Chicago Dermatological Society

November 2011
Monthly Educational Conference

Program Information
Continuing Medical Education Certification
and
Case Presentations

Saturday, November 19, 2011

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

Program

Conference Location

University of Chicago
Duchossois Center for Advanced Medicine (DCAM)
5758 S. Maryland Ave.

7:30 a.m.	**Registration Opens** *DCAM Main Lobby (near the elevators)*
8:00 a.m. - 9:00 a.m.	**Resident Lecture** – *4th Floor North Atrium* "Vitamin D" *Martin Weinstock, MD, PhD*
9:00 a.m. - 10:30 a.m.	**Clinical Rounds** Patient & Poster Viewing *Dermatology Clinic 3A (DCAM - 3rd floor)* Slide Viewing *DCAM 1st Floor, Suite D, Room 1333*
10:15 - 10:45 a.m.	**Break** – *4th Floor South Atrium*
10:45 a.m. - 12:00 p.m.	**General Session** - *4th Floor North Atrium*
10:45 a.m.	CDS Business Meeting
11:00 a.m.	LORINCZ LECTURE: "Melanoma Early Detection: The Public Health Perspective" – *Martin Weinstock, MD, PhD*
12:00 p.m. - 12:30 p.m.	**Box Lunches & visit with exhibitors** *4th Floor South Atrium*
12:30 p.m. - 2:30 p.m.	**Case Discussions** – *4th Floor North Atrium*
2:30 p.m.	**Meeting adjourns**

Mark the Date!

Next CDS monthly meeting will be the "President's Program" and awards luncheon:
Saturday, February 11, 2012 at the Stephens Convention Center in Rosemont.

Watch for details on the CDS website: www.ChicagoDerm.org
Save time and money – consider registering online!

Guest Speaker

MARTIN WEINSTOCK, MD, PHD

Professor of Dermatology and Community Health
Brown University
Providence, RI

Delivering the Allan Lorincz Lecture

Dr. Weinstock earned a PhD in epidemiology in 1982 from Columbia University Graduate School of Arts and Sciences and was awarded his MD degree in 1983 from Columbia University College of Physicians and Surgeons. He completed an internal medicine residency at the University of Pittsburgh (1984) and finished his dermatology residency at Harvard University Affiliated Hospitals (1987). He was a dermatology research fellow at Massachusetts General Hospital (1987) and was an Andrew W. Mellon Foundation Fellow in Clinical Epidemiology, Harvard Medical School (1987-88).

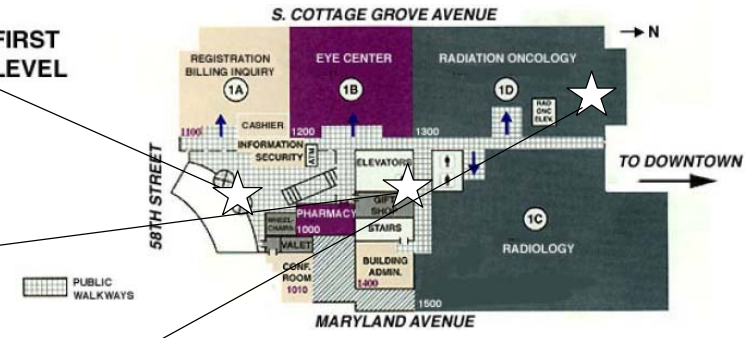
Dr. Weinstock has received a number of awards and honors and has participated in numerous professional organizations and committees. Current national and international activities include several editorial positions and more than a dozen committees, advisory boards, work groups and task forces.

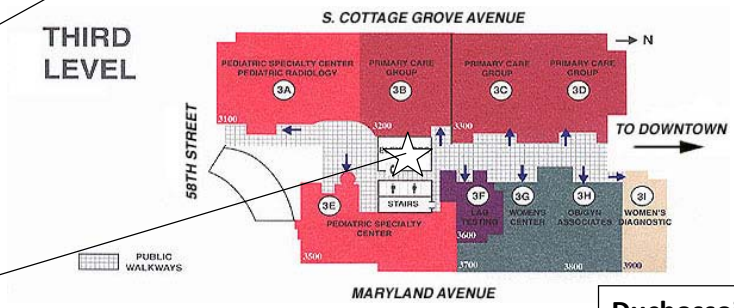
Registration:
Enter through DCAM main entrance. Table will be in Lobby near Elevators on 1st Floor.

