Chicago Dermatological Society

Monthly Educational Conference

Program Information
Continuing Medical Education Certification
and
Case Presentations

Wednesday, October 14, 2009

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

Program

Committees & Registration

8:00 a.m. - 9:00 a.m.	CDS Plans & Policies Committee *Feinberg Pavilion, Room B*
9:00 a.m. - 10:00 a.m.	IDS Board of Directors *Feinberg Pavilion, Room D*

Program Activities

9:00 a.m. - 10:00 a.m.	RESIDENT LECTURE "Infection, Vitamin D and Evidence-Based Medicine" Richard L Gallo, MD, PhD *Feinberg Pavilion, Room A*
9:30 a.m. - 11:00 a.m.	CLINICAL ROUNDS Patient & Slide Viewing *Dermatology Clinic, 676 N. St. Clair Street, Suite 1600*
11:00 a.m. - 12:15 p.m.	GENERAL SESSIONS *Feinberg Pavilion, Room A*
11:00 a.m.	Guest Lecture – “Understanding Skin Biology and Disease Through Innate Immunity” Richard L Gallo, MD, PhD *Feinberg Pavilion, Room A*
12:15 p.m. - 12:45 p.m.	Lunch & visit with exhibitors *Feinberg Pavilion - 3rd Floor Atrium*
12:45 p.m. - 1:00 p.m.	CDS Business Meeting *Feinberg Pavilion, Room A*
1:00 p.m. - 2:30 p.m.	Case Discussions *Feinberg Pavilion, Room A*
2:30 p.m.	MEETING ADJOURNS

Future Meeting Schedule – check the CDS meeting calendar on our website: www.ChicagoDerm.org

Next meeting – Wednesday, November 18 at the University of Chicago

CME Information

This activity is jointly sponsored by the Chicago Medical Society.

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

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

Commercial Support: There were no educational grants secured for this CME activity.

CME Credit Documentation

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

Evaluation Forms

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

CME Disclosure of Financial Interests

Speaker: Dr. Gallo is the cofounder and is a consultant to Skin Epibiotics.

Program Planning Committee Participants:

- Benjamin Dubin, MD, program chair, has no significant financial relationships to disclose.
- Richard Paul, CDS executive director, has no significant financial relationships to disclose.
- Roger L. Rodrigues, MD, Chairman, Chicago Medical Society's CME Subcommittee on Joint Sponsorship, has no significant financial relationships to disclose.
- Bapu P. Arekapudi, MD, Member of Chicago Medical Society's CME Subcommittee on Joint Sponsorship, has no significant financial relationships to disclose.
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- Hugo A. Alvarez, MD, Member of Chicago Medical Society's CME Subcommittee on Joint Sponsorship, has no significant financial relationships to disclose.
- Cecilia Merino, Chicago Medical Society, Director of Education, has no significant financial relationships to disclose.

Guest Speaker

Richard L. Gallo, M.D., Ph.D., is Professor of Medicine and Pediatrics, and Chief of the Division of Dermatology at the University of California, San Diego. His research focuses on the role of the innate immune system in skin health and disease, focusing on antimicrobial peptides and aspects of the basic functions of the skin immune system. His work is published in prominent scientific and medical journals and is well supported by grants from the NIH, the Veterans Administration, and private foundations. Dr. Gallo trained in Dermatology at Harvard Medical School where he also completed a post-doctoral fellowship in Cell and Developmental Biology. He received his MD degree at the University of Rochester, where he also received his PhD in Radiation Biology and Biophysics. Prior to dermatology, Dr. Gallo trained in Pediatrics at Johns Hopkins Hospital. Dr. Gallo practices primarily at the VA Medical Center in La Jolla, CA.author, editor or reviewer of ***journal articles, books, book chapters, and many other publications.***

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CHICAGO DERMATOLOGICAL SOCIETY **CASE #1**

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

HISTORY OF PRESENT ILLNESS

A 59 year-old Caucasian female with a history of hypothyroidism and presented in March 2009 for evaluation of dry, waxy, tight skin and soreness in her arms and legs. Her symptoms first began in August 2008 after being bitten by a cat. A few weeks after the bite, she began to develop pain and tightness in her upper and lower extremities. She also noted burning of her skin after strenuous exercise. Over the next few months, the patient developed increased tightness and soreness of her skin and joints, notably her knees, ankles, wrists and elbows.

PAST MEDICAL HISTORY

Hypothyroidism, Depression

MEDICATIONS

Prednisone, escitalopram, levothyroxine, fexofenadine, multivitamins

ALLERGIES

Sulfa

FAMILY HISTORY

Mother with rheumatoid arthritis, hypothyroidism

SOCIAL HISTORY

Remote history of tobacco use 8 years prior

PHYSICAL EXAM

Distal legs, arms, and posterior neck: woody induration with a waxy, peau d'orange appearance. No acrosclerosis or signs of Raynaud's phenomenon. Normal nailfold capillaries and no evidence of poikiloderma. Face and trunk: unaffected.

LABS

Absolute eosinophil count: 6000 K/ul
Bone marrow biopsy: normocellular marrow with marked eosinophilic hyperplasia but normal karyotype and cytogenetics
LDH: 206
Within normal limits: ANA, anti-dsDNA, anti-Scl 70, anti-Jo-1, anti-centromere, anti-RNA polymerase I and III, tryptase, ESR, SPEP, serum flow cytometry, complete metabolic panel, stool ova and parasites, c-kit mutation analysis, and Borrelia titers

HISTOPATHOLOGY

Left arm: within the deep subcutaneous tissue and fascia there is fibrinoid necrosis with edema and a mononuclear cell infiltrate with some plasma cells and rare eosinophils. Some inflammatory cells are also noted extending into the subcutaneous tissue. Vasculitis was not identified. Anti-treponemal antibody was negative. Colloidal iron stain was performed and demonstrates mild dermal and subcutaneous deposits of acid mucopolysaccharides. The DPAS stain was negative for fungi.

DIAGNOSIS

Eosinophilic fasciitis (Schulman's syndrome)

TREATMENT AND COURSE

The patient was started on prednisone 60 mg and imatinib 400 mg daily without improvement. Dapsone was attempted but discontinued secondary to renal impairment and hyperbilirubinemia. She is currently on methotrexate plus prednisone with modest improvement. The IL-5 inhibitor Mepolizumab is being considered but is not yet clinically available.

DISCUSSION

Eosinophilic fasciitis is a rare connective tissue disorder first described by Shulman in 1974 in patients presenting with scleroderma-like skin changes along with hypergammaglobulinemia, peripheral eosinophilia, and histologic evidence of diffuse fasciitis. It is most common in adults in the second to sixth decade of life but may occur in children. Classically the disease has an acute onset following strenuous exercise and begins on the distal extremities with spread to the trunk. Skin lesions begin as edematous plaques that progress to a peau d'orange appearance with hyperpigmentation, and finally to woody induration with skin tightness. Extracutaneous manifestations may occur and include inflammatory arthritis, flexion contractures, and carpal tunnel syndrome. Raynaud's phenomenon may be present but abnormal nailfold capillary microscopy should prompt an evaluation for other connective tissue disorders. Rarely, eosinophilic fasciitis may be associated with restrictive lung disease.

Association with hematologic abnormalities or malignancy has also been reported. Patients commonly have peripheral eosinophilia although this is not a prerequisite for diagnosis. Patients may have a monoclonal or polyclonal gammopathy, immune-mediated anemia or thrombocytopenia, aplastic anemia, myleodysplastic syndromes or lymphoproliferative disorders. Eosinophilic fasciitis has been described in association with malignancy including T and B cell lymphomas, multiple myeloma, polycythemia vera, metastatic colorectal carcinoma, and metastatic choroidal melanoma. For many of these malignancies, skin findings improved with treatment of the neoplasm suggesting that eosinophilic fasciits may represent a true paraneoplastic syndrome.

The etiology of eosinophilic fasciitis is not well understood but likely is related to an exaggerated immune reponse and pro-inflammatory environment. Elevated levels of Th2 cytokines, particularly IL-5, have been reported in active disease. IL-5 stimulates eosinophil chemotaxis and activation with subsequent eosinophil generation of TGF-beta, a pro-fibrotic stimulus, and toxic cationic proteins. Triggers for this alteration in immune reponse are unclear but may include preceding strenuous exercise, trauma, arthropod bites, or Lyme disease.

Diagnosis is confirmed by biopsy and appropriate laboratory findings including eosinophilia, hypergammaglobulinemia, and elevated inflammatory markers. A small study suggested that evidence of fascial thickening and signal abnormalities on MRI may be sufficient for the diagnosis of eosinophilic fasciitis. For many patients, the disease is self-limiting. First line treatment typically includes systemic corticosteroids which are effective in the majority of patients. For those unresponsive to systemic steroids, other possible therapies include physical therapy, cimetidione, D-penicillamine, antimalarials, sulfasalazine, methotrexate, cyclosporine, azathioprine, infliximab, dapsone, and combination UVA1 and oral retinoids.

REFERENCES

1. Bischoff L, Derk CT. Eosinophilic fasciitis: demographics, disease pattern and reponse to treatment: report of 12 cases and review of the literature. *International Journal of Dermatology* 2008;47:29-35.
2. Boin F, Hummers LK. Scleroderma-like fibrosing disorders. *Rheumatic Disease Clinics of North America*. 2008;34:199-220.
3. Endo Y, Tamura A, Matsushima Y, Iwasaki T, Hasegawa M, Nagai Y, Ishikawa O. Eosinophilic fasciitis: report of two cases and a systematic review of the literature dealing with clinical variables that predict outcome. *Clinical Rheumatology*. 2007;26:1445-51.

CHICAGO DERMATOLOGICAL SOCIETY **CASE #2**

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

HISTORY OF PRESENT ILLNESS

The patient is a 39 year-old Caucasian male with a past medical history significant for newly diagnosed acute myelogenous leukemia (AML), status post failure of 2 rounds of induction chemotherapy. He presented in October 2008 after transfer from an outside facility with profound neutropenia and tender, erythematous lesions on his face, scalp and extremities. Review of systems was positive for persistent malaise, fever, chills and night sweats.

PAST MEDICAL HISTORY

AML, *Pseudomonas* sepsis, osteomyelitis of right foot requiring amputation of 3rd and 4th digits

MEDICATIONS

Acyclovir, fluconazole, vancomycin, ciprofloxacin, meropenem and gentamicin

ALLERGIES

No known drug allergies

FAMILY HISTORY

Father with coronary artery disease, mother with brain tumor

PHYSICAL EXAM

Examination revealed 1.5 to 2 cm soft, erythematous nodules on the left brow, anterior scalp, right jaw line, and left forearm, a 2 cm erythematous nodule with a necrotic center on the right elbow, and 1 to 2 mm follicular- based papules and pustules on the abdomen.

LABS/IMAGING

White blood cell count: 0.5 K/uL, ANC unmeasurable, Hemoglobin: 9.7 g/dL, Platelets: 34 K/uL, D-dimer: 838 ng/mL, Fibrinogen: 776 mg/dL, PT: 14.5 seconds, INR: 1.2, Albumin: 1.7 g/dL, Alkaline phosphatase: 343 unit/L, AST: 124 unit/L, ALT: 121 unit/L, acute hepatitis panel: negative
Fungitel (1-3 beta-D-glucan) assay: 149 pg/mL (positive result >80)
Blood culture: positive for pseudomonas
Additional cultures (blood, central venous catheter, urine, pleural fluid*)*: negative.
Serum aspergillus, urine blastomyces, and urine histoplasmosis antigens: negative
Tissue culture: *Fusarium solani* species
Transthoracic Echocardiogram: no vegetations
MRI brain: left frontal scalp lesions suspicious for abscesses
CT sinus/chest: pan-sinus inflammation; right pleural effusion with ground glass nodular opacities noted in left lung

HISTOPATHOLOGY

Left forearm: Septic embolic disease with septated hyphae. There are extensive thrombi within vessels containing septated hyphal structures with dichotomous branching and fruiting bodies. The changes are most suggestive of septic embolic disease with a fungal organism.

DIAGNOSIS

Disseminated infection with *Fusarium solani*

TREATMENT AND COURSE

The patient was initially treated with liposomal amphotericin B (LAmB), voriconazole, terbinafine, and a short course of donor granulocyte transfusions. His skin lesions and nodular lung opacities improved significantly during his hospital stay. Based on tissue culture sensitivities, amphotericin and terbinafine were eventually stopped; voriconazole was continued and remains his current treatment. On hospital day 82, the patient was successfully discharged home. He subsequently underwent allogenic matched unrelated donor bone marrow transplant and is currently in remission. He has developed no additional skin lesions.

DISCUSSION

Fusarium species are saprophytic molds known to cause localized cutaneous infections, keratitis, and onychomycosis in immunocompetent hosts. They have recently gained recognition as emerging pathogens causing disseminated disease in immunocompromised hosts. Disseminated fusariosis is associated with significant mortality, approaching 75-90% in patients with hematologic malignancies and those undergoing allogenic hematopoietic stem cell transplant. While many *Fusarium* species have been implicated in causing human disease, *F. solani,* isolated in up to 50% of cases, is the most common and most virulent species. Cutaneous lesions are common in disseminated fusariosis, noted in 50-70% of cases. Patients classically present with numerous painful, erythematous papules and/or nodules, some with central necrosis and an ecthyma gangrenosum-like appearance on the extremities, face and trunk. Disease course is often rapid, with skin lesions evolving over a matter of days.

