sieve-like pattern. Immunostaining with human herpesvirus 8 is a highly sensitive and specific marker and is helpful in confirming the diagnosis.

The treatment of Kaposi's sarcoma is often unsatisfactory as recurrence rates are high and completely cure impossible. Local therapies for isolated skin lesions include surgical excision, cryotherapy, and laser surgery. Radiation therapy is also an option for localized Kaposi's sarcoma. Patients with widespread or rapidly progressive Kaposi's sarcoma should be evaluated for consideration for systemic chemotherapy.

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Presented by Tracy Campbell, MD, and Victoria Barbosa, MD
Department of Dermatology, RUSH University Medical Center

HISTORY OF PRESENT ILLNESS

The patient is a 33 year-old female who complains of a one year history of lesions on her face diagnosed as acne in the past. She states that she has tried Proactiv© and other over the counter remedies without resolution of her facial eruption. The patient has noticed a few more papules concentrated on her central face and no lesions on her back or chest. The patient first noticed new lesions 4 years prior and the appearance of light papules on her stomach, collarbone, chest, and upper arms. These lesions are asymptomatic.

PAST MEDICAL HISTORY

Nephrolithiasis (multiple) 1990, 1991, 1992, 1993, 1994
Partial parathyroidectomy surgeries 1994, 2006, 2008
Positive MENIN gene mutation 2006
Depression

MEDICATIONS

Duloxetine
Multivitamins

ALLERGIES

No known drug allergies

FAMILY HISTORY

Father's side of the family has an extensive history of MEN type 1.
All paternal aunts and half sister are positive for the MENIN gene and have undergone parathyroidectomies.
Paternal grandfather had surgery to remove a pancreatic tumor; patient does not known whether it was benign or malignant. The patient's 22 year-old half sister underwent removal of a non-malignant pancreatic tumor this year.
The patient has 1 adopted daughter.

SOCIAL HISTORY

Former smoker 1993-1998
Graduate student in interior designe

PHYSICAL EXAM

On the dorsal nose, right nasal ala, and upper lip there are numerous firm, flesh colored papules approximately 1-3 mm in size. Multiple smaller firm flesh colored papules are seen on the central face. There are no comedones or inflammatory papules noted. Three 2-10 mm hypopigmented firm papules on the abdomen, collarbone, and chest are noted.

HISTOPATHOLOGY

Nasal bridge, right nasal ala, and right lower lip lesions are all consistent with angiofibromas.

LABORATORY RESULTS

2006: MENIN gene positive
2009: Calcium, parathyroid hormone, and prolactin levels within normal limits

RADIOLOGY
2/2009 Dual Energy X-ray Absortiometry Scan (DEXA Scan): T score hip -1.5, spine T score -1.2, other T score -1.0 (normal bone density: higher than -1.0).
4/2008 Computed tomography scan (CT scan) abdomen/pelvis: Normal anatomy with no gross pancreatic tumors noted.

DIAGNOSIS
Multiple Endocrine Neoplasia (MEN) Type 1

TREATMENT AND COURSE
During the patient's visit a diagnosis of tuberous sclerosis was initially entertained. Upon further questioning, particularly about family history, it became apparent that the patient had MEN type 1. The patient was educated on the cutaneous manifestations of her genetic disease and three central facial papules were biopsied to confirm the diagnosis of angiofibromas. The patient was offered a biopsy of what appeared to be collagenomas that on her chest and abdomen, but she declined. The patient is monitored by her endocrinologist with calcium, parathyroid hormone and prolactin levels every six months, a DEXA scan every 2 years, and a CT scan of the abdomen and pelvis every 3 years. She follows up at Rush every six months for full skin exams due to her history of dysplastic nevi.

DISCUSSION
Multiple Endocrine Neoplasia (MEN) is a group of disorders with an autosomal dominant inheritance. They are characterized by the presence of a neoplasia or hyperplasia in 2 or more endocrine organs, often with associated mucoutaneous findings. MEN type 1, also referred to as Wermer syndrome is an autosomal dominant disease with a genetic mutation in the MENIN (a nuclear protein) gene. Mucocuaneous features include features very similar to tuberous sclerosis including facial angiofibromas, collagenomas, lipomas and confetti-like hypopigmented macules. Systemic features include pituitary tumors which can result in Cushing syndrome, acromegaly, or excess lactation due to a prolactinoma. The parathyroid is usually affected either by hyperplasia, adenoma, or manifests as hyperparapthyroidism, as in our patient. The pancreas can also be involved with islet cell hyperplasia, adenoma, or carcinoma. Rarely carcinoid tumors and adrenal cortical tumors can be associated with this disease as well.

In a recent study, the frequency of facial angiofibromas in Japanese patients with familial MEN 1 was examined.[5] Angiofibromas were identified in 43% (12/28) of the subjects. This frequency was significantly lower than that of Caucasian patients, but nonetheless almost equaled those of pituitary tumors and pancreas endocrine tumors.[5] Angiofibromas should be considered as one of major manifestations in MEN 1 regardless of patients' ethnic origin, and clinicians should pay careful attention to the cutaneous lesions in patients with endocrine tumors.[5]

Darling et al studied 32 individuals with previously diagnosed MEN1, none of whom had relatives with tuberous sclerosis.[3] Twenty-eight patients had multiple angiofibromas, with 16 patients having 5 or more. Collagenomas were observed in 23 patients, café au lait macules in 12 patients, lipomas in 11 patients, confetti-like hypopigmentation in 2 patients, and multiple gingival papules in 2 patients.[3]

Asgharian et al prospectively studied various criteria for MEN1 in 110 consecutive patients with gastrinomas, with or without MEN1.[4] Angiofibromas and collagenomas were more frequent in MEN1 patients (64% vs 8% and 62% vs 5%, $P < 0.00001$). Angiofibromas or collagenomas (single or multiple) had a 50-65% sensitivity for MEN1 and a 92-100% specificity. The combination criterion of multiple angiofibromas (more than three) and any collagenomas had the highest sensitivity (75%) and specificity (95%). This criterion has greater sensitivity than pituitary

or adrenal disease and is comparable to hyperparathyroidism in some studies of patients with MEN1 with gastrinoma. This criterion should have sufficient sensitivity/specificity to be clinically useful.[4] These findings were highly significant and confirmed that these lesions are a manifestation of the MEN1 syndrome.[4]

MEN 2A, also called Sipple syndrome and PTC syndrome has a mutation in the RET protein which is a tyrosine kinase receptor. This disease's cutaneous manifestations include lichen amyloidosis, nostalgia paresthetica, and macular amyloidosis. These patients are at risk for parathyroid adenomas, medullary thyroid cancer and hyperplasia, and adrenal tumors (pheochromocytoma).

