Chicago Dermatological Society

Monthly Educational Conference

Program Information
CME Certification
and
Case Presentations

Wednesday, September 21, 2011

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

Program Activities

9:00 a.m.	Clinic Registration Opens *Dermatology Clinic; 676 N. St. Clair, Suite 1600*
9:30 a.m. - 11:00 a.m.	Clinical Rounds -- Patient, poster & slide viewing *Dermatology Clinic*
10:15 a.m.	Conference Registration Opens *Lurie Building; 303 E. Superior, 1st Floor* *Outside the Hughes Auditorium*
10:15 - 11:15 a.m.	Coffee with the Exhibitors *Ryan Family Atrium, Lurie Building*
11:15 a.m. - 12:15 p.m.	Luncheon – *Ryan Family Atrium*
12:15 p.m. - 1:15 p.m.	General Session - *Hughes Auditorium* BLUEFARB LECTURE – "Skin Signs of Systemic Disorders" Dirk M. Elston, MD
1:15 p.m. - 3:15 p.m.	Case Discussions – *Hughes Auditorium*
3:15 p.m.	Meeting adjourns

Mark the Date!

Next CDS monthly meeting –
Wednesday, October 12, 2011
The University of Illinois at Chicago
Samuel T. Hwang, MD, Medical College of Wisconsin

Watch for details on the CDS website: www.ChicagoDerm.org

Northwestern University Medical School

Robert H. Lurie Medical Research Center
Hughes Auditorium
303 E. Superior Street - First Floor
Chicago, Illinois 60611

Registration: outside the Hughes Auditorium
Lunch, General Session & Case Discussions

Dermatology Clinic
676 N. Saint Clair Street, Suite 1600
Chicago, Illinois 60611

Patient/slide viewing & posters

Parking Garage Locations

At Saint Clair and Huron; enter from Huron (westbound) or Superior (eastbound).
Between Erie & Ontario just east of Fairbanks; enter from Erie (eastbound)

Discount Parking Coupons

Discounted parking coupons are available for the garages between Huron & Superior on Saint Clair and between Erie & Ontario just east of Fairbanks. The cost for discounted parking is $6.00 for a six-hour coupon or $12.00 for a twelve-hour coupon. <u>If you park longer than your coupon time allotment, your coupon is void; your fee in this case is the regular rate</u>. Cash is required, ***exact change preferred***. Purchase your discounted parking coupon at the Chicago Dermatological Society Meeting Registration table. A staff member from the NU Department of Dermatology will be present to handle your purchases.

Guest Speaker

Dirk M. Elston, MD

Dr. Elston is director of the Ackerman Academy of Dermatopathology in New York City. He formerly was the director of the Department of Dermatology and the Geisinger Medical Center, Danville, PA; and was chairman of the Department of Dermatology, Brook and Wilford Medical Centers. Dr. Elston earned his medical degree at the Jefferson Medical College in Philadelphia (1982). He completed his dermatology residency at Walter Reed Army Medical Center, Washington, DC (1986) and a fellowship in Dermatopathology at The Cleveland Clinic Foundation. He is the author/editor of 11 textbooks, 35 textbook chapters and more than 280 peer-reviewed publications. He is the Chief Editor of E-Medicine Dermatology and is Editor-in-Chief of Requisites in Dermatology.

Continuing Education Credit

Chicago Dermatological Society

"Chicago Dermatological Society Monthly Conference"

September 21, 2011 *Northwestern University* *Chicago, IL*

Participants must attend entire session to receive all types of credit. CFMC hosts an online evaluation system, certificate and outcomes measurement process. Following the conference, you must link to CFMC's online site (link below) to complete an evaluation form, in order to receive your continuing education statement of hours (certificate). Once the evaluation form is complete, you will automatically be sent a copy of your certificate via email.

Continuing Education evaluation and request for certificates will be accepted up to 60 days post activity date. The Colorado Foundation of Medical Care (CFMC) will keep a record of attendance on file for 6 years. CFMC contact information: 303-695-3300, ext. 3139.

Link address to evaluation form:
www.yourcesource.com/eval?act=591!09212011

JOINT SPONSOR STATEMENT

This Continuing Educational activity is Joint-sponsored by the **Colorado Foundation for Medical Care, Office of Continuing Education** and the **Chicago Dermatological Society**.

GOAL / PURPOSE

To broaden the clinical knowledge of dermatologists with respect to diagnostic and therapeutic options.

SESSION OBJECTIVES

Upon completion of sessions, participants will be able to apply new knowledge and skills in the area of physician learning.

After participating in this program, physicians should be able to:

- Describe skin signs which are indicative of lupus.
- Discuss the symptoms of dermatomyositis which can be observed on the skin.
- Explain how to recognize and diagnose scleroderma based on an examination of the skin.

CREDIT STATEMENTS

CME CREDIT

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 joint sponsorship of the Colorado Foundation for Medical Care, Office of Continuing Education (CFMC OCE) and Chicago Dermatological Society. CFMC is accredited by the ACCME to provide continuing medical education for physicians.

The Colorado Foundation of Medical Care designates this Live Activity for a maximum of 4.5 *AMA PRA Category 1 Credit(s)™*. Physicians should claim only the credit commensurate with the extent of their participation in the activity.

OTHER HEALTH CARE PROFESSIONALS

This educational activity has been planned and implemented following the administrative and educational design criteria required for certification of health care professions continuing education credits. Registrants attending this activity may submit their certificate along with a copy of the course content to their professional organizations or state licensing agencies for recognition for 4.5 hours.

DISCLOSURE STATEMENTS

All other members of the faculty and planning team have nothing to disclose nor do they have any vested interests or affiliations. **It is the policy of the Chicago Dermatological Society and Colorado Foundation for Medical Care (CFMC) that the faculty discloses real or apparent conflicts of interest relating to the topics of the educational activity.**

Case Presentations

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CHICAGO DERMATOLOGICAL SOCIETY **CASE #1**

Presented by Sonal Shah, MD and Joan Guitart, MD
Department of Dermatology, Feinberg School of Medicine, Northwestern University

HISTORY OF PRESENT ILLNESS

Patient is a 52yo Asian male who presented for evaluation of a lesion on his R cheek which began in December 2010. It began as a red bump and was pruritic. He saw a Dermatologist in February who thought it was possibly a bacterial infection and prescribed a course of oral antibiotics for 1 week, without any improvement. He was then prescribed another course of antibiotics and antivirals which did not improve the appearance of the nodule. He was then directed to Dr. Simon Yoo for biopsy of the lesion. Following the biopsy he noticed some clear drainage from the area. He denied any pain but admitted to a stinging sensation. He also noted some new lesions spreading to his R lower cheek and also to his L cheek which started in February, and were enlarging in size. He applied hydrocortisone 0.1% ointment occasionally to the area with mild improvement in pruritus. He also tried using some oral Chinese herbal medications, which he thought might have helped.

PAST MEDICAL HISTORY

Hepatitis B

MEDICATIONS

None

ALLERGIES

NKDA

FAMILY HISTORY

No history of malignancy

SOCIAL HISTORY

Married, works in accounting, previous smoker (quit 4 years ago)

PHYSICAL EXAM

The patient was a well developed, well nourished Asian male in no apparent distress. On the R lateral cheek there was a 3 cm erythematous to violaceous firm plaque composed of confluent nodules with some telangiectasias. On the R lower cheek there were two firm erythematous papules with no overlying surface change. On the L cheek there were 3 erythematous firm papules noted without any overlying surface change. There was a 1cm freely mobile lymph node noted at the R superior aspect of the cervical chain. There was some fullness palpated along the entire R neck. There was no axillary or inguinal lymphadenopathy.

LABS/IMAGING

Abnormal: Hepatitis B core antibody (total) Reactive [NR]; Hepatitis B Surface Antigen Positive [Neg]; Hepatitis B Surface Antibody Positive [Neg]; Hepatitis B Viral Quantitative PCR 240 copies [0]; platelets 120K/UL [140-390K/UL], AST 49U/L [0-40U/L]; ALT 70U/L [0-40U/L]; Total Bilirubin 1.4mg/dl [0-1.3mg/dl]; Total Protein 8.2gm/dl [6.0-8.0gm/dl]
Negative/normal: WBC with Differential, Hgb, Hct, Chem 7, Alk Phos, Albumin, Calcium, LDH, Uric Acid, Beta 2 microglobulin, Hepatitis A IgM, Hepatitis Be antigen and antibody, flow cytometry (skin & blood), quantitative immunoglobulins, bone marrow biopsy with cytogenetics
CT Chest/Abdomen/Pelvis 5/2/11: 2 mildly enlarged nonspecific peripancreatic lymph nodes

CT Neck/Larynx 5/2/11: Area of skin thickening and enhancement in the R cheek over the Right zygoma measuring 3cm in size. Mildly prominent bilateral submandibular lymph nodes suggestive of a reactive etiology
PET CT 5/6/11: Increased metabolic activity in the skin and superficial soft tissues over the right cheek

HISTOPATHOLOGY
3/14/11 R cheek: The epidermis shows mild spongiosis and focal exocytosis of lymphocytes. The dermis shows a dense superficial and deep lymphoid infiltrate with scattered irregular germinal centers. The infiltrate is composed of centrocytes and centroblasts with notable tangible body macrophages and variable mitotic activity. An interstitial lymphoplasmocytic infiltrate with numerous histiocytes and eosinophils is also noted. The infiltrate is composed of approximately a similar number of T cells (CD3+) and B cells (CD20+). The germinal centers express Bcl-6 while CD43 is expressed in the T cell zones. The infiltrate including the B cell zones are strongly positive for Bcl-2. The T-cells are positive for CD43 and CD5.
4/12/11 R cheek: The epidermis shows acanthosis and spongiosis with a focal serous exudate and hyperkeratosis/parakeratosis. There is a dense dermal infiltrate composed of small to medium-sized lymphocytes with a dense infiltration of eosinophils. There is also some vascular hyperplasia with telangiectasia and prominent endothelial cells focally vacuolated. Some margination of neutrophils is also noted. Immunohistochemistry revealed a similar number of T cells (CD3+) and B cells (CD20+). The T-cells are positive for Bcl-2. Bcl-6 is expressed in germinal centers.

DIAGNOSIS
Reactive Lymphoid Hyperplasia with Eosinophilia (Kimura's Disease)

TREATMENT AND COURSE
Given his active Hepatitis B, the patient was evaluated by Hepatology and started on tenofovir 300mg daily. He was started him on a 5 day course of prednisone 200mg/day with significant improvement. He was then started on rituximab 375mg/m^2 IV for 8 cycles. Upon follow up in Dermatology clinic, he received a course of intralesional triamcinolone 5mg/ml x 2 into the affected lesions. He was also initiated on hydroxychloroquine 200mg BID at the most recent visit. Overall he has noticed the most improvement in his facial lesions while on the high dose prednisone, and minimal improvement with rituximab and still continues to get new facial lesions.

DISCUSSION
Kimura Disease was first described in China in 1937 by Kim & Szeto as "eosinophilic hyperplastic granuloma", and was further elaborated upon by Kimura in 1948. It is characterized by the development of chronic, painless, single or multiple subcutaneous nodules, usually located on the head and neck (in 70% of all cases) with associated lymphadenopathy. It commonly occurs in young males of Asian descent, although there have been reports of it affecting all ethnicities.

The etiology is unknown but it is thought to be related to an autoimmune or delayed hypersensitivity reaction, possibly in reaction to an environmental or exogenous stimuli. Another thought is that it is an abnormal allergic response, as it can commonly be seen with associated asthma, atopic dermatitis, and allergic rhinitis. In addition hypereosinophilia is common; seen in up to 98% of patients as well as elevated IgE levels. Additional associated features described include nephrotic syndrome in 12-16% of patients, and proteinuria in 5% of patients, which both occur concurrently with the skin findings.

Pathology reveals dense lymphoid hyperplasia with germinal centers as well as a dense eosinophilic and plasma cell infiltrate. There can also be focal areas of necrosis forming eosinophilic microabscesses. In addition fibrosis is also seen, along with proliferation of post capillary venules.