Tissue culture is often necessary to diagnose infection with *Fusarium*, although up to 60% of patients will have positive blood cultures. Fusarial hyphae are similar to those of *Aspergillus* species with septate filaments that dichotomize at right angles. *Fusarium* species are often distinguished by "banana-shaped" macroconidia in addition to hyphae. PCR analysis allows for speciation. The 1,3-Beta-D-glucan test is a serological test that is often positive in the presence of invasive fungal infections; however it does not discriminate between various fungi.

Disease prognosis is proportional to host immune status, and treatment is often challenging due to *Fusarium*'s inherent resistance to various antifungal agents such as fluconazole and itraconazole. Though no standardized therapeutic strategy has been determined, high dose amphotericin B and extended spectrum triazoles such as voriconazole are among the more commonly used therapies, exhibiting moderate in vitro activity against *Fusarium* species. Posaconazole (PSC), a newer extended spectrum triazole available as an oral suspension, is a promising drug for the future. Frequent monitoring of serum levels of triazoles is critical due to their somewhat unpredictable bioavailability. Combination medical therapy as well as adjunctive therapy including granulocyte transfusions, G-CSF, GM-CSF and gamma interferon have also proven effective in several studies.

REFERENCES

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2. Stanzani, M. *et al.* 2007. Update on the treatment of disseminated fusariosis: Focus on voriconazole. Therapeutics and Clinical Risk Management.3(6):1165-1173
3. Nucci, M., Aniasse, E. 2007. *Fusarium* infections in immunocompromised patients. Clinical Microbiology Reviews. 20:695-704

CHICAGO DERMATOLOGICAL SOCIETY **CASE # 3**

Presented by David Reid, MD, Joan Guitart, MD, Pedram Gerami, MD
Department of Dermatology, Feinberg School of Medicine, Northwestern University

HISTORY OF PRESENT ILLNESS

This 38 year-old Caucasian male first developed an erythematous, nonpainful, nonpruritic eruption on the trunk and arms in July 2008. He initially developed seven subcutaneous nodules on the abdomen, arms, and hands. The lesions were stable for several months, but in March 2009, he developed new lesions, ulcerations, and drainage. He was unaware of any antecedent trauma. Review of systems was notable for easy bruising, but negative for fever, chills, night sweats, weight loss, or malaise.

PAST MEDICAL HISTORY

Mild asthma, diverticulitis

MEDICATIONS

Albuterol, fluticasone, salmeterol, loratidine

ALLERGIES

None

FAMILY HISTORY

Non-contributory

SOCIAL HISTORY

Lives with wife; works in industrial maintenance; no tobacco, alcohol, or illicit drugs

PHYSICAL EXAM

On the left abdomen, there is a large, poorly demarcated, indurated, eroded, erythematous plaque studded with yellow papules and producing serosanguinous drainage. The left posterior upper arm has an ill-defined erythematous nodule with overlying yellow papules. On the right hip, there is a 2 cm x 3 cm ulcer and two erosions with serosanguinous drainage. There is prominent edema extending from the right hip to the distal right leg. There is no palpable hepatomegaly or lymphadenopathy.

LABORATORY EVALUATION:

Bacterial, fungal, and atypical mycobacterial cultures: negative
Alpha-1 antitrypsin serum level: 33mg/dl (normal 90-120)
Alpha-1 antitrypsin phenotype: PI*ZZ
Complete blood count, comprehensive chemistry panel: within normal limits
Flow cytometry immunophenotyping: no abnormal cell population
CT chest/abdomen/pelvis: unremarkable
Pulmonary function testing: normal

HISTOPATHOLOGY

Right abdomen: Within the deep dermis and extending into the subcutaneous tissue, there is an interstitial proliferation of histiocytes with abundant eosinophilic cytoplasm and focal cytophagocytic changes (bean bag histiocytes). The process dissects collagen bundles forming a pseudo-vascular pattern with focal sheets of epithelioid shaped histiocytes. Atypia is minimal. Occasional mitotic figures are noted. Numerous erythrocytes are noted in the stroma, but there is no evidence of frank vasculitis. Numerous neutrophils and some eosinophils are also noted. Immunohistochemistry was performed on deparaffinized sections. All controls stained

simultaneously were reviewed and appeared adequate. The histiocytic infiltrate is CD68, CD163, lysozyme, CD45 positive with weak myeloperoxidase staining and negative for CD34. CD3 stained scattered lymphocytes. Rare aggregates of cells are CD20 positive. CD34 and CD31 label endothelial cells. CD23, CD21, CD117 markers are negative. Special stains (DPAS, Gram and acid fast bacilli) are negative for microorganisms. EBER-1 is negative.

DIAGNOSIS

Alpha-1 antitrypsin (A1AT) panniculitis

TREATMENT AND COURSE

In April 2009, the patient was started on dapsone 25mg twice daily. His lower extremity edema and skin lesions improved. The patient was subsequently referred to Dr. Kyle Hogarth at the Center for Advanced Lung Diseases at the University of Chicago. In July, he began weekly intravenous A1AT augmentation therapy with continued clinical improvement.

DISCUSSION

Alpha-1 antitrypsin deficiency, first described in 1963, is a relatively common genetic disorder characterized by defective production of alpha-1 antitrypsin. Deficiency of this glycoprotein, which is the most abundant circulating serine protease inhibitor, results most commonly in early onset emphysema and hepatic cirrhosis. Other clinical effects include pancreatitis, rheumatoid arthritis, vasculitis, and membranoproliferative glomerulonephritis. In a minority of cases, patients develop panniculitis. Over 120 different alleles are known to code for alpha-1 antitrypsin, accounting for several different forms and degrees of deficiency. Most individuals with A1AT deficiency inherit two copies of the PI*Z allele, resulting in a very high risk of chronic obstructive pulmonary disease, and a high risk of liver disease. A1AT panniculitis, however, can also result from heteropolymerization of unfolded protein forms, and MZ, SZ, and MS states have been reported as pathologic. Cases of panniculitis typically develop between the ages of 20 and 40, although childhood cases have been reported. Often, lesions occur after minor trauma, and appear as large, erythematous, tender plaques and nodules on the lower trunk. The flanks, buttocks, and thighs are other common sites of involvement. Nodules may spontaneously drain an oily discharge, and form deep, necrotic ulcerations. Noncutaneous features include fever, pleural effusions, and pulmonary emboli.

Histologic findings depend upon the stage of lesions. Early lesions manifest neutrophilic splaying of reticular dermal and subcutaneous septal collagen. Subsequently, there is dissolution and liquefactive degeneration of septae, resulting in a characteristic separation and free floating appearance of fat lobules. In some cases, suppurative and granulomatous infilammation with necrobiosis may be seen.

Intravenous replacement of alpha-1 antitrypsin is a highly effective, though expensive treatment. For mild cases, doxycycline or dapsone, which reduce neutrophil chemotaxis, may result in clinical improvement. Less beneficial therapeutic options include colchicine, cytotoxic agents, and immunosuppressants.

REFERENCES

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3. Korver G, Lue C, Petersen M. Alpha-1-Antitrpysin deficiency presenting with panniculitis and incidental discovery of chronic obstructive pulmonary disease. *Int J Dermatol* 2007; 46(10): 1078-80.
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CHICAGO DERMATOLOGICAL SOCIETY **CASE # 4**

Presented by Susan L. Boone, MD, Pedram Gerami, MD, and Mary Martini, MD
Department of Dermatology, Feinberg School of Medicine, Northwestern University

HISTORY OF PRESENT ILLNESS

This 17-year-old woman presented to our Pigmented Lesion Clinic with multiple pink and brown dome-shaped papules of approximately 12 months duration. Several lesions were first noted on her elbows and buttocks as pink and tan macules. She continued to develop more lesions over the next 10 months as many became enlarged to raised dome-shaped papules. Some of the lesions were slightly pruritic, and she denied lesional bleeding, pain, or tenderness. Prior to the eruption of these lesions she had ample sun exposure during a summer vacation. She denied any constitutional symptoms.

PAST MEDICAL HISTORY

None

MEDICATIONS

None

ALLERGIES

No known drug allergies

FAMILY HISTORY

No family history of melanoma

SOCIAL HISTORY

Student

PHYSICAL EXAM

Physical exam revealed more than 50 numerous pink, brown, and multi-colored macules and papules, measuring from less than 1mm up to 7mm, on the head and neck, bilateral elbows, extensor and flexor aspects of the arms, thighs and bilateral buttocks. There was no lymphadenopathy or hepatosplenomegaly detected. Dermoscopic evaluation showed features typical of Spitz nevi with most lesions showing a symmetric starburst pattern or a pink symmetric peripheral corona.

HISTOPATHOLOGY

A review of all biopsies performed over the last 18 months showed that many of the samples demonstrated classic histological features of Spitz nevi (left forearm, left lateral thigh, right lateral posterior thigh, left superior buttock, left mid buttock, right arm, and right wrist), while others were consistent with desmoplastic Spitz (chin, right knee) and Spitz nevi with some cytologic atypia (left ear, right buttock x 3, left elbow, right posterior upper arm, right medial thigh, right lateral anterior thigh). Typical lesions from the patient showed epithelial hyperplasia surmounting a symmetric neoplasm of epithelioid and spindled shaped melanocytes arranged in vertically oriented nests and fascicles with kamino bodies and good maturation. Occasional nuclear atypia was noted.

Four of the benign Spitz nevi from this patient were tested by fluorescence in situ hybridization (FISH). FISH analysis showed a significant population of tetraploid cells in three of the four cases while the fourth case showed typical diploid cells. The tetraploid cells showed balanced gains in 6p25, 6q23, 11q13, and Cep 6, with all cells having 3 or 4 identifiable copies of each chromosomal segment.

DIAGNOSIS
Eruptive Disseminated Spitz Nevi

TREATMENT AND COURSE
We continue to follow the patient every 6 months. Over the last year she has noted no new or changing lesions.

DISCUSSION
Spitz nevi (juvenile benign melanoma, spindle-cell nevus, epithelioid-cell nevus) are benign melanocytic neoplasms that can have a range of clinical presentations: solitary, agminated, and disseminated. Solitary Spitz nevi are the most common, with a clinical presentation ranging from red or pink dome-shaped papules to brown or black macules typically with symmetry. They are most commonly found in children younger than 10 years of age on the head, trunk, or extremities. More than 42 cases of the agminated type have been described, occurring most frequently on the face, back, and extremities. The disseminated variant is the most rare, with only 15 cases reported in the literature. Previous associations of disseminated Spitz nevi have been attributed to sunburn, intravenous drug use, pregnancy, and other types of cutaneous stimulation including trauma and radiotherapy.

In the cases of Spitz nevi presenting with an agminated or disseminated pattern, it is important to exclude melanoma with cutaneous in-transit disease or disseminated cutaneous metastases, which may clinically appear very similar. The average age of onset of in-transit or cutaneous metastases is >50 years and occurs most frequently with primary tumors on the lower extremity, whereas the average age of disseminated Spitz is 23 years of age without clear lesional predilection for location. Additionally cutaneous metastases dermoscopically lack the classic features of Spitz nevi such as starburst pattern and are more likely to have asymmetric features or present as a solitary blue-white nodule. Histologically, in-transit melanoma metastases tend to lie within the reticular dermis or subcutis. However epidermotropic cutaneous metastases may occur. Typical features of Spitz nevi including Kamino bodies, and prominent maturation would be unlikely, while high mitotic counts, asymmetry or expansile nodular growth would be more common in cutaneous metastases. Cutaneous metastases also frequently have more fibrosis and a greater inflammatory host response.

Our case highlights the importance of clinically and histologically differentiating between eruptive Spitz nevi and malignant melanoma with in-transit or distant cutaneous metastases, and that the FISH technique may have a role in distinguishing between the two melanocytic processes. In our patient, the acute onset and rapid growth of clinically classic Spitz nevi in a young patient, with typical dermoscopic features, and prototypical histologic findings including well developed large Kamino bodies, were consistent with a benign diagnosis of disseminated Spitz nevi. The FISH results also failed to show diagnostic changes of melanoma. The patient's general health has been excellent over the last 2.5 years after the onset of her skin lesions without evidence for metastatic disease. These results affirmed an overall diagnosis of benign disseminated Spitz nevi.

REFERENCES

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3. Pawlik TM, Ross MI, Thompson JF, Eggermont AM, Gershenwald JE. The risk of in-transit melanoma metastasis depends on tumor biology and not the surgical approach to regional lymph nodes. J Clin Oncol. 2005 Jul 20;23(21):4588-90.

CHICAGO DERMATOLOGICAL SOCIETY **CASE # 5**

Presented by Sonal Shah, MD and Joaquin Brieva, MD
Department of Dermatology, Feinberg School of Medicine, Northwestern University

HISTORY OF PRESENT ILLNESS

A 45 year-old female presented to the Emergency Department with complaints of a rash. She stated that the illness began two weeks prior to presentation with some left foot swelling and pain. The rash started five days prior to presentation as tender bumps on her arms and legs. She denied any lesions on her trunk. She was also complaining of a sore throat with some sinus pain and drainage as well as increased shortness of breath. She also noted arthralgias as well in her elbows, hands, knees, ankles and feet.