MEN 2B also called MEN type 3 or multiple mucosal neuroma syndrome, Wagenmann-Froboese Syndrome also has a mutation in the RET protein. The mucocutaneous features include multiple mucosal neuromas especially on the eyelid margin, lips, and tongue, and prominent lips, café au lait macules, circumoral lentingines, and a marfinoid habitus. These patients are at risk for medullary thyroid cancer, adrenal tumors (pheochromocytoma), and neuromatosis especially in the gastrointestinal tract.

We present this case to illustrate the similar cutaneous manifestations in tuberous sclerosis and MEN I.

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Presented by Jason Litak, MD, and Michael Tharp, MD
Department of Dermatology, RUSH University Medical Center

HISTORY OF PRESENT ILLNESS

A 22 year-old African American man presented with a history of severe ichthyosis since birth. He was born with a collodion membrane and has carried the clinical diagnosis of lamellar ichthyosis since childhood. He lacks the ability to sweat and becomes "over-heated" easily, which interferes with physical activity and employment. He also has noticed frontal hair loss and dry eyes. His only consistent treatment has been the application of petroleum jelly to his entire body daily.

PAST MEDICAL HISTORY

Hypertension
Gonorrhea urethritis (2/09)

MEDICATIONS

Petroleum jelly

ALLERGIES

No known drug allergies

FAMILY HISTORY

No family history of ichthyosis

PHYSICAL EXAM

Generalized large, dark, plate-like scale over entire skin surface
Frontal scarring alopecia
Bilateral ectropion

HISTOPATHOLOGY

Orthokeratotic hyperkeratosis and acanthosis

DIAGNOSIS

Lamellar Ichthyosis

TREATMENT AND COURSE

This patient presented to our clinic in February 2009. It had been many years since he had last seen a dermatologist. We have discussed the use of acitretin therapy, but he has been unreliable with his appointments and has been hesitant to initiate any treatment for his ichthyosis.

DISCUSSION

Lamellar Ichthyosis (LI) is a severe skin disorder involving the process of cornification and desquamation. It is recognized as part of a continuum along with congenital ichthyosiform erythroderma (CIE) and intermediate phenotypes. Lamellar ichthyosis has an estimated worldwide prevalence of 1 in 200,000 to 300,000 live births.

Lamellar Ichthyosis is genetically heterogeneous and in most families is inherited as an autosomal recessive trait, but autosomal dominant transmission has been observed. This

disorder has been mapped to at least three genetic loci, including the transglutaminase-1 (TGM1) gene on chromosome 14q12 (LI-1), the ATP-binding cassette transporter gene (ABCA12) on chromosome 2q35 (LI-2), and the cytochrome P450 CYP4F22 on chromosome 19p13.12. The majority of LI cases are caused by a deficiency of transglutaminase-1 due to deleterious mutations in both copies of the TGM1 gene. Transglutaminase-1 facilitates the formation of the insoluble protein envelope by catalyzing the cross-linking of numerous structural proteins in the upper layers of the epidermis (e.g. involucrin, small proline-rich proteins, loricrin, keratin intermediate filaments and desmosomal proteins) as well as attachment to the lipid envelope.

Lamellar Ichthyosis usually presents at birth with erythroderma and an overlying collodion membrane. During the first few weeks of life, the collodion membrane is replaced by large plate-like scales that form a “mosaic” or “bark-like” pattern with minimal to no erythema. These plate-like scales persist throughout life. Tautness of facial skin commonly results in ectropion and eclabium. Severe ectropion may lead to madarosis, conjunctivitis, and incomplete lid closure with ensuing keratitis. Traction and compression exerted by the taut skin causes scarring alopecia, especially at the periphery of the scalp. Intraepidermal constriction of sweat ducts often results in severe heat intolerance.

In the neonatal period, there is considerable clinical overlap with other congenital ichthyoses that present with a collodion membrane, such as CIE, self-healing collodion, and Sjogren Larssen syndrome. Later in life LI becomes more distinctive with its large, dark, plate-like scales without erythema and an associated ectropion. Congenital ichthyosiform erythroderma is clinically distinguished by the presence of marked erythroderma and small, white scales. Nevertheless, there is considerable variability and overlap between LI and CIE, and intermediate phenotypes do exist.

The histopathology of LI is not diagnostic. Massive orthokeratotic hyperkeratosis covers an acanthotic, sometimes psoriasiform or papillomatous, epidermis. Measurement of transglutaminase-1 levels and activity can be accomplished through cell culture, immunostaining, and expression/activity assays. DNA-based molecular genetic testing is commercially available for detecting pathogenic mutations in TGM1 and ABCA12. In families with known mutations, prenatal diagnosis can be performed through chorionic villus sampling or amniocentesis.

Any collodion baby should be treated and monitored carefully. After infancy, ichthyosis may be managed with topical therapies such as vitamin D3 derivatives, tazarotene, and special formulations of lactic acid and propylene glycol in a lipophilic cream base. Special care must be taken during treatment because of the propensity to skin irritation. Heat intolerance can be managed by frequent moistening of the skin with water, using air conditioners and humidifiers, and avoiding strenuous activity in hot climates.

The disease severity of LI may necessitate the use of oral retinoids, which are started slowly and titrated depending on response. Acitretin can be very effective in alleviating hyperkeratosis and scaling. Recent studies have shown that retinoic acid metabolism blocking agents (RAMBA’s) such as liarozole are also effective.

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CHICAGO DERMATOLOGICAL SOCIETY **CASE # 16**

Presented by William Huang, MD, and Arthur Rhodes, MD
Department of Dermatology, RUSH University Medical Center

Case A

HISTORY OF PRESENT ILLNESS
This 2 year-old Hispanic male presented for evaluation of hypopigmented lesions on the right anterior chest, right arm, and right leg noted since age 1 month. Lesions are asymptomatic and have not been previously treated. The patient is otherwise healthy and developing normally.