The clinical course is progressive but often becomes stable after a few years, but without spontaneous resolution. The presence of lymphadenopathy along with the classic skin lesions can often mimic malignancy; however there have been no reports of malignant transformation.

Multiple treatment methods have been explored for Kimura's Disease and are not well established. Surgical excision has been employed and it is usually effective, but recurrence rates are high. Oral corticosteroids can have a temporizing effect, with relapses being common. Radiation has also been used with one study showing a local response rate of 64.3% with no side effects in follow up, although some argue that it is not justified given that Kimura's Disease is not a true neoplasm. Cyclosporine at a dose of 5mg/kg/day has also been employed as well as antiallergic medications such as suplatast tonsilate (a Th2 inhibitor) and cetirizine. With regards to surgery, it is can be useful for cosmetically unacceptable tumors, however recurrence rate is high. In the literature there is one case report of a woman who had both Kimura's Disease as well as Mycosis Fungoides who was successfully treated with rituximab. Following treatment the lesions of Kimura's Disease on pathology revealed an absence of germinal centers as well as decreased B cell component, lending to the drug's mechanism of action.

REFERENCES

1. Chen, H. et al. 2004. Kimura Disease A Clinicopathologic Study of 21 Cases. Am J Surg Pathol.28(4):505-513.
2. Ghosn, S. et al. 2009. Concomitant Occurrence of Kimura Disease and Mycosis Fungoides in a Lebanese Woman: Significant and Response to Rituximab. Am J Dermatopathol.31(8):814-818.
3. Gocmen, H. et al. 2006. Kimura's Disease: Case Report and Brief Review of the Literature. The Journal of Otolaryngology.35(5):358-368.
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CHICAGO DERMATOLOGICAL SOCIETY **Case #2**

Presented by Lisa Arkin, MD, and Amy Paller, MD
Department of Dermatology, Feinberg School of Medicine, Northwestern University and Children's Memorial Hospital

HISTORY OF PRESENT ILLNESS

The patient is a 6 year-old African American female with multiple co-morbidities including severe developmental delay, failure to thrive, and chronic idiopathic liver disease. She presented for evaluation of severe generalized pruritus of 2 years duration. Her mother noted that the pruritus caused significant discomfort, as she often would wake from sleep scratching and crying. She had never had a facial rash although her mother reported one prior sunburn that developed after being outside for a brief period of time.

From a developmental perspective, she is unable to walk or speak more than a few words. She has a history of extensive dental caries requiring extraction of her upper incisors last year, as well as mild sensorineural deafness. She is followed by gastroenterology for failure to thrive and chronic elevation of her transaminases.

Treatment to date has included cholestyramine, ursodiol and various emollients, with minimal improvement.

PAST MEDICAL HISTORY

Premature (born at 32 weeks, with normal prenatal labs), failure to thrive with short stature (<3rd%), microcephaly, severe developmental delay, lower extremity joint contractures, spasticity, elevated liver enzymes of unknown etiology

MEDICATIONS

Neocate Junior via GT, ursodiol, diphenhydramine, polyethylene glycol, ranitidine, cetirizine, diazepam

ALLERGIES

Acetaminophen with codeine, amoxicillin/clavulanate (vomiting)

FAMILY HISTORY

Parents are non-consanguineous, mother without miscarriages, no siblings

PHYSICAL EXAM

The patient was generally well-appearing but small for age. She had microcephaly and dysmorphic features, notably narrow-set, sunken eyes, prominent everted ears, beaked nose and small mouth. There was no malar rash. Hair was sparse and thin. The arms and buttocks had scattered excoriations with post-inflammatory hyperpigmentation on arms and buttocks. The liver edge was palpable 2-3 cm below the right costal margin. No splenomegaly or lymphadenopathy.

LABS/IMAGING

Abnormal: alkaline phosphatase 621IU/L [< 200 IU/L]; ALT 179 IU/L [20-40 IU/L]; AST 95 IU/L [20-40 IU/L]; Liver biopsy: mild periportal fibrosis, no inflammation; ERCC6 gene- two novel mutations
Normal/negative: BMP, CBC, ANA, hepatitis A, B, and C panels, TSH and free T4, anti-smooth muscle antibody, liver kidney microscomal antibody, celiac panel, alpha-1 antitrypsin, genetic CF testing, karyotype 46, XX

Skeletal survey 12/2010: Cortical thickening of the long bones with near obliteration of medullary canals.
MRI brain 10/2010: Increased T2 signaling within the periventricular and subcortical white matter consistent with markedly delayed myelination.

DIAGNOSIS

Cockayne Syndrome Type II, with 2 novel mutations detected in the ERCC6 gene

TREATMENT AND COURSE

Her course has been complicated by persistently rising liver enzymes, now with evidence of both hepatitis and cholestasis. Ursodiol and cholestyramine were discontinued due to minimal improvement. A recent dilated ophthalmological exam confirmed bilateral cataracts. She has continued on emollients and hydroxyzine, with minimal improvement.

DISCUSSION

Cockayne syndrome is an autosomal recessive disorder caused by mutations in the ERCC6 or ERCC8 gene. These genes encode proteins involved in transcription-coupled DNA repair, which is the body's mechanism to correct errors in actively transcribing DNA. In contrast to patients with xeroderma pigmentosum who carry mutations in global excision repair, the mutations associated with transcription-coupled DNA repair produce accelerated aging without an increased risk of carcinogenesis.

Patients with Cockayne syndrome show a characteristic appearance described as "cachectic dwarfism," which is marked by microcephaly, sunken eyes, a beaked nose, and kyphosis. Neurologic development is severely delayed, and structural defects of the eye include cataracts, microophthalmos, and iris hypoplasia. Other features of the disorder include photosensitivity, dry skin and hair, progressive pigmentary retinopathy, and cataracts. Sensorineural hearing loss, dental caries, demyelinating neurologic disease, and thickening of the calvarium and cortical bones are often seen.

Several clinical subtypes exist, including CS Type I, in which patients develop symptoms after the first few years of life, and CS Type II, in which patients present with intrauterine growth restriction and markedly reduced postnatal increase in height, weight, and head circumference. CS type III is thought to be a milder form of the disease. Mutations in the genes ERCC2, ERCC3, and ERCC 5 cause an overlap syndrome with xeroderma pigmentosum, producing both a progeroid phenotype and an increased risk of malignancy by concomitantly impacting pathways of transcription-coupled and global excision repair.

The etiology of our patient's pruritus remains unknown, although her elevated liver enzymes are likely another manifestation of the disease. Ghaffar et al reported a series of 9 patients with genetic confirmation of Cockayne Syndrome, 7 of whom developed liver dysfunction ranging from episodes of severe cholestasis to fulminant hepatic failure. Stress or infection appeared to precipitate the attacks, which in all cases led to further neurologic deterioration and worsening liver function. Patients were treated with supportive care in conjunction with ursodeoxycholic acid and vitamin E, although these did not slow progression of the disease.

REFERENCES

1. Ghaffar TA, Elsobky, ES, Solaf M Elsayed. 2011. Cholestasis in patients with Cockayne syndrome and suggested modified criteria for clinical diagnosis. Orphanet J Rare Dis. Apr 8;6:13.
2. Hoeijmakers, JH. 2009. DNA Damage, Aging and Cancer. N Engl J Med. Oct 8;361(15):1475-85.
3. Laugel V et al. 2010. Mutation update for the CSB/ERCC6 and CSA/ERCC8 genes involved in Cockayne syndrome. Hum Mutat. Feb;31(2):113-26.

CHICAGO DERMATOLOGICAL SOCIETY **CASE #3**

Presented by Sarah Baker, MD and Bethanee J. Schlosser, MD PhD
Department of Dermatology, Feinberg School of Medicine, Northwestern University

HISTORY OF PRESENT ILLNESS
This 30 year old African American female with no significant past medical history presented for evaluation and treatment of painful lesions on her palms and soles present for approximately 5 years. The patient also noted more recent swelling of her proximal nail folds and abnormal appearing cuticles on her bilateral hands. She denied pustular lesions, but occasionally noted "blisters" on her soles and cracking on her palms. The patient had also noted several sores on her bilateral medial thighs which she attributed to ingrown hairs, as well as tender sores in her mouth. She denied similar lesions on her scalp or genitalia. Prior to presentation, she had been seen periodically in the emergency department when her lesions became particularly debilitating and had been given a preliminary diagnosis of palmoplantar psoriasis. She denied symptoms of fatigue, joint pain, muscle weakness, nosebleeds, ocular irritation, or odynophagia.

PAST MEDICAL HISTORY
None

MEDICATIONS
None

SOCIAL HISTORY
Single, 3 children, employed as a nurse's aide, no alcohol use, positive tobacco use (1/2 ppd)

FAMILY HISTORY:
No psoriasis, atopic dermatitis, palmoplantar keratodermas, or connective tissue disease

PHYSICAL EXAM
On the posterior buccal mucosa, pink centrally ulcerated plaques with surrounding hyperpigmentation were noted. There were confluent, erythematous sclerotic plaques with hyperpigmented borders, multiple fissures, and overlying scale on the palms and soles. Erythema, edema, and prominent dilated capillaries were noted on the bilateral proximal nail folds. The inner thighs had several erythematous scaly plaques with central ulceration and hyperpigmented borders. Multiple dark brown firm papules were noted on the extremities. The scalp, face, ears, nail plates, and vulva were uninvolved.

LABS
Abnormal labs: WBC 2.6 K/uL (ref 3.5-10.5), hemoglobin 10.8 gm/dL (ref 11.6-15.4), absolute neutrophil count 0.9 (ref 1.5-8.0), ANA 30 IU/mL (1:160-1:640 titer) (ref <7.5) homogenous and speckled pattern, SSA autoantibodies 101 units (ref <5), SSB autoantibodies 23 units (ref <5), urinalysis with small blood, positive nitrites and positive leukocyte esterase, initial urine culture positive for *Klebsiella pneumoniae* and repeat urine culture positive for *Escherichia coli*
Negative/normal labs: platelets, BUN, creatinine, ALT, AST, alkaline phosphatase, total bilirubin, C3, C4, glucose 6 phosphate dehydrogenase, thiopurine methyltransferase; dsDNA, Smith, RNP, Scl-70, cardiolipin, lupus anticoagulant, and beta 2 glycoprotein autoantibodies

HISTOPATHOLOGY
4/29/11 R volar 4th finger and L inner thigh: An atrophic epidermis with prominent hyperkeratosis and hypergranulosis was noted. There was a superficial band-like lymphohistiocytic infiltrate with focal squamatization of the basal cell layer and occasional necrotic keratinocytes. Numerous

melanin laden macrophages were noted. Colloidal iron stain was performed and demonstrated significant dermal deposits of acid mucopolysaccharides. Direct immunofluorescence of a L inner thigh lesion was negative for immune deposits.

DIAGNOSIS

Lupus erythematosus-lichen planus overlap syndrome

TREATMENT/COURSE

The patient was treated with fluocinonide 0.05% ointment for cutaneous and oral lesions as well as hydroxychloroquine 400 mg daily with little improvement noted after 2 months. She was also advised to discontinue smoking and was provided with a nicotine patch to facilitate smoking cessation. Rheumatology evaluated the patient and was highly suspicious for underlying systemic lupus erythematosus given the patient's laboratory abnormalities. We are currently considering other potential therapeutic options such as adding an additional antimalarial agent (i.e. quinacrine) or immunosuppressive medication (i.e. mycophenolate mofetil, azathioprine).

DISCUSSION

Lupus erythematosus-lichen planus (LE-LP) overlap syndrome is rare with fewer than 50 cases reported in the literature. LE-LP overlap syndrome encompasses a heterogenous group of individuals with cutaneous and/or mucosal lesions clinically and histopathologically displaying a combination of features of lupus erythematosus as well as lichen planus. Affected individuals are most commonly between the ages of 25 and 45 with a slight female predominance. Patients may also demonstrate increased titers of autoantibodies suggestive of lupus erythematosus.