Rm. 1005 (PPC and IDS Meetings):
On the first floor, right off the central elevators, before the public rest rooms.

Rm. 1333 Microscope Viewing
On the first floor, located in the radiation oncology clinic conference room, Suite 1D.

Derm Clinic 3A:
Take elevators up to 3rd floor for Patient Viewing.

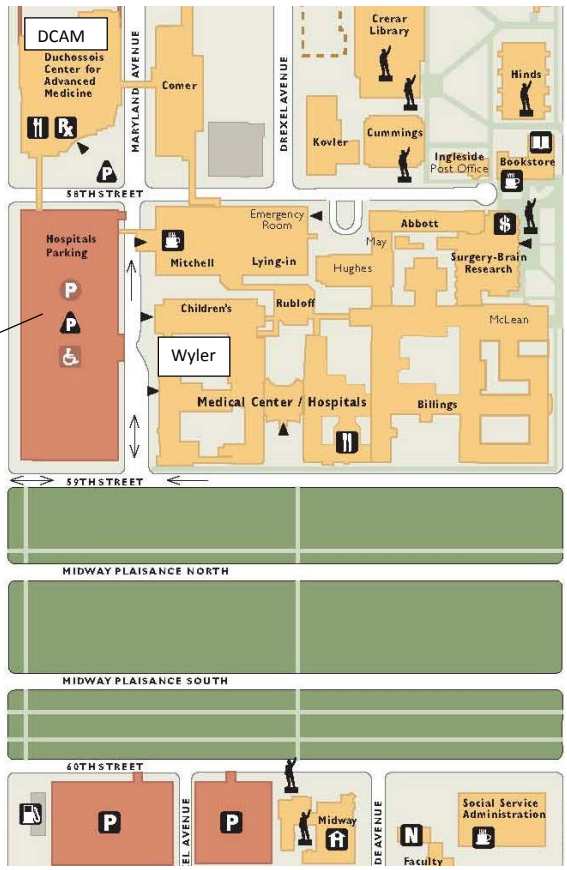




Duchossois Center for Advanced Medicine
5758 S. Maryland Avenue

PARKING INFORMATION

There is a parking lot that will be available for use located between 58th and 59th Street on Maryland Avenue.



CME Claims

Physicians wishing to receive Category 1 CME credit must complete a short online evaluation form managed by our joint sponsor, the Colorado Foundation for Medical Care. Once you complete this simple step, a certificate documenting the credit will be emailed to you automatically as a PDF attachment by CFMC.

It is the responsibility of each physician to claim and track CME credits earned. The Chicago Dermatological Society is not able to do this for you, nor is CDS allowed to provide you with the certificates that document CME credits you have earned. Our website does have information about claiming credit for previous meetings you may have attended.

To claim your credit for today's meeting:

Go to this website, enter your name and an email address. Then complete all of the questions and click on the "Submit" button at the bottom of the page. (Note – this web address also will be posted on the CDS website homepage on the day of the meeting.)

http://www.yourcesource.com/eval?act=600!11192011

Smartphone users:

This barcode also will take you to the online claim form . . .

Continuing Education Credit

Chicago Dermatological Society

"Chicago Dermatological Society Monthly Conference"

November 19, 2011 *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=600!11192011

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**. **CFMC is accredited by the ACCME to provide continuing medical education for physicians.**

GOAL / PURPOSE

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

SESSION OBJECTIVES

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

Physicians should be able to:

1. Describe the scientific justification (or lack thereof) for public health action on melanoma.
2. Discuss the adverse consequences of screening for melanoma.

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 for Medical Care designates this Live Activity for a maximum of 5.0 *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 5.0 hours.

DISCLOSURE STATEMENTS

All 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.**

TABLE OF CONTENTS

PRESENTERS
Erica R. Aronson, MD; Shani Francis, MD; Vesna Petronic-Rosic, MD, MSc; Sarah L. Stein, MD

HISTORY OF PRESENT ILLNESS
A 17 year old white female presented with a 2 year history of red and yellowish papules increasing in number on her chest and trunk. She denied pruritus or pain associated with these lesions. In addition to the skin findings, she described a greater than 4 year history of diffuse bony pain, most notable in the right knee, worsening over time, and intermittent abdominal discomfort.