PAST MEDICAL HISTORY
Non-contributory

MEDICATIONS
None

ALLERGIES
No known drug allergies

FAMILY HISTORY
No history of consanguinity

SOCIAL HISTORY
Lives with both parents

PHYSICAL EXAM
Right anterior chest/right arm/right leg – linear and whorled hypopigmented patches

TREATMENT AND COURSE
The patient was referred to pediatric neurology, ophthalmology, orthopedics, and dentistry. The patient is to follow-up in clinic once systemic evaluation has been completed.

Case B

HISTORY OF PRESENT ILLNESS
This 16 month-old African American male presented for evaluation of hypopigmented lesions on his right cheek and right neck noted at 1 month of age. Lesions are asymptomatic and have not been previously treated. The patient is otherwise healthy and developing normally.

PAST MEDICAL HISTORY
Non-contributory

MEDICATIONS
None

ALLERGIES
No known drug allergies

FAMILY HISTORY
No history of consanguinity

SOCIAL HISTORY
Lives with both parents

PHYSICAL EXAM
Right preauricular cheek/right lateral neck – linear and whorled hypopigmented patches

TREATMENT AND COURSE
The patient and family were reassured. The patient is being followed by his primary pediatrician. The patient is developing normally and meeting all milestones. He is to follow-up in dermatology clinic.

Case C

HISTORY OF PRESENT ILLNESS
This 6 month-old Hispanic female presented for evaluation of diffuse “light colored” lesions since birth. Lesions are asymptomatic and have not been previously treated. The patient is otherwise healthy and developing normally.

PAST MEDICAL HISTORY
Non-contributory

MEDICATIONS
None

ALLERGIES
No known drug allergies

FAMILY HISTORY
No history of consanguinity

SOCIAL HISTORY
Lives with both parents

PHYSICAL EXAM
Abdomen/back/legs/arms – hypopigmented patches in the lines of Blaschko crossing the midline

TREATMENT AND COURSE
The patient and family were reassured. The patient is being followed by her primary pediatrician. She is developing normally and meeting all milestones. She is to follow-up in the dermatology clinic.

DIAGNOSIS
Pigmentary mosaicism

DISCUSSION
Pigmentary mosaicism is a descriptive term of hypopigmentation or hyperpigmentation in a whorled or streaked pattern following lines of Blaschko, which may be associated with

neurological deficits, seizures, or abnormalities of other organ systems. Pigmentary mosaicism encompasses hypomelanosis of Ito where skin lesions are hypopigmented and linear and whorled nevoid hypermelanosis where the skin lesions are hyperpigmented. First described as a purely cutaneous disorder, further studies have reported an association with extracutaneous manifestations in 33% to 94% of cases. Present at birth or during the early neonatal period, patients have whorled, linear, or patchy hypopigmented or hyperpigmented lesions typically on the trunk and limbs in a variety of configurations. These lesions may occur unilaterally or bilaterally, and are asymptomatic. The differential diagnosis includes nevus depigmentosus and incontinentia pigmenti.

Pigmentary mosaicism appears to occur in a sporadic manner in all ethnicities with males and females equally affected. Reports of population prevalence from several studies range from 1 in 8,000 to 1 in 82,000. The condition is felt to reflect genetic mosaicism with a wide variety of chromosomal abnormalities having been reported including structural defects (i.e. chromosomal deletions and translocations), polyploidies, and aneuploidies. Any chromosome can be affected including autosomal and sex chromosomes leading to a heterogeneity of clinical phenotypes. Taibjee et al. reported 88% of cases of pigmentary mosaicism had chromosomal abnormalities which overlapped with one or more known pigmentary genes explaining why patients all share pigmentary changes in lines of Blaschko despite differences in their extracutaneous disease.

Rather than a diagnosis, many authors feel that pigmentary mosaicism is better characterized as a nonspecific phenotype or sign of genetic mosaicism. Besides their cutaneous lesions, patients may have systemic involvement with extracutaneous manifestations. Affected organ systems include central nervous system, eye, musculoskeletal, and cardiac. Current recommendations for evaluation of patients with hypopigmentation or hyperpigmentation in the lines of Blaschko include a full history and physical examination seeking extracutaneous abnormalities to direct further investigations. Pediatricians should be notified of the association of pigmentary mosaicism with systemic involvement, and asymptomatic patients should be evaluated on an annual basis, or sooner for signs or symptoms. Parents with pigmentary mosaicism and parents of children with this condition should be reassured of its non-heritable nature.

Histopathologic features of pigmentary mosaicism are nonspecific and biopsy of suspected lesions is not necessary to make the diagnosis. The pigmentary abnormalities in pigmentary mosaicism tend to remain constant, although long term follow-up studies are lacking. Currently, there are no special recommendations for the treatment of skin lesions and no precautions regarding sun exposure or the application of topical medications.

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Presented by Reshma Nair Haugen, MD, and Arthur Rhodes, MD
Department of Dermatology, RUSH University Medical Center

HISTORY OF PRESENT ILLNESS

A 13 year-old African-American female presented for recent worsening of lesions in her axilla, groin and neck that had been present since one year of age. These lesions are occasionally pruritic. Previous treatments have included urea 40% cream, 12% lactic acid, clindamycin lotion, mometasone ointment, benzoyl peroxide 2.5-5 % gel, tretinoin 0.05% cream, and 10% liquor carbonis detergens in aquaphor.