Clinically, lesions described in this condition have varying morphologies. Cutaneous lesions can display characteristics of discoid lupus erythematosus, subacute cutaneous lupus erythematosus, lichen planus or a combination thereof. The most commonly described lesions are tender scaling, reddish-blue, atrophic plaques or verrucous papules on the extremities. In addition, involvement of the trunk, head, neck; oral, vulvar, and ocular mucosa; and nail abnormalities have been reported. The etiology of lupus and lichen planus remains unclear. It has been postulated that development of these conditions may be secondary to autoimmunity, genetic predisposition, or an inciting viral infection in a predisposed host. There are also isolated reports of development of lupus erythematosus-lichen planus overlap syndrome in association with medications including isoniazid, procainamide, and acebutolol.

Direct immunofluorescence studies of lesional skin are thought to be useful in the diagnosis of lupus erythematosus-lichen planus overlap syndrome as they may show mixed features of both conditions. Lupus erythematosus typically displays granular or band-like deposition of immunoglobulins IgG, IgA and IgM as well as complement along the dermoepidermal junction, whereas lichen planus often demonstrates colloid bodies with positive IgM and fibrin deposition in a fibrillar or band-like pattern along the dermoepidermal junction. Although no standardized therapeutic regimens exist for this condition, there are reports of successful treatment with cyclosporine, hydroxychloroquine, systemic retinoids, and topical tacrolimus.

REFERENCES

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CHICAGO DERMATOLOGICAL SOCIETY **CASE #4**

Presented by Gunilla Carlsson Thorn, MD and Bethanee J. Schlosser, MD, PhD
Department of Dermatology, Feinberg School of Medicine, Northwestern University

HISTORY OF PRESENT ILLNESS

The patient is a 90 year-old Caucasian female with extramammary Paget's disease involving the vulva and perianal skin. The patient was first diagnosed with extramammary Paget's disease in 1997 and has undergone several surgical excisions, including a hemivulvectomy with flap reconstruction by plastic surgery, since her initial diagnosis. She was also treated with imiquimod 5% cream for 1 to 2 months with initial improvement but subsequent irritation and flare of Paget's requiring discontinuation of imiquimod. The patient reports constant pain and pruritus of the vulvar and perianal areas; aggravating factors include walking, rubbing and friction. She denies any vaginal discharge but notes occasional vulvar bleeding. The patient is currently applying pramoxine 1%/hydrocortisone 2.5% cream once daily with moderate improvement of her symptoms.

PAST MEDICAL HISTORY

Psoriasis, arthritis, hypertension, osteoporosis, cataracts, insomnia and depression

PAST SURGICAL HISTORY

Excision of extramammary Paget's disease lesions (1997, 2003, 2005, 2008), cholecystectomy

MEDICATIONS

Spironolactone, metoprolol, naproxen, venlafaxine, pramoxine 1%/hydrocortisone 2.5% cream, clobetasol 0.1% ointment (to psoriatic lesions only), calcium and vitamin D

ALLERGIES

Codeine

FAMILY HISTORY

Noncontributory

SOCIAL HISTORY

Nun, retired teacher, no alcohol or tobacco use

PHYSICAL EXAM

The exam was notable for widespread red erosions with intervening white macerated epithelium involving the majority of the vulva and perianal skin. There was severe vulvar dystrophy with narrowing of the vaginal introitus to less than 4mm and extensive surgical scarring. On the mons, medial thighs and hips were scattered erythematous patches and thin plaques with overlying scale consistent with psoriasis.

LABS/IMAGING

Abnormal: bacterial culture (vulva) methicillin-sensitive staphylococcus aureus; blood urea nitrogen 29mg/dl [8-26mg/dl]; creatinine 1.16mg/dl [0.4-1.10mg/dl]
Negative/Normal: fungal culture (vulva); CBC; ALT, AST, alkaline phosphatase, total bilirubin; PPD
Papanicolaou testing 4/10: negative
Chest X-Ray 6/11: no acute cardiopulmonary process
CT chest/abdomen 2000: negative
Mammography 2008: negative
Cystoscopy, colonoscopy: never performed

HISTOPATHOLOGY

3/15/11 L inner vulva: Atypical epithelial cells displaying pleomorphic nuclear detail and ample pale cytoplasm are noted at various levels of the epidermis. The dermis shows a variable, mostly perivascular lymphohistiocytic infiltrate. An invasive component is not identified. Immunohistochemical staining of the atypical cell population is positive for cytokeratin (AE 1/3), CK7 and CK5, and negative for S-100 protein, Mart-1 and CK20.

DIAGNOSIS

Extramammary Paget's Disease

TREATMENT AND COURSE

Additional evaluation (colonoscopy, CT chest/abdomen/pelvis) was discussed with the patient's primary care physician; given the patient's age and duration of disease, the decision was made not to pursue such testing. Severe narrowing of the vaginal introitus precludes cystoscopy and speculum examination with Papanicolaou testing. The patient was started on fexofenadine in an attempt to alleviate her pruritus.

Treatment options (additional surgical excision, photodynamic therapy, radiation therapy and topical imiquimod, topical 5-fluorouracil) were discussed with oncology, gynecologic oncology and radiation oncology. Given the extent of disease and potential treatment-related morbidities, none of these options were pursued. Instead, the patient was started on methotrexate 10mg PO weekly with supplemental folic acid 1mg PO daily. The patient was instructed to discontinue naproxen and to avoid all non-steroidal anti-inflammatory drugs while taking methotrexate. Radiation therapy is being considered as a subsequent mode of treatment pending the patient's course of disease and response to methotrexate.

DISCUSSION

Extramammary Paget's disease (EMPD) is a cutaneous adenocarcinoma of apocrine gland-bearing sites that is most commonly seen in the anogenital area of elderly Caucasian women. It is rare, with only a few hundred cases reported in the world medical literature, and is estimated to account for 1-2% of vulvar carcinomas. EMPD is divided into primary and secondary forms. The primary form arises as an intraepidermal neoplasm of apocrine origin and is not associated with any underlying adenocarcinoma. Secondary EMPD represents an epidermal extension of an underlying visceral malignancy (most commonly gastrointestinal or genitourinary) or adnexal adenocarcinoma.

EMPD classically presents as well-circumscribed, erythematous, scaly plaques that may demonstrate crusting, weepy erosions and ulcerations. Infiltrated nodules, vegetative lesions and regional lymphadenopathy may also be seen. While lesions are usually unifocal, multiple lesions with intervening normal skin can be present. Patients typically complain of intense pruritus, though some note burning or tenderness. The vulva is the most common site affected (65%), but involvement of the perianal area (20%) and male genitalia (14%) is also seen.

Histopathologic examination reveals an intraepidermal proliferation of large, round Paget cells with abundant, pale cytoplasm and central, pleomorphic nuclei. Immunohistochemical staining is essential to exclude other neoplasms that can present with pagetoid spead, including melanoma, Bowen's disease, mycosis fungoides and Langerhans cell histiocytosis. Initial staining with CK7 and CK20 has been suggested as primary EMPD stains CK7+/CK20-, secondary EMPD stains CK7+/CK20+ and conditions other than EMPD will stain negative for both markers.

The management of EMPD includes a thorough evaluation for internal malignancy including lymph node examination, colonoscopy and cystoscopy. Women should also undergo pelvic

and breast examination and imaging, while men require prostate examination and measurement of prostate specific antigen (PSA) level. Surgery (either Mohs micrographic surgery or conventional excision) remains the mainstay of treatment; however several newer modalities including radiation therapy, photodynamic therapy, topical 5-fluorouracil and topical imiquimod also show promise.

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CHICAGO DERMATOLOGICAL SOCIETY **CASE #5**

Presented by Julia Minocha, MD, Roopal V. Kundu, MD, and Joaquin Brieva, MD
Department of Dermatology, Feinberg School of Medicine, Northwestern University

PATIENT A

HISTORY OF PRESENT ILLNESS

The patient is a 15 year-old previously healthy female who presented for evaluation of a non-healing ulcer on her hand. She had travelled to Costa Rica on a school trip 2 months prior to presentation. During her trip to Costa Rica she sustained several insect bites. Approximately 1.5 weeks after returning from her trip, her left dorsal hand became swollen with a central dark papule. Approximately 2 weeks later, the lesion became ulcerated, tender to palpation, and mildly pruritic. There was no drainage or expanding erythema. She treated the area with neomycin and hydrogen peroxide regularly. She subsequently developed a similar papule on her left lower lip. She denied fevers, chills, shortness of breath, nausea, vomiting, or diarrhea.

PAST MEDICAL HISTORY

Febrile seizure at age 2

MEDICATIONS

None

ALLERGIES

NKDA

FAMILY HISTORY

Noncontributory

SOCIAL HISTORY

She is currently a high school student. She denies alcohol or tobacco use.

PHYSICAL EXAM

The patient was a well-developed, well-nourished female in no acute distress. On the left lower lip there was a 6mm erythematous edematous ill-defined papule with surrounding edema. On the right chin there was a 3mm crusted erythematous edematous papule. On the left dorsal hand there was a 1.5cm ulcerated erythematous discrete nodule with rolled borders.

LABS/IMAGING

Abnormal: Leishmania PCR and DNA Sequencing: *Leishmania panamensis*; Leishmania Real-Time PCR: positive; Leishmania Microscopy: positive; Leishmania Culture: positive; Hgb 10.9 gm/dL [11.6-15.4 gm/dL]; EKG: sinus bradycardia with sinus arrhythmia
Normal: WBC, platelets, potassium, creatinine, glucose, ALT, AST, lipase, and amylase

HISTOPATHOLOGY

5/12/2011 Left dorsal hand: Sections reveal an ulcerated process with pseudoepitheliomatous hyperplasia and a dense dermal infiltrate composed of histiocytes with numerous small and uniform round cytoplasmic inclusions measuring approximately 2-4 micrometers in diameter. Scattered lymphocytes, neutrophils and some plasma cells are noted.Giemsa stain highlights numerous mastigotes within histiocytes. The DPAS stain was negative for fungi.

DIAGNOSIS

Cutaneous Leishmaniasis

TREATMENT AND COURSE

The CDC was contacted and performed confirmatory testing and speciation with microscopy, culture, PCR, and DNA sequencing and identified *Leishmania panamensis* as the causative species. Although the patient had a lip lesion at presentation it was felt that the patient had three primary lesions of cutaneous leishmaniasis from multiple inoculations by the same sandfly vector. She had no evidence of mucocutaneous disease. Cutaneous leishmaniasis is often self-limited, however, because *L. panamensis* has a tendency to progress to mucocutaneous disease the patient was treated with amphotericin B 3mg/kg/day for 7 days followed by one dose on Day 14 and Day 21. Her lesions initially improved however, 6 weeks after completing therapy, her lesions progressed again so treatment was initiated with a pentavalent antimonial, sodium stibogluconate, 20mg/kg/d intravenously for 20 days. During the course of her treatment she developed mild leukopenia, hypokalemia, and transaminitis which did not interrupt her therapy.

PATIENT B

HISTORY OF PRESENT ILLNESS

The patient is a 16 year-old previously healthy female who presented for evaluation of a non-healing ulcer on her lower back. She had travelled to Costa Rica on the same school trip 2 months prior to presentation. After arriving home she developed a boil on her back that had grown in size and started to drain fluid. She had received an email from school stating that other children who had gone on the school trip to Costa Rica had developed similar skin lesions and were advised to see a physician. She denied fevers, chills, malaise, shortness of breath, nausea, vomiting, and diarrhea.

PAST MEDICAL HISTORY

None

MEDICATIONS

None

ALLERGIES

NKDA

FAMILY HISTORY

Noncontributory

SOCIAL HISTORY

She is currently a high school student. She denies alcohol or tobacco use.

PHYSICAL EXAM

The patient was a well-developed, well-nourished female in no acute distress. On the right waist there was a 1.5cm ulcerated erythematous discrete nodule with rolled borders.

