Chicago Dermatological Society

November 2008
Monthly Educational Conference

Program Information
Continuing Medical Education Certification
and
Case Presentations

Wednesday, November 12, 2008

Conference Host:
Section of Dermatology
University of Chicago Hospitals
Chicago, Illinois

Chicago Dermatological Society

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CDS Monthly Conference Program
November 2008 -- University of Chicago

November 12, 2008

8:00 a.m.	**REGISTRATION FOR RESIDENTS** *Billings Auditorium - Rm. P117*
8:00 - 10:00 a.m.	**REGISTRATION FOR PRACTICING DERMATOLOGISTS** *Dermatology Clinic - Room 6C, DCAM*
9:00 a.m. - 10:00 a.m.	**RESIDENT LECTURE** Dermatology Basic Science - Clinical Correlations *JEFFREY B. TRAVERS, MD* *Billings Auditorium - Rm. P117*
9:30 a.m. - 11:00 a.m.	**CLINICAL ROUNDS** Patient Viewing *Dermatology Clinic, Room 6C, DCAM* Slide Viewing *Room 1402, DCAM*
10:00 a.m.	**REGISTRATION CONTINUES** *Billings Auditorium - Rm. P117*
11:00 a.m. - 12:00 p.m.	**GENERAL SESSION** *Billings Auditorium - Rm. P117*
11:00 a.m.	CDS Business Meeting
11:15 a.m.	Insights into Staphylococcal Potentiation of Atopic Dermatitis *JEFFREY B. TRAVERS, MD*
12:15 p.m. - 1:00 p.m.	**LUNCHEON** *Served in room J-103*
1:00 p.m. - 2:30 p.m.	**AFTERNOON GENERAL SESSION** *Billings Auditorium - Rm. P117* Discussion of cases observed during morning clinical rounds *WARREN PIETTE, MD, MODERATOR*
2:30 p.m.	**MEETING ADJOURNS**

CME Information

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

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

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

Guest Speaker

Jeffrey B. Travers, MD, PhD
Kampen-Norris Professor & Chair of Dermatology; Professor of Pharmacology and Toxicology; Indiana University School of Medicine

A native of Ohio, Dr. Travers attended the Ohio State University receiving a bachelor's degree in chemistry, and a doctoral degree in pharmacology. He earned his medical degree there in 1991 . Dr. Travers completed his internship in transitional medicine at Riverside Methodist Hospital, Columbus, Ohio; his residency in dermatology at the University of Colorado Health Sciences Center in Denver (1995), and a fellowship at National Jewish Center for Immunology and Respiratory Medicine, also in Denver. Dr. Travers' primary research interest is in the mechanisms of skin inflammation, and he currently is the principal investigator on two National Institutes of Health grants, as well as co-investigator on three other NIH grants.

Speaker CME Disclosure of Financial Interests

Dr. Travers has no significant financial relationships to disclose.

CME Credit Documentation

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

Evaluation Forms

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

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PRESENTERS
Jessica Maddox MD, Vivek Iyengar MD, Vesna Petronic-Rosic MD MSc, and Aisha Sethi MD

HISTORY OF PRESENT ILLNESS
A 19-year-old Puerto Rican male was referred to our clinic for excision of painful growths in his axilla and groin. They first appeared several months previously as "boils" that enlarged over time and continued to drain purulent and hemorrhagic fluid despite a course of oral clindamycin.

PAST MEDICAL HISTORY
The patient had a known past medical history of nystagmus and Crohn's disease. He had required a blood transfusion during an admission for GI bleeding a year previously and complained of easy bruising. A maternal cousin was an albino.

MEDICATIONS
Infliximab infusions q 8 weeks, 6-mercaptopurine 75 mg PO daily, sulfasalazine 1 gram PO four times daily, and Pepcid 20 mg PO daily.

ALLERGIES
No known drug allergies

PHYSICAL EXAMINATION
On exam, it was noted that, in comparison to his mother who had Fitzpatrick skin type V, he had very pale skin, reddish-blond hair, blue eyes, and horizontal nystagmus. In his right axilla, there were two large, tender, beefy-red shiny nodules, with similar lesions in the groin. The axillary nodules were excised and noted to be deep, connecting as one large gelatinous neoplasm in the subcutaneous tissue. At the suture removal ten days later, he was noted to have hypertrophic papules along the incision line, as well as an adjacent, recurrent nodule.

LABORATORY DATA
Platelet function assay > 330 seconds [74 – 190]
Persistent normocytic anemia

DERMATOPATHOLOGY
Histopathologic examination revealed granulation tissue and a dense diffuse infiltrate of lymphocytes, histiocytes, and multinucleated giant cells. Keratin debris was noted, although there was no evidence of a cyst wall. Melan-A highlighted normal numbers of melanocytes at the dermal-epidermal junction. Mel-5 stained approximately 20% of the melanocytes stained by Melan-A.

FURTHER TESTING
EM of platelets: A complete absence of dense bodies was noted.
GeneDX: Homozygous for the 16 bp duplication in the HPS1 gene, which was denoted c. 1742_87Ddup on the cDNA level.

DIAGNOSIS
Hermansky-Pudlak Syndrome

TREATMENT AND COURSE
The patient was referred to genetics for counseling, as well as to hematology for evaluation of platelet function, pulmonology for evaluation of lung function and counseling, and ophthalmology. His gastroenterologist was informed of the diagnosis and opted to continue the current treatment regimen for colitis.

DISCUSSION

Hermansky-Pudlak Syndrome (HPS) is a rare autosomal recessive syndrome that predominantly affects patients of Puerto Rican decent. First described in 1959, HPS is a heterogeneous group of disorders of intracytoplasmic organelle-specific protein biosynthesis and trafficking. The organelles implicated include the dense bodies of platelets, the melanosomes of melanocytes, and the lamellar bodies of type II pneumocytes, resulting in the HPS phenotype of albinism and bleeding diathesis.

The various types of HPS are rare genetic diseases worldwide. However, *HPS1* is the most common single gene disorder in Puerto Rico. Some have estimated a frequency of about 1 case in 2000 population among Puerto Ricans, with an estimated carrier frequency of 1 in 21. In Puerto Rico, 5 out of 6 patients with OCA have HPS. For this reason, in Puerto Rico, a patient with OCA has HPS until proven otherwise. If an American patient of Puerto Rican heritage has OCA, HPS must be ruled out. HPS has an estimated prevalence of one in 500,000 to one in 1,000,000 in non-Puerto Rican populations. The *HPS1*, *AP3B1*, *HPS3*, *HPS4*, *HPS5*, *HPS6*, *DTNBP1*, and *BLOC1S3* genes are known to be associated with HPS.

Manifestations of HPS include tyrosinase-positive oculocutaneous albinism. In these individuals, the skin is very lightly pigmented, although they may have lentigines or nevi. Patients are at increased risk for UV-induced photodamage and non-melanoma skin cancer. Hair color varies from blond to red to light brown. Ocular involvement may include nystagmus, photophobia, strabismus, legal blindness, iris transillumination, and foveal hypoplasia.

The bleeding diathesis of HPS results from an absence or severe deficiency of dense granules in platelets. The dense bodies, which contain ADP, ATP, serotonin, calcium, and phosphate, release their contents upon stimulation to attract other platelets. This process constitutes the secondary aggregation response, which cannot occur in the absence of the dense bodies. There are normally four to eight dense bodies per platelet, but there are none in the platelets of individuals with HPS. Affected individuals experience variable bruising, epistaxis, gingival bleeding, postpartum hemorrhage, colonic bleeding, and prolonged bleeding during menstruation or after tooth extraction, circumcision, or other surgeries. Typically, cuts bleed longer than usual but heal normally. Affected individuals with colitis may bleed excessively per rectum.

Pulmonary fibrosis of HPS typically causes symptoms in the thirties and is fatal within a decade. The pulmonary fibrosis has been described largely in individuals with HPS1 but also occurs in other subtypes. The fibrosis consists of progressive, restrictive lung disease with an extremely variable time course. A bleeding granulomatous colitis resembling Crohn's disease presents, on average, at 15 years of age. The colitis is severe in 15% of cases and occasionally requires colectomy; affected individuals may have the inflammatory bowel disease of HPS without the explicit diagnosis of colitis. Although the colon is primarily involved, any part of the alimentary tract, including the oral mucosa and gingiva, can be affected. Studies have shown infliximab to successfully treat the colitis associated with HPS. Cardiomyopathy and renal failure have also been reported in HPS. Pulmonary fibrosis, granulomatous colitis, cardiomyopathy, and renal failure have been attributed to the lysosomal accumulation of ceroid lipofuscin, but this relationship is speculative.

The diagnosis of HPS is established by clinical findings of hypopigmentation of the skin and hair, characteristic eye findings, and demonstration of absent dense bodies on whole mount electron microscopy of platelets. Molecular genetic testing of the *HPS1* gene is available on a clinical basis for individuals from northwestern Puerto Rico. Homozygosity for a16-bp duplication is found in approximately 75% of all affected individuals of Puerto Rican ancestry and in virtually all affected individuals from northwestern Puerto Rico.

This young Puerto Rican man remained without a diagnosis, despite the classic oculocutaneous signs and associated bowel disease. The excessive granulation tissue and granulomatous inflammation in response to cutaneous injury is likely associated with this syndrome, although it has not been reported in the literature. This case highlights the importance of diagnosis, as possible complications, prognosis, and genetic counseling should be relayed to the patient.

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PRESENTERS
John C. Fox MD, Vesna Petronic-Rosic MD MSc, Keyoumars Soltani MD, and Aisha Sethi MD

HISTORY OF PRESENT ILLNESS
A 16 year-old Hispanic female presented with a 10-day history of a progressive, blistering skin eruption with associated chills and rigors. Early skin changes involving the left foot, left thigh, and hairline were treated by an outside pediatrician with trimethoprim-sulfamethoxasole for a presumed infectious etiology. Seven days after the onset of skin changes, the patient was seen by an outside dermatologist who discontinued TMP-SMX and started a regimen of oral prednisone, triamcinolone cream, and retapamulin cream. Symptoms continued to worsen over the subsequent four days, and the patient came to the University of Chicago Dermatology clinic for further management.

PAST MEDICAL HISTORY
Eczema, seasonal allergies

MEDICATIONS
Prednisone, retapamulin cream, triamcinolone cream

ALLERGIES
No known drug allergies

PHYSICAL EXAMINATION
Physical examination revealed a young woman in mild distress with numerous erythematous targetoid plaques with dusky centers and pink urticarial plaques with overlying vesicles and bullae involving greater than 70% of BSA.

LABORATORY DATA
CBC: WBC 17.5 K/uL (ref 3.5 – 11) with Eosinophils 21%, Bands 1%, Myelocytes 1%, Neutrophils 49%, Lymphocytes 22%, Reactive Lymphs 1%, Monocytes 5%.
LFT, CMP: within normal limits.
Hepatitis panel, RPR: non-reactive.

DERMATOPATHOLOGY
H & E: Histopathologic evaluation of a punch biopsy from involved skin over the left thigh revealed a subepidermal blister, the cavity of which was filled with eosinophils. The underlying and adjacent dermis contained a perivascular and interstitial infiltrate with numerous eosinophils.
IF: Direct immunofluorescence studies demonstrated linear deposition of IgG and C3 at the epidermal basement membrane zone, as well as numerous immunoglobulin-bearing cells in the dermis. IgA deposition was not detected. Indirect immunofluorescence with patient serum and monkey esophagus showed pemphigoid antibodies at titers >1280. Similar studies on salt-split skin showed antibodies binding only to the epidermal side of the dermal-epidermal separation.

DIAGNOSIS
Chikdhood bullous pemphigoid (possibly drug-induced)

TREATMENT AND COURSE
The patient was admitted to the University of Chicago Burn ICU, and a dermatology consult was obtained for ongoing management of her bullous pemphigoid. She was initially placed on oral prednisone, mycophenolate mofetil, topical tacroliumus, and fluocinonide cream for immunosuppression, and high-dose therapy was continued during her ICU stay until her skin

symptoms stabilized with no new lesion development. During the course of her admission, the patient developed bullae and erosions involving the oral and esophageal mucosa. Upper endoscopy with biopsy of esophageal tissue was sent for histopathologic examination and immunofluorescence. H&E illustrated a severe esophagitis with deep ulceration involving the muscularis propria with occasional cells demonstrating atypia suggestive of, but not diagnostic of, viral changes. Immunostaining was negative for EBV, CMV, and HSV, and DIF revealed non-specific staining patterns with IgG, IgM, IgA, and complement. The etiology of her esophageal involvement remains unclear, though unlikely a manifestation of her pemphigoid. The patient was discharged home after a 21-day admission on mycophenolate mofetil 1000 mg PO BID, prednisone 60 mg PO daily, Nexium 40 mg PO daily, and triamcinolone cream 0.1% BID. Bullae have subsequently healed without scarring or recurrence, but with significant hyperpigmentation that continues to gradually fade with time. She has successfully completed a slow taper and eventual discontinuation of oral prednisone without recurrence of visible disease, and we are currently in the process of reducing the dose of mycophenolate mofetil. Currently, the patient is not on topical corticosteroid therapy.