PAST MEDICAL HISTORY

Endometriosis with subsequent total abdominal hysterectomy, Irritable bowel syndrome, asthma

MEDICATIONS

Ibuprofen, estradiol

ALLERGIES

Codeine

FAMILY HISTORY

Mother - Crohns's Disease

SOCIAL HISTORY

Married, works as a book keeper, Non-smoker, denies illicits, occasional alcohol use

PHYSICAL EXAM

On the bilateral upper and lower extremities there are numerous edematous erythematous, tender papules and pseudovesicular papules coalescing into plaques. Two edematous erythematous papules are noted on the back. The posterior pharynx shows mild erythema and cobblestoning.

HISTOPATHOLOGY

Right Arm: Spongiosis of the epidermis with some exocytosis of neutrophils. Dermis shows marked papillary edema with abundant diffusely scattered neutrophils and histiocytes with some karyorrheixis. No vasculitis is noted. Dense and deep perivascular and interstitial lymphohistiocytic infiltrate.

DIAGNOSIS

Histiocytoid Sweet's Syndrome

TREATMENT AND COURSE

The patient was discharged from the ED with prednisone 10mg daily and doxycycline 100 mg for seven days. She noticed significant improvement within 24 hours. Further diagnostic testing and imagine was pursued. Chest CT showed hilar lymphadenopathy suggestive of sarcoidosis. M mediastinoscopy with lymph node biopsy revealed compact granulomas consistent with sarcodosis. She has been following with Pulmonary and has been noticing some shortness of breath for which she is using albuterol with good relief 2-3 times each day. Her rash has resolved and she is currently tapering off of the Prednisone.

DISCUSSION

Sweet's Syndrome is a skin disorder characterized by leukocytosis, fever, and a rash consisting of erythematous plaques that show dermal neutrophilia on biopsy. Classically Sweet's Syndrome can be seen following an upper respiratory tract infection. Associated conditions (present in 29-50% of cases) include inflammatory bowel disease, other chronic inflammatory disease, infectious diseases, and pregnancy. In addition malignancy can also be seen with Sweet's Syndrome in 10-20% of cases. Lofgren's Syndrome is a subset of sarcoidosis that is characterized by erythema nodosum, bilateral hilar lymphadenopathy, and arthritis of the ankles, wrists, or elbows. It accounts for 19% of all cases of sarcoidosis. There have been only 12 reported cases in the literature in which these two entities co-exist simultaneously.

These few cases in which Sweet's Syndrome and Lofgren's syndrome are associated, it is noted that patients tend to be younger with a female predominance. The distribution of skin findings tends to less likely to involve the face and trunk and have a predilection for the arms as opposed to patients with idiopathic Sweet's Syndrome. In addition, these lesions are more papular than the classical ones seen with Sweet's Syndrome. All of the patients were reported to have a benign course and self limiting disease. The presence of co-existing Sweet's Syndrome in the setting of sarcoidosis may be a favorable prognostic sign.

Histologically, Sweet's Syndrome typically appears with intense edema of the papillary dermis, dense dermal inflammatory infiltrate mostly with mature neutrophils. In rare cases, such as with this patient, the infiltrate can be composed of histiocytoid mononuclear cells with large, elongated, kidney shaped basophilic nuclei. In a study looking at 41 patients with typical lesions of Sweets Syndrome with histiocytoid mononuclear cells seen on pathology, these cells were found to be immunophenotypically indicative of thee monocytic-histiocytic lineage. In addition they stained intensely for myeloperoxidase. This may indicate that these cells are immature myeloid cells, which are precursors for neutrophils. These in turn may be replaced by mature neutrophils later within the disease course.

The mechanism triggering both Sweet's Syndrome and sarcoidosis are largely unknown. Several etiologies have been proposed, both infectious and non-infectious, but no solid evidence exists that any one thing is responsible for their development. Both diseases are through to be the result of immunopathological response to a triggering antigen. It has been suspected that an antigen produced by a sarcoidal granuloma may be the triggering antigen for Sweet's Syndrome. Both sarcoidosis and Sweets Syndrome have an increase in both IL-2 and IFN-γ (T1 helper cytokines) and a decreased T2 helper cytokines. This relationship may also contribute to the association of the two diseases.

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CHICAGO DERMATOLOGICAL SOCIETY **CASE # 6**

Presented by Katherine Brown, MD and Peter Lio, MD
Department of Dermatology, Feinberg School of Medicine, Northwestern University

HISTORY OF PRESENT ILLNESS

This 26 year-old African American man presented for evaluation of two nodules on his left elbow for one year. They were not symptomatic but were slowly enlarging. Review of systems negative for fever, chills, night sweats, GI symptoms, or associated arthralgias. A biopsy done 5 months prior was suggestive of a collagenoma but was too superficial to render a definitive diagnosis. Tissue cultures for bacteria, mycobacteria, and fungal organisms were negative at that time.

PAST MEDICAL HISTORY

Hepatitis B, acne

MEDICATIONS

Adapalene 0.1% cream, benzoyl peroxide, clindamycin cream

ALLERGIES

No known drug allergies

FAMILY HISTORY

Hypertension, diabetes mellitus

SOCIAL HISTORY

The patient works in retail. No tobacco, illicit drug, or ETOH use.

PHYSICAL EXAM

Exam reveals an African American man in no distress. On left elbow there is a deep firm mobile 5 mm flesh-colored nodule and an adjacent 2 cm x 2 cm deep firm heterogeneous mobile nontender plaques with surface nodularity. The remainder of the cutaneous exam was unremarkable.

HISTOPATHOLOGY

Elbow: There is a dense superficial and deep perivascular and interstitial dermal infiltrate composed of neutrophils and mononuclear cells. The vessels reveal focal fibrinoid necrosis with perivascular fibroplasia and karyorrhexis. An interstitial histiocytic process with some necrobiosis is also noted.

DIAGNOSIS

Erythema Elevatum Diutinum

TREATMENT AND COURSE

A trial of oral dapsone and niacinamide is planned; however, a commitment to compliance with follow-up blood work and appointments is needed on the patient's part prior to initiation of this agent.

DISCUSSION

Erythema elevatum diutinum (EED) is a rare form of small vessel vasculitis and its clinical and pathologic manifestations are dependent on the stage of disease. This entity was initially described in 1889 by Hutchinson and since that time numerous associations have been reported in the literature including autoimmune conditions (inflammatory bowel disease, rheumatoid arthritis, systemic lupus erythematous, celiac disease, relapsing polychondritis), chronic infections

(streptococcal infection, HIV disease), and hematologic conditions (IgA monoclonal gammopathy, multiple myeloma). It is hypothesized that the formation of immune complexes and complement deposition resulting in leukocytoclastic vasculitis is the underlying mechanism of disease. Interestingly, however, systemic vasculitis is not usually a feature.

EED presents as symmetric red- brown, violaceous, or yellowish papules, plaques, or nodules distributed on the extensor surfaces of joints of buttocks. The face and ears may become involved. Early in the course lesions are soft and mobile, but become more firm and fibrotic with time and residual hyperpigmentation or scarring may result. Lesions are often asymptomatic but may be described as painful or burning. Successive crops of lesions occur over a period of several months followed by a waxing and waning course for many years. The prognosis of EED tends to follow the course of spontaneous regression in 5-10 years, although cases persisting up to 20 years have been reported.

Histological exam of acute lesions demonstrates necrotizing leukocytoclastic vasculitis with neutrophils in the upper and mid-dermis. Eosinophils may be prominent. By contrast, chronic lesions show fibrosis, an infiltrate composed of macrophages, plasma cells, lymphocytes, and cholesterol deposits.

Therapeutic options are limited although numerous agents have been tried. Dapsone tends to be most effective with acute lesions, achieving rapid resolution of symptoms and gradual tumor shrinkage. However rapid recurrence is common with discontinuation, particularly when lesions are in a fibrotic phase. Other treatment modalities reported include niacinamide, systemic steroids, sulfapyridine, tetracycline, chloroquine, colchicine, or excision of bulky lesions. Because the cutaneous manifestations may precede any hematologic disorders by an average of six years, a work-up to rule out an underlying hematologic, autoimmune, or chronic infection should be considered. Treatment aimed at underlying condition may improve EED manifestations.

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CHICAGO DERMATOLOGICAL SOCIETY **CASE # 7**

Presented by Sandra Han, MD and Amy Paller, MD
Department of Dermatology, Feinberg School of Medicine, Northwestern University

HISTORY OF PRESENT ILLNESS

The patient is a 3 day-old Hispanic girl born at 38 weeks gestation at an outside hospital to a 29 year old G2P0 female via Caesarian section secondary to fetal distress. At birth, she was noted to be bright red with large areas of denuded skin. Her father is certain he saw two teeth at birth. However, she did not have any hair, fingernails, or toenails. On day of life #3, the patient had an arterial pH of 6.97, potassium of 8.8, and sodium of 156. She was intubated and transferred to Children's Memorial Hospital for further care.

PAST MEDICAL HISTORY

Her mother reports that at 28 weeks of gestation, ultrasound revealed intrauterine growth retardation.

MEDICATIONS

Petrolatum-mineral oil, albuterol, ampicillin, cefotaxime, sodium polystyrene, regular human insulin, fentanyl, total parenteral nutrition

FAMILY HISTORY

The patient's parents are first cousins, once removed. Her mother previously had twins that miscarried at 10 weeks gestation due to an unknown cause. There is no family history of erosive skin diseases, dental problems, or alopecia. There are no healthy siblings at home.

SOCIAL HISTORY

The patient's parents are immigrants from Ecuador.

PHYSICAL EXAM

The baby is small for her gestational age. She has extensive sloughing of the epidermis on her forehead, upper eyelids and glabella. Widespread erosions are present throughout the chest, abdomen, arms, and legs. The vaginal mucosa shows superficial erosions on an erythematous base. Total alopecia is noted. She has absent nails on her fingers and toes. There is an endotracheal tube in place that limits examination of the oral cavity.

HISTOPATHOLOGY

H&E sections reveal suprabasal acantholysis with prominent acantholysis and dyskeratosis of the adnexal units. Immunomapping reveals a normal linear expression along the dermal-epidermal junction of all the tested components including cytokeratin, plectin, type XVII collagen (BP 180), α6 integrin, β4 integrin, laminin 3.2.2, and type VII collagen. Immunohistochemistry for herpes simplex virus and varicella zoster virus are both negative.

LABORATORY DATA

Toxoplasma IgG: positive; Toxoplasma IgM: not tested; Herpes simplex virus IgM: not detected; Rubella IgM: negative; Urine cytomegalovirus rapid shell antibody: negative

Direct sequencing of the patient's DNA reveals a single homozygous deletion in the region of the *DSP* gene that encodes the intermediate filament binding region in the C-terminal domain of the desmoplakin protein. This leads to a premature stop codon downstream of the mutation.

DIAGNOSIS

Lethal acantholytic epidermolysis bullosa.

TREATMENT AND COURSE

The patient was dressed in Aquaphor and Mepilex dressings and placed in a protective isolette. Immediate attention was given to correcting her metabolic derangements due to insensible losses and dehydration. Her skin showed evidence of rapid re-epithelialization; the face was virtually re-epithelialized within 5 days as was most of the trunk. Cardiac echocardiograms were normal. Attempts to extubate the patient were unsuccessful due to respiratory distress, since the airway filled with sloughed mucosal material. She developed severe anemia and thrombocytopenia requiring multiple transfusions. Wound and blood cultures obtained on day of life #16 grew *Candida parapsilosis*. Based on her overall prognosis and her critically ill state, her parents expressed their wish to extubate the patient on day of life #26.

DISCUSSION

Lethal acantholytic epidermolysis bullosa (LAEB) was first described by Jonkman *et al.* in 2005, and this remains one of only three known cases. The phenotype for this disorder includes severe skin and mucous membrane fragility present at birth, universal alopecia, neonatal teeth, and anonychia. The condition was lethal for the baby in this report due to immense transcutaneous fluid loss leading to compensation with great volumes of intravenous fluids and secondary heart failure.

The genetic basis for this disorder is mutations in the *DSP* gene that result in truncation of the cytoplasmic protein desmoplakin. Desmoplakin is a component of the desmosome and, in skin, connects keratin filaments with plakoglobin and plakophilin. Desmoplakin plays a similar role in desmosomes of cardiac myocytes, although desmin, rather than keratin, is the intermediate filament. Desmoplakin has three plakin repeat domains (A, B, and C) in its C-terminal region that bind intermediate filaments. In the report of LAEB, novel mutations of both *DSP* genes resulted in loss of all three keratin binding domains.

Other mutations in *DSP* have been described and affect skin, heart, and hair. These conditions include striate palmoplantar keratoderma (PPK), arrhythmogenic right ventricular dysplasia, "skin fragility / woolly hair syndrome with striate PPK," and Carvajal syndrome, among others. Differences in clinical presentation are attributed to abnormalities at different intermediate filament binding sites of the desmoplakin protein.

Histopathology of LAEB demonstrates suprabasal clefting and acantholysis leading to "tombstoning" of the basal layer. Immunofluorescence demonstrates normal staining of pan-keratin and all components of the basement membrane known to cause disease. Electron microscopy reveals disconnection of keratin from desmosomes in all layers of the epidermis. The desmosomes themselves appear normal in number and diameter.

Our patient displayed the same clinical features as that of the patient reported with LAEB, and DNA analysis confirms homozygous mutation of the *DSP* gene, putting her among one of the first known cases. As a child of consanguineous parents, her parents are asymptomatic heterozygous carriers of the mutation in *DSP*, and our patient inherited the disorder in an autosomal recessive fashion. Further biochemical and immunofluorescence testing is underway to further characterize the cellular effects of the mutation.