PAST MEDICAL HISTORY

Severe insulin resistance
Hyperandrogenemia

MEDICATIONS

As above

ALLERGIES

No known allergies

FAMILY HISTORY

No family history of acanthosis nigricans, diabetes, thyroid disease, pernicious anemia, Addison's disease, lupus or scleroderma

PHYSICAL EXAM

Inferior nares, columella, nasal alae, anterior neck, bilateral conchal bowl, bilateral axilla, bilateral inguinal folds and labia majora: well-demarcated dark brown velvety and hyperkeratotic plaques

HISTOPATHOLOGY

Left axilla and neck: epidermal papillomatosis with overlying marked hyperparakeratosis, with focal areas of hypogranulosis

LABORATORY RESULTS

The following tests were abnormal: insulin level 329 units (2-17), free testosterone 26.6 units (0.95-4.3), total testosterone 140 units (1-80), sex hormone binding globulin 13 units (18-114)

The following tests were normal: TSH, dihydrotestosterone, androstenedione, DHEAS, 17-OH progesterone, BUN, creatinine, liver function tests, triglycerides, cholesterol, insulin-like growth factor, luteinizing hormone, follicle-stimulating hormone, prolactin, urinalysis

RADIOLOGY

Pelvic ultrasound: Normal pelvic ultrasound. No sonographic adrenal or ovarian abnormalities.

DIAGNOSIS

Atypical acanthosis nigricans in the setting of insulin resistance and hyperandrogenemia, consistent with HAIR-AN syndrome

TREATMENT AND COURSE

Multiple treatment regimens were attempted. The patient is currently using urea 40% cream to her axilla and ears twice daily, benzoyl peroxide 5% gel to her neck, and petrolatum USP to her groin and nasal alae. This therapy has thinned out her plaques considerably. The patient is currently in the midst of an ongoing evaluation for specific insulin receptor mutations or antibodies against her insulin receptors.

DISCUSSION

Acanthosis nigricans (AN) are symmetric lesions characterized by hyperpigmented, velvety cutaneous thickening that can occur on any part of the body, but characteristically affects the axillae, neck, groin, antecubital and popliteal surfaces, and umbilicus. The lips and mucous membrane of the mouth, upper respiratory tract, and external genitalia are affected in unusual cases[2]. In nondiabetic obese hirsuite hyperandrogenic women, the vulva was the most likely site of involvement[1]. Older lesions turn to verrucous or papillomatous plaques[2].

Acanthosis nigricans is thought to be caused by insulin resistance. The mechanisms are not entirely defined. It is thought that severe insulin resistance produces compensatory hyperinsulinemia[2]. Excessive amounts of insulin interact with insulin-like growth factor-1 receptors (IGFR) in peripheral tissues[2]. Human keratinocytes and fibroblasts have IGFR on their surface, and thus increased binding of insulin to IGFR boosts their proliferation.

HAIR-AN syndrome is an acronym for hyperandrogenism, insulin resistance and acanthosis nigricans[3]. Insulin resistance is categorized as type A or B. Type A occurs when there are mutations of insulin receptors. These mutations impair insulin function by reducing the receptor's ability to bind insulin or undergo insulin-stimulated phosphorylation, thus diminishing the number of effective insulin receptors on the surface of target cells[1]. Patients with type A syndrome are usually black females who have the onset of AN in infancy or childhood[1]. The AN is usually generalized, with rapid progression during the peripubertal period and early reproductive years[1]. Children often have high plasma levels of testosterone. Some patients with type A insulin resistance have hirsuitism and polycystic ovaries[1]. In type B insulin resistance, there are autoantibodies against insulin receptors. Average age of onset is 39 years old[1]. Many of these patients have other autoimmune disorders, including systemic lupus erythematosus and scleroderma.

Treatment should be directed at the underlying problem. Weight loss and lifestyle changes are extremely important. There are various pharmacological approaches to improve insulin sensitivity and/or reduce hyperinsulinemia[2]. Metformin is a biguanide drug that suppresses endogenous glucose production by increasing both the peripheral response to insulin and the cellular glucose metabolism[2,3,4]. It can also reduce androgen blood levels and increase sex-hormone-binding globulin concentrations. Other antiandrogenic agents may also be used, including oral contraceptives, spironolactone, flutamide and finasteride[3].

Cholecalciferol (vitamin D_3) analogs increase keratinocyte differentiation while inhibiting their proliferation; thus, topical calcipotriene ointment may be an effective treatment[2,4]. Oral retinoids may also be of some benefit in these patients, but their effect is transient, and lesions reoccur when the medication is stopped[2,4].

Patients with extensive AN including HAIR-AN syndrome must be monitored for diabetes mellitus and coronary artery disease. Hyperinsulinemia itself has been labeled as an independent risk factor for cardiovascular disease[1].

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Presented by Tracy Campbell, MD, and Michael Tharp, MD
Department of Dermatology, RUSH University Medical Center

HISTORY OF PRESENT ILLNESS

This 54 year old white female with history of dermatomyositis was admitted to Rush Hospital for left leg erythema and pain. The patient noticed a "bruise like" discoloration 3 months prior to admission after she fell onto her shoe. She was admitted to an outside hospital as presumed cellulitis in February of 2009 and treated with intravenous antibiotics without improvement. She was then readmitted in March 2009 and received vancomycin with some improvement. She was discharged on sulfamethoxazole/trimethoprim and dicloxacillin. Despite antibiotic therapy the patient noted increasing erythema extending down her lower posterior leg, and was readmitted 2 weeks later and given intravenous clindamycin which did not improve the redness. We were consulted to evaluate the patient for lower leg cellulitis. The patient denied pain, fever, chills, weight loss, night sweats or pulmonary symptoms. She only noted slight muscle weakness which she contributed to her dermatomyositis. Two biopsies were obtained for histopathologic evaluation and culture.

PAST MEDICAL HISTORY

Dermatomyositis 2003

MEDICATIONS

methotrexate 30 mg weekly
hydrochlorothiazide
potassium chloride
metoprolol succinate
olmesartan medoxomil
folic acid
prednisone 15 mg daily

ALLERGIES

No known drug allergies

FAMILY HISTORY

Non-contributory

SOCIAL HISTORY

Non-contributory

PHYSICAL EXAM

Minimally blanching erythema on the left posterior leg extending downward towards the knee. No left inguinal lymphadenopathy. Physical exam otherwise unremarkable.

HISTOPATHOLOGY

3/27/2009: Left leg punch biopsy: Interface dermatitis with underlying minimal perivascular inflammation, compatible with dermatomyositis. AFB, Fite, GMS stains negative for organisms.