DISCUSSION

Bullous pemphigoid (BP) is an acquired, chronic subepidermal vesiculobullous disease mediated by autoantibodies toward antigens located in the hemidesmosomes and lamina lucida of the dermo-epidermal junction, specifically 230-kD BP antigen (BPAG1, BP-230) and 180-kD BP antigen (BPAG2, BP-230). Histologic examination of affected skin reveals subepidermal bulla formation with numerous eosinophils, and direct immunofluorescence demonstrates linear deposition of IgG and complement along hemidesmosomes and the upper lamina lucida of the basement membrane zone. Indirect immunofluorescence similarly shows IgG binding the epidermal side of salt-split skin.

In certain patients, possibly those with an underlying genetic diathesis, systemic medications can lead to the development of bullous pemphigoid. The mechanism for this induction has not been described, but it is proposed that the offending drug acts as a trigger for modifying the affected individual's immune response or altering antigenic properties of the epidermal basement membrane. Many pharmacologic agents have been implicated, the most frequent being diuretics (e.g. furosemide, bumetanide), D-penicillamine, antibiotics (e.g. amoxicillin, ciprofloxacin), potassium iodide, gold and captopril. Given both the number and diversity of medications suggested to play a role in drug-induced bullous pemphigoid, it is necessary to conduct a thorough drug history to exclude the possibility of a triggering agent which if promptly discontinued may result in rapid improvement.

BP most commonly affects the elderly, and while childhood disease is rare, it is still the most common IgG-mediated subepidermal bullous disease in children. The disease is clinically similar to its adult counterpart with the exceptions of mucous membrane involvement being more common in children, and involvement of the hands and feet being far more common in infants younger than one year. Most cases of childhood bullous pemphigoid have a good to excellent prognosis with disease duration of one year or less.

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PRESENTERS
Christiane Querfeld MD and Christopher R. Shea MD

HISTORY OF PRESENT ILLNESS
This 32-year-old African-American man presented with an eight-month history of asymptomatic, enlarging plaques on the trunk and buttocks. Prior to his appointment, he was treated with topical clindamycin lotion that led to partial regression of some lesions. The patient had no other complaints and was in good general health.

PAST MEDICAL HISTORY
Unremarkable

MEDICATIONS
Multivitamins

ALLERGIES
No known drug allergies

FAMILY HISTORY
Non-contributory

SOCIAL HISTORY
He is a teacher at a local university. He does not smoke, drinks alcohol socially, and denies illicit drugs. He has had recent travels within the United States.

PHYSICAL EXAMINATION
Well-defined, soft, brown to yellow plaques with violaceous nodules in a cobblestone-like pattern were present on the left flank, bilateral hips and buttocks. There was no lymphadenopathy or hepatosplenomegaly noted.

LABORATORY DATA
CBC, CMP, LDH, ANA, and ESR were all within normal limits. Serologic tests for RPR and HIV 1/2 were negative. The serum protein level was normal without evidence of a monoclonal gammopathy.

HISTOPATHOLOGY
Left buttock: There was a dense, deep dermal and subcutaneous, inflammatory infiltrate composed of macrophages and foamy histiocytes, admixed with plasma cells and lymphocytes. Within histiocytes were well-preserved inflammatory cells. Histiocytes were positive for CD68 and S-100, and negative for CD1a. The Gram, Fite, PAS, and Warthin-Starry stains were negative for bacteria, mycobacteria, fungi, and spirochetes.

IMAGING
CT scans of chest, abdomen, and pelvis are pending.

DIAGNOSIS

Cutaneous Rosai Dorfman disease

TREATMENT & COURSE
Treatment with topical steroids (fluocinonide 0.05% ointment) was initiated. He was referred to Hematology/Oncology for further evaluation and input.

DISCUSSION

Histiocytoses are a heterogeneous group of disorders that are characterized by the proliferation and accumulation of reactive or neoplastic histiocytes. A recent classification of histiocytic disorders developed by the World Health Organization's Committee on Histiocytic/Reticulum Cell Proliferations and the Reclassification Working Group of the Histiocyte Society separates tumors of histiocyte and accessory dendritic cells into three groups based on the lineage of lesional cells and their biological behavior. Dendritic cell-related entities such as Langerhans cell histiocytosis and macrophage-related entities such as Rosai-Dorfman disease (sinus histiocytosis with massive lymphadenopathy) have varied biological behavior and are separated from those that are malignant.

Rosai–Dorfman disease is a rare disorder characterized by a nonmalignant proliferation of distinctive histiocytic/phagocytic cells within lymph node sinuses as well as lymphatics in extranodal sites first described by Rosai and Dorfman in 1969 as sinus histiocytosis with massive lymphadenopathy (SHML). The primary cutaneous form of SHLM, also referred to as cutaneous Rosai Dorfmann disease (RDD), is rarer still and has been defined as a distinct clinical entity because of its lack of systemic involvement.

The etiology remains unknown, but an exuberant response to an undetermined immunologic trigger has been suggested. Antibodies to pathogenic organisms including EBV and HHV-6 have been reported, but consistent serologic findings are lacking. Immunologic abnormalities are found in a significant number of patients and often lead to a clinically unfavorable disease course. Polyclonal hypergammaglobulinemia is found in 90% of patients. A small subset of patients also has concurrent neoplasia including non-Hodgkin lymphoma, multiple myeloma, other histiocytic proliferations, melanoma or carcinoma. RDD shares features of defective apoptosis found in autoimmune lymphoproliferative syndrome affecting the Fas/FasL pathway.

Histopathologic evaluation is the key to diagnosis. Cutaneous findings are similar to those found in lymph nodes, demonstrating a dermal, dense infiltrate of histiocytes with large vesicular nuclei and abundant pale pink cytoplasm and an accompanying inflammatory background of lymphocytes, plasma cells, neutrophils or epithelioid cells. Histiocytes of RDD are positive for S-100, negative for CD1a, and variably positive for CD68 an contain engulfed intracytoplasmic inflammatory cells (emperipolesis).

The clinical course of SHML/RDD is characterized by a protracted clinical course with spontaneous resolution in most cases. Topical or intralesional steroid therapy may be instituted for cutaneous lesions. Surgical excision or localized irradiation may be indicated for cosmetic reasons or symptomatic relief. Cutaneous lesions have also responded to thalidomide therapy. For systemic disease, surgical debulking, radiation therapy, or a combination of both may be used in cases where vital organ function is compromised. The lack of response to high-dose chemotherapy with alkylating agents for severe SHML suggests that chemotherapy may not be a mainstay of therapy in this disease. Rituximab with and without concomitant chemotherapy and interferon-alpha have also been reported with various success rates.

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PRESENTERS
Justin Wasserman MD, Christopher R. Shea MD, and Keyoumars Soltani MD

HISTORY OF PRESENT ILLNESS
A 66-year-old Caucasian woman presented with a growth on her proximal left arm. Of note, she had a history of significant lymphadenopathy and renal failure in June 2007 and was diagnosed with Burkitt lymphoma by flow cytometry and bone marrow biopsy. She subsequently underwent 7 rounds of chemotherapy to treat Burkitt lymphoma, complicated by respiratory failure during course two which necessitated placement of a tracheotomy. Following her treatment, there was resolution of the patient's lymphadenopathy, but she developed a new smooth dome-shaped growth on her proximal left arm. The lesions were asymptomatic but occurred suddenly and grew very quickly in size.

PAST MEDICAL HISTORY
Burkitt lymphoma, hypertension, borderline diabetes mellitus type II, acute renal failure – resolved, respiratory failure with tracheotomy

MEDICATIONS
Albuterol, magnesium, olmesartan, fluticasone/salmeterol, pantoprazole, furosemide, propoxyphene/acetaminophen, ciprofloxacin

ALLERGIES
Sulfa, iodine

PHYSICAL EXAMINATION
Vital signs within normal limits. Well-developed obese female in no acute distress. The patient presented with a 3 cm by 3 cm firm, non-tender, shiny, round white nodule with an erythematous border on the left lateral proximal arm with no surface change, erosion, or ulceration.

DERMATOPATHOLOGY
H & E: Skin and subcutaneous tissue with a dense confluent proliferation of darkly basophilic cells with a "starry sky" appearance at low magnification due to scattered small lucencies within the lymphoid nodule. The cells occupy the entire dermis with focal infiltration of the epidermis, and extension of the basophilic infiltrate to the inferior margin of the specimen within the subcutaneous fat. The cells contain enlarged nuclei with granular chromatin and scant cytoplasm, Numerous mitotic figures are present throughout the specimen.

Hematopathology: CD19(+), CD20(variably +), CD10(+), CD24(+), CD52(+), CD79a(+), HLA-DR(+), CD38(+), BCL6(+), BCL2(+), Ki67(+). T-cell and myeloid markers negative. TdT(-), CD34(-). t(14;18) and t(3;8;14) translocations involving c-myc, bcl2, and bcl6 were identified.

DIAGNOSIS
Atypical cutaneous Burkitt lymphoma

TREATMENT AND COURSE
Following the initial 7 rounds of chemotherapy and the subsequent lack of remission, the patient chose to seek a second opinion at an outside institution and is currently alive and receiving experimental chemotherapy regimens. Despite these treatments the patient continues to have active disease with no sustained remission.

DISCUSSION

Burkitt lymphoma (BL) is a B-cell lymphoma with a high proliferation rate, which often presents in extranodal sites or as an acute leukemia. No single parameter is diagnostic of BL but several diagnostic techniques in concert, such as morphology, cytogenetics, and immunophenotyping, are needed to make this diagnosis. Three clinical variants of BL are reported.

Endemic BL is a variant that occurs in equatorial Africa, and represents the most common childhood malignancy in this region. It has a 2:1 male to female predominance and the average age of onset is between 4-7 years old. The Epstein-Barr virus (EBV) genome is present in the majority of neoplastic cells in all patients. The jaw and facial bones are the most common site of presentation occurring in 50% of cases, central nervous system, gastrointestinal, gonads, kidney, long bones, thyroid, salivary glands, and breasts are other sites of extranodal involvement. Peripheral blood involvement has not been reported.

Sporadic BL is seen throughout the world and affects mainly children and young adults, It is relatively rare comprising only 1-2% of lymphomas in western Europe and the US, but it makes up 30-50% of childhood lymphomas. There is a male predominance and the average age of adult onset is 30 years. EBV can be detected in up to 30% of sporadic cases. Clinically the majority present as abdominal masses, jaw involvement is rare. Ovaries, central nervous system, kidneys, and breasts are also frequently involved. Lymph node presentation occurs more often in adult patients than children.

Immunodeficiency-associated BL is primarily seen associated with HIV infection and can often be the initial manifestation of Acquired Immunodeficiency Syndrome (AIDS). EBV is identified in only 25-40% of cases BL usually occurs early in the progression of HIV while CD4 counts are still high, which suggests that BL may not be directly related to immunosuppression. Clinical presentations include central nervous system, nodal localization, and bone marrow involvement.

Regardless of subtype patients often present with bulky disease and a high tumor burden, once therapy is initiated tumor lysis syndrome can occur due to rapid tumor cell death. Rarely BL can present as a leukemia with only peripheral blood and bone marrow involvement..

Morphologically the cells are medium sized and show a diffuse monotonous pattern of growth, the cytoplasm is deeply basophilic, there is a high mitotic index and a high fraction of apoptosis. A “starry sky” pattern is present due to benign macrophages that have ingested apoptotic tumor cells. Occasional reports of plasmacytoid differentiation of the cells have been reported in children and immunodeficiency-associated cases. The immunophenotype of BL consists of membrane IgM, B-cell markers (CD19, CD20, CD22), CD10, BCL6, CD38, CD77, CD43. BCL2 may be positive in about 20% of cases and TdT is uniformly negative. Ki67 shows proliferation rates around 100%. Most cases have a translocation involving the MYC locus on chromosome 8 with the most common being t(8;14) to the IG heavy chain region.