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CHICAGO DERMATOLOGICAL SOCIETY **CASE # 8**

Presented by Bryan Gammon, MD and Joaquin Brieva, MD
Department of Dermatology, Feinberg School of Medicine, Northwestern University

UNKNOWN

CHICAGO DERMATOLOGICAL SOCIETY **CASE #9**

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

HISTORY OF PRESENT ILLNESS

A 2 day-old female presented with tense blisters and several areas of denuded skin present since birth. Progression of the skin lesions with development of new bullae and poor feeding presumed secondary to discomfort was noted on day of life one, and the infant was transferred to Children's Memorial Hospital Neonatal Intensive Care Unit for further evaluation and management.

BIRTH HISTORY

Labor induced at 36 weeks secondary to oligohydramnios and intrauterine growth restriction; Apgars were 9 at 1 minute and 9 at 5 minutes

MEDICATIONS

None

ALLERGIES

None

FAMILY HISTORY

Mother was diagnosed with epidermolysis bullosa acquisita at age 28. She had a history of esophageal strictures and ocular involvement and had been treated in the past with cyclophosphamide and oral prednisone. She discontinued immunosuppressive therapy during the first trimester of her recent pregnancy. Three older siblings born prior to mom's diagnosis are healthy without any blistering history. No history of a genetic blistering disorder.

SOCIAL HISTORY

Noncontributory

PHYSICAL EXAM

The infant was well appearing, but small for gestational age. There were multiple superficial and deep erosions on her face, chest, abdomen and extremities, and scattered intact vesicles and bullae. The most prominent involvement was noted on the hands, ankles and feet. Her lips and right naris revealed vesicles, and open erosions with mild crusting. The oral mucosa was clear and the nails were normal.

HISTOPATHOLOGY

Left thigh- Pauci-inflammatory subepidermal blister
Direct immunofluorescence (DIF)-Linear deposition of IgG1, IgG4, IgM and C3 at the dermal-epidermal junction on the dermal side of the blister. Ig A and fibrinogen were negative for immune deposits and the intercellular epidermal space was free of deposits.
Indirect Immunofluorescence (IIF)-Positive staining of IgG at the dermal-epidermal junction involving the dermal side on all dilutions 1:10 to 1:40.
Enzyme-linked immunosorbent assay (ELISA)- Increased levels of IgG anti-collagen VII autoantibodies

DIAGNOSIS

Neonatal Epidermolysis Bullosa Acquisita

TREATMENT AND COURSE

Given the expected spontaneous taper in our patient's circulating antibody level we did not initiate immunosuppressive therapy. Our patient did very well with supportive treatment and meticulous wound care. Pain was well controlled with Tylenol. During her 1 week hospitalization, new blister development was rare and her feeding improved. On follow up at 3 weeks of age there was no new blister formation. At 2 months of age, all of the erosions were healed and the areas of old blistering were studded with milia.

DISCUSSION

Epidermolysis bullosa acquisita (EBA) is a rare, chronic autoimmune blistering dermatosis of the skin and mucous membranes characterized by IgG autoantibodies against the non-collagenous terminus of the alpha chain of Collagen VII, resulting in decreased anchoring fibrils in the lamina densa. There are two distinct phenotypes of EBA. The inflammatory type mimics other bullous diseases including bullous pemphigoid, Linear IgA bullous disease and cicatricial pemphigoid. The more common, "classic-type" EBA is phenotypically similar to dystrophic epidermolysis bullosa with skin fragility, trauma-induced blistering, scarring and milia.

Skin biopsy classically reveals a subepidermal pauci-inflammatory blister. Inflammatory EBA has neutrophils and eosinophils within the blister cavity. DIF should demonstrate linear deposition of IgG at the dermal-epidermal junction on the dermal side of the blister, and IIF should also demonstrate positive staining of IgG at the basement membrane zone on the dermal side. ELISA will detect the presence of collagen VII autoantibodies.

The majority of cases are acquired in adulthood with an estimated incidence of 0.25 per million in Western Europe while rare childhood cases have been reported. This is the first reported case of EBA in a neonate. In contrast to adult disease, childhood disease is more typically inflammatory, has an increased incidence of mucosal involvement and has a better response to treatment (typically oral prednisone and dapsone) and therefore a better long term prognosis.

Autoimmune neonatal transient blistering skin disease characterized by placental transfer of maternal IgG autoantibodies is rare. It has been documented in infants born to mothers with pemphigus vulgaris, gestational pemphigoid and pemphigus foliaceous. It has not been reported with EBA, likely because EBA is extremely rare and does not typically affect individuals of child bearing age. Experience with neonatal pemphigus has shown that neonatal disease appears to be self-limited and resolves with supportive therapy. As this is the first reported case of neonatal EBA, it is premature to make conclusions regarding long-term prognosis, but we expect our patient to do very well.

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CHICAGO DERMATOLOGICAL SOCIETY **CASE #10**

Presented by Elizabeth Grossman, MD, Annette Wagner, MD, and Pedram Gerami, MD
Department of Dermatology, Feinberg School of Medicine, Northwestern University

HISTORY OF PRESENT ILLNESS

A one-day old female, born at 40.6 weeks to a G1P1 mother, presented at birth with a giant congenital melanocytic nevus with multiple nodules and a large area of ulceration. On the second day of life, two biopsies were performed: one of the ulcerated area and one of a large nodule on the right lateral back.

PAST MEDICAL HISTORY

Delivery via Caesarian section due to chorioamnionitis and failure of labor to progress.

MEDICATIONS

None

FAMILY HISTORY

No family history of melanoma. Mother's prenatal care was routine.

PHYSICAL EXAM

There was a large hyperpigmented plaque with hypertrichosis in a garment distribution involving the posterior trunk, anterior trunk, and superior portion of the buttocks and a 4 cm ulcerated nodule on the left paraspinal. There were numerous exophytic melanocytic nodules within the nevus. Satellite lesions were noted ranging in size from several millimeters to several centimeters on the scalp, extremities, buttocks, trunk and chin. No cervical, axillary, inguinal, clavicular lymphadenopathy. No hepatosplenomegaly.

LABORATORY TESTS:

Comparative genomic hybridization of tissue: gains in chromosome 8,10,13 with losses in chromosome 7 and 14 and 11q.
MRI (4 months of age): Focal area of T1 hyperintensity at the right frontal lobe consistent with neurocutaneous melanosis. No evidence of lesions consistent with rhabdomyosarcoma.

HISTOPATHOLOGY

Left paraspinal: Within the dermis are sheets of small spindle to epitheliod cells, with focal hemorrhage and necrosis. Aggregates of small epitheliod cells with scant and partially pigmented cytoplasm are present. There are rhabdoid morphological features. There are numerous mitosis and apoptotic cells, with rare abnormal mitosis. Immunohistochemistry: high proliferative ratio (Ki-67). Negative for S-100, MART-1, CD34, smooth muscle actin, neuron specific enolase, CD 99 and Calponin. MITF is positive and Desmin focally positive. FISH targeting 6p25, 6q23 and 11q23 showed no aberrations at these loci.
Right lateral back: sheets of small spindle cells are noted with irregular aggregates of small cells with high nuclear: cytoplasmic ratio and mitotic activity.

Excision left paraspinal: The dermis has alternating cellular and myxoid areas. The cellular areas have cells with primitive round, hyperchromatic nuclei and indistinct cytoplasm with high mitotic activity. The cellular areas transition into myxoid areas that are mitotically active with relatively uniform, slender, spindled cells arranged in a storiform pattern. Clusters of larger oval or elongated fusiform cells resembling rhabdomyoblasts are present. There are bizarre multinucleated rhabdomyoblasts and areas of cartilaginous differentiation. Immunostains: S-100 protein, Melan-A and HMB 45 positive. Desmin and Myogenin positive in spindled cells. Smooth muscle actin diffusely positive. EMA and synaptophysin negative.

DIAGNOSIS
Embryonal rhabdomyosarcoma arising within a giant congenital melanocytic nevus

TREATMENT AND COURSE
The patient was discharged home on day #4 of life. At day #14 of life, the patient was evaluated for poor healing of the left paraspinal ulceration, and it was noted the nodule was enlarging. Given a negative wound culture, mupirocin ointment was replaced with triamcinolone. At two months of age, the patient underwent resection of the now 5cm x 6.5 cm nodule by plastic surgery. Pathology was consistent with embryonal rhabdomyosarcoma.

At three months of the age, the patient had multiple new satellite lesions and another slowly enlarging nodule on the buttock. She is scheduled for re-excision with placement of tissue expanders of an enlarging nodule at the site of her rhabdomyosarcoma. The patient continues to thrive with normal development and without evidence of seizures. Physical exam remains negative for lymphadenopathy or hepatosplenomegaly.

DISCUSSION
Giant congenital melanocytic nevi (GCMN) defined as >20 centimeters in diameter, occur in 1 in 20,000 live births; the bathing trunk type occur in 1 in 500,000 live births. A variety of tumors have been noted to appear in congenital melanocytic tumors; of greatest concern is the potential for malignant melanoma to arise in GCMN.

Proliferating nodules are well documented to arise from GCMN. These benign entities are cellular melanocytic proliferations arising from the dermis that may closely resemble melanoma both clinically and histologically. Proliferative nodules most typically present in the neonatal period and demonstrate slow growth. Differentiation from melanoma is based on low mitotic index, lack of necrosis, and absence of uniform high grade atypia. On histology, the nodule blends in with the surrounding tissue, while melanoma shows a more abrupt transition. Proliferative nodules may ulcerate, particularly in the neonatal period. Though there may initially be high mitotic activity, there is spontaneous regression of cellular activity and the mitotic rate decreases. Chromosomal analysis of tissue from proliferative nodules classically show gain in chromosome 10 and loss of chromosome 7. Proliferative nodules do not require treatment; they regress and spontaneously involute.

Embryonal rhabdomyosarcoma (ERMS) has rarely been reported in GCMN. On histology, ERMS tumors resemble various stages in the embryogenesis of normal skeletal muscle. The cells have committed to a myogenic lineage, but arrest prior to terminal differentiation. The cell of origin is thought to be a human skeletal muscle myoblast, and the tumor is characterized by the presence of rhabdomyoblasts. Because of its origin in embryonal mesenchyme, RMS can arise virtually anywhere in the body. There are several subtypes of rhabdomyosarcoma, with embryonal representing 70-80% of tumors. Immunohistochemical staining is positive for desmin and muscle specific actin. In ERMS, the classic chromosomal abnormality seen is loss of heterozygosity at 11p15. However, other aberrations reported include gains on chromosome 2, 7, 8, 11, 12, 13 and 20 and losses on chromosomes 1, 6, 9 14 and 17.

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CHICAGO DERMATOLOGICAL SOCIETY **CASE # 11**

Presented by Sapna Patel Vaghani, MD and Prashant Singri, MD
Department of Dermatology, Feinberg School of Medicine, Northwestern University

HISTORY OF PRESENT ILLNESS

A 45 year old Caucasian female with a clinical history of psoriasis presented with a red, painful eruption of one year. She complained of her whole body burning, followed by peeling and sloughing of her skin. The rash was circular and scaly, and was accompanied by chills, malaise, and nausea. It recurred every 4-5 weeks, lasted a few weeks each time, but never completely cleared between cycles. She has a history of a hysterectomy and therefore does not have menses but noted tender breasts in the few days prior to the flares. During this time, she received monthly oral steroids for asthma flares, which temporarily helped calm her skin. Treatment for this problem included etanercept and clobetasol, neither of which helped, and doxycycline, which caused significant nausea.

PAST MEDICAL HISTORY

Asthma, sinusitis, herniated disk, diabetes mellitus (type II)

PAST SURGICAL HISTORY

Hysterectomy, laparoscopy, appendectomy, cesarean section, cholecystectomy

MEDICATIONS

Clobetasol, doxycycline, hydroxyzine, loratadine, metaxalone, etanercept, albuterol, acetominophen, budesonide, fluticasone/salmeterol, metformin

ALLERGIES

Latex (anaphylaxis), NSAIDs, cephalexin, niacin, garlic supplements

FAMILY HISTORY

Allergic rhinitis, eczema, psoriasis, asthma, uterine cancer, arthritis, diabetes mellitus, hypertension, tuberculosis, psoriatic dermatitis

SOCIAL HISTORY

Married, nurse, no tobacco or alcohol use

PHYSICAL EXAM

Fitzpatrick skin phototype II. Face: confluent erythema of central face, especially cheeks. Trunk & buttocks: diffuse polycyclic annular scaling patches with trailing scale and tiny peripheral pustules, telangiectasias at the active border. Lower extremities: numerous small erythematous scaling papules. Abdomen and lower extremities: erythematous, scaly papules and plaques with overlying white scale.

HISTOPATHOLOGY

Right shoulder: Subcorneal neutrophils and nuclear debris. Upper dermis- mixed inflammation with some exocytosis of neutrophils. No vasculitis. DPAS negative.
Abdomen: Subcorneal pustules consistent with pustular psoriasis. DIF negative.

LABORATORY:

Within normal limits: TSH, CBC, ESR, CMP, ANA, anti-dsDNA, anti-Scl 70, anti-Jo-1, anti-centromere, anti-RNA polymerase I and III.