LABORATORY RESULTS

CRP 48.9 (0-8 mg/l), ESR 36 (0-27mm/hr)
WBC 7 (4-10), Hemaglobin 10.7 (12-16), Hematocrit 35.4 (37-47), Platelets 323 (150-400)

Tissue culture biopsy: AFB Smear – Negative
DNA probe assay from tissue smear: Mycobacterium Avium Complex (MAC)

RADIOLOGY
Lower extremity ultrasound: no evidence of deep vein thrombosis.

DIAGNOSIS
Cutaneous Mycobacterium Avium Complex (MAC) secondary to immunosupression

TREATMENT AND COURSE
The patient followed up in the dermatology outpatient clinic where she was placed on doxycycline 100 mg twice daily and referred to infectious disease for evaluation and treatment. She was placed on rifabutin 300 mg, ethambutol 1200 mg and azithromycin 500 mg daily. Doxycycline was discontinued. The patient is being followed by infectious disease and continues to improve.

DISCUSSION
Mycobacterium avium-intracellulare or complex (MAI or MAC) is the atypical mycobacterium most commonly associated with human disease. It is primarily a pulmonary pathogen that affects individuals who are immune compromised. Although the prevalence of MAC infection has increased following the AIDS epidemic, it remains an extremely rare cause of skin disease. Buruli ulcers caused by M. ulcerans are the most prevalent atypical mycobacteria skin infections worldwide, and M. mariunum is the most common pathogen observed for cutaneous infection in the U.S.[2]

Cutaneous manifestations of MAC infection include scaling plaques, crusted ulcers, ecthyma-like lesions, verrucous ulcers, inflammatory nodules, panniculitis, pustular lesions, and draining sinuses.[2]

In Taiwan 63 patients with culture proven, non-tuberculous mycobacteria (NTM) skin infections were reviewed.[3] Seventy-three percent of these lesions involved the extremities, and overall 30% of the patients had immune suppression. Immunsuppression was observed in 100% of patient with MAC, and 60% of patient with M. kansasii infections.[3]

Diagnosing NTM infections of the skin continues to be challenging because of variation in the clinical presentation and histologic findings.[4] The usual delay from presentation to diagnosis of NTM infections is 7.1 months because of these variables.[4] Histopathology patterns include dermal and subcutaneous abscesses, superlative granulomas, tuberculoid granulomas, and granulomas with a perifollicular distribution.[5] In a recent series of 25 NTM cutaneous cases, tissue culture and PCR proved to be the most sensitive and specific tests for diagnosis of NTM.[4]

In our patient, it is unclear if the original inoculation was secondary to trauma when the patient fell on her shoe, or if she had disseminated infection and the traumatic experience facilitated the the bacteria to seed at this site. Cutaneous lesions can be the first and only sign of NTM disease, and tissue culture or biopsy with PCR still remains the definitive diagnostic procedure. Although MAC remains an extremely rare cause of cutaneous infection, it should be included in the differential diagnosis in immune compromised patients with nonhealing cutaneous lesions resistant to antibiotic treatment.

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Presented by Lauren Campbell, MD, and Arthur Rhodes, MD
Department of Dermatology, RUSH University Medical Center

HISTORY OF PRESENT ILLNESS

A Hispanic male presented at two weeks of age to the dermatology clinic with blisters on his buttocks, arms, legs, head, and back that were first noted at birth. No treatment was attempted. The family denied fevers, chills, loss of appetite, diarrhea, vomiting, or other systemic signs.

PAST MEDICAL HISTORY

Full term spontaneous vaginal delivery without complications

MEDICATIONS

None

ALLERGIES

No known drug allergies

FAMILY HISTORY

No history of similar lesions in family members

SOCIAL HISTORY

The patient lives at home with his mother and father. The family immigrated to the U.S. from Mexico 2 years ago. The patient has no siblings. The patient's mother denied a history of previous unsuccessful pregnancies.

PHYSICAL EXAM

Well-developed, well-nourished two week-old male infant who appeared alert and well. There were vesicles and crusted papules in a linear configuration on both thighs, legs and feet, (right>>left), buttocks, right lateral trunk and right arm. Total mucocutaneous examination revealed no other suspicious lesions. Oral and ocular mucosae were normal.
Examination of the patient's mother revealed no obvious dysmorphic features, and no obvious dental, eye, or hair abnormalities. There were no hypopigmented atrophic streaks. She was of normal intelligence.

HISTOPATHOLOGY

Hematoxylin and eosin: Intra-epidermal vesicular eosinophilic dermatitis.
Direct immunofluorescence: negative for deposition if immunoglobulins or complement.

LABORATORY RESULTS

Polymerase chain reaction for HSV-1 and HSV-2 negative

DIAGNOSIS

Incontinentia pigmenti, possibly segmental or mosaic in a male child

TREATMENT AND COURSE

The patient did not develop new blisters after the initial visit at two weeks of age. All existing blisters eventually crusted and healed with post-inflammatory hyperpigmented patches, without scarring. By age 6 months, he had barely perceptible hyperpigmented macules and patches. With time, the patient had lesions only on the right thigh, leg, buttock, and forearm; no lesions

were visible on the left side. He is now 10 months old and is being followed every three months. He continues to do well and is reaching normal developmental milestones. He has shown no evidence of neurologic or ophthalmologic difficulties. The patient has been referred to pediatric ophthalmology and will be evaluated by pediatric dentistry when he develops teeth. Genetic studies are pending.

DISCUSSION

Incontinentia pigmenti (IP), also known as Bloch-Sulzberger syndrome, is a relatively rare genodermatosis that is traditionally considered to be lethal in male infants in utero. Although the vast majority of patients diagnosed with IP are female (approximately 97%), there have been reports of male infants with the disease.

IP is inherited in an X-linked dominant manner. Most cases in female patients are associated with a mutation in the NEMO gene (NF kappa B essential modulator) on chromosome Xq28. It is characterized by skin manifestations occurring within Blaschko's lines in four stages which are variably present. In stage one, in 90% of patients, vesicles are present at birth or a few weeks later. Stage 2 is the verrucous phase, occurring usually between two and eight weeks of age. Stages 3 and 4 have linear and swirled hyper- and hypopigmentation, respectively, not recurring in the same areas. Approximately 40-60 % of patients have cicatricial alopecia. Nail dystrophy is variably present. A commonly encountered extra-cutaneous finding, occurring in about 70-95% of female patients, is dental abnormalities, manifested as peg teeth, delayed dentition, or partial anodontia. Neurologic problems occur in about 30% of patients and include seizures, mental retardation, and/or spasticity. Eye changes are not uncommon and may include strabismus, cataracts, optic atrophy, and blindness.