LABS/IMAGING

None

HISTOPATHOLOGY

5/18/2011 Right waist: Sections reveal an ulcerated lesion with a dermal infiltrate composed of histiocytes with numerous small and uniform round cytoplasmic inclusions measuring approximately 2-4 micrometers in diameter. Scattered lymphocytes, neutrophils and some plasma cells are noted. Small calcific cytoplasmic concretions are noted.

Pseudoepitheliomatous hyperplasia is noted. Giemsa stain highlights focal intracytoplasmic amastigotes. The DPAS stain was negative for fungi.

DIAGNOSIS

Cutaneous Leishmaniasis

TREATMENT AND COURSE

The CDC was contacted and recommended treating the patient for infection of *L. panamensis* based on the results of her travelling companions lab testing. The patient received amphotericin B 3mg/kg/day for 7 days followed by one dose on Day 14 and Day 21. Her lesion healed and she did develop any new lesions.

DISCUSSION

Leishmaniasis is an umbrella term that covers a spectrum of chronic parasitic infections including cutaneous leishmaniasis, mucocutaneous leishmaniasis, and visceral leishmaniasis caused by more than 15 species of the flagellated protozoa (Class Mastigophora) of the family Trypanosomidae, called Leishmania. The disease is endemic in Central and South America (New World), as well as, the Mediterranean basin, and parts of Asia and Africa (Old World). Cutaneous leishmaniasis (Old World; *L. tropica, L. major, L. aethiopica, L. infantum*; and New World; *L. mexicana, L. guyanensis*) is the most common clinical presentation and typically occurs in the Old World but can also occur in the New World. Mucocutaneous leishmaniasis, or espundia, (*L. braziliensis, L. panamensis*) occurs almost exclusively in the New World and visceral leishmaniasis (*L. donovani, L.infantum*) has a worldwide distribution. Globally there is an annual incidence of 400,000 new cases and a prevalence of approximately 12 million infected people. Leishmaniasis species are obligate intracellular parasites which exist and multiply in their vectors, the sandfly, in the promastigote flagellated form. Once inoculated into their host; human, canine, or rodent; they are engulfed by histiocytes and transform into mastigotes.

Cutaneous leishmaniasis first presents as a small discrete papule at the inoculation site which progresses into a nodule that may be verrucous or become ulcerated with an erythematous rolled border. Exposed areas (ear, extremities) are the most commonly involved. Affected individuals typically have solitary lesions but a minority may develop secondary satellite lesions. Disseminated cutaneous leishmaniasis, or anergic leishmaniasis, can be associated with *L. aethiopica* (Africa) and *L. mexicana* (Americas) and is characterized by multiple nonulcerated papules and plaques which may cover the entire body. This disease subtype is progressive and often recalcitrant to therapy. Some affected individuals (<5% *L. braziliensis, L. panamensis*) will develop mucocutaneous disease months to years after initial infection. Recent studies suggest that infection of the leishmania parasite with an endogenous virus, called Leishmania RNA virus-1 (LVR1) allows the parasite to subvert the host immune response leading to development of mucocutaneous lesions. Early mucosal lesions include hyperemia of the nose and lips which may ulcerate. Lesions can progress to invade the septum, palate, and laryngeal cartilage resulting in extensive loss of mouth and nasal tissue and loss of phonation due to vocal cord destruction. Leishmaniasis recidivans (*L. tropica*) is cutaneous disease that recurs at the periphery of the inoculation site up to 2 years later.

Visceral leishmaniasis (kala-azar) is due to infection of the reticuloendothelial system; the liver, spleen, lymph nodes, and bone marrow; by the parasite. After a 1-4 month incubation period, systemic symptoms of fever, weight loss, cough, hepatosplenomegaly, and lymphadenopathy most commonly occur. Laboratory abnormalities such as pancytopenia, hypergammaglobulinemia, and hypoalbuminemia are frequently seen. Resultant immunosuppression can result in pulmonary, gastrointestinal, and oral infections which may lead to death.

Histologically lesions appear as an ulcer with pseudoepitheliomatous hyperplasia and a dense infiltrate of histiocytes, lymphocytes, plasma cells, and neutrophils. Amastigotes are present in dermal macrophages and can be stained with Wright, Giemsa, and Feulgen stains. In chronic lesions caseation necrosis may be present. The diagnosis can be confirmed by demonstration of mastigotes in dermal histiocytes, culture of parasites in Nicolle–Novy–MacNeal (NNM) or chick embryo media (positive in 40% of cases), or in chronic cases by a positive Montenegro skin reaction test (positive in 90% of patients with cutaneous and mucocutaneous leishmaniasis). Speciation with PCR and DNA sequencing is recommended to guide appropriate therapy.

Old World cutaneous leishmaniasis is often self-limited and resolves within 6-18 months. Treatment decisions should weigh the degree of morbidity against the potential side effects of therapy. Pentavalent antimonials (20 mg/kg/day for 10-20 days, 30 days for mucosal involvement) are the standard therapy for New World leishmaniasis as well as severe cases of Old World leishmaniasis (*L. tropica, L. major)*, however, side effects may include cardiotoxicity (prolongation of the QT interval and ST-T wave changes), pancreatitis, hepatitis, thrombocytopenia, and, rarely, acute renal failure. Additional therapeutic options include intralesional injections of pentavalent antimonials, heat therapy, cryotherapy, pentamidine, oral anti-fungals, amphotericin B, and allopurinol. Newer therapies including vaccines against leishmanial antigens are under investigation. Our two patients were treated with a course of amphotericin. One patient relapsed and was then treated with sodium stibogluconate, a pentavalent antimonial.

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CHICAGO DERMATOLOGICAL SOCIETY **CASE #6**

Presented by Sapna Patel, MD, Joaquin Brieva, MD, and Bethanee J. Schlosser, MD, PhD
Department of Dermatology, Feinberg School of Medicine, Northwestern University

HISTORY OF PRESENT ILLNESS
The patient is a healthy 27 year-old African American female who presented to the emergency room with fever to 105ºF, diarrhea, emesis, sore throat, and bilateral eye redness with pain. Her symptoms started five days prior to presentation. Her internist initially diagnosed her with a viral syndrome and started her on acetaminophen and ibuprofen. She returned two days later to her internist and was started on sulfacetamide eye drops for conjunctivitis. The next day, she presented to the emergency department with worsening symptoms. She was diagnosed with an allergic reaction to sulfacetamide drops, which were discontinued, and she was started on ophthalmic moxifloxacin drops. The morning of presentation, she was seen by a community dermatologist and was started on valacyclovir. That evening, she presented to the emergency room for further progression of the eruption and persistent fever. She denied visual changes, dysuria, sick contacts, other new exposures, travel, and sexual activity in the preceding six years. There was no prior history of cold sores.

PAST MEDICAL HISTORY
None

PAST SURGICAL HISTORY
None

MEDICATIONS
Ibuprofen, acetaminophen, moxifloxacin ophthalmic drops

ALLERGIES
NKDA

FAMILY HISTORY
Noncontributory

SOCIAL HISTORY
Single, 4th grade teacher, no alcohol or tobacco use

PHYSICAL EXAM
Eyes: eyelids markedly edematous, conjunctival injection bilaterally with mild crusting at lid margins, no exudate. Chest, forehead, & cheeks: numerous brown to dusky thin papules coalescing into large plaques, few small flaccid bullae on the upper forehead draining clear fluid. Lips: small erosions with ulceration along the upper and lower vermillion border. R lower back: cluster of small vesicles. Palms, soles, vulva: clear

LABS/IMAGING
Abnormal: WBC 2.9K/UL [3.5-10.5K/UL]; (N73/L20); AST 146U/L [0-40U/L]; ALT 203U/L [0-48U/L]; albumin 3.3g/DL [3.5-5 g/DL]; PT 15.3S [9.2-13s]; INR 1.4 [0.8-1.2]; ANA 1:320 [<7.5IU/mL]**;** UA: 1.023, protein 100, glucose 100, ketones 15, moderate leukocyte esterase, >100 WBC, >100 RBC, 2+bacteria, 1+ epithelial cells, 6-10 hyaline casts, negative bilirubin & nitrites
Negative/Normal: Hemoglobin, platelets, renal function, alkaline phosphatase, bilirubin

HISTOPATHOLOGY

6/26/11 Right Flank: Sections demonstrate full-thickness necrosis of the epidermis with detachment of the epidermis and vesicle formation. Scattered single apoptotic cells are seen lateral to the area of full thickness necrosis. A sparse superficial perivascular inflammatory infiltrate is noted. There is also some edema and telangiectasia of the upper dermis. Clusters of neutrophils and some bacteria in the pilosebaceous unit are noted. Direct immunofluorescence of perilesional skin is negative.

DIAGNOSIS

Stevens-Johnson Syndrome / Toxic Epidermal Necrolysis secondary to ibuprofen

TREATMENT AND COURSE

The patient was given one dose of piperacillin-tazobactam, clindamycin, vancomycin, and ketorolac in the emergency room, which were discontinued upon inpatient admission. In addition to supportive care, IV acyclovir was started. Dysuria developed overnight and for the first three days of admission, she had progressively increasing erosions of the nasal, oral, and vulvar mucosa as well as bullous lesions on the face and trunk. IVIg 1g/kg/day for three days was started out of concern for development of toxic epidermal necrolysis and clobetasol suppositories were started to decrease vulvovaginal mucosal inflammation and the potential for associated scarring. Exams by consulting services revealed bilateral corneal abrasions with subconjunctival hemorrhage and erosions of the epiglottis as well as mild to moderate edema of both the epiglottis & arytenoids. She was subsequently started on dexamethasone 10mg IVq8 and transferred to the intensive care unit for further airway monitoring. Liver function tests gradually improved and by the fourth day of admission, she had no new bullae, could fully open her eyes, and could tolerate soft solids. The patient was then transferred to the burn unit at Loyola University Medical Center, where nasoduodenal feeds and use of Acticoat (nanocrystalline silver) tampon were started. She was discharged home after a total of 17 days in the hospital and a follow-up exam was notable for significant dyschromia, facial pustules, extensive xerosis, atrophic plaques with focal erosion of the labia minora extending to the labia majora, and agglutination of the clitoral hood. Nightly use of intravaginal clobetasol suppository 0.05% and clobetasol ointment externally to the vulva were resumed.

DISCUSSION

More than 95% of patients with toxic epidermal necrolysis (TEN) report the use of at least one medication prior to onset of symptoms, however 50% of Stevens-Johnson syndrome (SJS) cases are linked to infections or vaccines. To date, more than 100 drugs have been associated with SJS and TEN, most commonly antibiotics, non-steroidal anti-inflammatory drugs (NSAIDs), and anticonvulsants. A 2011 review of 71 patients with SJS and TEN reports the average number of suspected drugs per patient as 2.3 with the most common being painkillers, NSAIDs, and antiepileptic agents.

A1995 European review of 245 patients with SJS and/or TEN found that sulfonamide antibiotics were the most commonly associated medications with a relative risk (RR) of 172, followed by cephalosporins (RR 14) and quinolones (RR 10). Among drugs more commonly used for months or years, increased risk was largely confined to the first two months of treatment and relative risks were highest with carbamazepine (RR 90), corticosteroids (RR 54), and phenytoin (RR 53). Only oxicam-derived NSAIDs were significantly associated with disease (RR 22), as was acetaminophen in most regions (RR 9.3). The risk with cyclooxygenase-2-selective NSAIDs, such as celecoxib and rofecoxib, is less clear since they were introduced after the completion of most large epidemiologic studies.