In endemic and sporadic cases the tumor is aggressive but curable. Staging is usually related to tumor burden. Bone marrow, central nervous system, high LDH, and unresected tumors greater than 10 cm in diameter are poor prognostic factors. Intensive combination chemotherapy gives the best chance of cure with 90% rates in patients with limited disease and 60-80% of patients with advanced disease. Children typically have a better prognosis than adults. If relapse occurs it usually occurs within one year of the diagnosis.

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PRESENTERS
Irene Vergilis MD, Christiane Querfeld MD, Diana Bolotin MD PhD,
Vesna Petronic-Rosic MD MSc, and Aisha Sethi MD

HISTORY OF PRESENT ILLNESS

A 46-year-old white man was referred for a single, recalcitrant, enlarging, and vegetative plaque on his left upper thigh for about one year that initially presented as a papulopustular lesion. Bacterial and fungal cultures from this plaque performed at an outside dermatology office 2 months prior to his visit revealed rare Gram-positive cocci and Trichophyton species. The patient subsequently received trimethoprim/sulfamethoxazole and, and mupirocin for three weeks without improvement, and currently was on no medication.

PAST MEDICAL HISTORY

The patient reported a dry cough, but otherwise good general health. He had no history of immune compromise**.**

MEDICATIONS

None

ALLERGIES

None

FAMILY HISTORY

Non-contributory

SOCIAL HISTORY

He works as an aircraft mechanic, and reported occasional exposure to airborne soil, dust, and dirt particles. He does not smoke or drink, and denies recreational drugs. His travel history was unremarkable.

PHYSICAL EXAMINATION

A large vegetative plaque with a verrucous surface and sharply delineated, rolled borders was present on the left upper thigh. There was no lymphadenopathy noted.

LABORATORY DATA

Serum glucose was elevated at 263 mg/dL, otherwise a complete blood cell count with differential, comprehensive metabolic panel, liver function tests, and CRP were all within normal limits. HIV1/HIV2 antibodies were negative.

Fungal culture (tissue): *Blastomyces dermatitidis*

HISTOPATHOLOGY

Left thigh: Pseudoepitheliomatous hyperplasia and numerous intraepidermal and dermal abscesses composed of neutrophils, lymphocytes, histiocytes, and multinucleated giant cells. The PAS and Giemsa stains highlight budding spores up to 30 microns in size. Multiple spores are also present within the abscesses. The Gram and Fite stains were negative for bacteria and mycobacteria.

IMAGING

Chest radiography: No acute disease

DIAGNOSIS
Cutaneous blastomycosis

TREATMENT & COURSE
The patient was started on itraconazole 200 mg PO daily and is currently being followed by dermatology and infectious diseases.

DISCUSSION
Blastomycosis, also referred to as North American blastomycosis, is an uncommon, soil-born, chronic, granulomatous disease caused by the dimorphic fungus *Blastomycosis dermatitidis* endemic to the south-central and north-central states of the United States bordering the Mississippi and Ohio Rivers. Pulmonary blastomycosis is the most common route of infection through inhalation of spores, but hematogenous dissemination to other sites occurs in 25% to 30% of cases. The most common secondary site is the skin, followed by bone, genitourinary, and central venous system. Rare cases of cutaneous inoculation blastomycosis have been described as a chancriform ulcer at the trauma site with varying degrees of lymphangitis and lymphadenitis.

B. dermatitidis has a thermally dimorphic nature and grows in mycelial phase at room temperature (25^0 C), and in yeast form in tissues (37^0 C). Spores formed in the saprophytic phase (25^0 C) are 2 to 10 μm in diameter and are seen on the lateral or terminal branches of the mycelium. It grows as a slow-growing brown, wrinkled yeast colony at body temperature and as a white, fluffy colony at room temperature on Sabouraud's dextrose agar.

Clinically, cutaneous blastomycosis presents as a pustule that progresses into a verrucous plaque and/or ulcer, which may be mistaken for squamous cell carcinoma, scrofuloderma, lupus vulgaris, nocardiosis, American leishmaniasis, or other deep fungal infections. The diagnosis of cutaneous blastomycosis can be made by histopathologic identification of thick-walled budding spores of *B. dermatitidis* in tissue using PAS or Gomori methenamine-silver stains, and by fungal cultures.

Cutaneous blastomycosis should be managed in accordance with the guidelines for disseminated blastomycosis. Oral itraconazole (200-400 mg daily) is the preferred regimen for those with mild-to-moderate cutaneous disease without CNS involvement and should be continued for at least 6 months or until the skin lesions have resolved. Ninety percent cure rates have been reported after a 6-month regimen of itraconazole.

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PRESENTERS
Ingrid Polcari MD, Diana Bolotin MD PhD, Vesna Petronic-Rosic MD MSc, and Sarah L. Stein MD

HISTORY OF PRESENT ILLNESS
An 11-year-old male presented for evaluation of a rash on his fingers which had been present for the past 4 years. He recalls his fingers having been itchy in the past, but denies this currently. He was treated with a topical antifungal medication for one year without improvement. He admits to chewing and rubbing his fingers sometimes.

PAST MEDICAL HISTORY
The patient has seasonal allergies.

FAMILY HISTORY
No family members have similar skin findings. He has an aunt with thyroid disease.

MEDICATIONS
None

ALLERGIES
No known drug allergies

PHYSICAL EXAMINATION
The distal aspect of all 10 fingers have well-demarcated pink, hypopigmented lichenified plaques on the dorsal surface. The distal aspect of the palmar fingers are pink and peeling. His fingernails are normal. There are no skin changes on the feet and the remainder of his skin exam is normal. He has full range of motion and muscle strength and his cranial nerves are intact.

LABORATORY DATA
None

DERMATOPATHOLOGY
Mild regular hyperplasia with compact orthokeratosis which is more prominent on a lateral portion of the specimen. There is some increased space in between the collagen bundles of the dermis. Colloidal iron stain demonstrates a mild focal increase of mucin. This is accentuated in the area with thicker compact orthokeratosis. An elastic stain shows reduced and fragmented elastic fibers in the same area of the specimen.

DIAGNOSIS
Pachydermodactyly

TREATMENT AND COURSE
Topical mometasone was prescribed with no change in the skin findings.

DISCUSSION
Pachydermodactyly is a rare form of fibromatosis of the fingers. It has been described as a dense fibrosis and fibroblastic proliferation around one or more proximal interphalangeal joints. It typically spares the thumbs and fifth fingers and rarely extends proximally to the wrists. However, recent case reports have discussed a “distal” form in which all distal fingertips are involved.

Pachydermodactyly was first reported in the literature in 1975 in a young man and was thought by the authors to be a variant of knuckle pads. Most initial case reports were in adolescent males leading to the hypothesis that hormones may be a trigger, but more recent papers have reported cases in an elderly man and an elderly woman. Although some authors have noted associated mechanical trauma or compulsive rubbing or biting of the fingers, many of the cases have had no such association.

Clinical changes are symmetrical, diffuse, painless swelling of the skin on the lateral aspects of the phalanges and interphalangeal joints. In the so-called "distal pachydermodactyly," there are non-tender, skin-colored longitudinally furrowed intradermal plaques on the middle and distal phalanges. Our patient's clinical findings are more consistent with the distal form.

Histopathologic characteristics include thickening of the dermis, with coarse collagen bundles and a mild proliferation of fibroblasts. Sometimes there are small deposits of mucin noted. Elastic fibers are reduced. There is no inflammation. Epidermal changes include mild hyperplasia and a compact orthokeratosis.

There is no known effective treatment for pachydermodactyly. Intralesional steroids have been reported to bring about improvement in some cases, while topical steroids seem to have little to no benefit. There is also one reported case of attempted surgical excision.

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PRESENTERS
Diana Bolotin MD PhD, Vesna Petronic-Rosic MD MSc, and Christopher R. Shea MD

UNKNOWN CASE

A 60-year-old Italian man with a history of deep venous thrombosis, lupus anti-coagulant, obstructive pulmonary disease, and sinusitis presented with a two month history of pruritic and tender papules and plaques on the forehead, scalp and lower extremities.

PRESENTERS
David Mann MD, Vesna Petronic-Rosic MD MSc, and Aisha Sethi MD

HISTORY OF PRESENT ILLNESS
A 58-year-old Ukrainian male was referred for consultation by endocrinology for the evaluation of facial papules. Present for many years, the patient had noticed several asymptomatic, discrete growths on his upper lip and nose. Otherwise, the patient had been feeling well despite some progressive dyspnea and occasional fatigue. The patient denied any symptoms of cough, weight loss or anorexia.

PAST MEDICAL HISTORY
Carcinoid lung cancer (status post pneumonectomy, one of fifteen positive lymph nodes, refused radiation therapy but received four cycles of adjuvant cisplatin and etoposide); parathyroid adenoma complicated by hypercalcemia; history of meningioma (stable by serial neuroimages).

FAMILY HISTORY
Family history was significant for a sister with uterine cancer. There was no history of any other cancers, lung disease or endocrinologic disorders in the family.

SOCIAL HISTORY
The patient emigrated from the Ukraine, was employed as a draftsman, is divorced and lives alone. He denied ever using tobacco products, alcohol or use of illicit drugs.

MEDICATIONS
Sensipar

ALLERGIES
No known drug allergies

PHYSICAL EXAMINATION
Three firm, pink, 4-5 mm dome shaped papules were present on the face (two on the nasal sidewall, one on the upper cutaneous lip). The left third toenail had a 3 mm pink papule extending from the proximal nail fold consistent with a periungual fibroma.

LABORATORY DATA
PTH intact: 219 pg/ml [15-75]
Thyrotropin: 1.5 mcU/ml [0.3-3.8]
Calcitonin: < 5 pg/ml [< 16 basal, <= 130 peak]
Vitamin D 1,25: 40 pg/ml [22-67]
Alkaline phosphatase: 95 U/L [30-120]
Inorganic phosphate: 2.4 mg/dL [2.5-4.4]
CBC – WBC: 4.6 H/H: 13.6/39.5 Plat: 184
BMG - Creatinine: 1.0 Calcium: 11.6 mg/dL [8.4-10.2]

DERMATOPATHOLOGY
A biopsy of a facial papule revealed a fibrotic dermis containing stellate fibroblasts and multinucleated floret type cells, consistent with an angiofibroma.

DIAGNOSIS
Multiple endocrine neoplasia type 1

TREATMENT AND COURSE

Genetic testing for multiple endocrine neoplasia type 1 was positive. The patient is being followed by endocrinology, pulmonary, and general surgery for other possible endocrinologic tumors.

DISCUSSION

Multiple endocrine neoplasia type 1 (MEN1) is a familial syndrome associated with tumors of the parathyroid, pancreatic, and pituitary glands. Its frequency is estimated at 1 in 30,000 individuals, with no racial or gender predilection. As demonstrated in our patient, the disorder is often discovered from elevated parathyroid and calcium levels as the parathyroid gland is most commonly affected. In addition to gastrinomas, insulinomas, prolactinomas, and carcinoid tumors, cutaneous tumors are often associated with this condition. While common, the skin findings are often subtle and therefore may be missed on examination. We present this case to highlight the cutaneous features of this syndrome and to discuss the relevancy of such findings in making the diagnosis.

MEN1 is caused by a mutation in the tumor suppressor gene MEN1, on band 11q13. The gene product, Menin, appears to be a nuclear-bound protein whose function remains unclear. Only when both copies are mutated is there tumor proliferation.

Clinically, the skin lesions are composed of angiofibromas, collagenomas, and lipomas. In MEN1, the morphology and histopathology of these lesions are classic for the most part. What distinguishes these tumors is their increased prevalence in MEN1 patients. Angiofibromas have been reported anywhere from 5 to 88% in patients with MEN1. Collagenomas have been described in the literature being present in 63-72% of patients with MEN1, with 83-91% of patients having multiple lesions. Lipomas have been reported in 3-34% of patients with MEN1.

In one prospective 2004 study, a cohort of patients with Zollinger-Ellison syndrome due to gastrinomas angiofibromas were found to be present in 64% of MEN1 patients vs. 8% of controls. Similarly, collagenomas were noted at 62% vs. 5% of controls. Of even greater significance was the finding that three or more angiofibromas along with one or more collagenomas served as a highly sensitive (75%) and specific (95%) marker for the diagnosis of MEN1. This had greater sensitivity than pituitary or adrenal disease for MEN1 and comparable sensitivity to hyperparathyroidism in some studies of patients with MEN1 with gastrinoma.