Histopathologically, in the first stage of IP, there is a vesicular dermatitis with eosinophilic spongiosis. Peripheral eosinophilia is present in about 70% of patients, and may last up to four or five months.

Approximately forty cases of IP in male infants have been reported. The male phenotype has not been well characterized. Although boys with IP have a similar overall phenotype to girls, there are distinct differences noted in a recent case series of males with IP. Only 32% of male infants with IP had peripheral eosinophilia. Only 15 % of male patients had a unilateral presentation, which is an unusual occurrence, especially in the early stages. Boys may also have unilateral extracutaneous manifestations. Abnormalities of the teeth were the most common extracutaneous manifestation in male patients. The explanation for unilateral involvement in male babies is not known, but may represent a partial expression of an unstable mutation early in embryogenesis. In the largest series, only five of 42 male patients had a NEMO mutation. The International IP Consortium proposed three mechanisms by which males with a NEMO mutation can survive: 1). hypomorphic alleles 2). Klinefelter syndrome (XXY), and 3). somatic mosaicism.

Male patients with IP seem to have a similar phenotype to female patients, but due to lack of an identifiable NEMO mutation in most male patients, phenotypic/genotypic correlations cannot be made. Treatment of IP is mostly supportive, and includes genetic counseling and referral to appropriate specialists for extracutaneous problems.

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CHICAGO DERMATOLOGICAL SOCIETY **CASE # 20**

Presented by Melinda Simon, MD, and Mark D. Hoffman, MD
Department of Dermatology, RUSH University Medical Center

HISTORY OF PRESENT ILLNESS

A 43-year-old woman presented with a two day history of diffuse, pruritic facial redness and right sided facial edema, followed by the appearance of an erythematous papular eruption on her face, upper torso, and arms. She denied a history of similar lesions. Although the patient has a history of acne she noted these lesions were different from her usual acne lesions. The patient had received an abatacept (Orencia) infusion for rheumatoid arthritis one day prior to the onset of these signs, prompting concern that her lesions were a medication reaction despite having received abatacept monthly for one year without incident.

PAST MEDICAL HISTORY

Rheumatoid arthritis, acne for four years (mostly comedonal and confined to the forehead and well controlled with topical clindamycin lotion 1% daily and tretinoin cream 0.025% nightly, with occasional premenstrual flares), migraine headaches.

MEDICATIONS

Abatacept 75 mg every four weeks
Methylprednisolone 5 mg daily
Methotrexate 7.5 mg weekly
Nabumetone 750 mg twice daily

PHYSICAL EXAM

The face was erythematous and studded with numerous pinpoint pink pustules; fewer pink papules were present on the neck, chest and bilateral arms. Two light brown scaling patches were noted on the patient's upper back.

KOH of facial pustules showed scores of demodex mites [greater than 100 per cm^2]; no yeast or mycelia were observed. KOH of the upper back revealed innumerable yeast forms and dense tangles of mycelia.

HISTOPATHOLOGY

Right forearm punch biopsy: mild perifollicular inflammation with a dilated follicular infundibulum harboring one demodex mite.

Right chest punch biopsy: mild perivascular and interstitial infiltrate consisting of lymphocytes and many eosinophils. Deeper sectioning failed to reveal a follicle.

DIAGNOSIS

Demodicosis and tinea versicolor associated with abatacept infusions

TREATMENT AND COURSE

Treatment consisted of topical metronidazole to her face and chest BID, and ciclopirox shampoo to her face, trunk and arms daily. Her pruritus, erythema, and pustules began to improve within days. At the time of her follow up visit eleven days later she was nearly clear, and the tinea versicolor also appeared to have resolved. Our patient has continued on this topical regimen and has not had any further lesions after her abatacept infusions.

DISCUSSION

Demodicosis, also known as demodicidosis, is the name given to cutaneous disorders that are attributed to the Demodex mite. Two demodex species can occupy human skin: *D brevis* which occupies the sebaceous ducts, and *D folliculorum* which is found in the infundibulum. Although these mites are common commensals of the human pilosebaceous unit, skin disease has been ascribed to these organisms when they are present in abnormal numbers or locations. The demodex mite has been implicated in causing, *inter alia,* papulopustular and / or granulomatous rosacea, perioral dermatitis, blepharitis, and facial hyperpigmentation. Because incontrivertable proof for a causative role of demodex in these conditions has not been produced, "demodicosis" remains controversial. More recently, a role for the bacterium *Bacillus oleronius*--which has been isolated from a demodex mite--has been postulated in the pathogenesis of papulopustular rosacea.

Demodex is typically found in the upper pilosebaceous follicle, and in control populations the mite density is ordinarily < 1 mite per cm^2. The mite has been deemed pathogenic when found in an atypical location (within the dermis) or at high densities (> 5 mites per cm^2). Skin scrapings or "standardized skin surface biopsy" [using cyanoacrylic adhesive applied to microscope slide] are more sensitive than biopsy when attempting to quantify the mite burden. Nevertheless, in a study examining 1,124 consecutive biopsies for presence of demodex, 10% these tissue specimens were infested. The prevelance of demodex was highest on the face; no mites were identified on a biopsy of an extremity[1].

Hsu, Hsu and Lee[2] described 15 Taiwanese patients with clinical and pathologic findings of demodicosis. They found the mean age was 38.7 years with a female predominance. Their patients were not immunocompromised. Similarly, a report of 115 patients with demodicosis authored by Forton et al found less than 5% of cases to have a known immunodeficiency[3]. Many isolated reports of demodicosis associated with documented or presumed immunodeficiency have appeared in the literature, suggesting links with: HIV[2]; MF during treatment with electron beam therapy; UVB phototherapy; hemodialysis[4;] and leukemia ALL[5,6]. Pimecrolimus and tacrolimus have also been associated with induction of demodicosis.