In a review of 32 pediatric patients with SJS and TEN, ibuprofen (alone or in combination with another medication) was involved in 47% of cases, and many of these children experience complications, including genitourinary problems. All children who experienced either cutaneous, mucosal, or both types of complications had taken ibuprofen, and chi-square analysis revealed the relationship between ibuprofen and complications to be statistically significant. Another review of 89 patients with SJS, TEN, or SJS-TEN overlap noted complications of vaginal and labial commissure synechiae. Vulvar involvement is under recognized in SJS and TEN. In a prospective study of 40 patients, 70% had genital lesions during the acute period. 89% of these patients had lesions confined to the vulva and 11% also had vaginal lesions. Five of these patients (12.5%) had long-term sequelae, including synechiae and dyspareunia.

Given the high morbidity and mortality associated with SJS and TEN, some have argued that early diagnosis is helpful in regards to management. It has been shown that granulysin levels are elevated in the serum of patients with SJS & TEN prior to blister formation. The rapid test for detecting serum granulysin in this group of patients recently published by Fujita et al is promising in this regard, with 80% sensitivity and 96% specificity.

Treatment for SJS and TEN remains controversial with systemic corticosteroids and IVIg being the most commonly used medications. Anecdotal evidence supports the role of topical corticosteroids in the vulvar area to prevent formation of scar tissue however there are no such cases described in the literature.

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CHICAGO DERMATOLOGICAL SOCIETY **CASE #7**

Presented by Anne Goldsberry, M.D., M.B.A. and Anthony Mancini, M.D.
Department of Dermatology, Feinberg School of Medicine, Northwestern University and Children's Memorial Hospital

UNKNOWN

CHICAGO DERMATOLOGICAL SOCIETY **CASE #8**

Presented by Benjamin Marks, MD, PhD and Maria Colavincenzo, MD
Department of Dermatology, Feinberg School of Medicine, Northwestern University

HISTORY OF PRESENT ILLNESS
Patient is a 64 year-old male with past medical history significant for HIV and Hepatitis C who presented to the dermatology clinic for evaluation of blisters on the dorsum of the hands and arms for the past six months. He first noticed the blisters at the start of the summer after he had mowed his lawn. Over the next few months, the blisters continued to increase in number and were occasionally painful. He denied any trauma to his hands. He never had anything like this before. He was unaware of any relationship to sun exposure.

PAST MEDICAL HISTORY
HIV: more than 20 years, acquired from IV drug use, Hepatitis C, Hypertension, steatohepatitis

SOCIAL HISTORY
Tobacco use > 20 pack years, history of IV drug use (clean for > 20 years), denies EtOH

MEDICATIONS
efavirenz/emtricitabine/tenofovir, lisinopril, hydrochlorothiazide, atorvastatin, tiotropium

ALLERGIES
NKDA

PHYSICAL EXAM
The bilateral dorsum of hands and arms had several intact firm blisters without surrounding erythema, multiple erosions with hemorrhagic crust and several hyperpigmented macules. His face did not have erosions or blisters but showed slight hypertrichosis on cheeks.

Wood's lamp exam of urine is positive for a pink fluorescence.

LABS/IMAGING
Abnormal: AST 105U/L [0-40U/L]; ALT 129 U/L [0-48U/L]; Urine Porphyrins: Uroporphyrin 6116.6ug/gCreat [<22.0ug/gCreat], Coproporphyrins 352.7ug/gCreat [23-130ug/gCreat], Total Porphyrins 10237.3ug/gCreat
Negative/normal: CBC, BMP, alkaline phosphatase, bilirubin, iron, iron binding capacity, ferritin
CT of liver 12/13/2010: Findings of cirrhosis and portal hypertension including mild splenomegaly and small gastroesophageal varices

HISTOPATHOLOGY
12/2/10 R hand: Sections demonstrate variable subepidermal bullae. There is some epidermal necrosis without spongiosis or acantholysis. There is vascular basement membrane thickening and homogenization. The dermal-epidermal junction membrane is of normal thickness. Upper dermal edema is noted. Festooning of dermal papillae is also noted. A variable perivascular lymphohistiocytic infiltrate is identified. Occasional eosinophils are noted in the dermis. DPAS shows thickening of the upper dermal vessel walls and focal thickening of the basement membrane.
12/2/10 Direct Immunofluorescence, R hand: IgG1 and IgA showed perivascular deposits. C3 show granular basement membrane staining. IgG4 and IgM were negative.

DIAGNOSIS
Porphyria cutanea tarda

TREATMENT AND COURSE
Given the patient's normal hemoglobin and iron levels, therapeutic phlebotomy was pursued. Unfortunately, access to the patient's veins was challenging, (related to previous IV drug use) and phlebotomy was discontinued. He started hydroxychloroquine 200mg twice a week. He was instructed to use a sunscreen with physical blockers such as zinc oxide or titanium dioxide. He continues to get new blisters but urine porphyrins levels have improved.

DISCUSSION
Porphyrias are a group of metabolic disorders involving the heme biosynthetic pathway. Porphyria cutanea tarda (PCT) is an uncommon disease with an estimated prevalence of 1:10,000, but is the most common within this group of disorders. PCT is due to a defect in uroporphyrinogen decarboxylase (UROD), the fifth enzyme in the heme synthetic pathway. This defect prevents conversion of uroporphyrinogen III to coproporphyrinogen III, so that the former is elevated in serum and urine.

PCT is the only porphyria that is not inherited solely as a monogenetic trait. In fact, PCT is divided into an acquired, Type I and inherited, Type II, forms. In Type I PCT, UROD deficiency is limited to the liver, in contrast to Type II in which the enzyme deficiency is in all cell types, including red blood cells. There is also an inherited form of PCT that has normal red blood cell UROD activity, designated Type III PCT. More than 100 mutations in UROD gene have been identified, reflecting the high degree of molecular heterogeneity. In addition, there is a disease entity with identical clinical presentation to PCT but without defective UROD enzyme activity. This subset is referred to as pseudoporphyria and is usually due to chronic renal disease or medications.

Clinically, type I and II PCT are identical. Overt disease occurs when UROD activity falls below roughly 25% of normal levels. As UROD function decreases, hepatic accumulation of uroporphyrinogen increases which then is oxidized, in an iron-dependent reaction, to uroporphomethene. This later agent serves as a competitive inhibitor of UROD and thus causes a further decrease in enzymatic activity. Symptoms manifest on sun exposed areas in the form of photosensitivity, skin fragility, vesicles, bullae, erosions and crusts. As lesions resolve, hypo- or hyperpigmented scars and milia develop. Hypertrichosis with non-virilizing hair can develop on the temples and cheeks. In rare cases, sclerodermoid skin changes and purplish red discoloration periorbitally can occur.

A variety of triggers have been identified that exacerbate the clinical manifestations of PCT. Ethanol may have direct inhibitory effect on UROD and other enzymes in the heme biosynthetic pathway as well as increase gut absorption of iron. Iron levels are often elevated in PCT and inheritance of hemochromatosis genes has been linked to PCT development. Estrogen therapy has increased the incidence of PCT in females. Hepatitis C and HIV are associated with PCT. Up to 91% of PCT patients are Hepatitis C positive. The mechanism is not known but may be related to viral hepatotoxic effects. Finally, 60-70% of patients with PCT have chronic liver disease.

Diagnosis of this disease primarily involves the evaluation of blood, urine and stool for elevated porphyrins. PCT presents with accumulation of uroporphyrin, hepta-carboxylated porphyrins and coproporphyrin in the urine. Elevated uroporphyrin can be appreciated by use of Wood's lamp (UVA) illumination, which highlights a pink to red fluorescence or exposure to natural light that turns the urine red to brown after several hours. Fecal analysis reveals elevated coproporphyrin and isocoproporphyrin. Histopathology demonstrates a pauci inflammatory subepidermal blister. The blood vessels of the superficial dermal plexus have thickened walls.

DIF usually reveals C3 deposits around the upper dermal vascular plexus and may show linear deposition of IgG or IgA at the DEJ.

Treatment involves counseling on avoidance of UV light exposure, particularly 400-410nm. The patient should use sun protective clothing and frequent application of physical blocking sunscreens such as zinc oxide or titanium dioxide. Treatment of choice is either phlebotomy or low dose chloroquine or hydroxychloroquine. Phlebotomy has been recommended at 500ml every two weeks or weekly of 300ml. This usually leads to resolution of skin fragility and blistering within 2-4 months and normalization of urinary porphyrins in about 9-12 months. The antimalarials are thought to work by forming water-soluble complexes with porphyrins, which are removed from hepatocytes by exocytosis. Other effects may be a partial inhibition of porphyrin synthesis and a decrease in iron load. Standard therapy is chloroquine 125-250mg twice weekly or hydroxychloroquine 100-200mg twice weekly and complete remission can be expected in 6-9 months.

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CHICAGO DERMATOLOGICAL SOCIETY **CASE #9**

Presented by Bryan Gammon, MD, and Anthony J. Mancini, MD
Department of Dermatology, Feinberg School of Medicine, Northwestern University and Children's Memorial Hospital

HISTORY OF PRESENT ILLNESS
The patient is a 9 year-old healthy girl who presented for evaluation of a one year history of asymptomatic pigmented macules on the legs. Her mother notes that these initially began on the distal extremities, and then spread proximally to involve her thighs and recently the upper arms. The lesions may have slight substance or "feel firm" when they first develop, but are largely characterized by hyperpigmented macules. Her mother denies a family history of lupus, rheumatoid arthritis, miscarriage, photosensitivity or autoimmune conditions.

PAST MEDICAL HISTORY
Non-contributory

MEDICATIONS
None

ALLERGIES
NKDA

FAMILY HISTORY
No relevant family history

SOCIAL HISTORY
Unremarkable

PHYSICAL EXAM
Upon initial evaluation, the patient was well-appearing. She had numerous linear, stellate and circinate hyperpigmented patches ranging in size from 5-40 mm on the anterior and posterior legs. A few of the lesions were noted to be slightly indurated, and non-tender to palpation. There was no associated violaceous erythema, subcutaneous nodules, ulceration, necrosis, eschar or scarring. Mucosal surfaces were unremarkable. Palms and soles were clear.

LABS/IMAGING
Negative/normal: CBC, BMP, LFTs, CRP, ESR, ANA, dsDNA, anti-Sm, C3, C4, CH50, Protein C, Protein S, Factor V Leiden, Antithrombin III, beta-2 glycoprotein, anti-phospholipid antibodies, D-dimer, Von Willibrand Factor, p-ANCA, c-ANCA.

HISTOPATHOLOGY
4/28/11 L posterior leg: The sections reveal and unremarkable epidermis and dermis. Within the subcutaneous tissue and deep reticular dermis there is a vessel with marked concentric fibroplasia and occlusion of the lumen with a minimal inflammatory infiltrate with rare plasma cells. Vasculitis or fibrin was not identified. The elastic stain highlights an internal elastic lamina. Colloidal iron demonstrates the lack of significant dermal mucopolysaccharides. Although initially interpreted as being consistent with cutaneous polyarteritis nodosa, a thorough literature review was performed, and based on the clinical and histopathologic features; the findings were subsequently felt to be more consistent with macular lymphocytic arteritis.

DIAGNOSIS
Macular lymphocytic arteritis

TREATMENT AND COURSE

The patient remains asymptomatic and has not developed new lesions since presentation. She will be followed clinically for the development of any further clinical signs or symptoms of vasculitis or connective tissue disease, with intermittent laboratory evaluations.

DISCUSSION

Macular lymphocytic arteritis (MLA) is a recently recognized entity first published in the literature in 2003. Subsequently, 16 cases with similar histologic and clinical findings have been reported using varied nomenclature. In 2009, Saleh and Dutasim proposed the term Macular Lymphocytic Arteritis as a nomenclature, which draws attention to the unique clinical and histologic findings of the disorder. While this term has gained traction within the United States, some investigators prefer using the term Lymphocytic Thrombophilic Arteritis in an effort to draw attention to the unique feature of luminal fibrin deposition in the affected vessel.