DIAGNOSIS

Autoimmune progesterone dermatitis

TREATMENT AND COURSE

The patient continued antihistamines and began triamcinolone 0.1% ointment twice daily but the lesions worsened and remained very tender. Etanercept was stopped and she was started on acetretin 10mg daily, which she did not tolerate secondary to tingling of the hands and feet. She then started cyclosporine 200mg twice daily with good results. The severity of the lesions and degree of pruritus improved, and the pain resolved. Etanercept was restarted as cyclosporine was tapered, but the monthly flares returned. An intradermal progesterone test was done. One hour later, a 2cm area of induration was noted. She was started on Estratest, a combination of esterified estrogen and methyltestosterone. After one month, she reports decreased pruritus and that the rash is much less widespread.

DISCUSSION

Autoimmune progesterone dermatitis is a rare disease, reported in 50 patients to date worldwide. It typically occurs in 20-30 year old women with a history of exogenous progesterone intake and less commonly after exposure to endogenous progesterone during menarche or pregnancy. The pathogenesis is unclear but exposure to exogenous progesterone may induce a hypersensitivity to endogenous progesterone. It is characterized by recurrent, cyclic flares of dermatitis that correspond to the luteal phase of the menstrual cycle when progesterone levels are elevated. On average, the eruption develops one week prior to menses with monthly recurrence and it partially or completely resolves within a few days of menstruation. Patients present with localized or generalized urticaria, papulovesicles, erythema multiforme, or angioedema and usually have by eczematous changes. Mucosal lesions are rare. Patients can evolve towards spontaneous remission but also towards anaphylaxis in the most severe cases. The disease either improves or worsens with pregnancy and resolves with menopause.

It is important to differentiate the condition from perimenstrual flares and exacerbations of chronic conditions such as acne, psoriasis, and lupus erythematosus. Diagnosis requires demonstration of progesterone sensitization. This can be done via an intradermal, oral, or intramuscular dose of progesterone; detection of circulating antibodies to progesterone, cutaneous biopsies with indirect immunofluorescence with IgG, or the basophilic degranulation test. The majority of patients who react to an intradermal skin test develop urticaria within 30 minutes and/or erythema and induration at 24-28 hours. In the presence of a negative progesterone test, estrogen dermatitis should be evaluated for with an intradermal estrone test.

Therapeutic benefits of antihistamines, topical, and oral steroids appear limited. Treatment is aimed at inhibiting ovulation via estrogen-containing medications. Therapy with tamoxifen and danazol has also been reported. Bilateral oophorectomy offers definitive therapy for intractable cases.

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CHICAGO DERMATOLOGICAL SOCIETY **CASE # 12**

Presented by Sonal Shah, MD and Joaquin Brieva MD
Department of Dermatology, Feinberg School of Medicine, Northwestern University

CASE A

HISTORY OF PRESENT ILLNESS

A 70 year-old man with a history of diverticular bleeds presented with bright red blood per rectum and syncope. He was admitted to the intensive care unit for management of the GI bleed and hypotension. He was started on vancomycin, ciprofloxacin, and pipercillin-tazobactum for presumed sepsis. During his hospital course an acute eruption developed over his chest and abdomen. It was asymptomatic and he denied prior episodes similar to this. He denied any fevers, chills, weight loss, or night sweats.

PAST MEDICAL HISTORY

Coronary heart disease, s/p 5 vessel CABG, Pulmonary Hypertension, s/p Biventricular and AICD placement, prostate cancer s/p radical prostatectomy, diverticulosis with history of diverticular bleed, thrombocytopenia of unknown etiology

MEDICATIONS

Albuterol-ipratropium nebulizers, ciprofloxacin, docusate, esomeprazole, piperacilin-tazobactum, vancomycin, acetaminophen, furosemide

ALLERGIES

No known drug allergies.

FAMILY HISTORY

Father – coronary heart disease

SOCIAL HISTORY

Married, lives at home with wife, previous history of alcohol use, denies tobacco or ililcits

PHYSICAL EXAM

Predominantly on the chest and abdomen and sporadically on the back there were blanching erythematous to purpuric macules and somewhat firm papules. Some of the firm papules appeared follicularly-based. Face and extremities were spared.

HISTOPATHOLOGY

Abdomen: a dense dermal infiltrate with lichenoid changes and some superficial hemorrhage are present. The infiltrate is composed of intermediate size mononuclear cells with fairly abundant granular cytoplasm and oval nuclei. Some plasmacytoid cells are noted. The cells are somewhat hyperchromatic with fragile nuclear detail. Some mitotic figures and numerous erythrocytes are noted.
Immunohistochemistry shows that CD3 stains numerous scattered cells, some of which exhibit CD8 positivity. TIA-1 and granzyme are positive. CD20, CD5, CD123, CD1a, CD4, gamma M3 is negative. CD56, BF1, CD117 stain rare cells.

DIAGNOSIS

Atypical Mononuclear Cell Infiltrate – suggestive of leukemia cutis

LABS AND STUDIES
Bone marrow biopsy was negative for any evidence of leukemia. T cell receptor rearrangement by PCR showed a monoclonal rearrangement.

TREATMENT AND COURSE
The patient's hospital course was complicated by intractable thrombocytopenia and anemia thought due to Idiopathic Thrombocytopenia Purpura. Dexamethasone and IVIG were started with no improvement and the patient died shortly thereafter following a sudden cardiac arrest.

CASE B

HISTORY OF PRESENT ILLNESS
A 56 year-old male with a past medical history of chronic myeloproliferative disorder presented to the hospital with a rapidly increasing WBC count. The patient complained of fatigue and a new eruption on his abdomen and lower legs of hyperpigmented nodules for 2-3 weeks. These lesions were asymptomatic and he denied prior episodes. The patient denied any recent fevers, c hills, or weight loss.

PAST MEDICAL HISTORY
Chronic myeloproliferative disorder (9/08)- BCR-ABL, JAK2 and CHIC2 negative, Flourescent In Situ Hybridization for imatinib responsiveness negative, cerebellar intraparenchymal hemorrhage, latent tuberculosis

MEDICATIONS
allopurinol, acyclovir, fluconazole, bisacodyl, folic acid, busulfan, isoniazid, multivitamin, prochlorperazine, vitamin B6, hydroxyurea, acetaminophen-hydrocodone

ALLERGIES
No known drug allergies

FAMILY HISTORY
Father – coronary artery disease

SOCIAL HISTORY
20 pack-year smoking history, previously drank one 6 pack of beer/day, occasional cocaine use

PHYSICAL EXAM
Revealed numerous annular infiltrative plaques with purpuric border on bilateral lower extremities. On abdomen there were several purpuric infiltrative plaques. Face, back and arms were spared.

HISTOPATHOLOGY
Right leg: Monomorphous infiltrate composed of intermediate size mononuclear cells with abundant cytoplasm and oval nuclei. The cells are scattered throughout the reticular dermis. The cells are hyperchromatic with fragile nuclear detail. Some mitotic figures are noted. Numerous erythrocytes extravasated are noted in the dermis.

Immunohistochemistry was performed. Tumor cells are positive for myeloperoxidase, lysozyme, and negative for CD3, CD20, CD123, kappa, and lambda. The changes are consistent with Acute Myelogenous Leukemia.

DIAGNOSIS
Leukemia Cutis

TREATMENT AND COURSE
Bone marrow biopsy from previous admission was consistent with his known myeloproliferative/myelodysplastic syndrome. Upon admission the patient was started on high dose hydroxyurea and continued on busulfan for his increased white blood cell count in addition to leukopheresis, which temporarily improved his counts. The patient had a sudden cardiac arrest and was then noted to be in disseminated intravascular coagulopathy. As a result he suffered a large subarachnoid hemorrhage. Given his poor prognosis, care was withdrawn prior to the results of his skin biopsy being known.

DISCUSSION
Aleukemic monoblastic leukemia cutis is a rare cutaneous manifestation of a systemic hematologic condition that presents with a dermal infiltrate of monoblasts, which occurs prior to any changes seen on peripheral or bone marrow examination. Clinically it can manifest as pale or bright erythematous papules or subcutaneous nodules that are usually asymptomatic. Occasionally large hemorrhagic plaques or a monomorphic purpuric exanthema can be seen. Generally there are no secondary changes associated with the lesions. Monocytic aleukemic leukemia cutis can occur in both acute monoblastic and chronic myeloproliferative leukemias. The skin lesions typically precede the usual symptoms associated with the onset of leukemia by months.

Histologically one can see an infiltration in the reticular dermis and subcutaneous tissue with a monomorphous infiltrate of leukemic cells arranged in horizontal strands that can spread to the adnexa, and can occasionally be hemorrhagic. Immunohistochemistry is especially important to help differentiate between both T and B cell lymphomas and for identification of infiltrative cells. It is necessary to identify markers for monocytes, macrophages, and granulocytes, as well as a lack of T and B cell markers.

It is unknown why the leukemic cells first appear in the skin as opposed to the peripheral blood or bone marrow. There are some thoughts that these leukemic cells originate in the bone marrow as a localized process and then seed the extramedullary sites quickly within the disease process. Other ideas are that the cells originate in the dermal hematolymphoid tissue with hematogenous spread to the bone marrow and peripheral blood.

Aleukemic leukemia cutis has an extremely poor prognosis. Death occurs within 3-4 months following diagnosis. Chemotherapy has been found to be insufficient in treating this disease process.

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CHICAGO DERMATOLOGICAL SOCIETY **CASE# 13**

Presented by Gunilla Carlsson Thorn, MD and Mark Gendleman, MD
Department of Dermatology, Feinberg School of Medicine, Northwestern University

HISTORY OF PRESENT ILLNESS

This is a 53 year-old male with a history of Carney complex who presented to the dermatologist in 2008 for removal of several benign verrucous skin lesions. The patient was also found to have lentigenes on the back, a blue nevus on the right forearm and fleshy lesions on the left areola consistent with cutaneous myxomas. The patient's disease first presented at the age of 5, at which time he developed testicular cancer, treated with a bilateral orchiectomy and radiation therapy. At age 17 he developed Cushing's syndrome and was treated with hormonal supplementation. At age 27 he had a myocardial infarction, attributed to coronary vasospasm when cardiac catheterization showed normal coronary arteries. At age 33 a melanotic schwannoma was excised from his sacral spine and the diagnosis of Carney complex was rendered (1988). A screening echocardiogram revealed multiple cardiac myxomas and mitral valve prolapse, which were managed through four separate open-heart surgeries over the next two years. At age 41 and 45, the pt was found to have a retroperitoneal malignant fibrous histiocytoma and another melanotic schwannoma, respectively.

PAST MEDICAL HISTORY

Carney complex, hypothyroidism, ventricular fibrillation s/p biventricular Implantable Cardiac Defibrillator (ICD)

MEDICATIONS

Ramipril, metoprolol, digoxin, atorvastatin, coumadin, testosterone enanthate, amiodarone, levothyroxine, calcium citrate

ALLERGIES

None

FAMILY HISTORY

Sister with Wegener's granulomatosis and brother with developmental delay. Both parents alive and well in their 80s. Family members have deferred genetic testing for Carney complex.

SOCIAL

The patient is married and works in medical manufacturing. He does not use alcohol, tobacco or illicit drugs. He has no children.

PHYSICAL EXAM

Exam notable for few scattered brown macules on the back, a bluish-black dome-shaped papule on the right forearm, and skin-colored fleshy papules around the left areola.

HISTOPATHOLOGY

Patient refuses biopsy of current cutaneous lesions. All prior pathology results performed remotely over twenty years prior.

DIAGNOSIS:

Carney complex

TREATMENT AND COURSE:
The patient is currently managed by a multidisciplinary team, including his general internist, cardiologist, electrophysiologist, and dermatologist. The patient is actively participating in a research study on the syndrome with Dr. Constantine Stratakis at the NIH.

DISCUSSION
Carney complex was first described by Dr. J. Aiden Carney in 1985. It is a rare genetic syndrome characterized by cardiac myxomas, cutaneous myxomas, mammary myxomatosis, spotty mucocutaneous pigmentation, primary pigmented nodular adrenocorticoid disease, large cell calcifying Sertoli cell tumors of the testes, acromegaly, thyroid carcinomas, psammomatous melanotic schwannomas, blue nevi, multiple breast ductal adenomas and osteochondromyxomas. A diagnosis of Carney complex is made when a patient either exhibits two or more of the aforementioned manifestations or exhibits one of the aforementioned features and either has an affected first-degree relative or a confirmed inactivating mutation of the protein kinase A type I-a regulatory subunit (*PRKAR1A*) gene.

The *PRKAR1A* gene is located on chromosome 17 and codes for a regulatory subunit of protein kinase A (PKA). PKA is a second messenger-dependant enzyme involved in a wide range of cellular processes, including transcription, metabolism, cell cycle regulation and apoptosis. It is also thought to act as a tumor-suppressor gene and mutations have been documented in approximately half of patients with Carney complex.

The cutaneous manifestations of Carney complex include lentigenes, blue nevi, and cutaneous myxomas. The lentigenes present as small, brown to black, irregularly shaped macules, typically distributed on the lips, eyelids, conjunctival mucosa, ears and genitalia. Though often present at birth, these lesions generally do not assume this characteristic distribution until puberty. Histologically, the lesions demonstrate hyperpigmentation of the basal epidermal layer and hyperplasia of melanocytes with or without elongation of the rete pegs. The blue nevi present as larger, blue to black dome-shaped papules that histologically demonstrate localized accumulation of spindle-shaped melanocytes with elongated, dendritic processes in the upper dermis. The cutaneous myxomas typically present as asymptomatic, flesh-colored, sessile papules frequently located on the eyelids, external ear canal, breasts and nipples. Histology reveals well-circumscribed collections of mesenchymal cells, evenly distributed capillaries, and few collagen bundles within an abundant myxoid stroma.