PAST MEDICAL HISTORY
Transient transaminitis in 2007, liver biopsy demonstrated normal liver parenchyma.

FAMILY HISTORY
No family history of skin disorders

MEDICATIONS
Naproxen sodium as needed for bony pain

ALLERGIES
No known drug allergies

PHYSICAL EXAMINATION
Discrete red-brown to yellow papules and nodules on the chest and back, with interspersed pink atrophic plaques. Additional violaceous minimally raised papules are scattered over the lower abdomen.

DERMATOPATHOLOGY
Three biopsies of the skin lesions have demonstrated collections of foamy histiocytes, spindle cells, and Touton giant cells that stain positive with anti-CD68 and negative with anti-CD1a, consistent with juvenile xanthogranulomas.

LABORATORY DATA
Skeletal survey: bilateral patchy bone sclerosis in the long bones, lumbar vertebral bodies and pelvis.
99m Tc bone scintigraphy: multifocal regions of increased radiotracer uptake in the bilateral upper and lower extremities.
Bone biopsy: sampling from a sclerotic lesion in the distal right femur identified no bone disease; specifically there was no evidence of a histiocytic infiltrate.
Bone Marrow biopsy: normocellular bone marrow with slightly thickened bone.
Complete blood count: Leukocytes 6.4 K/μL (3.5-11.0), hemoglobin 14.0 g/dL (11.5-15.5), platelets 235 K/μL (150-450)
ESR: 29 mm/hr (0-20mm/hr)

DIAGNOSIS
Erdheim-Chester Disease

TREATMENT AND COURSE.
The patient continues to develop new lesions and experience knee pain bilaterally. A trial of oral prednisone 40mg daily was initiated. After three weeks of treatment, the patient reported no improvement of symptoms, but complained of numerous side effects from the steroids and they were discontinued. Application of imiquimod 5% cream to selected nodules resulted in slight flattening of treated lesions.
The patient was started on weekly interferon-alpha therapy in August, 2011. She reports minimal

improvement of her bony pain but feels she has not developed any new cutaneous lesions since initiating this therapy.

DISCUSSION

The non-Langerhans cell histiocytoses (LCH) are a diverse group of diseases characterized by the accumulation of histiocytes that are CD1a negative and do not possess the characteristic Birbeck granules seen in Langerhans cells. The non-LCH may be seen as a spectrum of disorders which can be categorized into those affecting only the skin, those that affect the skin and have a systemic component, and those disorders that primarily affect extracutaneous sites, though skin lesions may be present. The non-LCH can be further subdivided based on the immunophenotype of the cells composing the cutaneous lesions. The cells of the juvenile xanthogranuloma family stain positively for CD-68, Factor XIIIa, CD163, fascin, and CD14 while staining negatively for CD1a and S100.

Erdheim-Chester disease (ECD) is a rare, primarily extra-cutaneous non-LCH which is defined primarily by the skeletal findings. The skeletal findings are seen on Xray as bilateral and symmetric cortical osteosclerosis of the diaphyseal and metaphyseal regions in the long bones. Bone scintigraphy findings are quite specific, demonstrating symmetric and abnormally increased uptake at the distal ends of the long bones of the lower and occasionally upper limbs. Fifty percent of cases are associated with extraskeletal organ involvement, most commonly the nervous system, heart, lungs, and retroperitoneum. Skin findings have been reported infrequently. ECD has been classified within the juvenile xanthogranuloma family based on histopathology of skin lesions demonstrating a dermal infiltrate of bland histiocytes with xanthomatous cytoplasm and Touton-like giant cells with intervening fibrosis. Immunophenotyping is consistent with that of JXG. Similar pathological findings from sites such as the lung, retroperitoneum and bone have been reported. The diagnosis of ECD is rarely made by skin biopsy, but rather requires a multidisciplinary evaluation of clinical, radiological and pathological findings.

ECD is usually diagnosed in the fifth to seventh decade of life and cutaneous involvement is seldom the presenting symptom. Only a handful of pediatric cases of ECD have been reported in the literature. This disorder is often fatal with death occurring in >50% of patients due to cardiac and pulmonary involvement. Prognosis is dependent on the extent of visceral involvement. There are no standard treatments for ECD and therapeutic options are largely based on case reports and anecdotal evidence. A variety of chemotherapeutic agents have been utilized though most have not produced a lasting clinical response. Interferon-alpha has had success in patients without CNS or cardiovascular involvement and has been effective in the few pediatric cases of ECD reported in the literature.