MLA presents as an asymptomatic eruption on the bilateral lower extremities that may occasionally involve the upper extremities. The characteristic lesion is a hyperpigmented oval to stellate macule or patch. It has been observed primarily in African American and Asian patients, with only one reported case occurring in a Caucasian patient. The disorder is predominantly seen in females, with a female to male ratio of 4:1. While discoid lupus erythematosus was observed in 2 reported cases, and several patients have had low positive titers of anti-nuclear antibodies (ANA), investigation for a unifying underlying systemic disease has been unrevealing. Similarly, there is no commonality of drug exposure to suggest that medications play a role in the pathogenesis of MLA. Interestingly, of the 6 patients diagnosed with lymphocytic thrombophilic arteritis, 4 had positive antiphospholipid antibodies.

The histologic findings of MLA are characteristic. The epidermis, dermis and subcutaneous fat are essentially unremarkable. In all reported cases, a small artery in the superficial fat near the junction with the deep reticular dermis was infiltrated and surrounded by a lymphocytic infiltrate and an absence of neutrophils. The lumen of the vessel is often narrowed by deposition of fibrinous material from the luminal side. There is no frank destruction of the vessel wall, and elastin stain reveals an intact elastic lamina.

Based upon the relatively few cases reported in the literature, MLA runs a chronic but indolent course without evolution into a systemic vasculitis. The cutaneous lesions remain asymptomatic but may progress in number. The primary differential diagnosis based upon clinical and histopathologic grounds is cutaneous polyarteritis nodosa (PAN), which can similarly run an indolent, chronic course. Resolved lesions of PAN may leave retiform hyperpigmented macules in their wake. In fact, it has been suggested by some that these two entities exist on a continuum, and that MLA represents the most indolent presentation of PAN. We believe, however, that the distinction between MLA and cutaneous PAN can be made, based on clinical characteristics. While resolved lesions of PAN may mimic MLA, it has not been reported to present solely as hyperpigmented macules. Additionally, most patients with cutaneous PAN present with features lacking in MLA, such as purpura, necrosis, gangrene, nodules and/or livedo reticularis. The demonstration of an intact elastic lamina further argues against characterizing MLA as a variant of PAN, which would be expected to result in a discontinuous elastic lamina.

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CHICAGO DERMATOLOGICAL SOCIETY **CASE #10**

Presented by Lisa Shen, MD and Joaquin Brieva, MD
Department of Dermatology, Feinberg School of Medicine, Northwestern University

HISTORY OF PRESENT ILLNESS

The patient is a 26 year-old previously healthy African American female who developed asymptomatic skin colored papules on bilateral calves during the middle of her first pregnancy in 2005. A biopsy performed at an outside institution demonstrated mucin and was interpreted as "self-healing juvenile cutaneous mucinosis." The lesions subsequently resolved towards the end of pregnancy without intervention. Review of systems was negative at that time for malar rash, photosensitivity, oral ulcers, Raynaud phenomenon, arthralgias, pleuritic chest pain, hematuria, or headaches.

Four years later she presented to the Northwestern dermatology clinic with papules and subcutaneous nodules on her arms and legs. She also reported fatigue, occasional fevers and chills, pallor, and myalgias. The patient was started on hydroxychloroquine 400mg daily, which was discontinued after ophthalmologic evaluation revealed a paracentral scotoma and familial drusen. The patient progressively developed large firm plaques on her arms, thinning hair, and joint pain and swelling in bilateral wrists. The diagnosis of systemic lupus erythematosus was made in March 2010 based on clinical symptoms and laboratory data. Azathiaprine 50mg daily was initiated by a rheumatologist in June 2010 but was stopped 5 months later due to elevated transaminases. Prednisone 20mg daily was then started in September 2010 and slowly tapered down to a current dose of 5mg daily as the patient noticed occasional headaches and left sided numbness (involving face, arms, and legs). Mycophenolate mofetil 500mg twice daily was initiated in October 2010 and the dose was titrated up to a current dose of 1500mg in the morning and 1000mg in the evening.

In April 2011 the patient developed pink plaques on the scalp which she noted to be itchy, irritated, and sore. Fluocinonide 0.05% solution was prescribed for these discoid lupus lesions, with good efficacy.

PAST MEDICAL HISTORY

Systemic lupus erythematosus, anemia, history of eclampsia, deep venous thrombosis in arm and clot near right ovary

MEDICATIONS

Prednisone, mycophenolate mofetil, fluocinonide solution (for scalp)

ALLERGIES

NKDA

FAMILY HISTORY

Hypertension (both parents), prostate cancer (father)

SOCIAL HISTORY

Married with one son (healthy), no significant alcohol or tobacco history.

PHYSICAL EXAM

On the bilateral forearms, posterior elbows and dorsal aspects of the feet there were numerous 1-3cm subcutaneous indurated rubbery nodules. Scattered across the arms and legs were dozens of monomorphic 4-6mm yellowish firm dome-shaped papules.

LABS/IMAGING
Abnormal: WBC 2.7 K/UL [3.5 - 10.5K/uL]; hemoglobin 10g/dL [11.6-15.4g/dL]; ESR 88mm/hr [2-25mm/hr]; ANA 50 IU/mL (1:320 - 1:1280) [<7.5 IU/mL]; dsDNA autoantibodies 337 IU/mL [<5 IU/mL]; C3 33mg/dL [90-180mg/dL]; C4 4mg/dL [16-47mg/dL]; SSA autoantibodes 123 units [<5 units]; SSB autoantibodies 9 units [<5 units]; SPEP: IgG 4520mg/dL [750-1700mg/dL], serum alpha-2 0.5g/dL [0.6-1.0g/dL), serum gamma 3.8g/dL [0.7-1.5g/dL], kappa light chain 3660mg/dL [629-1350mg/dL], lambda light chain 1560mg/dL [250-723mg/dL]
Negative/normal: TSH, CK, aldolase, IgM Ab, IgA Ab, Scl-70 Ab, urinalysis

HISTOPATHOLOGY
3/17/10 L upper arm & R leg: The epidermis and upper dermis are unremarkable. Sections demonstrate dense deposits of mucin in the reticular dermis and subcutis consistent with papulonodular mucinosis. There is a proliferation of dermal dendritic cells with some fibroplasia. A colloidal iron stain shows prominent dermal deposits of mucin. CD34 staining shows a sparse but present infiltrate of dermal dendritic cells.

DIAGNOSIS
Papulonodular mucinosis associated with systemic lupus erythematosus (SLE)

TREATMENT AND COURSE
Due to the patient's inability to tolerate traditional therapies, belimumab is now being discussed as a treatment option for papulonodular mucinosis associated with SLE.

DISCUSSION
Papulonodular mucinosis is an unusual clinical presentation of lupus erythematosus occurring in approximately 1.5% of patients with lupus erythematosus. The clinical presentation includes asymptomatic, flesh-colored papules and nodules which may create a 'lumpy' appearance on the skin of the trunk, upper extremities, and occasionally face. The lesions sometimes have a central depression and pigmentation. The temporal relationship of the lesions with respect to diagnosis of SLE may vary (preceding SLE in up to a third of cases), though it has been linked to disease severity. It is also associated with renal disease and arthritis in up to 75% of patients.

The histologic findings are characterized by marked deposition of mucin in the upper and mid dermis, separation of intradermal collagen bundles, and a mild to moderate perivascular lymphocytic infiltrate. Of note, the histopathologic changes of lupus erythematosus are typically absent from the epidermis. Direct immunofluorescence typically reveals linear or granular depositis of IgG, IgM, and C3 at the dermal-epidermal junction.

The pathogenesis of papulonodular mucinosis has been attributed to the overproduction of glycosaminoglycans by fibroblasts, possibly driven by circulating antibodies. There have also been reports of triggers such as ultraviolet light. Finally, the increased ratio of males to females with papulonodular mucinosis (18:13) as compared to the ratio for SLE alone (1:9) is quite dramatic, suggesting a possible role for sex hormones.

Various treatment options for papulonodular mucinosis include antimalarials, corticosteroids, cyclophosphamide, methotrexate, and injection of lesions with hyaluronidase. Response is variable with a reported 20% of patients responding well to antimalarial medications. In March 2011, belimumab, a new biologic agent targeting human B-lymphocyte stimulator protein, was approved for treatment of active autoantibody-positive SLE. It is a humanized monoclonal antibody, which selectively reduces CD20+ B lymphocytes and short-lived plasma cells as well as anti-dsDNA antibody titers in SLE patients. It has been shown in phase 3 trials to lower disease

activity as measured by the SLE responder index. However, there is no literature on its efficacy in the treatment and management of papulonodular mucinosis associated with SLE.

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CHICAGO DERMATOLOGICAL SOCIETY **CASE #11**

Presented by Jennifer Sorrell, MD and Anthony J. Mancini, MD
Department of Dermatology, Feinberg School of Medicine, Northwestern University and Children's Memorial Hospital

HISTORY OF PRESENT ILLNESS
The patient is a 5 year-old previously healthy Caucasian female who presented to pediatric dermatology clinic due to maternal concerns about her hair. Her mother had noted that her hair was very light in color, fine and sparse. She had never had a haircut. Upon questioning, her mother noted that her nose did not look similar to anyone else's in the family. Review of systems was otherwise unremarkable.

PAST MEDICAL HISTORY
Unremarkable

FAMILY HISTORY
Unremarkable

MEDICATIONS
None

ALLERGIES
NKDA

PHYSICAL EXAM
The patient was short in stature (<5th%ile for age). She had mild facial dysmorphism with a pear shaped, bulbous-appearing nose. On the scalp, there was very thin, wispy, light blonde colored hair. A few hairs were easily extracted without pressure. Examination of the nails showed some loss of cuticles and slightly flattened distal phalanges. No significant brachydactyly or other obvious digital abnormalities.

LABS/IMAGING
Bilateral hand X-ray 3/7/2010: There is a cone-shaped appearance of the index finger middle phalangeal growth plate bilaterally with evidence of central premature growth plate closure. The little finger middle phalanges are also small. These findings are compatible with the clinically suspected diagnosis of trichorhinophalangeal syndrome**.**
Trichogram 2/17/2011: Several hairs with ruffled cuticle and dystrophic anagen bulb.

DIAGNOSIS
Trichorhinophalangeal syndrome, likely Type 1 with loose anagen syndrome

TREATMENT AND COURSE
The patient was referred to Genetics for evaluation given the associations of short stature as well as increased risk of bony exostoses, hip problems and early osteoarthritis.

DISCUSSION
Trichorhinophalangeal syndrome type I (TRPS I) is an autosomal dominant genodermatosis caused by a mutation in the TRPS gene. This gene encodes for a unique GATA transcription factor, Trps 1 protein, located on chromosome 8q24.1. This transcription factor is thought to cause repression of nuclear transcription in vertebrates.

Three subgroups of TRPS have been identified. TRPS I is characterized by craniofacial abnormalities, hair changes and skeletal anomalies. The most common craniofacial abnormalities include a bulbous, pear shaped nose, a thin upper lip, a long philtrum, and maxillary prognathism (overbite) with mandibular hypoplasia. Hair changes such as hypotrichosis of the scalp, fine, slow growing hair, a high frontal hairline and scant lateral eyebrows have been reported. Patients may also present with skeletal abnormalities that include brachydactyly, short stature, hip malformation, and deviation and distension of middle phalanges. The classic findings on plain radiographs are cone-shaped epiphyses, primarily at the base of the third phalanges, though short metacarpals, short phalanges, and Perthes disease-like femoral head changes may be also seen on radiographic imaging. Patients may develop nail changes and present with broadened, shortened nails (the "racket" nail) or slow growing, thin fragile nails.

TRPS III is similar clinically to TRPS 1 and I results from a missense mutation in exon 6 of the TRPS 1 gene. Patients have similar clinical features to TRPS 1, but typically develop more severe growth retardation, severe brachydactyly, and abnormalities of the phalanges and metacarpals. TRPS II is caused by a larger deletion and involves the genes for TRPS I and hereditary multiple exostoses (EXT1). The EXT1 gene is more telomeric and localizes to the 8q24.11-8q24.13 region. When larger pieces of 8q are deleted, mental retardation is more commonly associated with TRPSII. TRPSII can be distinguished from TRPSI when multiple cartilaginous exostoses or redundant skin are present. Additional findings in TRPS II include mental retardation, conductive hearing loss, delayed speech development and microcephaly. Management of TRPS primarily involves a skeletal survey to look for any bony abnormalities and genetic counseling.