Abatacept is a biologic agent indicated for RA and juvenile idiopathic arthritis that operates as a selective costimulatory modulator. It consists of a CTLA-4 domain linked to a modified IgG Fc component, and it functions by competing with CD 28 for binding to CD 80 / CD 86 on antigen presenting cells, thus interfering with T cell activation mediated by the CD80/86 with CD 28 costimulatory signal. To our knowledge, demodicosis associated with use of abatacept has not been reported.

Treatment of demodicosis may include topical and systemic agents depending on disease severity. Topical therapies that have been utilized include metronidazole, permethrin, sodium sulfacetamide, crotamiton, 10% sulfur, 1% lindane, retinoids, benzyl benzoate (BB), and salicylic acid[5-8]. Since there is evidence for acaricidal activity with only two of them (crotamiton and BB), some therapies may work via promotion of desquamation and prevention of follicular plugging, or through anti-inflammatory mechanisms. Systemic therapy may include ivermectin and metronidazole[2,7]. Our patient was successfully treated with topical metronidazole with a response within one week of starting therapy. She continues to do well.

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Presented by Melinda Simon, MD, Kastytis A. Jucas, MD, and Michael Tharp, MD
Department of Dermatology, RUSH University Medical Center

HISTORY OF PRESENT ILLNESS

A 25-year-old Lithuanian man presented to a clinic in the United States for a second opinion for a seven year history of "bumps," which began in the inguinal area and spread to the right axilla and flexural areas of the arms, legs, and groin. The patient had a history of intense itching in the affected areas six months prior to the initial eruption. New lesions continued to appear. The patient denied shortness of breath, wheezing, frequent urination, visual disturbances, and/or headaches. He did have symptoms of depression, which were attributed to his altered appearance from his dermatologic condition.

PAST MEDICAL HISTORY

None

MEDICATIONS

None

ALLERGIES

NKDA

FAMILY HISTORY

Non-contributory

PHYSICAL EXAM

The patient had extensive nodular purple-yellow tinged linear plaques in the axilla, antecubital fossa, popliteal fossa, and groin-inguinal areas.

HISTOPATHOLOGY

The patient previously had two previous biopsies performed at the University of Vilnius, Lithuania. Both reports were unavailable, but the diagnosis given was xanthoma disseminatum.

Histopathology of an excisional biopsy from the antecubital fossa showed the collapse of dermal normal stromal structure, collagen fiber degeneration, necrobiosis, and infiltration with lymphocytes and histiocytes. No atypical cells were identified. A diagnosis of necrobiotic granuloma was given. Review of this biopsy by our department showed an unremarkable epidermis with a dense infiltrate of foamy histiocytes admixed with few neutrophils. A diagnosis of xanthoma disseminatum was given.

LABORATORY RESULTS

Laboratory evaluation revealed a normal CBC with differential and LDH, negative ANCA, ANA, and double stranded DNA and no monoclonality. Patient reported a normal lipid profile, although results were unable to be obtained.

RADIOLOGY

Chest X-ray showed lymphadenopathy. Ultrasound studies revealed hepatomegaly, but a normal upper and lower gastrointestinal system and normal spleen.

DIAGNOSIS
Xanthoma disseminatum

TREATMENT AND COURSE
The patient returned to Lithuania for further treatment of xanthoma disseminatum and subsequently developed diabetes insipidus, further supporting the diagnosis. He has been lost to follow up.

DISCUSSION
Originally described by Montgomery and Osterberg in 1938[1], xanthoma disseminatum, (XD), is a rare non-langerhans cell disorder of histiocytic proliferation affecting the skin and mucous membranes as well as the central nervous system, gastrointestinal, respiratory, and ocular systems[2]. Rarely the skeletal system is affected[3]. Roughly 100 patients have been reported[4]. The pathogenesis is unknown. Since most patients are normolipemic, it has been speculated that this disorder represents a reactive histiocytic proliferation with secondary lipid deposition[5].

Patients with XD may have the classic triad of cutaneous xanthomas, mucous membrane xanthomas, and diabetes insipidus[6-7]. XD affects males more than females, typically in childhood or young adulthood. The cutaneous xanthomas are red, yellow or brown papules and are symmetrical, often involving the flexural and intertriginous areas. Lesions may be grouped, atrophied, locally destructive and disfiguring. Age at presentation ranges from 8 months to 85 years[8]. Forty to sixty percent of patients will have mucous membrane involvement but only twenty percent have abnormal lipid levels. Forty percent of patients have hypothalamus and pituitary lesions, which can result in diabetes insipidus [6,8]. Vision can be impaired with ocular lesions involving the cornea and conjunctivae. Thyroid disorders, plasma cell disorders and monoclonal gammopathy are rarely found in XD patients[8].

Histologically, early lesions have a dense histiocytic infiltrate in the dermis with few inflammatory or foamy cells. Later lesions contain many foam cells and histiocytes, lymphocytes, plasma cells, neutrophils, and characteristic Touton cells. Histiocytes are CD68, CD11b, CD11c, CD14, Factor XIIIa positive and stain for α1-antitrypsin and lysozyme. The cells are S-100 and CD1a negative and do not have Birbeck granules[4,6].

There is no standard therapy for XD. Cyclophoshamide has been shown to be useful for mucosal lesions. Other therapy for cutaneous lesions include intralesional corticosteroids, cryotherapy, excision, radiotherapy, electrocoagulation, and dermabrasion[8,9]. Carpo et al. reported impressive cosmetic improvement using the CO2 laser. The response of cutaneous lesions to clofibrate treament has been varied[8]. Oral and topical corticosteroids have not proven useful[8]. Klaus et al. described a therapeutic combination of 3 lipid lowering agents of rosiglitazone 4mg daily, acipimox 250mg twice daily, and simvastatin 10mg daily. This combination induced a partial remission with regression of lesions for 2 years in one patient [5]. Radiotherapy is typically used for upper airway obstruction. Diabetes insipidus responds well to DDAVP (Vasopressin).

Caputo et al. described three forms of XD distinguished by their prognosis[8]: the self healing form, a more common persistent form, and an extremely uncommon progressive form which can be fatal and have extensive gastrointestinal and pulmonary involvement[10]. Our patient likely represents the more common persistent form of xanthoma disseminatum. The fact that XD may progress highlights the need for close follow up in these patients.