Cutaneous tumors may precede symptoms associated with the endocrine tumors. Unlike in tuberous sclerosis, the angiofibromas in MEN1 tend to be smaller, less numerous, and involve the upper lip and vermillion border. Additional skin findings include café au lait macules, hypopigmented macules (confetti-like hypopigmented macules), gingival papules, and solitary periungual fibromas.

Treatment is directed at correcting the underlying endocrinologic disorder. Skin manifestations can be treated for cosmetic purposes with simple procedures (shave excisions) or laser therapy with CO2 ablation, though risks of recurrence, scarring and hypopigmentation must be taken into consideration.

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PRESENTERS
Roger Kapoor MD, Christiane Querfeld MD, Vesna Petronic-Rosic MD MSc, and Aisha Sethi MD

HISTORY OF PRESENT ILLNESS
A 53-year-old African American man presented with a 3-month history of a pruritic, erythematous rash on the face, neck, trunk, and extremities. At that time, he was being treated with a one-month course of prednisone with mild improvement. He had also received various topical steroids and anti-itch medications with only slight relief of his symptoms. The patient denied any new and/or any change in medications, the use of any new cosmetic or household products, or recent illnesses.

PAST MEDICAL HISTORY
Hypertension

MEDICATIONS
Metoprolol, amlodipine/enalapril, prednisone

ALLERGIES
No known allergies

FAMILY HISTORY
Non-contributory

SOCIAL HISTORY
He started to work in a florist shop prior to the onset of his rash. He denies tobacco, or illicit drug use, but drinks beer regularly. He has no risk factors for sexually transmitted diseases or HIV. No recent history of foreign travels.

PHYSICAL EXAMINATION
On the face, neck, upper chest in a V-distribution, and distal upper and lower extremities, including dorsal hands, were diffuse, erythematous and brown papules and plaques with lichenification and overlying scale. The skin under his wristbands bilaterally appeared uninvolved. There were oval patches with collarette scale on his trunk.

LABORATORY DATA
Elevated SGOT at 118U/L and SGPT at 72U/L, otherwise complete blood cell count with differential, and comprehensive metabolic panel were within normal limits. ANA and anti-SSA/SSB antibodies were absent. Serologic tests for Hep B and C, HIV, and RPR were negative.

DERMATOPATHOLOGY
Multiple skin biopsies from the back and right arm: Spongiotic dermatitis with a superficial, dermal, perivascular infiltrate of lymphocytes. The PAS stain was negative for fungi or basement membrane thickening.

DIAGNOSIS
Chronic actinic dermatitis

TREATMENT AND COURSE
Over the course of the following 12 months the patient was treated with topical corticosteroid ointments of various strength with mild to moderate improvement, but continued to flare in

photodistributed areas, despite the concomitant use of sunblocks and sun protective clothing. The patient was also treated with tacrolimus ointment for three months without significant relief. He was subsequently started on oral prednisone and tapered over the next four weeks followed by oral mycophenolate mofetil (1gm daily). At the same time he discontinued his job at the florist store. A follow-up visit two months later showed almost complete clearing of his lesions in the photodistributed areas. A recent flare in August 2008 was precipitated by temporary discontinuation of his immunosuppressive drug and a visit to a local baseball game without sunprotection.

DISCUSSION

Chronic actinic dermatitis represents a spectrum of photosensitive dermatoses, which includes persistent light reactivity, photosensitive eczema, and actinic reticuloid. These conditions were originally defined based on the following three criteria: a persistent eczematous eruption of infiltrated papules and plaques that predominantly affects sun-exposed skin that may extend to sun-protected areas; a skin biopsy with abnormalities resembling chronic eczema to cutaneous T-cell lymphoma; and photo-test abnormalities with reduction in the minimal erythema dose to UVB and UVA.

CAD is most commonly reported in temperate climates and can affect Caucasians, Latin Americans, African-Americans, Japanese and Indians. The prevalence is higher in elderly men and not as common in women.

A delayed T-call mediated cellular hypersensitivity to an unknown photoinduced cutaneous antigen is thought to be the underlying etiology. On histology, a predominant $CD8^+$ T-cell infiltrate is found along with dermal dendrocytes. CAD is commonly associated with both allergic contact dermatitis and photoallergic contact dermatitis, but the mechanisms that lead to a persistent light reactivity remain unclear. Sesquiterpene lactone extracts from compositae plants (chrysanthemum flowers), fragrances, colophony, rubber and sunscreens are commonly identified as allergens. Our patient's previous occupation in a florist store with work-related flares did suggest an occupational allergy. However, his chronic skin condition did not allow for patch testing. In addition, the rash continued to flare with sun exposure alone after the patient lost his job due to closing down of the florist shop.

Treatment of chronic actinic dermatitis is a challenge and involves foremost avoidance and protection from UV-light. Frequently applied sunscreens and sun-protection are mandatory. Azathioprine, hydroxychloroquine, UVB, PUVA, topical and oral corticosteroids, tacrolimus ointment, thalidomide, cyclosporine, and most recently mycophenolate mofetil have been used with various success rates.

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PRESENTERS
Shaily Patel MD, Vesna Petronic-Rosic MD MSc, Christopher R. Shea MD, and Keyoumars Soltani MD

HISTORY OF PRESENT ILLNESS
A previously healthy 44-year-old woman presented to our clinic with a two-year history of multiple, non-healing facial ulcers. She had been diagnosed with granuloma faciale per multiple outside biopsies and treated with multiple excisions by a plastic surgeon. She subsequently presented to our clinic with a three-month history of a non-healing facial lesion that had developed within a prior excision scar. It was neither painful nor pruritic and seemed to be gradually increasing in depth and diameter. She was not on any treatment at the time of presentation. She denied any travel prior to onset of her lesions or any occupational exposures. Upon repeated questioning, the patient revealed that she has a small fish tank at home.

PAST MEDICAL HISTORY
Seasonal allergies and asthma as a child.

FAMILY HISTORY
Family history significant for hypertension.

SOCIAL HISTORY
She works as an assistant manager, smokes 2-3 cigarettes/day, and denies alcohol or illicit drug use.

MEDICATIONS
None

ALLERGIES
Augmentin

PHYSICAL EXAMINATION
All vital signs were within normal limits. The patient was a well-appearing female in no acute distress. Skin examination revealed a 1.2 by 1.5 cm round, erythematous, indurated plaque with central ulceration. The base was yellowish and the borders were irregular and raised. The plaque was within a prior linear scar. There was no other skin involvement and no lymphadenopathy.

LABORATORY DATA
Quantitative G6PD: 12.5
CBC: WBC: 8.6, H/H: 13.3/37.9, Plt: 316
HIV: Nonreactive
Tissue culture: A pigmented rapidly growing acid-fast bacillus was isolated after 14 days. Fungal culture was negative. Sensitivity testing revealed a mycobacterium susceptible to doxycycline.

DERMATOPATHOLOGY
Outside pathology report: Epidermis with focal spongiosis and acanthosis. A superficial and deep perivascular and interstitial infiltrate composed of lymphocytes, plasma cells, neutrophils, macrophages and abundant eosinophils was noted. Foci of granuloma formation were present. Immunoperoxidase staining was positive for a mixture of B and T-cells without light chain restriction. Atypical cells were not observed.
L cheek biopsy: Skin with no epidermis and with extensive dermal fibroplasia. The dermis had a nodular and diffuse, mixed inflammatory cell infiltrate composed of lymphocytes, histiocytes,

neutrophils, plasma cells and scattered eosinophils and extravasated red blood cells. Polarization revealed birefringent foreign material multifocally throughout the dermis. The Fite stain revealed exceedingly rare acid-fast organisms, while the Ziehl-Neelsen stain was negative.

DIAGNOSIS
Unknown pigmented atypical mycobacterium

TREATMENT AND COURSE
After dermatology evaluation and based on the outside pathology report, the patient was initially started on prednisone 20 mg daily and dapsone 50 mg daily. Once acid-fast bacilli were noted on tissue culture, prednisone was immediately discontinued and dapsone was increased to 100 mg daily. Sensitivity testing was procured about 1 month into her course, at which time she was switched to doxycycline 100 mg BID for three months. This treatment was discussed and agreed upon by the infectious disease service. The patient noted complete resolution of her lesion in a few weeks, with no recurrence. Genotyping via PCR analysis of the mycobacterium is currently pending.

DISCUSSION
Atypical mycobacteria were first identified and isolated in 1931; however, their importance as human pathogens was not recognized until many years later. These mycobacteria are found not only in the environment, but also in dairy products, cold-blooded animals, and human feces. They are transmitted by accidental inoculation via inhalation, ingestion, or percutaneous penetration. This subsequently leads to pulmonary, lymph node or skin disease. Disease severity is often determined by the immune status of the host, although there have been increasing reports of atypical mycobacterial infection in immunocompetent individuals.

The mycobacteria are classified based on rate of growth *in vitro* and pigment production following exposure to light. Over 100 species are now recognized, with many of them having cutaneous involvement. *M. ulcerans, M. marinum, M. kansasii, M. fortuitum, M. chelonae, M. avium intracellulare, M. haemophilum,* and *M. scrofulaceum* are the most common.

The clinical presentation may be of a single, firm inflammatory nodule or pustule or a keratotic plaque involving the skin and subcutaneous tissue. Eventually, the lesion may ulcerate and typically spread in a sporotrichoid pattern. The most common primary location is the extremities; facial involvement is rare. Disseminated infections are most commonly seen in immunocompromised hosts.

Histologically, findings can range from acute and chronic inflammation to tuberculoid granulomas. In addition, the changes will vary based on the species of the mycobacterium. Fibrinoid deposits and caseation necrosis have also been observed. The infiltrate is polymorphonuclear, and can contain neutrophils, lymphocytes, eosinophils, histiocytes and plasma cells. Acid-fast bacilli should be observed on special staining although organisms may be quite difficult to find in immunocompetent individuals.

Treatment varies by some authors based on the pathogen; however surgical excision has been suggested as the therapy of choice for ulcers. Continuous local heating to 40ºC by circulating water jackets and hyperbaric oxygen can be useful. Systemic treatment should be tailored based on sensitivity testing of the organism. Evidence is lacking as to whether single versus combination therapy should be employed. In addition, therapy tends to be long-term, usually in the range of three to six months, depending on the immune status of the patient, severity of infection, and resistance pattern of the mycobacterium.

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PRESENTERS
Jessica S. Maddox MD, Vesna Petronic-Rosic MD MSc, and Maria Tsoukas MD

HISTORY OF PRESENT ILLNESS
A 38-year-old woman presented for evaluation of a growth on her posterior scalp. This sizeable mass had been present for over twenty years but had recently become larger and tender, interfering with supine positioning. In addition, she had other innumerable growths on the body that were cosmetically concerning.

PAST MEDICAL HISTORY
She had a history of neurofibromatosis type 1 (NF1), with seizure disorder, mood disorder, and developmental delay, as well as hypertension. Her father also had NF1.

MEDICATIONS
Olanzapine 5 mg PO QHS, lorazapam 0.5 mg PO BID PRN, buspirone 5 mg PO BID, hydrochlorothiazide 23 mg PO daily, benztropine 2 mg PO BID, loratadine 10 mg PO daily, Necon OCP, and docusate sodium 100 mg PO QHS.

ALLERGIES
No known drug allergies

PHYSICAL EXAMINATION
On exam, a six centimeter firm mass was noted on the occipital scalp. It was mobile and appeared well circumscribed. There were multiple soft, fleshy nodules and tumors of various sizes diffusely, as well as multiple hyperpigmented patches, axillary freckling, and freckling of the irides. She exhibited marked scoliosis and limb-length discrepancy, as well as divergent strabismus. An excision of the scalp mass was performed, revealing a four centimeter rubbery, pink-tan tumor with a thin, translucent membrane.

DERMATOPATHOLOGY
Histopathologic sections displayed densely packed spindle cells with hyperchromatic nuclei, marked atypia, and mitotic figures, some of which were atypical. Multiple small foci of tumor necrosis and areas of extensive hemorrhage were present. Tumor cells were positive for S-100 and CD34.

DIAGNOSIS
Malignant peripheral nerve sheath tumor in patient with neurofibromatosis type 1

TREATMENT AND COURSE
The patient was referred to oncology for further work-up. A head CT revealed the persistence of a soft tissue mass of the occipital scalp. A CT of the chest, abdomen, and pelvis was performed to identify metastases, and was normal. She was referred to plastic surgery for wide excision and oncology for further management.

DISCUSSION
Neurofibromatosis type 1 (NF1), or von Recklinghausen's disease, is a multisystem autosomal disorder. The disease is due to a mutation or deletion of the *NF1* gene on chromosome 17 which codes for the tumor suppressor, neurofibromin. Occurring in 1 out of 3000 people, NF1 is the most common genodermatosis.