Patients with Carney complex should be followed closely, as early intervention for several of the disease components is crucial. For the same reason, first-degree relatives of affected individuals should also be evaluated. Generally, the most serious components of the Carney complex are the cardiac myxomas, which are present in more than two thirds of patients. These tumors may be present in any cardiac chamber and are frequently multiple. Potential complications include embolization, cyst and microabscess formation, syncope, and sudden death. Regular screening by echocardiography with subsequent surgical removal of any lesions is advised.

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CHICAGO DERMATOLOGICAL SOCIETY **CASE # 14**

Presented by Sandra Han, MD, and Bethanee Schlosser, MD
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HISTORY OF PRESENT ILLNESS

The patient is a 77 year-old Hispanic female who presented with a 7-month history of a pruritic, burning, and tender rash of her vulva and thighs unsuccessfully treated with oral erythromycin, fluconazole, and topical antifungal creams. Six months after onset of the rash, she reports new involvement of her neck, shoulders, and inframammary folds. Biopsy records from an outside hospital were suggestive of pemphigus. She was prescribed clobetasol 0.05% ointment but discontinued it soon after initiation because she did not like the texture of the medication. She returned five months later with large lesions involving her labia majora and medial thighs.

PAST MEDICAL HISTORY

Hypertension, atrial fibrillation, allergic contact dermatitis to "Polygrip" powder

MEDICATIONS

Tramadol, enalapril, coumadin

FAMILY HISTORY

The patient reports her father had a similar, intermittent rash around his neck. Her daughter and grandchildren have no history of skin diseases.

SOCIAL HISTORY

The patient moved to the US from Mexico 20 years ago. She is a homemaker and lives with her husband, daughter, and grandchildren.

PHYSICAL EXAM

Left axilla and inframammary fold: solitary 1 to 1.5 cm violaceous, erythematous plaques with overlying microerosions
Left lateral neck: 2 cm x 3 cm ill-defined erythematous patch
Right labia majora to the right medial thigh: 6 cm vegetative, erythematous plaque with overlying erosions
Left labia majora to the left medial thigh: 1.5 cm vegetative, erythematous plaque with overlying erosions

HISTOPATHOLOGY

H&E: Suprabasal acantholytic blister. Sections reveal an intraepidermal blister with prominent acantholysis without dyskeratosis. Tombstone changes of the basal cell layer are noted. The process extends to involve follicular structures. The dermis also shows a variable mostly perivascular lymphohistiocytic infiltrate with some eosinophils.
IIF: No immune deposits; **DIF**: No evidence of intercellular anti-epithelial antibodies

LABORATORY

Anti desmoglein-1 and desmoglein-3 antibodies negative

DIAGNOSIS

Benign familial chronic pemphigus (Hailey-Hailey disease), predominantly vulvar

TREATMENT AND COURSE

The erosive plaques were treated with fluocinonide 0.1% ointment and chlorhexidine 4% solution. Her poorly controlled hypertension excluded the use of systemic corticosteroids. She used the

fluocinonide ointment only briefly due to disliking the texture of the medication. She reported stinging with use of chlorhexidine resulting in its discontinuation as well. Her disease remitted significantly, however, without specific treatment. At follow up, her topical steroid was changed to clobetasol 0.05% cream.

DISCUSSION

Benign familial chronic pemphigus (BFCP) was first described in 1939 by Howard Hailey and Hugh Hailey. In their case report of two brothers, they described a condition characterized by intermittent, recurrent small blisters of the neck that became "wet and crusted" within a few days. The lesions were pruritic and exacerbated by perspiration.

Since that time, the disease has been found to be transmitted in an autosomal dominant manner, although 30% of patients have no known family history. Cutaneous symptoms usually arise after puberty, during the second or third decade of life. Affected sites are the intertriginous areas and include the neck, axilla, genitofemoral folds, and perineum. 70% of patients have multiple asymptomatic, white, longitudinal bands of their fingernails.

Microscopic examination of BFCP reveals suprabasilar acantholytic vesicles and bullae. Intercellular edema with loss of intercellular attachments leads to partial acantholysis and the appearance of a "dilapidated brick wall" in the lower epidermis. The acantholytic cells have a well-defined nucleus and well-preserved cytoplasm.

The pathogenesis of BFCP was established in 2000 to be due to mutations in the *ATP2C1* gene. This gene encodes the hSPCA1 protein isoforms that act as ATPases to transport Ca^{2+} into the cellular endoplasmic reticulum. It is hypothesized that abnormal calcium homeostasis leads to adverse desomosomal protein processing, thereby resulting in impaired desmosome formation and epidermal acantholysis.

The mainstay of treatment for BFCP has been topical corticosteroids. Because inflammation from bacterial superinfection can potentiate acantholysis, clearance of superinfection with topical or oral antibiotics is advocated. Some patients benefit from the long-term use of low-dose antibiotics. Other treatments reported to be successful in case reports include topical tacrolimus, topical calcitriol, topical and oral retinoids, dapsone, CO_2 and Erbium:YAG lasers, dermabrasion, botulinum toxin A, photodynamic therapy, and excisional surgery.

The neck is the most common site of presentation of BFCP. Initial presentation of the vulva is uncommon, and in the few reported cases, all were initially diagnosed as other conditions such as lichen simplex chronicus, condyloma acuminatum, candidiasis or genital herpes simplex. In addition to presentation with extensive vulvar plaques, our case is unusual in that the patient was in her eighth decade at disease onset. This case highlights the importance of obtaining a full history, including a family history, and performing a careful clinical exam, with histologic confirmation as warranted, in any patient presenting with erosive vulvovaginal plaques.

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CHICAGO DERMATOLOGICAL SOCIETY **CASE # 15**

Presented by Sarah Baker, MD and Joaquin Brieva, MD
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HISTORY OF PRESENT ILLNESS

Patient is a 62 year-old Caucasian male with a past medical history significant for hypertension, who presented for evaluation of a perianal ulcer which had been present for approximately 6 months. Treatment for this problem had included antibiotic ointment. The patient described the lesion as tender and pruritic. He also noted blood on his toilet tissue after defecation. He had no personal or family history of Crohn's disease or ulcerative colitis. Patient also denied history of anal intercourse, groin radiation, or known arsenic exposure.

PAST MEDICAL HISTORY

Hypertension, hyperlipidemia

MEDICATIONS

Lisinopril, atorvastatin

ALLERGIES

No known drug allergies

FAMILY HISTORY

Brother with colon cancer

SOCIAL HISTORY

Smokes 1 pack of cigarettes per day, denies alcohol use

PHYSICAL EXAM

On the left perianal region, there was a 2.5 cm by 2.5cm erythematous ulcerated nodule with pearly rolled borders and surrounding maceration. No inguinal lymphadenopathy or other pertinent skin findings were noted.

HISTOPATHOLOGY

The epidermis is unremarkable. Within the dermis there are large irregular lobules of basal cells with hyperchromatic nuclei and scant cytoplasm. At the periphery of the lobules, palisading of the cells with stromal retraction are noted. The stroma shows fibromyxoid changes with a variable lymphohistiocytic infiltrate.

DIAGNOSIS

Perianal basal cell carcinoma, nodular type

TREATMENT AND COURSE

Patient was referred to Northwestern Memorial Hospital, Department of Surgical Oncology for excision of lesion. He has since transferred his care to the University of Illinois at Chicago and is awaiting colonoscopy and further surgical management.

DISCUSSION

Basal cell carcinomas are the most common skin malignancy. They typically occur on sun exposed areas of the body and are rarely found on sun protected regions. Perianal basal cell carcinomas (BCC) represent approximately 0.2% of all anorectal tumors. In a recent retrospective review at Mayo clinic, they found 51 cases of perianal and genital basal cell

carcinoma in an 11 year period, 15 of which were perianal. The average age of diagnosis was 73 years and the average size was approximately 2 cm. One third of the patients presented with ulcerated lesions, suggesting possible diagnostic delay due to location and vague symptomatology. No definite risk factors have been identified in the development of perianal BCC. Suggested etiologies include chronic irritation, immunosuppresion, and pelvic radiation. HPV DNA, predominately type 16, has been rarely isolated from BCC's of sun exposed areas in several studies, however no convincing correlation has been seen between HPV and the pathogenesis of genital or perianal BCC.

Histologically, it is important to differentiate perianal BCC from basaloid carcinoma (BC) of the anus, which may have similar histological appearance but follow a much more aggressive course. Typically BC's lack the prominent nuclear palisading seen with BCC and often display atypical mitoses as well as central necrosis of tumor nests and squamous metaplasia. In addition, the cytokeratin profile expressed by BCC differs from that of BC. BCC displays cytokeratins 10 and 11; whereas, BC is positive for cytokeratin 19. BC's have also been shown to express the immunohistochemical markers CEA, EMA and UEA 1, which have not been demonstrated with BCC. Flow cytometry reveals an increased S-phase fraction in BC as opposed to BCC. The distinction between these two entities is important because BCC rarely metastasizes and may be treated with wide local excision, whereas BC has been shown to metastasize to inguinal lymph nodes in up to 50% of instances and is often treated with chemotherapy and radiation with possible wide abdominoperineal resection.

There has been only one report of metastasis of a perianal basal cell carcinoma to inguinal lymph nodes in the literature. However, high recurrence rates of up to 20% have been reported with genital, particulary vulvar, BCC. Recommended treatment for these lesions includes wide local excision with clear margins. Mohs surgery is often recommended if lesion is large or histologically aggressive. Larger defects may be closed with the aid of a split thickness skin graft and/or local rotational flap, unilateral or bilateral V-Y flaps, or various myocutaneous flaps.

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CHICAGO DERMATOLOGICAL SOCIETY **CASE # 16**

Presented by Bryan Gammon, MD and Amy Paller, MD
Department of Dermatology, Feinberg School of Medicine, Northwestern University

HISTORY OF PRESENT ILLNESS

This is a 12 year-old girl followed since infancy for an ichthyotic condition and hemidysplasia. She had a history since birth of psoriasiform plaques on the left side of her body as well as marked shortening of the left arm and leg with ectrodactyly of the residual digits. She had undergone an above the knee amputation and wears a prosthesis, although wearing the prosthesis for ambulation had become more uncomfortable, given the intermittent development of verrucous nodules on the stump as well.

After not being seen for 4 years, she presented again at 11 years of age with the progressive development of tender verrucous lesions involving the left side of the vulvar region. The region was draining purulent material, despite recent treatment with amoxicillin.

Various topical agents have been prescribed to treat the psoriasiform dermatitis (up to class II topical corticosteroids, tar) have been poorly tolerated. She tolerates the application of Aquaphor. Trials of topical cholesterol and Epiceram have led to no detectable change. Hydroxyzine partially ameliorates her bouts of pruritus.

PAST MEDICAL HISTORY

8 lb. 2 oz. female neonate born at term via C-section due to failure to progress to a G2P1 mother. Gestation was complicated by vaginal bleeding and concern for placenta previa as well as oligohydramnios. On ultrasound she was found to have skeletal abnormalities involving the left side. Amniocentesis had previously revealed a 46,XX karyotype

MEDICATIONS

No oral medications. Aquaphor topically.

ALLERGIES

Possible sulfa drug allergies, leading to urticaria

FAMILY HISTORY

Mother with one early gestation spontaneous miscarriage

SOCIAL HISTORY

Unremarkable

PHYSICAL EXAM

Left sided torticollis is evident as well as slight prominence of the left side of the skull relative to the right. Her right-sided extremities are normal; left forearm and left femur are severely shortened with ectrodactyly. The left tibia, fibula and foot are absent. Her left arm and axillary skin are thickened with moderate erythema. The entire left side from the mid-chest to the stump similarly shows well-demarcated erythema and edema. The stump area is covered in slightly telangiectatic firm, non-compressible pink papules without crust or necrosis. Erythema and scale strictly respect the midline. The left labial area showed bright red friable verrucous mucosal papules, forming a pendulous mass from the entire vulvar area and extending to the anal region. These sites were tender and associated with slight purulent drainage.

HISTOPATHOLOGY

Labial and perianal mass: Verruciform Xanthoma. The sections reveal large fragments of an exuberant exophytic and papillomatous process. The epithelium shows hyperplasia, papillomatosis, and neutrophilic exocytosis. Within the papillary dermis, there are collections of foamy histiocytes. There is a perivascular lymphohistiocytic dermal infiltrate. Aggregates of plasma cells are noted. Atypia was not identified.

Gluteal Cleft: Verruciform Xanthoma. The epidermis shows acanthosis with papillary projections. There is marked hyperkeratosis and parakeratotic cells on top of the papillae. Thickened granular layer with perinuclear haloes are focally identified. In between the papillary tips are numerous xanthoma cells as well as neutrophilic infiltrate.

Electron Microscopy:

Biopsies were taken from the normal left side and symmetric area of abnormal skin on the right side for electron microscopic evaluation by Dr. Peter Elias at UCSF. The affected skin shows widespread abnormalities of the lamellar body secretory system, as well as complete disorganization of the extracellular matrix. The "unaffected" sample also showed distinctive changes in ultrastructure; i.e., abnormal lamellar body contents, and extensive areas of lamellar/non-lamellar phase separation, but was milder than those in the affected sample.