Loose anagen syndrome is a benign condition that is self-limited and most frequently seen in females with blond hair between the ages of 2 and 6 years. Many parents report wispy, lusterless hair that has never required a haircut. In patients with loose anagen syndrome, the anagen hairs do not have an internal or external root sheath. On trichogram, the anagen hairs have a "floppy sock" appearance, which occurs from ruffled cuticles and a distorted proximal hair shaft. Misshapen anagen bulbs and long, tapered and twisted hairs may also be seen.

Loose anagen syndrome has been reported anecdotally with trichorhinophalangeal syndrome. When seen in tandem with a known syndrome however, it is most commonly associated with coloboma, Noonan syndrome and hypohidrotic ectodermal dysplasia. This possible association with LAS and TRPS is an interesting observation and warrants consideration in patients with TRPS.

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CHICAGO DERMATOLOGICAL SOCIETY **CASE #12**

Presented by Anne Goldsberry, M.D., M.B.A. and Joan Guitart, M.D.
Department of Dermatology, Feinberg School of Medicine, Northwestern University

PATIENT A

HISTORY OF PRESENT ILLNESS

The patient is a 31 year-old African American male who presented with a ten month history of nodules in the groin. He initially attributed the nodules to folliculitis, but when the lesions persisted, he presented to an outside dermatologist. Biopsy at that time was consistent with Rosai-Dorfman disease. In the six months prior to his presentation, he continued to develop new, enlarging lesions at the base of the penis and on the back, right shoulder, and right breast. He also complained of chronic nasal congestion and rhinorrhea over the same time period. He denied fevers, chills, night sweats, and weight loss.

PAST MEDICAL HISTORY

Allergic Rhinitis, Attention Deficit Hyperactivity Disorder

MEDICATIONS

Methylphenidate

ALLERGIES

NKDA

FAMILY HISTORY

Non-contributory

SOCIAL HISTORY

Denies tobacco, alcohol intake, or drug use.

PHYSICAL EXAM

The base of the penis and the back were notable for multiple soft, pink plaques and nodules. There were soft, hyperpigmented papules and plaques on right trapezius and in the right inframammary fold. There was no lymphadenopathy.

LABS/IMAGING

Abnormal: Absolute Lymphocytes 4.2k/ul [1-4k/ul]; Absolute Monocytes 1.3k/ul [0.2-0.9k/ul]; Total Protein 8.7gm/dl[6-8gm/dl]
Negative/normal: CBC, platelets, BMP, LFT, ANA
CT Chest/Abdomen/Pelvis 1/31/2011: No definite enlargement of lymph nodes in chest, abdomen, or pelvis. Bilateral inguinal and axillary lymph nodes are mildly prominent. Asymmetric nodular areas of skin thickening present in right inframammary region and back.
CT Sinus 1/31/2011: Soft tissue opacification in the bilateral anterior nasal cavity with the appearance of polyps. Mild scattered mucosal thickening in the bilateral ethmoid air cells and maxillary sinuses.

HISTOPATHOLOGY

11/17/2011 Left Groin: Skin and subcutaneous tissue with nodular histiocytic proliferation consistent with cutaneous Rosai Dorfman disease. Immunohistochemistry positive for S100 and CD68 and negative for keratin AE1/3, HMB46, MART1, CD1a; CD20+ and CD3+ cells identified. Failed to demonstrate light chain restriction.

2/15/11 Left shoulder: Unremarkable epidermis. Dermis with dense deep dermal and subcutaneous infiltrate composed of small lymphocytes with extensive confluent sheets of histiocytes. Extensive areas with fibroplasias noted. Numerous plasma cells. Histiocytes with large abundant pale and granular cytoplasm. Focal emperipolesis. No atypia. Immunohistochemistry was positive for S100 and CD68.

DIAGNOSIS
Cutaneous Rosai-Dorfman disease

TREATMENT AND COURSE
The patient underwent a CT of the chest, abdomen, pelvis and sinuses to rule out systemic involvement. The imaging identified small axillary and inguinal lymph nodes that were determined to be insignificant. Chronic congestion and rhinorrhea was evaluated by ENT who suggested that he had similar lesions of the nasal mucosa and right cervical/ submandibular region. Initially patient desired surgical excision of lesions but on reconsideration, he had too many to treat surgically. The most bothersome lesions were treated with intralesional triamcinolone resulting in decreased size of the lesions. He was also started on acitretin 25 mg po three times weekly.

PATIENT B
HISTORY OF PRESENT ILLNESS
The patient is a 20 year-old Indian female who presented with an eleven year history of multiple deep-seated nodules on her thighs, upper arms, back and buttocks. A biopsy from ten years prior was read as consistent with benign reactive lymphoid hyperplasia. During the four to six months leading up to presentation, the lesions grew in size and number prompting the patient to seek further evaluation. She denied fevers, chills, night sweats, and weight loss.

PAST MEDICAL HISTORY
None

MEDICATIONS
None

ALLERGIES
NKDA

FAMILY HISTORY
Non-contributory

SOCIAL HISTORY
No tobacco or drug use. Admitted to social alcohol intake.

PHYSICAL EXAM
The upper arms, upper thighs, and lower back were notable for multiple deep-seated nodules and plaques with overlying bluish with a total body surface area of 5%. No palpable lymphadenopathy.

LABS/IMAGING
Abnormal: Lymphocytes 14% [15-50%]; Neutrophils 76% [34-73%]; Alkaline Phosphatase 40u/L [61-295u/L]; Protein Total 8.5gm/dl [6-8gm/dl]
Normal: CBC, CMP, LDH, ANA panel, rheumatoid Factor, Ebstein Barr Virus IgM, T cell rearrangement of the serum

HISTOPATHOLOGY

Right arm: Unremarkable epidermis. Dense deep dermal and subcutaneous infiltrate composed of aggregates of small lymphocytes with extensive confluent sheets of histiocytes. Extensive fibroplasia. Numerous plasma cells with some Russell bodies. Focal eperipolesis. Immunohistochemistry showed the histiocytes stained positively for CD 68 and negative for CD1a. S100 was non-contributory.

DIAGNOSIS

Cutaneous Rosai-Dorfman disease, subcutaneous variant

TREATMENT AND COURSE

The slides from her previous biopsy were reviewed at Northwestern Dermatopathology and found to be consistent with cutaneous Rosai-Dorfman disease. The lesion on her right forearm was re-biopsied and subsequently excised. The biopsy was again consistent with Rosai-Dorfman disease. Given the asymptomatic and limited nature of her presentation, the patient elected to pursue a course of close follow up without active intervention. She has not had any progression of her lesions since her initial presentation in 2008.

DISCUSSION

Rosai-Dormfann disease, or sinus histiocytosis with massive lymphadenopathy, was first described in 1965 by Destombes and was later recognized as a unique entity by Rosai and Dorfman in 1969. The systemic form is an uncommon histiocytiocytosis that primary involves the lymph nodes. It involves extranodal sites in approximately 43% of cases with the most common location being the skin in 10% of patients. In 1978, Thawerani et al. reported a case of Rosai-Dorfman disease that was limited to the skin. Since that time, fewer than 100 cases of cutaneous Rosai-Dorfman have been reported in the literature. The unique population affected, non-specific clinical findings, and variable histopathologic findings compared to the systemic form may complicate diagnosis of this rare subtype.

Cutaneous Rosai-Dorfman disease appears to affect a distinct population from systemic Rosai-Dorfman disease. Systemic disease affects males in the second or third decades of life and is more common in African Americans and Caucasians. In contrast, cutaneous limited disease affects women in their 40s, favoring Asians over other racial groups.

Cutaneous Rosai-Dorfman disease also has a non-specific clinical presentation. Systemic disease traditionally presents with massive cervical lymphadenopathy, fever, malaise, and hematologic or immunologic abnormalities. Cutaneous disease can be more subtle, presenting with single to multiple asymptomatic lesions on the trunk, head, neck, lower and upper extremities. It may be associated with uveitis, systemic lupus erythematosus, HIV, diabetes mellitus, hyperlipidemia, aortic stenosis, positive borrelia serology, elevated Ebstein Barr Virus IgG tiers, and anemia.

Histology ranges from a nodular and diffuse to a patchy and interstitial infiltrate of 'Rosai-Dorfman cells' or characteristic histiocytes with abundant amorphous cytoplasm, indistinct borders, and a large vesicular nuclear with prominent nucleoli. These cells stain positively for S100, negatively for CD1a and variably for CD68. This combination of staining for both monocyte/macrophage markets (lysozyme, MAC-387, CD68) and dendritic/langerhans cell markers (S100) is key in diagnosis. The histiocytes also show emperipolesis or phagocytosed inflammatory cells in histiocytes. Other variable histologic features include an infiltrate of lymphocytes, plasma cells, and neutrophils; vascular proliferation, neutrophilic microabscesses, lymphoid aggregates with germinal centers, stromal fibrosis and epidermal changes.

Cutaneous limited disease has a benign clinical course with no reported cases progressing to the systemic disease. The lesions heal spontaneously with time but can also be treated with surgical excision, topical, intralesional, and systemic corticosteroids, liquid nitrogen, radiotherapy, and high dose thalidomide.

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CHICAGO DERMATOLOGICAL SOCIETY **CASE #13**

Presented by Tracy Donahue, MD and Jonathan Cotliar, MD
Department of Dermatology, Feinberg School of Medicine, Northwestern University

HISTORY OF PRESENT ILLNESS
The patient is a 41 year-old male with Acute Myelogenous Leukemia and neutropenia who developed a painful right thumbnail four days following a matched sibling donor hematopoietic stem cell transplant (HSCT). Two months prior, the patient noted distal separation of all of his fingernails following induction chemotherapy with cytarabine and idarubicin. A month later he noticed asymptomatic, dark discoloration of the first through third fingernails of his right hand. Four days after his HSCT he developed a painful right thumbnail that loosened over the next day. He then developed a hemorrhagic bulla of the distal thumb and erythema of the thenar hand that tracked from the medial wrist to the antecubital fossa. He subsequently lost sensation in the distal thumb. He was febrile to 101°F despite treatment with vancomycin, cefepime, and clindamycin. Review of systems also revealed oral mucositis and *C. difficile* diarrhea.

PAST MEDICAL HISTORY
AML: diagnosed 3 months prior to admission, Bladder cancer s/p surgical excision 5 years prior

MEDICATIONS (abbreviated list)
IVIg (weekly), tacrolimus, acyclovir, cefepime, clindamycin, pentamindine, vancomycin, voriconazole, hydromorphone

ALLERGIES
NKDA

PHYSICAL EXAM
The right hand was notable for significant soft tissue edema of the thumb and thenar eminence. Erythema extended linearly from the dorsal right hand to the antecubital fossa. The thumb had a periungual tense, hemorrhagic bullae. A second linear bulla, surrounded by a purpuric plaque, was located over the DIP joint. The right thumbnail also revealed proximal and lateral onycholysis with near-avulsion of the nail and underlying blue-green discoloration. There was no subungual debris. There was limited range of motion at the right first DIP and MCP joints. Sensation to light touch at the distal fingertip was decreased. The remaining nine fingers had distal onycholysis. There was yellow-green discoloration of the proximal right second and third fingernails and left fourth fingernail. Lymphadenopathy along the right arm and axilla was absent but there was tenderness and fullness of the right axilla.

LABS/IMAGING
Abnormal: WBC 0.1 k/uL [3.5-10.5 k/uL; Hb 7.9 g/dL [13.0-17.5 g/dL]; platelets 7 k/uL [140-390 k/uL]; culture (bulla): few *Pseudomonas aeruginosa;* blood culture (central and peripheral): *Pseudomonas aeruginosa*; tissue culture (R thumb, 2.5 weeks after presentation): *Enterococcus faecium* (vancomycin resistant)
Normal: urine culture

DIAGNOSIS
Green Nail Syndrome/Cellulitis

TREATMENT AND COURSE
The patient's physical exam findings were concerning for *Pseudomonal* nail infection, which was confirmed by tissue culture following incision and drainage of the bulla on the right thumb.