The diagnosis of NF1 is made when 2 of 7 criteria are met: 1) six or more café-au-lait macules greater than 5 mm in diameter in children younger than 10 years and greater than 15 mm in adults, 2) axillary or inguinal freckles (Crowe's sign), 3) two or more typical neurofibromas or one plexiform neurofibroma, 4) two or more iris hamartomas (Lisch nodules), 5) optic nerve glioma, 6) bony abnormalities which may include sphenoid dysplasia or pseudarthrosis, and 7) a first-degree relative with NF1. MRI may detect benign hamartomas in the brain parenchyma seen more often in patients with learning disabilities. The major causes for morbidity and mortality in these patients are hypertension and malignancy.

Malignant peripheral nerve sheath tumors (MPNSTs) are rare, aggressive soft tissue sarcomas. These tumors arise from peripheral nerve branches or the nerve sheath and are likely derived from Schwann cells or other nerve sheath cells. The most common sites are on the extremities, with involvement often of the sciatic nerve, brachial plexus, or sacral plexus. Pain is the most common presenting symptom, although neurologic deficits may occur in the distribution of the affected nerve branch.

In total, MPNSTs account for 5-10% of all soft tissue sarcomas. Approximately two-thirds of all MPNSTs are associated with neurofibromas, particularly the plexiform variant, and 40 – 60% of MPNST occurs in the setting of NF1. Sporadic MPNSTs are most common between 40 and 50 years of age, while those occurring in the setting of NF1 are diagnosed on average 10 years earlier. A recent study of patients with NF1 has indicated that the lifetime risk of developing a MPNST is 8 – 13% percent. Rapid enlargement of an existing neurofibroma should be considered a sign of malignant transformation until proven otherwise.

Histologically, MPNSTs are characterized by the presence of pale spindle cells often arranged in fascicles with alternating cellular and myxoid areas. There are variable degrees of mitotic activity, necrosis, and calcification, the evaluation of which contribute to tumor grade. There is often evidence of adjacent neurofibroma. S-100 protein is expressed in 50 – 90% of tumors.

MPNST is often a highly aggressive tumor with a poor prognosis. Prognosis is generally worse in patients with tumors greater than five centimeters in diameter and in those with NF1, with the five-year survival rate of 10 – 20% for NF1 patients with MPNST, compared to 40 – 50% for sporadic cases. Wide surgical resection is the treatment of choice; however, the recurrence rate after excision is fifty percent. Post-operative chemotherapy and radiation are often used as adjuvant therapy. Metastases occur hematologically and are found primarily in the lung.

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PRESENTERS
John C. Fox MD, Christopher R. Shea MD, and Sarah L. Stein MD

HISTORY OF PRESENT ILLNESS
A six-year-old female with congenital erythropoietic porphyria (CEP) presented for her annual follow-up. Her family reported only very occasional sores on the back of the hands or face, mostly occurring in late summer and fall. They acknowledge the persistence of hypertrichosis, erythrodontia, and dyspigmented and hypertrophic scars involving the cheeks, chest, and back. There were no active vesicles, bullae, or erosions on the day of presentation.

PAST MEDICAL HISTORY
Prenatal course was significant for pre-eclampsia, maternal hypertension secondary to hyperaldosteronism, and premature delivery at 32 weeks gestation. The infant was immediately transferred to the neonatal ICU for prematurity, respiratory distress, and possible sepsis. Hyperbilirubinemia developed on the second day of life, and phototherapy with shielded fluorescent bulbs was initiated. Within hours, the infant became anemic, hypotensive, and developed respiratory distress requiring mechanical ventilation and vasopressor support. The acute drop in the RBC count, hemoglobin, and hematocrit necessitated several blood transfusions. The combination of history, findings on physical examination and skin biopsies, and laboratory values led to the diagnosis of CEP. The patient was treated with immediate discontinuation of phototherapy and was transferred to a dark room. The patient was repeatedly transfused with packed RBCs, fresh frozen plasma, platelets, and cryoprecipitate. This produced stabilization of her anemia, suppressed production of abnormal porphyrins, and allowed her general condition to improve.

MEDICATIONS
Beta-carotene 30 mg PO daily, multivitamin with Vitamin D.
Careful use of sun-protective clothing, physical blocking sunscreens and sun avoidance.

ALLERGIES
No known drug allergies

PHYSICAL EXAMINATION
Physical examination demonstrates a well-appearing, well-developed, and friendly 6-year-old in no distress. The teeth are red in color, and there is hypertrichosis of the face, controlled with depilatories. Mildly hypertrophic scars involving the cheeks, chest, and back have flattened significantly over time, and previously notable dyschromia involving the extremities has much improved. Over the dorsal hands and wrists there are hyperpigmented patches, but no active blisters or erosions. Nails are normal, and there is no appreciable hepato- or splenomegaly.

For clinical interest, we have included photographs of the initial physical examination on DOL#2, which revealed an intubated and sedated infant with skin fragility, blisters, and erosions on the trunk, neck, and face, and dusky, mottled discoloration of the skin over the chest wall. Abdominal distention, poor perfusion, and hepatosplenomegaly were also noted. On DOL#6, physical examination disclosed a generalized, dusky, mottled discoloration and more extensive blistering with angulated, widespread erosions.

LABORATORY DATA

5/11/07

Porphyrins, Fecal	Porphyrins, Urine
Total Porphyrins 56.5 ug/dl (<1)	Pentacarboxylporphyrins 544 ug/24hr (<7)
Hexacarboxyl I 21ug/24hr (<10)	Hexacarboxyl porphyrins 156 ug/24hr (<6)
Isohexacarboxyl 84 ug/24hr (<10)	Heptacarboxyl porphyrins 186 ug/24hr (<7)
Pentacarboxyl I 489 ug/24hr (<20)	**Uroporphyrin 1839 ug/24hr (<25)**
Isopentacarboxyl 165 ug/24hr (<80)	**Coproporphyrin 2126 ug/24 hr (<110**)
Coproporphyrin I 25616 ug/24hr (<500)	Uroporphyrinogen synthase 12.6 nmol/s/L (>7)
Coproporphyrin III 5620 ug/24hr (<400)	
Isocoproporphyrin 534 ug/24hr (<200)	

Prophyrin profile is consistent with CEP (Mayo Medical Laboratories, Rochester, MN)

DERMATOPATHOLOGY

Day of Life #6 (presented for clinical interest)

Punch biopsy of abdominal skin exhibited epidermal atrophy with focal dermal-epidermal separation and incipient necrosis. The dermis exhibited scant inflammation and dilated blood vessels. A biopsy specimen of involved skin of the left thigh revealed a non-inflammatory, subepidermal blister with slightly hyalinized dermis. PAS stain demonstrated mild thickening of the basal membrane as well as thickening of dilated dermal vessels.

DIAGNOSIS

Congenital erythropoietic porphyria (CEP, Günther disease)

TREATMENT AND COURSE

Erosions over the face, chest, and back have healed with significant hypertrophic scarring and post-inflammatory pigmentary changes. The patient has subsequently undergone normal physical and cognitive development and has suffered only minimal ongoing cutaneous blistering. Her anemia has resolved, and so far she has not been transfusion-dependent. As is consistent with the diagnosis of CEP, her teeth have erupted red, she has developed hypertrichosis, and her urine continues to be intermittently red. The family continues to shield the child from sunlight as much as possible, but gradual exposure to incandescent and fluorescent light has not provoked skin lesions. The potential for hematopoietic stem cell transplantation was discussed with the family, as were the numerous potential risks. A sibling transplant donor is not available. Also of clinical interest, mutational analysis of DNA has failed to demonstrate the presence of any of the known gene mutations associated with CEP, representing the possibility of a novel mutation.

DISCUSSION

Congenital erythropoietic porphyria (CEP, Günther disease) is the rarest of the inherited porphyrias, a diverse group of inborn errors of heme biosynthesis. There are approximately 150 reported cases of CEP in the medical literature, representing diverse racial and demographic groups. Named after German physician Hans Günther who first recognized the disease as an inborn error of metabolism in 1911, CEP is presently recognized to originate from an inherited, autosomal recessive mutation in the uroporphyrinogen III synthase (U3S or UROS) gene, resulting in marked deficiency in functional activity of the enzyme. The subsequent accumulation and deposition of photoactive heme precursors in skin, erythrocytes, bone, and teeth results in the unique syndromic manifestations of severe photosensitivity, hypertrichosis, hemolytic anemia, and erythrodontia.

Onset and clinical severity of CEP are highly variable, ranging from presentation as non-immune hyrops fetalis to milder forms in which cutaneous involvement develops in adult life. Investigation to date has revealed 36 known mutations in the UROS gene, and a close relationship has been demonstrated between residual enzyme activity and patient phenotype, with minimal enzyme activity and larger porphyrin excess correlating with more severe disease. CEP is often a devastating disorder with potential for mutilating scarring, disfigurement, necessity for chronic transfusions, and shortened life expectancy. Currently, stem cell transplant is the only curative therapy.

The possibility of stem cell transplant was recently reviewed and discussed with the patient's family; however, given her excellent recovery and the manageable role the disease activity plays in her daily life, the consensus has been that the risk of a transplant would be too great given the mild expression of the disease at this time. The favorable course of her disease is of clinical interest and it is posed that this may be due to the inherent photo-protective qualities of her natural pigmentation and perhaps a previously yet unidentified mutation in the UROS gene that has allowed for some residual function of the enzyme.

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PRESENTERS
Christiane Querfeld MD, Justin Wasserman MD, Vesna Petronic-Rosic MD MSc, Christopher R. Shea, MD, and Keyoumars Soltani, MD

Patient A

HISTORY OF PRESENT ILLNESS
A 56-year-old white man presented with a two-month history of asymptomatic nodules on the right thigh and buttock. Histopathological evaluation of an outside biopsy was described as atypical lymphocytic infiltrate with a dense dermal infiltrate of lymphocytes and plasma cells.

PAST MEDICAL HISTORY
Remote history of fever and fatigue three years ago without clinical or pathologic findings. Negative HIV-test 10 years ago.

MEDICATIONS
Multivitamins

ALLERGIES
No known drug allergies

FAMILY HISTORY
Negative for non-Hodgkin lymphoma.

SOCIAL HISTORY
Works as a statistician. Does not smoke or drink, and denies illicit drugs.

PHYSICAL EXAMINATION
Two soft, violaceous nodules were present on the right upper thigh and buttock. There was no lymphadenopathy or hepatosplenomegaly noted.

LABORATORY DATA
SGOT slightly elevated at 37U/L, otherwise complete blood cell count with differential, comprehensive metabolic panel, and LDH were all within normal limits.
Normal serum and urine protein levels without evidence of monoclonal gammopathy.

HISTOPATHOLOGY
H&E: Right buttock: Deep, dense, nodular and diffuse infiltrate of medium-sized to large lymphoid cells, interspersed with small lymphocytes and focal aggregates of plasmacytoid cells. A grenz zone sparing the epidermis was present. Neoplastic cells were pleomorphic, with large, round to oval nuclei and prominent nucleoli. Scattered atypical mitotic figures were noted. Tumor cells were positive for CD20, CD45, CD79, CD138, Bcl-2, Bcl-6, and MUM-1 and negative for CD10 and EBV-encoded RNA.
T- and B-cell rearrangement studies: polyclonal for T-cells and monoclonal for B-cells.

IMAGING
9/30/2008 CT scan of chest, abdomen, and pelvis revealed no peripheral lymphadenopathy, but mild periceliac adenopathy.

DIAGNOSIS
Large B-cell lymphoma, leg type

TREATMENT & COURSE
The patient is followed by dermatology and hematology/oncology. He is currently being evaluated for systemic chemotherapy such as R-CHOP (cyclophosphamide, doxorubicin, Oncovin® [vincristine], and prednisone with rituxumab) versus radiation therapy. The patient otherwise feels well.

Patient B
HISTORY OF PRESENT ILLNESS
This 72-year-old white woman presented with a two-week history of an erythematous rash on the thighs and pretibial areas, and bilateral leg edema. She complained of an enlarged right inguinal lymph node for about one month. She had been on chronic immunosuppression primarily with cyclosporine A and intermittently with prednisone for the last 20 years following a liver transplant in 1987, but had been doing well prior to the onset of the rash.

PAST MEDICAL HISTORY
Hepatitis C diagnosed in 1966, status post liver transplant in 1987 with recurrent cirrhosis, endocarditis, and osteoporosis.