DIAGNOSIS

1. CHILD syndrome (Congenital Hemidysplasia Ichthyosis and Limb Defects).
2. Verruciform xanthomas with secondary streptococcal infection.

TREATMENT AND COURSE

The patient was treated with cephalexin for secondary infection of the vulva. The patient underwent surgical excision of the xanthomatous mass of the left labia and perianal area and transposition flaps were performed. These included a flap from the normal right side to the abnormal left side on the trunk, and a flap from the normal-appearing left arm to the abnormal-appearing left arm regions. The flaps were performed to determine whether the skin from the right ("unaffected") side would be able to retain its normal appearance on the left side, and whether the "unaffected" skin from the left side would be able to retain its normal appearance when flapped into an area showing the psoriasiform dermatitis.

Numerous samples were taken for keratinocyte culture in the Northwestern Skin Disease Research Center's Keratinocyte Core including a) normal skin on the right side, b) abnormal-appearing skin from the left side at the same site; and c) normal-appearing skin on the left side. DNA was extracted from each culture, and sent to Dr. Maurice van Steensel in the Netherlands for NAD(P)H steroid dehydrogenase-like protein (NSDHL) gene testing and methylation analysis. We assume that the genotype of each keratinocyte will be identical, but will test whether the degree of methylation correlates with the clinical outcome (e.g. that there is extensive methylation of the abnormal X chromosomal allele in keratinocyte DNA from the right side and "unaffected" left side compared to keratinocyte DNA from the psoriasiform site). This would be consistent with the finding of abnormalities in lamellar bodies from both "unaffected" and "affected" skin, although more severe in "affected" skin.

DISCUSSION

CHILD (Congenital Hemidysplasia Ichthyosis and Limb Defects) syndrome was first reported in 1948. Since the first report, fewer than 50 cases have been reported. CHILD syndrome is an X-linked dominant genodermatosis thought to be lethal in males, although there have been occasional reports of affected males with either Klinefelter syndrome or post-zygotic mosaicism. CHILD syndrome results from inactivating mutations in the gene on chromosome Xp28 that

encodes NSDHL, an important early enzyme in the post-squalene cholesterol biosynthetic pathway.

The cutaneous findings of CHILD syndrome include unilateral erythematous plaques, most commonly on the right side of the body, with thick waxy yellow scale. These plaques are sharply demarcated from unaffected skin at the midline. Large areas of skin are usually affected, but the face is usually spared. Rarely, the contralateral side is involved. With time, the erythema lessens in severity, while the verrucous plaques become more prominent. Ipsilateral alopecia, and nail dystrophy is common, while the teeth are generally normal. Skeletal abnormalities range from hypoplasia of digits to amelia. Ipsilateral visceral organ hypoplasia also occurs; the most commonly affected organs are the brain, kidney, heart and lungs.

There have been reports of treatment of the cutaneous lesions with topical or systemic retinoids, or surgical excision, while emollients and corticosteroids are largely palliative. Multidisciplinary care is indicated for management the multiple affected organ systems. Given the defect in cholesterol biosynthesis, a trial of cholesterol was undertaken in the past without improvement; further consideration suggested that the combination of 2% lovastatin and 2% cholesterol would make more sense. A 24 year-old with CHILD syndrome in the Canary Islands recently found considerable improvement with this combination within 2 months and a trial is planned for our patient in the near future.

The intriguing question in patients with CHILD syndrome is why lesions lateralize, as this distribution is not consistent with the patterning along Blaschko's lines seen with other X-linked dominant disorders. The studies to investigate methylation patterns in skin from a variety of skin sites may begin to address the underlying mechanism.

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CHICAGO DERMATOLOGICAL SOCIETY **CASE #17**

Presented by Elizabeth Grossman, MD, Simon Yoo, MD, and Joaquin Brieva, MD
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HISTORY OF PRESENT ILLNESS

A 64 year old Asian female with a past medical history significant for kidney transplantation presented for evaluation of a rash on her extremities that had been present for two weeks. The rash began as small erythematous papules that gradually enlarged. The lesions were asymptomatic, and the patients denied any vesiculation or bullae formation.

PAST MEDICAL HISTORY

Living donor kidney transplant 8/14/08 for IgA nephropathy, hospitalization for CMV 4/1/09, hypertension, hyperlipidemia, osteoporosis, hysterectomy1989

MEDICATIONS

Mycophenolate mofetil, tacrolimus, lamivudine, valganciclovir, trimethoprim/ sulfamethoxazole, famotidine, simvastatin, felodipine, metoprolol, citracal, iron, fish oil, multivitamin,

ALLERGIES

Adhesive tape

FAMILY HISTORY

Non-contributory

SOCIAL HISTORY

Married. Emigrated to the United States from the Philippines.

PHYSICAL EXAM

There are numerous annular plaques with erythematous to violaceous borders and central hyperpigmentation on the dorsal hands, arms, and thighs.

LABS

Bullous Pemphigoid antigen 1 (230 kd) positive

HISTOPATHOLOGY

Left thigh: There is prominent spongiois with exocytosis of eosinophils and mononuclear cells. Eosinophils are noted in the upper dermis and at the dermal-epidermal junction. There is focal clefting as well as dermal edema and perivascular lymphocytic infiltrate.

Left hand DIF on salt-split skin: Mild granular C3 deposits at the dermal-epidermal junction. IgA, IgG1, IgG4, IgM and fibrinogen all negative for immune deposits.

DIAGNOSIS

Urticarial bullous pemphigoid in an immunosupressed patient

TREATMENT AND COURSE

The patient was started on clobetasol 0.05% cream twice daily with improvement of her existing lesions. The erythema did remit and although the patient continues to develop new lesions, she develops them less frequently then previously.

DISCUSSION

First described as a distinct entity by Lever in 1953, bullous pemphigoid is the most common autoimmune blistering skin disorder. Bullous pemphigoid is a disease primarily of the elderly, with the estimated incidence of 10 cases per million thought to be rising as the population continues to age. Classic lesions present as tense bullae on either inflamed or non-inflamed skin. The lesions are typically symmetrically distributed and they predominate in flexural areas, limbs, and lower trunk. Histopathology of classic lesions reveals subepidermal bullae with eosinophils

The pathophysiology of bullous pemphigoid has been well documented. The disease is associated with circulating and tissue-bound autoantibodies directed against either Bullous Pemphigoid Antigen 1 (a 230-kDa intracellular molecule of the hemidesmosone) or Bullous Pemphigoid Antigen2 (a 180-kDa transmembrane molecule with a collagenous extracellular domain). Antibodies are typically directed at the intracellular C terminal region of BP230, while on BP180, the extracellular NC16A domain is largely recognized as the most immunogenic site. Direct immunofluorescence (DIF) reflects the pathophysiology with IgG and C3 binding in a continuous linear pattern at the dermal-epidermal junction. On salt-split skin, the antibodies are localized to the roof of the tissue.

The clinical presentation and course of bullous pemphigoid may be quite variable. Subtypes of bullous pemphigoid include localized bullous pemphigoid, pemphigoid nodularis, pemphigoid gestationis, erythrodermic pemphigoid, polymorphic pemphigoid, and non-bullous pemphigoid. Complicating the clinical picture is that one third to two thirds of patients with classic bullous pemphigoid may have prodromal symptoms lasting from weeks to years. These findings include pruritus, erythema, papules, papulovesicles, plaques, wheals, nodules or erythema multiforme-like lesions. Direct immunofluorescence performed in the prodromal state is typically negative. However, if the patient is re-biopsied during the bullous phase, the DIF will reveal the classic linear staining pattern. This differentiates patients in the prodrome stage from patients with the non-bullous variant, who will have a positive DIF with IgG and C3 staining along the basement membrane.

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CHICAGO DERMATOLOGICAL SOCIETY **CASE #18**

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

HISTORY OF PRESENT ILLNESS

The patient is a 31-year-old Asian female with no significant past medical history, who presented in August 2009 for evaluation and treatment of facial and body hyperpigmentation. Her symptoms first started several years ago in high school, when she developed flat, hyperpigmented, reddish/brown lesions initially on her face, and subsequently on her neck, chest, back, and arms. Since that time, the lesions became increasingly prominent and raised. Specifically, she noted dramatic changes in the lesions with each of her two pregnancies. Previous treatment for presumed rosacea with metronidazole cream, topical tretinoin, and topical steroids had been unsuccessful.

PAST MEDICAL HISTORY

Ovarian Cysts, Seasonal allergies

MEDICATIONS

Multivitamin

ALLERGIES

NKDA

FAMILY HISTORY

Father with coronary artery disease, prostate cancer, and diabetes

SOCIAL HISTORY

Software manager

PHYSICAL EXAM

The face had numerous erythematous, indurated plaques in a Blaschkoid distribution. There was an overlying umbilicated to cobblestoned surface extending from the scalp down to the neck with intermixed areas of sparing. The back and chest had tan, thin plaques with a cobblestone texture in a whirling or Blaschkoid distribution. Similar plaques were located on the bilateral arms, ranging on the left from the shoulder to the forearm, and on the right from the shoulder to the index finger. A cluster of skin-colored verrucous papules were on the right dorsal hand.

HISTOPATHOLOGY

Right forehead: Corrugated epidermis with prominent sebaceous lobules possibly consistent with a nevus sebaceous.
Right hand: Verrucous hyperplasia of the epidermis consistent with an epidermal nevus.

DIAGNOSIS

Linear organoid nevus with both nevus sebaceous and keratinocytic epidermal nevi

TREATMENT AND COURSE

The patient was very healthy and had no history of seizures, visual disturbances or spinal disease. It was felt that, in light of her age and clinical presentation, brain or spinal imaging was not necessary at that time. She was referred to ophthalmology for further evaluation. We are currently attempting to obtain insurance coverage for possible fractionated carbon dioxide laser treatments.

DISCUSSION

The term "organoid nevus" was first coined by Jadassohn in 1895 as a label to differentiate keratinocytic and appendageal hamartomas from melanocytic nevi. There are several variants of organoid nevi, including nevus sebaceous and keratinocytic epidermal nevi. Nevus sebaceous is a common congenital hamartoma that typically presents with sebaceous differentiation but may also show epithelial, trichilemmal, or apocrine differentiation. It most commonly occurs on the face or scalp. Keratinocytic epidermal nevi typically present as linear or whorled hyperpigmented plaques on the trunk or extremities.

In patients with extensive organoid nevi or linear nevus sebaceous, one should consider the possibility of an epidermal nevus syndrome. Lawrence Solomon first proposed the term "epidermal nevus syndrome" to describe the association of epidermal hamartomas with extracutaneous abnormalities. There are six defined epidermal nevus syndromes, including Schimmelpenning-Feuerstin-Mims syndrome, Proteus syndrome, CHILD syndrome, Becker's nevus syndrome, nevus comedonicus syndrome, and phakomatosis pigmentokeratotica. Schimmelpenning-Feuerstin-Mims syndrome describes the presence of a linear or Blaschkoid nevus sebaceous coupled with extracutaneous manifestations involving the CNS, ocular, or skeletal systems. The most common CNS manifestations include seizures and mental retardation, but structural anomalies (brain dysgenesis, cortical dysplasia, hemimegaloencephaly) and neoplasms (glial hamartomas and low-grade gliomas) have been reported. Ocular abnormalities include strabismus, colobomata, choristomas, cataracts, corneal opacities, exo/esotropia, retinal changes, ptosis, macroophthalmia, and conjunctival growth disorders. Skeletal anomalies include fibrous dysplasia of the cranium, scoliosis, and other primary and secondary bony defects. Vitamin D dependent rickets has also been described. Our patient has no known extracutaneous involvement, although her clinical presentation is highly suspicious for Schimmelpenning-Feuerstin-Mims syndrome.

The occurrence of epidermal nevus syndromes is sporadic and non-Mendelian in transmission. It is hypothesized that these disorders are the result of genetic mosaicism involving a lethal autosomal dominant gene. Epidermal mosaicism accounts for the majority of findings but mesodermal mosaicism is also found in 18% of patients and may result in some associated extracutaneous syndromes.

Interestingly, our patient denied congenital presence of her nevus sebaceous and keratinocytic epidermal nevi, maintaining that the lesions did not manifest until puberty. Most keratinocytic epidermal nevi are present at birth, but onset may occur during infancy to early childhood. At initial presentation, they are often flat, but over time they become elevated, verrucous, and darker in color. In comparison, nevus sebaceous are virtually always present at birth but may not be noticed until later childhood or puberty. Under the influence of hormonal changes at puberty, these lesions often become thickened with papillomatous epidermal hyperplasia. A histopathologic study of androgen receptor positivity in nevus sebaceous showed evidence of more intense staining within sebaceous glands as compared to normal skin. In addition, eccrine and apocrine glands as well as basal layer keratinocytes demonstrated androgen receptor positivity in nevus sebaceous, which was not noted in normal skin. These differences account for the intense changes noted in these lesions at puberty and perhaps explain why, in our patient, significant changes seemed to occur with each pregnancy.