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Presented by Tracy Campbell, MD, and Michael Tharp, MD
Department of Dermatology, RUSH University Medical Center

HISTORY OF PRESENT ILLNESS

This 49 year-old male presented to the Rush emergency department in May, 2008 with a 2 week history of extremely painful, ulcerating lesions on the dorsum of both hands. The lesions were biopsied by our consult service for histopathology and for fungal, bacterial, and viral cultures. The patient denied pulmonary symptoms or nights sweats, but admitted to subjective fevers, chills and malaise. A chest x-ray was done and revealed consolidation in the right middle lobe. A computed tomography (CT) exam was then preformed which revealed a possible abscess in the right middle lobe. The patient was then admitted for four days and placed on itraconazole 200 mg daily by the infectious disease team for presumed blastomycosis. After four days the patient left against medical advice, at the time of discharge, microbiology and pathology from his hand biopsies were not yet definitive. The patient was placed on itraconazle 200 mg daily for presumed blastomycosis and asked to follow up in the dermatology and infectious disease outpatient clinics.

The patient failed to follow up, and was admitted to the hospital six weeks later when he was again seen by the dermatology consult service. The patient stated that his hand lesions had completely resolved with itraconazole 200 mg daily x 1 month, but had returned 2 weeks ago after he had run out of medication. A chest X-ray was preformed along with another biopsy for histopathology and tissue cultures for fungal, bacterial, and viral elements. The patient was again placed on itraconazole while we awaited the results of the biopsy and culture.

PAST MEDICAL HISTORY

Hepatitis C
Alcohol Abuse
Illicit drug abuse (cocaine per patient history)
Diabetes Mellitus
Depression

MEDICATIONS

Norco (hydrocodone bitartrate and acetaminophen)
Gabapentin
Humulin
Insulin
Pregabalin

ALLERGIES

No known drug allergies

FAMILY HISTORY

Non-contributory

SOCIAL HISTORY

The patient smokes approximately one pack per day, drinks daily, and abuses cocaine. He is a former construction worker.

PHYSICAL EXAM

Right dorsal hand with a well circumscribed 4-5 cm superficial ulceration with an undermined

border and serum and heme crust. Three edematous papules with overlying serum heme crust are seen on his left dorsal hand.

HISTOPATHOLOGY

5/23/2008: Left dorsal hand punch biopsy: ulcer with dense neutrophilic inflammation and pseudoepitheliomatous hyperplasia. Special stains for fungus, AFB, and bacteria were negative. No granulomas were seen. The histologic changes were consistent with pyoderma gangrenosum.

7/30/2008: Dense diffuse neutrophilic dermatitis consistent with pyoderma gangrenosum. GMA, PAS and Fite stains are negative for microorganisms.

LABORATORY RESULTS

HSV1, HSV 2 negative
Tissue biopsies for culture were negative for fungi, AFB, and bacteria

RADIOLOGY

Chest X-ray: Right middle lobe consolidation with an air/fluid level.

DIAGNOSIS

Neutrophilic dermatosis of the dorsal hands

TREATMENT AND COURSE

The patient was given clobetasol ointment 0.05%, placed on a five day supply of prednisone (60 mg daily), and was asked to follow up in the dermatology clinic. The patient failed to return to clinic and presented 3 months later to our clinic with a recurrence of his hand lesions. The patient stated the lesions completely resolved with the 5 day course of prednisone, but the "rash" had returned and was extremely painful. The patient was again placed on 60 mg per day of prednisone, topical clobetasol ointment 0.05% twice daily, and started on dapsone 25 mg daily. He was only given 1 week of medication because of his noncompliant history. The patient returned in 1 week with dramatic improvement; the lesions nearly resolved. At this visit his prednisone was decreased to 50 mg, and dapsone was increased to 50 mg. He was asked to return in 2 weeks. The patient returned completely healed except for one erosion on the right dorsal hand that he admitted to traumatizing. At this visit the prednisone was decreased further to 40 mg daily for 2 weeks, then 30 mg daily for 2 weeks; the dapsone remained at 50 mg. The patient was to follow up in 2 weeks, but never returned and has been lost to follow up for 10 months.

DISCUSSION

Dr. Sweet from Plymouth, England first described acute febrile neutrophilic dermatosis in 1964. This entity is more common in women and appears as tender erythematous or violaceous plaques and nodules, predominantly on the face, upper trunk, and extremities.[7] Skin biopsy specimens demonstrate dense dermal neutrophilic infiltrates with leukocytoclasis. Associated findings may include fever, peripheral blood neutrophilia, and an elevated erythrocyte sedimentation rate.[7]

Pustular vasculitis of the dorsal hands was first described by Strutton *et al*. in 1995.[3] This entity can clinically and histologically resemble Sweet's syndrome except for the presence of a leukocytoclastic vasculitis. Lesions are usually limited to the dorsal hands, often with a predilection for the lateral aspect of the hand between the thumb and index finger. This entity has been renamed and "neutrophilic dermatosis of the hands" which is now considered a subset of Sweets Syndrome.[6,7,9]

Histological findings of this entity are almost identical to that of Sweet's syndrome with a predominant neutrophilic infiltration in the dermis, papillary dermal edema, with or without the presence of leukocytoclastic vasculitis. This entity is also unique because of the rapid response to steroid treatment.[5,6]

Many different treatments have been used in Sweet's syndrome, with different rates of success and relapse. These include topical and systemic corticosteroids, dapsone, potassium iodide, colchicine, clofazimine, azathioprine, danazol, tetracyclines, cyclosporine and indomethacin.[8] Systemic corticosteroids have been found to be the most common first-line therapy, as prescribed in our patient. However, there are significant side-effects associated with prolonged courses of high-dose steroids and relapses can occur in up to 30% of cases when tapering the dose. Up to 30% of cases can resolve spontaneously.[3,6,9]

We present this case because the clinical appearance and histopathologic findings often lead to the misdiagnosis of a cutaneous infection. Thus, atypical pyoderma gangrenosum, bullous Sweet's syndrome, and pustular vasculitis of the hands are best understood as variations of a single disease entity, which is now most commonly designated as neutrophilic dermatosis of the dorsal hands.[3]

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