MEDICATIONS
Cyclosporin A, alendronate, calcium, furosemide, levothyroxine, multivitamins, vitamin E, and selenium

ALLERGIES
Penicillin, codeine

FAMILY HISTORY
Mother with history of malignant melanoma

SOCIAL HISTORY
She is widowed with 6 children and 16 grand children. She denies tobacco, alcohol, or illicit drugs.

PHYSICAL EXAMINATION
There were tender, ill-defined and indurated erythematous plaques involving the lower extremities with 2+ pitting edema. She had a single right inguinal lymphadenopathy, but no other adenopathy or organomegaly was noted.

LABORATORY DATA
Decreased white blood cell count at 3.1/μL and hematocrit of 32.7%, elevated LDH at 981U/L, SGOT at 59U/L and total protein at 8.9g/dL, otherwise normal platelets, and comprehensive metabolic panel.

HISTOPATHOLOGY
H&E: Right thigh: Deep, dense dermal and subcutaneous infiltrate with diffuse infiltrate of large atypical cells with large hyperchromatic nuclei and prominent nucleoli. Numerous mitotic figures and areas of tumor necrosis were present. There was a grenz zone sparing the epidermis. Tumor cells were positive for CD20, CD45, Bcl-6, and Ki-67, and negative for CD10, Bcl-2, MUM-1, ALK-1, and EBV-encoded RNA.
Cytogenetic studies: positive for c-MYC translocation.

Bone marrow: normocellular bone marrow with peritrabecular, small atypical lymphoid aggregates. Morphologic features of large B-cell lymphoma were not present.

IMAGING
3/6/2008 CT scans of chest, abdomen, and pelvis without lymphadenoathy or organomegaly. There was chronic liver disease and portal hypertension. PET scans revealed hypermetabolic tumors in mediastinum, abdominal wall, and lower extremities.

DIAGNOSIS
B-cell lymphoma with features of diffuse large B-cell lymphoma and Burkitt lymphoma

TREATMENT & COURSE
The patient is being followed by hematology/oncology, hepatology and dermatology. She was started on R-CHOP regimen, but significant tumor lysis syndrome necessitated discontinuation of her therapy. She subsequently was transferred to ICU for sepsis with acute renal failure. However, in view of the poor prognosis of her lymphoma hospice care was arranged.

DISCUSSION
Diffuse large B-cell lymphoma (DLBCL) is an aggressive malignancy of large B lymphoid cells. It is the most common type of non-Hodgkin lymphoma and accounts for 30% to 40% of new diagnoses. However, DLBCL is heterogeneous both clinically and morphologically and patients with DLBCL have highly variable clinical courses.

Morphological, molecular, immunophenotypical, and clinical studies have subdivided DLBCL into prognostically significant subgroups and distinct disease entities. A large number of cases, however, do not fit into other categories of better defined subtypes and remain not otherwise specified. Besides considering the morphology and growth pattern of the neoplastic B-cell population immunophenotyping studies of CD20, CD79, Bcl-2, Bcl-6, CD10, and MUM-1 are generally required to make a diagnosis.

As with patient A some subtypes can present in the skin exclusively. In the consensus WHO–EORTC classification for primary cutaneous lymphomas, three distinct primary cutaneous B cell lymphomas are distinguished: primary cutaneous marginal zone B-cell lymphoma (MZL), primary cutaneous follicle center lymphoma (FCL) with tumors preferentially localized on upper extremities, trunk, and scalp, and primary cutaneous DLBCL, leg-type, with tumor localization mostly restricted to the legs. Recent studies demonstrated that patients with primary cutaneous DLBCL, leg-type differ from other cutaneous B-cell lymphomas by a later age of onset, more frequent dissemination to extracutaneous sites and a poorer prognosis. Unlike primary cutaneous FCL, most DLBCL, leg-type, express Bcl-2 and MUM-1 protein.

Patient B presented with widespread disease on both legs, but developed her B lymphoid malignancy as a consequence of chronic immunosuppression following a liver transplant. Post-transplant lymphoproliferative disorders (PTLD) comprise a spectrum ranging from indolent to EBV-positive or EBV-negative proliferations indistinguishable from lymphomas that may occur in immunocompetent patients. PTLD appear to be most commonly associated in liver or lung allograft recipients. Although extranodal involvement in PTLD is common, cutaneous presentation is rare.

The clinical and morphologic features are highly variable. Our patient presented with histologic features of both DLBCL and Burkitt lymphoma. Although EBV-encoded RNA was negative,

cytogenetic abnormalities such as MYC translocation and a high proliferation index as shown by Ki67 staining of nearly 95% of the neoplastic cells was found.

Currently, the prognosis of patients with systemic DLBCL is estimated using the clinical parameters of the International Prognostic Index (IPI). Despite the use of anthracycline-based chemotherapy (CHOP), durable remissions are achieved in only 40% to 50% of patients. The addition of the CD20 antibody rituximab has led to a marked improvement in survival. Rituximab in the treatment of DLBCL, leg type, either as single agent therapy or in combination with systemic chemotherapy remains to be established as long-term follow-up data are not available.

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PRESENTERS
Justin Wasserman MD, Christopher R. Shea MD, Robert Chen MD, and Aisha Sethi MD

HISTORY OF PRESENT ILLNESS
A 81 year old Caucasian male with no significant past medical history presented to the dermatology clinic because of a rapidly enlarging mass on the scalp over a 4-5 day period. The lesion was asymptomatic otherwise. No other areas of his body were affected.

PAST MEDICAL HISTORY
Actinic keratoses on the scalp treated with cryotherapy, elevated cholesterol, cataracts

MEDICATIONS
Atorvostatin, aspirin

ALLERGIES
No known drug allergies

PHYSICAL EXAMINATION
Vital signs within normal limits. Well developed well nourished male in no acute distress. The patient presents with a 3 cm by 3 cm non-tender asymmetric violaceous nodule on the right anterior scalp with no surface change, erosions, or ulceration.

DERMATOPATHOLOGY
H & E: Diffuse nodular and interstitial infiltrate of atypical cells forming irregular vascular spaces within the dermis, dissecting between collagen bundles. "Hobb-nailing" of endothelial cells is identified within vessels. Considerable cytologic atypia is noted with prominent nuclear enlargement and hyperchromasia. Necrosis and hemorrhage are abundant.
Immunohistochemistry: HHV8 staining is negative within the tumor cells.

DIAGNOSIS
Angiosarcoma

TREATMENT AND COURSE
Following the diagnosis the patient was immediately scheduled with plastic surgery for complete excision of the tumor with follow-up chemotherapy and radiation treatment. He is currently doing well with no signs of recurrence.

DISCUSSION
The term angiosarcoma is traditionally used to denote any high grade malignant neoplasm of endothelial origin, either of lymphatic or vascular differentiation. Angiosarcomas are rare neoplasms that usually occur in the adults and the elderly. Examples that occur in younger populations are usually associated with an underlying disease state such as chronic lymphedema, chronic radiodermatitis or immunosuppression.

The most common form of angiosarcoma is cutaneous angiosarcoma without lymphedema which occurs in the elderly. Over 70% of these tumors occur in patients over the age of 40 years, and the highest incidence is in patients over the age of 70 years. Fifty percent of these lesions occur in the area of the head and neck. There is a higher incidence of this tumor in Caucasians and it has a 2:1 predilection for males.

Clinically, angiosarcomas often present as bruise like lesions on the head and neck, which can often appear very benign. With time these lesions become violaceous, nodular, bleed easily, and may ulcerate. They spread in a centrifugal manner and can ultimately cover large areas of the head and neck. Angiosarcomas that arise in the setting of chronic lymphedema present as firm violaceous plaques or nodules within a background of non-pitting edema. Most lymphedema associated angiosarcomas arise after mastectomy and lymph node dissection and occur on the inner surface of the upper arm. Post-irradiation angiosarcomas present as infiltrative plaques or nodules in previously irradiated areas. Angiosarcomas are aggressive and multicentric, and they have a high rate of metastasis to regional lymph nodes and the lungs.

Histologically, angiosarcomas can have a variable degree of differentiation within the tumor itself. Well differentiated areas appear as anastomosing networks of sinusoidal vessels lined by a single layer of endothelial cells with mild to moderate cytologic atypia. These vessels infiltrate through collagen bundles and adipose cells. Poorly differentiated areas have poor lumen formation, high mitotic rates, and blood filled cavities may be present. Most angiosarcomas will stain with CD34 or CD31. Unlike Kaposi's sarcoma, which can be in the differential, angiosarcomas do not stain with HHV-8.

The prognosis of this tumor is very poor, with a 5 year survival of less than 15%. Lesions should be treated aggressively with wide surgical excision. Chemotherapy and radiation are often used palliatively but have not been found to improve survival.

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PRESENTERS
Roger Kapoor MD, Diana Bolotin MD PhD, Christopher R. Shea MD, and Sarah L. Stein, MD

HISTORY OF PRESENT ILLNESS
The patient is an 11-year old female with Goltz syndrome (focal dermal hypoplasia) who presented for evaluation of new dark spots within areas of hypopigmentation on her legs, developing over the last 1-2 years. The patient notes that she developed a sore near the right knee about a year ago, which drained yellow material for weeks to months and doesn't seem to have completely healed. Lastly, over the past few weeks, she developed rough, white bumps on her right knee and elbow that are asymptomatic.

PAST MEDICAL HISTORY
Goltz syndrome (microcephaly, growth delay, umbilical hernia, simple ear, cleft lip s/p correction, notched ala nasi, bifid uvula and syndactyly of the 2nd and 3rd left toes).
Neonatal herpes.

MEDICATIONS
None

FAMILY HISTORY
Biological mother was on methadone at the time of delivery.
Patient raised in foster care.

PHYSICAL EXAMINATION
The patient demonstrates facial asymmetry as well as a few perioral pink papillomatous papules. Hypopigmented, atrophic, linear plaques following the lines of Blashko are present in widespread distribution, favoring the right side of the body. White, keratotic, rough papules are present within the atrophic areas on the right elbow and knee. Numerous, well-demarcated, stellate, dark brown to black macules are found scattered within hypopigmented atrophic plaques. Just below the right knee, there is a dark brown macule with an overlying pink irregular scar with some scale. No active drainage was noted at the time of evaluation. Syndactyly of the left 2nd and 3rd toes along with nail dystrophy of the right great toenail, 4th and 5th fingernails was noted.

DERMATOPATHOLOGY
A punch biopsy of the hyperpigmented lesion and the scar near the right knee demonstrated flattening of epidermal rete ridges over an area of dermal fibrosis. Melanophages were present in the dermis.

DIAGNOSIS
Goltz syndrome with lentigo-like pigmentation

TREATMENT AND COURSE
Given the patient's craniofacial dysmorphism, she continues to be followed regularly by the craniofacial, speech, plastic surgery, ophthalmology and genetics teams. Her skin changes are followed by dermatology. The patient recently underwent a cleft lip revision using dermal fat graft to her right upper lip and has had multiple previous surgeries including a tonsillectomy and adenoidectomy for sleep apnea and a reconstruction of her nose by rotation flaps.

DISCUSSION

Goltz syndrome, or focal dermal hypoplasia, was initially reported in 1962. It is an X-linked dominant genodermatosis with characteristic skin findings and a wide number of defects that may affect the eyes, teeth, skeletal, urinary, gastrointestinal, cardiovascular and central nervous systems. This condition is thought to be embryonically lethal in most males and is therefore seen predominantly in females due to the mosaic lyonization of the X-chromosome. Concordantly, skin lesions in Goltz syndrome follow the lines of Blashko and typically consist of dermal atrophy with telangiectasias, fat herniation, and perioral or perianal papillomatous papules. Hair is frequently sparse and nail dystrophy is occasionally seen. Skeletal defects may include syndactyly, or lobster-claw deformity, and osteopathia striata. Eye abnormalities such as coloboma or micropthalmia are often seen. Histopathology demonstrates a reduction in dermal collagen. Adipose tissue may be present in the upper dermis and often directly abuts the epidermis. Skin appendages are typically sparse.

Recently, the genetic defect has been identified as a mutation in the PORCN gene on the X chromosome. PORCN encodes a protein in the endoplasmic reticulum that targets Wnt signaling proteins to the cell membrane. Wnt proteins have a multifocal role in skin development through effects on adipogenesis, osteoblast differentiation and hair follicle formation. The presence of keratotic follicular papules within areas of dermal hypoplasia seen in our patient is intriguing in terms of the role of Wnt signaling on hair follicle formation. Whether these keratotic papules represent aborted hair follicles remains an open question.