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CHICAGO DERMATOLOGICAL SOCIETY **CASE #19**

Presented by Katherine Brown, MD, Thomas Cibull, MD, and Ken Gordon, MD
Department of Dermatology, Feinberg School of Medicine, Northwestern University and Northshore University Health System

HISTORY OF PRESENT ILLNESS

This 74 year-old Japanese man with a history of Castleman's disease presented for a one year history of dark lesions on his back and chest. He noted that over the preceding three months, the lesions had become more numerous and progressively darker. He denied any associated pain or pruritus. He reported no new medications or history of skin blisters. He denied photosensitivity and had noted no apparent relationship between sun exposure and skin lesions. Review of systems was positive for fatigue.

In 2005, he was noted to have weight loss and microscopic hematuria on routine blood work. Imaging revealed a perinephric mass and inguinal lymphadenopathy. Biopsies of perinephric tissue and several nodes were consistent with multicentric Castleman's disease, plasma cell variant. Bone marrow biopsy was without evidence of involvement by Castleman's disease. The patient was monitored clinically for one year then opted for treatment due to anemia and proteinuria thought related to Castleman's. In August 2006, he began seven cycles of cyclophosphamide which resulted in decreased proteinuria, improved fatigue, and stable CT scan involvement. No skin lesions were noted at initial presentation; however, the patient developed intermittent maculopapular eruptions and some hyperpigmented macules on his back during follow-up which his oncologist treated with triamcinolone or fluocinonide cream.

PAST MEDICAL HISTORY

Castleman's disease (2005), hypertension, membranous glomerulonephritis/chronic kidney disease, hearing loss

MEDICATIONS

Lisinopril, nifedipine

FAMILY HISTORY

Hypertension

SOCIAL HISTORY

The patient is retired from data processing and lives with wife. He rarely drinks alcohol and has a 8 pack-year smoking history, quit 20 years ago.

PHYSICAL EXAM

Scattered on upper chest, back, and shoulders, there were too numerous to count 5 mm –1 cm red to brown indurated dermal nodules without overlying scale. Some lesions were violaceous and partially blanching. There was no lymphadenopathy or hepatosplenomegaly.

LABS:

2005: anemia (Hgb 9.6 gm/dl), hypogammaglobulinemia, HHV-8 negative
2009: A CBC was normal and a metabolic panel was notable for a BUN 29 mg/dl (H) and creatinine 2.4 mg/dl (H). Patient declined further recommended tests including HIV, CMP, ESR, CRP, SPEP.

HISTOPATHOLOGY

Left chest and right shoulder: superficial and deep perivascular and perieccrine inflammatory infiltrate forming dense nodular aggregates within the dermis composed primarily of

mononuclear cells and abundant plasma cells. Immunohistochemical stains revealed a polytypic infiltrate by Kappa/lambda. Negative for IgG4 and human herpesvirus 8 by immunohistochemistry.

DIAGNOSIS

Cutaneous involvement by Multicentric Castleman's disease, plasma cell variant

TREATMENT AND COURSE

A trial of topical tacrolimus ointment was recommended. He has been followed by oncology who determined no further systemic therapy was currently indicated.

DISCUSSION

Castleman's disease, described first as angiofollicular lymph node hyperplasia in 1956, is an atypical B cell lymphoproliferative disorder, classified into localized or multicentric disease. There are three described histologic variants: hyaline-vascular subtype, plasma cell subtype, and a mixed type. The plasma cell variant is least common (10%) and most often multicentric. Cutaneous multicentric Castleman disease (MCD) is rare and is limited to a few case reports in the literature. In these reported cases, the cutaneous manifestations run concurrently with the initial diagnosis and can vary from maculopapular eruptions, infiltrated nodules and plaques, and pemphigus vulgaris.

In our patient with MCD, the cutaneous manifestations developed several years following his initial diagnosis. A systemic variant of Castleman's disease, MCD presents with generalized lymphadenopathy, hepatosplenomegaly, polyclonal hypergammaglobulinemia, anemia, constitutional symptoms, and elevated ESR and IL-6. It is most commonly reported in an Asian or Pacific Islander population. The leading hypothesis is that immune dysregulation or hyperproduction of IL-6 leading to B cell proliferation is an important factor in development of the disease. Epidemiological data have suggested human HHV-8 is associated with MCD in all HIV+ cases and in nearly 50% in HIV-negative cases. The HHV-8 genome encodes a human IL-6 homologous gene, which may be the link to increased IL-6 production in this condition.

MCD generally has a good prognosis; however, plasma cell variant tends to have poorer outcomes. Other lymphoproliferative disorders must be excluded and clinical follow-up is recommended due to reports of development of T-cell lymphomas with long standing disease. Treatment with pimicrolimus cream, chimeric murine anti-human IL-6, cyclophosphamide, rituximab, valacyclovir, and prednisolone have been reported.

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CHICAGO DERMATOLOGICAL SOCIETY **CASE # 20**

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

HISTORY OF PRESENT ILLNESS

This is an 11 month-old Caucasian female who presented for evaluation of redundant skin folds. Initially thought to be overweight, the patient was noted to have prominent, redundant, symmetric skin folds at approximately 5 months of age. The skin folds were most marked over both upper and lower extremities. She also had long eyelashes. Her past medical history was notable for short stature (amongst the 25th percentile in height) and physical motor delay. Her physical motor delay involved an inability to crawl or stand without support.

PAST MEDICAL HISTORY

Gastroesophageal reflux disease, Motor delay

MEDICATIONS

Lansoprazole

ALLERGIES

None

FAMILY HISTORY

Non-contributory

SOCIAL HISTORY

She lives at home with her parents. She has no siblings.

PHYSICAL EXAM

Bilateral symmetric, ring-like skin folds of her upper and lower extremities. No dysmorphic facial features, no cutaneous vascular stains, no cutaneous epidermal nevi, no palmar or plantar hyperplasia, no asymmetry or hemidysplasia, no macrodactyly and no hypertrichosis.

LABORATORY

Growth Hormone level: 0.58 (normal 2-10 ng/ml).
Within normal limits: TSH, fasting glucose, hemoglobin A1C.
Normal echocardiogram

DIAGNOSIS

Michelin Tire Syndrome

TREATMENT AND COURSE

Our patient is currently being followed by dermatology, genetics and endocrinology. A biopsy of the skin folds will be performed.

DISCUSSION

Michelin Tire Syndrome is a rare hamartomatous disorder, characterized by excessive skin folding that involves either adipose tissue or smooth muscle. First described by Ross in 1969 as Michelin Tire Syndrome (MTS) due to the physical resemblance of these patients to the Michelin Tire mascot, fewer than 25 cases have been reported. MTS is associated with a number of non-cutaneous abnormalities and has been described as a clinical presentation, reflecting multiple underlying disorders with multiple causes, clinical, histologic and genetic differences.

The pathogenesis of MTS remains unknown; however chromosomal abnormalities involving the deletion of the short arm of chromosome 11 and paracentric inversion of the long arm in chromosome 7 have been reported. The condition may be also be familial with an autosomal dominant pattern of inheritance.

Clinically, MTS is characterized by multiple, asymptomatic, circumferential skin folds. The folds are often present since birth and most commonly involve the extremities. Trunks, palms and soles may also be involved. Some patients develop hypertrichosis of the affected areas. MTS is associated with a number of congenital anomalies including facial dysmorphism such as microcephaly, micrognathia, up-slanting palpebral fissures, long and curled eyelashes, bushy eyebrows, bilateral epicanthic folds, low set ears, hypoplastic teeth. Mental retardation, developmental delay, seizure disorders, congenital heart defect, pectus excavatum, rocker bottom feet, metatarsus abductus, and undescended testis with histologic abnormalities have also been reported.

Histological studies reveal anomalies in both smooth muscle and adipose tissue. Published cases demonstrating both diffuse lipomatous nevi involving the deeper dermis and smooth muscle harmartomas have been reported. In one patient, fragmented elastic fibers in addition to a smooth muscle hamartoma were found, suggesting that abnormal elastic fiber formation may be a pathogenic factor in MTS.

There is no specific treatment for MTS. In most affected children, skin folds diminish over time and disappear without intervention. In the few familial cases reported, some older members continue to have remnants of deep skin folds. However, because every case of MTS is different, patients should be evaluated for underlying congenital abnormalities and treatment should be directed as necessary. Further study of this rare condition is needed.

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CHICAGO DERMATOLOGICAL SOCIETY **CASE # 21**

Presented by Gunilla Carlsson Thorn, MD, Mario Lacouture, MD, and Prashant Singri, MD
Department of Dermatology, Feinberg School of Medicine, Northwestern University

CASE A

HISTORY OF PRESENT ILLNESS

This is a 42 year-old female with a history of BRCA1 mutation and bilateral breast cancer, uterine fibroids, and cutaneous leiomyomas. The patient states she has had cutaneous leiomyomas for 14 years, but that the lesions began to spread six years ago, after receiving chemotherapy consisting of adriamycin, cytoxan and taxotere for breast cancer. She has had multiple leiomyomas excised in the past, mostly due to discomfort.

PAST MEDICAL HISTORY

Bilateral breast cancer, benign right ovarian cyst, fibroids, polycythemia vera, hypertension, depression, asthma

PAST SURGICAL HISTORY

Bilateral mastectomy, hysterectomy, right salpingo-oophrectomy

MEDICATIONS

Fluticasone and salmeterol inhaler, albuterol, anastrozole, clonidine, alendronate, losartan hydrochlorothiazide, sertraline

ALLERGIES

Codeine, penicillin, aspirin, caffeine, shellfish

FAMILY HISTORY

Brother deceased from metastatic renal cell carcinoma

SOCIAL

The patient is single and works as a paralegal. She consumes alcohol occasionally but does not use tobacco or illicit drugs.

PHYSICAL EXAM

Exam notable for numerous exophytic, rubbery papules on face and upper chest.

HISTOPATHOLOGY

Right jaw and chest: Pilar leiomyoma. Within the dermis, there are identifies bundles of cigar shaped spindle cells with abundant pink cytoplasm with numerous vacuoles. Atypia was not identified. The dermis also shows a variable perivascular lymphohistiocytic infiltrate. Staining was positive for PDGFR and negative for EGFR.

DIAGNOSIS

Multiple cutaneous and uterine leiomyomatosis (Reed Syndrome)

TREATMENT AND COURSE

The patient was educated about the syndrome and several tender lesions were removed. She was encouraged to follow-up with her oncologist for ongoing screening for renal disease.

CASE B

HISTORY OF PRESENT ILLNESS
This is a 40 year-old female with a history of uterine fibroids who presented for evaluation of tender firm papules on her right forearm that began developing 20 years ago. She periodically develops new lesions. She had no prior diagnostic work-up or treatment of the lesions.

PAST MEDICAL HISTORY
Fibroids, irritable bowel syndrome

PAST SURGICAL HISTORY
Appendectomy, partial hysterectomy

MEDICATIONS
None

ALLERGIES
Seasonal allergies

FAMILY HISTORY
Father and two paternal uncles with colon cancer, mother with epilepsy

SOCIAL
The patient is married, works as a teacher, and denies alcohol, tobacco, and illicit drug use.

PHYSICAL EXAM
Exam notable for multiple 3-4 mm reddish-brown, firm, tender papules on arms.

HISTOPATHOLOGY
Within the dermis, there are identifies bundles of cigar shaped spindle cells with abundant pink cytoplasm with numerous vacuoles. Atypia was not identified. The dermis shows a variable mostly perivascular lymphohistiocytic infiltrate.

DIAGNOSIS
Multiple cutaneous and uterine leiomyomatosis (Reed Syndrome)

TREATMENT AND COURSE
The patient was educated about the syndrome and had several bothersome lesions excised. She was encouraged undergo yearly screening for renal cancer.

DISCUSSION
Multiple cutaneous and uterine leiomyomatosis, also known as Reed Syndrome, was first described by Kloepfer in 1958. It is an autosomal-dominant condition characterized by multiple cutaneous leiomyomas in affected males and cutaneous and uterine leiomyomas in affected females. In a rare variant of the disorder, known as hereditary leiomyomatosis and renal cell carcinoma, affected individuals are also predisposed to aggressive renal cell cancer.

Cutaneous leiomyomas are derived from the smooth muscle cells of the erector pili apparatus. Onset of cutaneous lesions typically occurs in the teens, 20s or 30s. The lesions present as clustered intradermal papules or nodules, usually 2-20 mm, distributed diffusely or in a Blaschkonian pattern fashion. The majority of patients report lesions are painful, particularly in

response to low temperatures or trauma. Uterine leiomyomas present earlier than in the general population, are markedly symptomatic, and frequently require hysterectomy for managment.

Recent research has revealed that patients with multiple hereditary cutaneous and uterine leiomyomatosis and renal cell carcinoma possess a germline mutation in a single copy of the fumarate hydratase gene. The gene product is a Krebs cycle enzyme that catalyzes the conversion of fumarate to malate. It is theorized that the fumarate hydratase gene acts as a tumor suppressor gene. Interestingly, loss of both copies of the fumarate hydratase gene results in a different clinical presentation. This condition, known as autosomal-recessive fumarate hydratase deficiency, occurs when there are either homozygous or compound heterozygous germline mutations in both fumarate hydratase genes. It is a severe metabolic disease characterized by neurological dysfunction and survival of only a few months to years. No tumor formation has been noted in this syndrome.

Management of patients with multiple cutaneous and uterine leiomyomatosis focuses on symptom control, as the lesions are otherwise benign. Cutaneous lesions that are tender to the patient can be surgically excised and symptomatic uterine lesions often warrant hysterectomy. A proportion of patients with cutaneous and uterine leiomyomatosis are predisposed to develop aggressive renal cell cancer; therefore, screening is advised.

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