Clindamycin was discontinued and IV piperacillin-tazobactam and IV tobramycin were started for double coverage of *Pseudomonas*. The patient became afebrile hours later. Tobramycin was changed to IV ciprofloxacin after 2 days based on culture susceptibility results. Aggressive pain management was continued with a PCA pump. Daily blood cultures were ordered to ensure clearance of *Pseudomonas*. Nails were kept dry and dressed with Vaseline-impregnated gauze daily; the right arm was elevated. A TED stocking was placed on the right arm for lymphangitis. White blood cell counts recovered following GCSF and leukocyte transfusions, but the green nails and lymphangitic streaking persisted two weeks later. Macerated skin on the right thumb was excised and sent for a second culture and was positive for vancomycin resistant *Enterococcus faecium*. Ciprofloxacin was continued, and piperacillin-tazobactam was changed to linezolid. Erythema and edema of right thumb and right arm improved greatly by the next day. The patient was discharged on oral ciprofloxacin.

DISCUSSION

Green Nail Syndrome (GNS) presents as distal nail onycholysis with green discoloration in the region of separation and is often accompanied by acute paronychia. These nail changes are caused by overgrowth of *Pseudomonas aeruginosa,* which produces the pigments pyocyanin and pyoverdan. When in high concentrations, these pigments have been shown to stain nails even without the direct invasion of *P. aeruginosa* into the nail plate. In one small case series, 23 out of 26 green nails cultured grew *P. aeruginosa*. *P. Aeruginosa* does not typically survive on healthy dermis and requires a wet, occluded, or traumatized surface for invasion. For this reason, GNS is more commonly seen in individuals whose occupations involve frequent hand washing and exposure to detergents. There are also a few reports of *P. aeruginosa* infection of the toenails associated with military footwear. Other nail conditions, such as *Trichophyton rubrum* infection or nail psoriasis may locally predispose a patient to *P. aeruginosa* infection of the nail.

Green Nail Syndrome is typically a clinical diagnosis but may be confirmed by gram stain and culture of nail fragments and debris. *Aspergillus* and *Candida* have also been reported to cause green nails. The differential diagnosis also includes subungual hematoma, melanocytic nevus, or melanoma.

Treatment of GNS typically lasts several months and includes clipping the nail back and avoiding precipitating factors. The affected digit can be soaked in 1% acetic acid solution twice daily. Topical fluoroquinolone and aminoglycoside solutions are often used.

It is important to note that hospitalized patients may become infected with *P. aeruginosa* from contact with health care workers who have GNS. Surgical wound infections have been traced back to surgeons or nursing staff with *P. aeruginosa* nail infection confirmed by culture.

Infection with *P. aeruginosa* in immunocompromised patients can be life threatening. Bacteremia or cutaneous trauma can predispose patients with *Pseudomonas* to a secondary cellulitis and/or ecthyma gangrenosum. Patients with ecthyma gangrenosum present with opalescent, tense vesicles or pustules with necrotic centers surrounded by pink to violaceous halos. Elastase secreted by *Pseudomonas* allows the organism to infiltrate subcutaneous tissue and proliferate. Further exotoxins and proteases are released, causing eventual ulceration. Lesions are most commonly found on the buttocks or extremities.

Ecthyma gangrenosum is most commonly seen in neutropenic patients with *P. aeruginosa*, but it has also been reported in patients with diabetes and HIV. Other causative organisms include *Pseudomonas mesophilica, Escherichia coli, Klebsiella pneumonia, and Stenotrophomonas maltophilia.*

Ecthyma gangrenosum is an important clinical finding that may herald the onset of *Pseudomonal* sepsis. Blood cultures usually reveal *P. aeruginosa.* Prompt treatment with IV antipseudomonal antibiotics is crucial. Granulocyte-macrophage colony-stimulating factor can be used adjunctively to stimulate immune recovery in neutropenic patients. Debridement of necrotic lesions is often necessary.

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CHICAGO DERMATOLOGICAL SOCIETY **Case #14**

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

HISTORY OF PRESENT ILLNESS

Patient is a 50 year-old Caucasian female with a history of asthma and chronic sinusitis with nasal polyposis who presented for evaluation of diffuse arthralgias, hemoptysis and purpuric papules on her hands, elbows, and feet. Her symptoms first began in 2007 when she was diagnosed with severe persistent asthma. Over the last year, her asthma worsened requiring frequent courses of oral steroids. In 2009, she was diagnosed with chronic sinusitis with nasal polyposis. Three weeks prior to presentation, she first noted arthralgias with pain in both wrists that soon progressed to her hands, elbows, shoulders, hips, knees and ankles. She was treated with oral steroids and ibuprofen, with near resolution of symptoms. However, symptoms recurred after discontinuation of steroids and one week prior to presentation she developed non-pruritic, non-tender purpuric papules on the palmar surface of her hands, dorsal feet and elbows. She had symptoms of hemoptysis, coughing up a quarter-sized amount of dark red sputum four to five times daily. On the day of presentation, she was found to have an absolute peripheral eosinophilia of 16.5 K/μL.

Her review of systems was notable for numbness in her right foot, dyspnea with exertion, orthopnea, and chest tightness. She had no changes in her mental status, fevers, chills, hematuria, diarrhea, or abdominal pain.

PAST MEDICAL HISTORY

Asthma, chronic sinusitis with nasal polyposis, specific antibody deficiency, migraines

MEDICATIONS

Sertraline, montelukast, fluticasone nasal inhaler, fluticasone and salmeterol inhaler, ciclesonide inhaler, ibuprofen as needed

SOCIAL HISTORY

The patient is married. She does not smoke and drinks 2 alcoholic beverages weekly.

PHYSICAL EXAM

The patient had discrete 1-2 mm palpable purpuric papules over the dorsal right foot, plantar left foot, and the digits of left hand. On the extensor surface of her elbows she had symmetrically distributed, indurated erythematous 2-3 mm papules with adherent heme crust.

LABS/IMAGING

Abnormal: White cell count 27.7K/μL [3.5-10.5 K/μL]; absolute peripheral eosinophils 16.5K/μL [0-0.6 K/μL]; p-ANCA 1:640 [<1:40]; myeloperoxidase: 71U [0-20U]; ESR 65mm/hr [2-25 mm/hr]
Negative/normal: hemoglobin, platelets, creatinine, liver function tests, C-ANCA, proteinase 3, ANA
CT Chest 7/12/2011: Patchy ground glass opacities bilaterally, most marked in the upper lobe and right lower lobe with centrilobular nodules in the mid lower lung fields, concerning for eosinophilic pneumonia or pulmonary hemorrhage.

HISTOPATHOLOGY

7/12/11 L 3rd digit: Along the superficial vascular plexus there is fibrinoid necrosis with vasocclusive changes and extravasation of erythrocytes. Interstitial eosinophils, some neutrophils and nuclear debris (karyorrhexis) are noted.

DIAGNOSIS
Churg Strauss Syndrome

TREATMENT AND COURSE
The patient was admitted to Northwestern Memorial Hospital. She was immediately started on intravenous (IV) methylprednisolone 125mg IV every 6 hours and seen by Rheumatology, Allergy, Neurology, and Dermatology. One day after admission, she developed chest pain, with work-up revealing elevated troponins and electrocardiogram changes concerning for ischemia. Her dyspnea and hemoptysis worsened and she was transferred to the medical intensive care unit, where she received high dose IV methylprednisolone at 250mg IV every 6 hours, cyclophosphamide at 750mg/m^2 IV once, and intravenous immunoglobulins (IVIG) at 50gm IV for 4 doses. Her hemoptysis, dyspnea and joint pain resolved. Further cardiac work-up revealed myocarditis secondary to Churg Strauss Syndrome. Her symptoms continued to improve upon discharge and her skin lesions have nearly resolved. She remains on 60mg of prednisone and will receive 1-2 more doses of 750mg/m^2 of IV cyclophosphamide and IVIG.

DISCUSSION
Churg Strauss syndrome (CSS) is a systemic necrotizing vasculitis, first described in 1951 by the pathologists Churg and Strauss. Characterized by asthma, hypereosinophilia and systemic vasculitis, CSS primarily involves small to medium-sized vessels within multiple organ systems. CSS is a rare disorder, with an incidence of 0.1 to 2.6 new cases per million population per year with a slight female predominance. Clinically, CSS is described as a 3-stage disorder: a prodromal phase dominated by asthma, rhinosinusitis and nasal polyposis; a second phase characterized by peripheral blood and tissue eosinophilia with respiratory infections and gastrointestinal symptoms; and a third phase with systemic vasculitis with granulomatous inflammation.

Nearly all patients with CSS present with adult-onset asthma as the primary feature of the prodromal phase. Over time, the asthma becomes more severe and often refractory to standard inhalational therapy. The latency between onset of asthma and the vasculitic phase is typically estimated to be 3-9 years and may in part be explained by treatments for asthma control, including oral corticosteroids. Allergic rhinitis, nasal polyps and recurrent paranasal sinusitis frequently accompany asthma in the prodromal phase of CSS.

More than half of patients with CSS present with cutaneous findings in the third phase, reflecting involvement of small vessels. Palpable purpura on the lower extremities is the most common manifestation, followed by subcutaneous nodules on the scalp or lower extremities. Less frequently, urticaria, livedo reticularis, retiform purpura and papulonecrotic lesions may be present.

In the third phase, CSS often affects 2 or 3 other internal organs. The lung is a common target and patients can present with patchy pulmonary infiltrates, ground glass opacities, and bronchial wall thickening, seen on high resolution CT. Involvement of the neurologic system is a distinctive feature of CSS, with many patients developing peripheral neuropathy and mononeuritis multiplex, a vasculitic process involving the peripheral nerves resulting in foot or wrist drop. Granulomatous infiltration of the myocardium is the leading cause of death of patients with CSS and may present as myocarditis, arrhythmias, and sudden death. The gastrointestinal tract may be affected by either eosinophilic intestinal infiltration or mesenteric vasculitis. The kidney is not frequently involved and less than a quarter of patients develop focal segmental glomerulonephritis. Patients may also present with constitutional symptoms including malaise, rapid weight loss, diffuse myalgias, and polyarthralgias.

The differential diagnosis for CSS includes Wegner's granulomatosis (WG), microscopic polyangiitis (MPA) and hypereosinophilic syndrome. The diagnosis of CSS is often challenging as there is no pathognomonic presentation or diagnostic study for the disease. Rather, many patients present with a constellation of findings that have evolved over several years and are often misdiagnosed with worsening asthma. Patients with CSS typically develop peripheral eosinophilia (>10% on differential or 1.5 $x10^9$/L) with the majority of ANCA directed against myeloperoxidase. Histologically, infiltrates of eosinophils, formation of extravascular granulomas, and necrotizing vasculitis of small to medium vessels may be seen.

The prognosis for CSS is very good. CSS is considered a mild vasculitis with an overall lower mortality compared to other systemic vasculitides. Corticosteroids and systemic immunosuppressants such as cyclophosphamide are standard therapies to induce remission. Although CSS has a higher remission rate that of WG or MPA, maintenance of CSS can be challenging and patients often remain on immunosuppressant therapy with corticosteroids alone or in conjunction with methotrexate, cyclosporine, or azathioprine to prevent or treat relapse. For refractory or frequently relapsing patients, plasma exchange, IVIG, tumor necrosis factor - α inhibitors, and rituximab have also proven efficacious.

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CHICAGO DERMATOLOGICAL SOCIETY **CASE #15**

Presented by Bryan Gammon, M.D.
Departments of Dermatology, Feinberg School of Medicine, Northwestern University and University of Pennsylvania

UNKNOWN