In addition, our patient demonstrated an unusual finding of lentiginous macules within areas of focal dermal hypoplasia that has only been described in one previous report in the literature. Clinically, both of these cases presented with numerous lentigo-like macules developing in areas of affected skin. Histopathologically, both of these cases show an increase in dermal melanophages. Previous authors speculated that this finding may be due to an increase in tyrosinase activity within melanocytes in areas of focal dermal hypoplasia. Whether Wnt signaling is involved in the development of these lesions remains an unanswered question.

A multidisciplinary team approach is recommended to care for patients with Goltz syndrome. Regular surveillance to detect anomalies and timely preventative and corrective treatment are appropriate. Surgical correction of the various soft-tissue, dental and skeletal anomalies is performed as needed.

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PRESENTERS
Ingrid Polcari MD, Christiane Querfeld MD, and Sarah L. Stein MD

HISTORY OF PRESENT ILLNESS
An almost 3 year old Hispanic male was referred by his pediatrician to the pediatric dermatology clinic for evaluation of skin changes on his hands and feet. His mother stated that the soles of his feet have been discolored since birth. She had recently noticed some hard bumps on the soles of his feet and some discoloration on the dorsal aspects of his feet and hands. She felt that the child sweat normally.

PERTINENT PAST MEDICAL HISTORY
Birth History: Full term infant, uncomplicated pregnancy. 1 month NICU stay after birth for hyperbilirubinemia, hypoglycemia and poor feeding.
Family History: Family is from Mexico but the patient was born in the United States. No family members with similar skin findings.

MEDICATIONS
None

ALLERGIES
No known drug allergies

PHYSICAL EXAMINATION
Well appearing boy in no distress. Weight 12.8 kg (10-25% for age). The hands are small with short fingers. The palmar and plantar surfaces of the hands and feet show reticulated hypo and hyperpigmentation, hyperlinearity and are somewhat atrophic. The tips of the fingers have a smooth texture with the absence of dermatoglyphics. The fingernails appear normal. The balls/heels of the plantar feet have some crateriform lesions with a keratotic plug. There is a small amount of hyperkeratotic scaling on the heels. There is reticulated hypo and hyperpigmentation over the dorsal feet and extending onto the ankles. Some of the toenails appear somewhat irregular. The remainder of the skin exam and skeletal exam is normal. Facial features appear normal with the exception of a somewhat flattened nasal philtrum. Teeth and hair appear normal. There are no oral lesions. Neurologic exam is non-focal. His motor and verbal skills are normal for age.

LABORATORY DATA/IMAGING
IgG, IgA, IgM: within normal limits.
X-rays of clavicle, spine and hands: slightly short terminal phalanx and slight pointing of the distal aspects of the index finger (non-specific findings).
Ophthalmology exam: normal

DERMATOPATHOLOGY
None

DIAGNOSIS
Huriez syndrome (palmoplantar keratoderma with scleroatrophy)

TREATMENT AND COURSE
The patient's family was advised to use Vaseline liberally on the hands and feet. The child was referred for a genetics evaluation where they agreed with the diagnosis of Huriez syndrome.

DISCUSSION

Huriez syndrome, otherwise known as palmoplantar keratoderma with scleroatrophy, was first described in 1968 when it was noted in 44 members of 3 French families. It is a rare inherited disorder of keratinization characterized by diffuse scleroatrophic keratoderma of the palms and soles, sclerodactyly, nail anomalies and possible squamous cell cancer (SCC) of affected skin. The inheritance is autosomal dominant. Gene mapping has not reliably revealed the mutation(s) responsible for this condition. There have been reports of this condition in France, Germany and the United Kingdom but no reported cases in the United States.

Clinical changes are usually present at birth or during early childhood and progress throughout adult life. Case reports describe discrete hyperkeratosis with atrophy, diffusely covering especially the palmar skin, with less severe involvement of the plantar skin. Atrophic plaques may be present on the dorsal hands and fingers. Sclerodactyly that strongly resembles that seen in scleroderma is observed. Nail changes include aplasia, ridging and clubbing. Half of cases have associated hypohidrosis. There is a risk of development of squamous cell carcinoma on the affected skin as early as in the third or fourth decade, with an estimated 15% of Huriez patients being affected. These carcinomas tend to be aggressive with early metastases.

Histopathologic changes are nonspecific although the absence of Langerhans cells in affected skin has been noted in some cases. It has been suggested that this results in decreased immune surveillance and therefore increased incidence of carcinoma.

Treatment is symptomatic. Emollients can soothe the dry, tight skin and prevent fissures. There is one case report of topical retinoid use in a patient with previous SCCs, this patient did not develop any further SCCs during the five year treatment period. Patients should be monitored periodically for development of these cancers.

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PRESENTERS

Diana Bolotin MD PhD, Vesna Petronic-Rosic MD MSc, and Aisha Sethi MD

HISTORY OF PRESENT ILLNESS

A 53-year-old African American woman with a history of well controlled hypothyroidism and gut dysmotility disorder presented with a two-week history of a rash on her face, dorsal hands and groin. The rash was somewhat pruritic and tender. She denied using any medications to treat this condition prior to presentation. The patient's bowel dysmotility disorder was diagnosed five months prior to her presentation. Initially, she was unable to tolerate oral nutrition (PO), thus requiring total parenteral nutrition (TPN). The initial infusion of TPN was complicated by a hypersensitivity reaction that was attributed to either the lipid or trace mineral supplements within the TPN. Since at that point the patient was able to tolerate small amounts of PO intake, the trace mineral and lipid supplements were discontinued. One month prior to her presentation she again stopped taking any nutrition by mouth.

PAST MEDICAL HISTORY

Relevant history includes hypothyroidism and gut dysmotility disorder. Surgical history includes cholecystectomy and splenectomy secondary to ruptured spleen due to a car accident.

FAMILY HISTORY/SOCIAL HISTORY

Non-contributory

MEDICATIONS

Synthroid, Prevacid and Reglan

ALLERGIES

Penicillin

PHYSICAL EXAMINATION

On physical exam, the patient was emaciated but in no distress. She had a flat affect and appeared forgetful. Her oral mucosa was dry and her tongue smooth. Flat topped, hyperpigmented and lichenified papules coalescing into plaques were present on the dorsal aspect of the hands overlying the metacarpophalangeal joints and extended into the interdigital spaces. A well demarcated pink plaque with slight scale and peripheral pustules was present in the anogenital area.

DERMATOPATHOLOGY

A 4-mm punch biopsy from the groin lesion showed confluent parakeratosis overlying the epidermis that had spongiosis, psoriasiform hyperplasia with hypogranulosis and an intraepidermal spongiotic neutrophilic pustule. Papillary dermal edema, dilated blood vessels and a dense perivascular mixed inflammatory infiltrate were present within the dermis. The PAS stain was negative for microorganisms. A second 4-mm punch biopsy from the right dorsal hand showed compact hyperkeratosis overlying confluent parakeratosis. There was regular acanthosis with mild spongiosis and patchy areas of keratinocyte pallor present in the suprabasal layers of the epidermis. A scant, primarily lymphocytic infiltrate was seen in the dermis.

LABORATORY DATA
CBC: Hemoglobin 10.3 g/dL (NL 11.5-15.5 g/dL)
Serum vitamin and mineral levels: niacin <0.5 μg/mL (0.5 - 8.45 μg/mL), zinc 0.14μg/mL (0.66-1.1 μg/mL), copper 0.57μg/mL (0.75-1.45 μg/mL), free retinol 343 μg/L (360-1200 μg/L), α-tocopherol of 6.3 μg/L (5.5-17.0μg/L)
Serum essential fatty acid measurement: Triene to tetraene ratio 0.084 (0.01-0.038)

DIAGNOSIS
Acquired combined nutritional deficiency presenting as psoriasiform dermatitis

TREATMENT AND COURSE
The patient was admitted for anaphylaxis monitoring as TPN with trace mineral and lipid supplementation was restarted. By the third day of parenteral supplementation, the patient's skin lesions improved considerably and were completely resolved within 2 weeks of initiating supplementation. Of note, the patient tolerated re-initiation of trace mineral and lipid supplementation without any adverse reactions.

DISCUSSION
Nutritional deficiency, a prevalent problem worldwide, remains rare in developed countries. In the US, acquired nutritional deficiencies have been reported in patients with anorexia nervosa, malabsorption syndromes, those on long term parenteral nutrition and patients with food allergies. Given the significant morbidity and sometimes mortality associated with certain nutritional deficiencies, their prompt recognition, diagnosis and treatment by clinicians is of great importance. Many nutritional deficiencies have classic cutaneous presentations that are valuable clinical diagnostic tools. However, acquired multiple nutritional deficiencies may put forth a mixed clinical picture that could be easily mistaken for another condition, such as, in this case, psoriasis. There is a paucity of reports of cutaneous presentations of combined nutritional deficiency in dark-skinned patients and of the expected time-course of resolution with resupplementation.

Zinc deficiency may be genetic, as in acrodermatitis enteropathica (AE), or acquired due to a deficiency in the patient's diet. Cutaneous presentation of zinc deficiency classically includes erythematous scaly plaques present on the extremities, anogenital and periorificial areas. Histologically, zinc deficiency classically shows necrolysis, a term used to describe cytoplasmic pallor and vacuolization of keratinocytes in the spinous and granular layers of the epidermis. In our case the patient had both clinical and pathologic features that were consistent with psoriasiform dermatitis. Interestingly, the first case attributed to zinc deficiency was porcine parakeratosis, otherwise known as swine psoriasis. Other reports have shown that more chronic cases of zinc deficiency share a number of histopathologic features with psoriasis, including parakeratosis with variable neutrophils, psoriasiform hyperplasia of the epidermis, hypogranulosis and epidermal pallor. Importantly, cutaneous signs of zinc deficiency resolve with nutritional supplementation, without the need for additional anti-inflammatory therapy as would be necessary in psoriasis. Our case illustrates the capacity of nutritional deficiency dermatitis to clinically mimic psoriasis in a dark-skinned patient and documents a timeline for complete resolution with parenteral nutritional resupplementation.

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PRESENTERS
David Mann MD and Sarah L. Stein MD

HISTORY OF PRESENT ILLNESS
An 11-month-old Caucasian female presented for evaluation of light patches of skin. Present from birth, these asymptomatic, white patches were most prominent on the legs while less obvious on the trunk and forehead. Her parents noted several islands of pigmentation that had developed within these areas over time. The patient was otherwise healthy.

PAST MEDICAL HISTORY
Full-term infant, uncomplicated pregnancy and delivery. Immunizations were up to date.

FAMILY HISTORY
Multiple paternal family members with similar areas of depigmentation and white hair including the patient's father, three of four uncles, grandfather, and great-grandmother. No family history of different colored irides or deafness.

MEDICATIONS
None

ALLERGIES
No known drug allergies.

PHYSICAL EXAMINATION
Vital signs are within normal limits on this well-developed, 11-month-old in no acute distress. On the mid portion of her legs bilaterally, there are well-demarcated geographic patches of depigmentation with islands of normal pigmentation within. There is subtle hypopigmentation on the anterior trunk and a less obvious patch on the upper forehead at the hairline. There is no noticeable white hair. The irides appear to be of the same color and there are no other notable dysmorphic facies. The patient's father is also noted to demonstrate hypo and hyperpigmented patches with white hairs on the mid legs. In addition, he has a clearly defined white forelock of hair.

LABORATORY DATA
None

DERMATOPATHOLOGY
None

DIAGNOSIS
Piebaldism

TREATMENT AND COURSE
Sun protection, offered genetics evaluation, and provided ideas for cosmetic interventions if the child is interested in the future.

DISCUSSION
Piebaldism is a rare, autosomal dominantly inherited disorder of congenital patterned areas of depigmentation (leukoderma) and white patches of hair (poliosis). Mutations in the *KIT* proto-oncogene encoding for a tyrosine kinase cell surface receptor for mast/stem cell growth factor are primarily responsible for the disorder. The location of the mutation within the KIT gene has been

shown to correlate with clinical severity, with mutations in the intracellular tyrosine kinase domain associated with the most severe phenotypes. In addition, deletions in the transcription factor SLUG and zinc finger transcription factor SNAI2 have also been described in the literature.

Pathophysiologically, the abnormal pigmentation results from both defective migration of melanoblasts from the neural crest to the central midline and from a defect in the differentiation of melanoblasts to melanocytes. Ultrastructural studies have shown an absence of melanocytes and melanosomes in the hypomelanotic areas. There have been reported cases of progressive depigmentation, and also of partial repigmentation following exposure to ultraviolet light.

Clinically, there are hypopigmented patches with islands of repigmentation classically located on the anterior and poster aspects of the legs from the midthigh to midcalf. They sometimes contain hyperpigmented borders and generally remain unchanged throughout life. Other areas of involvement include the chin, anterior neck, anterior trunk/abdomen, and anterior and posterior aspects of the midarm to the wrist. Often the lesions are bilateral but not necessarily symmetric. As seen in our patient's father, 80 to 90% of piebald individuals also demonstrate a white forelock with a depigmented triangular patch of the scalp and forehead (including portions of the eyebrows and eyelashes).

Waardenburg syndrome has similar dyspigmentation features, but notably also involves deafness, different colored irides, and facial dysmorphism (lateral displacement of inner canthi).

Unlike vitiligo, the lesions in piebaldism are typically present from birth, lack convex borders, include hyperpigmented macules of depigmented and normal skin, and have a predilection for ventral surfaces. Generally, patients with piebaldism are otherwise healthy and live normal life spans.

Treatment is typically centered on sun protection and cosmetic interventions, such as makeup or the more invasive technique of autologous cultured epidermal grafts. One study showed dermabrasion and split-skin grafting followed by mini-grafting to be successful for twelve adults. A few patients have shown improvement from phototherapy (PUVA), though the disease is generally considered unresponsive to medical or light treatment. However, our patient's father feels that his skin has repigmented significantly over time, though the white body hair remains.

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PRESENTERS
Irene J. Vergilis-Kalner MD, Darryl Oble MD PhD, Vesna Petronic-Rosic MD MSc, and Maria M. Tsoukas MD

HISTORY OF PRESENT ILLNESS
A 37-year-old Hispanic male with a history of common variable immunodeficiency, Hodgkin's and non-Hodgkin lymphomas in remission for 3 years following chemotherapy, was admitted to the University of Chicago Medical Center with colonic pneumonitis, intra-abdominal free air, and diffuse lymphadenopathy. One month prior to his admission, an enlarging lung mass in the right lower lobe was noted on CT scan. Dermatology was consulted for evaluation of asymptomatic skin lesions on his face which had been present for approximately one month. The patient denied any prior history of similar eruption.

PAST MEDICAL HISTORY
Common variable immunodeficiency, Hodgkin's lymphoma, non-Hodgkin lymphoma, gastrointestinal malabsorption

PAST SURGICAL HISTORY
Appendectomy, splenectomy

FAMILY HISTORY
Non-contributory

MEDICATIONS ON ADMISSION
Total parenteral nutrition, intravenous immunoglobulin

ALLERGIES
No known drug allergies

PHYSICAL EXAMINATION
On the forehead, upper eyelids, and dorsal feet bilaterally there were multiple red to light brow, indurated, deep-seated papules and nodules, with surrounding erythema, ranging from 0.5 to 1.5 cm in diameter. In addition, other cutaneous findings included impetiginized herpes simplex viral infection perinasally and diffuse verrucous papules and plaques on the trunk and extremities clinically consistent with verrucae. Examination of the palms, soles, mucous membranes, and nails did not reveal any changes, but the patient did have appreciable cervical, axillary, and inguinal lymphadenopathy.

LABORATORY DATA
The following were negative or within normal limits:
Comprehensive metabolic panel, white blood cell count, platelet count, coagulation studies, calcium, magnesium, inorganic phosphate, total protein, albumin, total and conjugated bilirubin, SGOT, SGPT, plasma lactate, anti-double-stranded DNA antibody.

The following were abnormal:
Hemoglobin 10.7-12.3 g/dl (normal 11.5-15.5 g/dl), hematocrit 31.6-36.7 % (normal 36-47 %), alkaline phosphatase 188-333 U/L (normal 30-120 U/L).

Infectious Disease studies:
Negative / Nonreactive:
CMV IgM Antibody, quantitative CMV by PCR studies, EBV Capsid antibody, infectious mononucleosis antibody, urinary *Blastomyces* antigen, urinary *Histoplasma* antigen, urinalysis, RPR, HIV1/HIV2 antibody, wound drainage culture from papule on leg, bacterial, viral and fungal tissue culture from medial eyebrow area, multiple bacterial and fungal blood cultures, respiratory bacterial and fungal cultures, right lower lobe cavity lesion bacterial culture, urine cultures, feces culture for AFB, direct exam for ova and parasites, *C. difficile* assays.

Microbiological Cultures Positive for Mycobacterium szulgai*:*
Tissue culture from the medial eyebrow area grew 4+ acid fast bacilli, identified as Mycobacterium *szulgai* by DNA sequencing.
The same organism was also identified in pathology specimens from a cervical lymph node and bone marrow biopsies, and was further cultured from sputum and blood.

Imaging Studies:
On infused CT of soft tissue on neck: enhancing cervical lymph nodes worrisome for neoplastic versus inflammatory or infectious involvement.
On infused CT of chest, upper abdomen, lower abdomen and pelvis: lobulated centrally necrotic right paraspinal mass, and mediastinal and left inguinal adenopathy.

DERMATOPATHOLOGY
Punch biopsy specimen from skin papules at the medial eyebrow and left leg revealed dense dermal nodular and diffuse infiltrates composed of neutrophils, lymphocytes, histiocytes, and plasma cells. Within the infiltrates, there were rod-shaped microorganisms, 1-2 micrometer wide by 10-20 micrometers long, staining positive with Gram, PAS, GMS, and Fite stains.

DIAGNOSIS
Systemic *Mycobacterium szulgai* infection

TREATMENT and CLINICAL COURSE
After the organism was isolated and identified the patient was started on antimycobacterial treatment including moxifloxacin, azithromycin, and rifampin. The patient's disease, however, continued to progress until the time of his death in July 2008.

DISCUSSION
Mycobacterium szulgai is a rare nontuberculous mycobacterium (NTM) first identified in 1972. Since then, it has most frequently been reported to cause pulmonary infection, but also septic arthritis, bursitis, tenosynovitis, keratitis, lymphadenitis, disseminated infection, osteomyelitis and skin lesions. Of the eight *M. szulgai* cases reported in literature involving the skin, four presented as skin infections only and four manifested as skin lesions and osteomyelitis.

Classified as Runyon Group II (slow-growing scotochromogen), very little is understood with respect to *Mycobacterium szulgai* epidemiology. Cases occur worldwide and humans are reported to have become infected via ice water, tropical fish, and aquarium water. There are no reports of human-to-human transmission. Affected individuals have been reported from ages 6 months to 62 years with a median age of 50 years. Although infections have been shown in healthy individuals, predisposing conditions include tobacco use, chronic lung disease, alcohol use, previously healed or active tuberculosis, AIDS, or sustained immunosuppression after bone marrow transplant.

M. szulgai is relatively susceptible to conventional antimycobacterial agents including streptomycin, capreomycin, isoniazid plus rifampin, and ethambutol. Other in vitro studies have shown the organism to be susceptible to ciprofloxacin, levofloaxacin, tetracycline, erythromycin, and clarithromycin. There is wide variation in resistance patterns with most frequent resistance reported to isoniazid, followed by cycloserine, rifampin, and para-aminosalycilic acid. There is no standard treatment for this infection, however two or more drugs are typically required to result in clinical improvement. Treatment courses range from 9-24 months with relapses occurring anywhere from 10 months to 5 years post treatment.

Gene amplification and sequencing is optimal for positive identification of *M. szulgai*. Reported biochemical properties include nitrate reduction, catalase activity, pigment production in the dark, delayed Tween hydrolysis, and urease production though strains are variable. According to routine staining for mycobacteria, Ziehl-Neelsen reveals acid-fast bacilli and Gram staining shows no pathogen.

This patient presented with disseminated Mycobacterium *szulgai* infection. The history of common variable immunodeficiency, as well as both Hodgkin's and non-Hodgkin lymphoma, are predisposing factors for infection with many possible organisms including *M. szulgai*. It is important to recognize patients susceptible to atypical mycobacterial infections, as these organisms may sometimes be difficult to culture. *M. szulgai* is a rare but clinically relevant organism to consider when immunocompromised patients present with cutaneous nodules or infiltrates and it should be included in the differential of atypical mycobacterial infections of the skin.

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PRESENTERS
Shaily Patel MD, Vesna Petronic-Rosic MD MSc, and Christopher R. Shea MD

HISTORY OF PRESENT ILLNESS
This 82-year-old woman presented to the emergency room with nausea, vomiting and abdominal pain. Workup revealed a serum lipase level of 18,890 U/L, and she was admitted for acute pancreatitis. At the time of admission, the patient was noted to have diffuse erythema of her lower extremities. Over the course of the next day, she began to run low-grade fevers, experienced worsening erythema, and was complaining of calf and shin tenderness. A punch biopsy was performed for histopathologic evaluation and tissue cultures.

PAST MEDICAL HISTORY
Atrial fibrillation, s/p Colles fracture, sensorineural hearing loss, NMSC status post Mohs surgery, 2006.

FAMILY HISTORY
Non-contributory

SOCIAL HISTORY
She lives at home, denies smoking, alcohol or illicit drug use.

MEDICATIONS
Diltiazem, coumadin

ALLERGIES
Codeine

PHYSICAL EXAMINATION
Vital signs were within normal limits. Physical examination revealed an elderly woman in no acute distress. Both lower extremities were notably edematous and with varicosities. Erythema and tender, indurated nodules were noted on both shins. A few of the nodules were fluctuant, ill-defined and freely mobile.

LABORATORY DATA
Lipase: 18,890 U/L
CBC: WBC: 8.8, H/H: 12.4/37.3, Plt: 225
CMP: Na: 122, K: 3.6, Cl: 102, CO2: 28, BUN 22, Cr 0.9, Glu 122, Ca 8.2
Protein 6.9, total bilirubin 0.8, direct 0.2, indirect 0.7, ALT 26, AST 22, alkaline phosphatase 60
Bacterial culture swab: No organisms
Tissue culture: No organisms

DERMATOPATHOLOGY
There was a superficial and deep mixed inflammatory cell infiltrate admixed with numerous extravasated red blood cells and extensive necrosis of the deep dermis and subcutaneous fat with foci of shadow cells. Sheets of inflammatory cells and necrotic debris were present at the base. Gram stain highlighted clusters of Gram-positive cocci in the dermis. The PAS stain was negative for fungi.

DIAGNOSIS
Pancreatic panniculitis

TREATMENT AND COURSE

The patient was medically managed for pancreatitis and her lipase dropped down to normal at time of discharge. The cause of her pancreatitis was not discovered, as there was no evidence of gallstones or obstruction on imaging and the patient had no history of hyperlipidemia or alcohol abuse. She was not started on antibiotics as there was no evidence of infection per culture results. At follow-up one week after discharge, some of the fluctuant nodules had ulcerated, discharging a yellowish oily material. The patient was advised to use polyurethane foam and to keep her legs elevated. She continued to follow up with wound care twice weekly and had complete resolution of the lesions within a few weeks.

DISCUSSION

Pancreatic panniculitis was first described in 1883 and is a rare complication of pancreatic disease, occurring in less than 2% of cases. This complication is significant and may occur prior to detection of the underlying pancreatic disorder, including acute and chronic pancreatitis, pancreatic carcinoma, pseudocysts, pancreatic divism and traumatic pancreatitis.

The pathogenesis is not well understood; however, evidence suggests that pancreatic enzymes including lipase, amylase and trypsin are involved in producing the lesions. Elevated enzyme levels have been observed in both blood and skin lesions, with lipase having the clearest relationship to the panniculitis. It is thought that amylase and trypsin promote increased vascular permeability, thus allowing lipase to hydrolyze fat. This in turn leads to fat necrosis and inflammation.

Clinically, subcutaneous nodules most frequently occur on the lower legs, but have also been observed on the abdomen, chest, arms, and scalp. The lesions may be erythematous, edematous and subsequently fluctuant and ulcerate, extruding oily contents. Fever, abdominal pain, polyarthritis, ascites, and pleural effusions may also occur. Lesions may involute within a few weeks, and in acute pancreatitis, lesions resolve as the acute inflammatory phase passes.

Histologically, the process may start as a septal panniculitis, with progression to lobular or mixed septal and lobular. Fat necrosis and liquefaction with microcyst formation are observed. Lipocytes may lose their nuclei and form "ghost cells." Fat saponification results in both granular and homogenous basophilic calcific deposition. Macrophages, eosinophils, neutrophils and giant cells may also be present. Later in the process, fibrosis and lipoatrophy are seen.

Treatment includes effective management of the underlying pancreatic disorder. Octreotide may be used to inhibit pancreatic enzyme production. In addition, gentle wound care is advisable and antibiotics are generally not warranted.

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