REFERENCES

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4. Dehner, LP. Juvenile Xanthogranulomas in the first two decades of life: A clinicopathologic study of 174 cases with cutaneous and extracutaneous manifestations. *Am J Surg Pathol* 27(5): 579-593, 2003. Jeon, I, Lee, SS, and Lee, MK. Chemotherapy and Interferon-alpha Treatment of Erdheim-Chester Disease. *Pediatr Blood Cancer* 2010; 55:745-747.
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PRESENTERS
Shani Francis, MD, Carol Semrad, Christopher R. Shea, MD

HISTORY OF PRESENT ILLNESS
This 20-year-old male, with a past history of iron-deficiency anemia and a recent abnormal video capsule endoscopy notable for small bowel hemorrhage, presented to the gastrointestinal procedures unit for double-balloon enteroscopy. During the procedure, his mucosa was notably friable and he was admitted to hospital for observation and monitoring of potential procedural complications, with a suspicion of underlying connective tissue disorder. Review of systems was significant for fatigue, a lifelong history of easy bruising, and occasional stools mixed with streaks of blood.

PAST MEDICAL HISTORY
Iron-deficiency anemia; history of splenic rupture after minimal trauma while playing soccer; history of two colonic perforations, status-post partial colonic resections at ages 17 and 18, last procedure complicated by abdominal hematoma requiring mesh placement.

FAMILY HISTORY
Non-contributory. There was no history of sudden death, nor of inflammatory bowel or connective tissue disease.

SOCIAL HISTORY
Current occasional marijuana use; former tobacco use, quit three months prior to presentation. Remote history of alcohol use, quit two years prior to presentation.

MEDICATIONS
Iron sulfate, ascorbic acid

ALLERGIES
Hydromorphone

PHYSICAL EXAMINATION
Thin, average-height man with pale, translucent skin and prominent chest vasculature. On his central abdomen there is a wide, atrophic, linear surgical scar. Several additional horizontal thin, papyraceous scars are also noted on the abdomen surrounding the surgical defect. Joint hypermobility of the fingers of both hands, with passive dorsiflexion of the little fingers beyond 90 degrees, and passive apposition of the thumbs to the flexural aspects of the forearms. Gorlin's sign is not appreciated.

LABORATORY DATA
Complete blood count: WBC 7.9K/µL (3.5-11), hemoglobin 8.6g/dL (13.5-17.5), platelets 356K/µL (150-450), MCV 74 fL (81-99)
Differential: Neutrophils 63%, lymphocytes 19%, monocytes 14%, basophils 2%

Prothrombin time 15.8 sec (12.1-14.9), INR 1.2 (0.9-1.1), partial thromboplastin time 29.0 sec (24.0-34.0), platelet function analyzer-100: 98 sec (60-120 sec)

PROCEDURAL IMAGING

Video capsule study (12/15/10): focal plume of red blood at 47 minutes without an underlying lesion in the proximal small bowel; flecks of blood are also present in the area. They do not appear to have the appearance of arteriovenous malformations or vascular ectasias.

Double balloon enteroscopy (01/06/11): Friable mucosa with submucosal trauma in a segment of jejunun. No native bleeding lesion identified in the proximal small bowel.

GENETIC STUDIES

DNA sequencing reveals a c.557 G>A transition in exon 7 of the COL3A1 gene. This change converts a codon for a triple helical glycine (GGT) to a codon for aspartic acid (GAT). We have previously identified a change in the identical codon resulting in a Gly186Arg substitution. This finding is consistent with a disease-causing mutation. The patient is heterozygous for the mutation.

DIAGNOSIS

Ehlers-Danlos syndrome, vascular type

TREATMENT AND COURSE

Genetics follow-up was recommended following hospitalization. The Genetics service considered that his clinical presentation was consistent with vascular-type Ehlers-Danlos syndrome and offered consultation while negotiations with insurance company to cover genetic testing ensued. Anticipatory guidance was given and he was directed to a support group and to social work services for long-term health insurance, and given information on a possible NIH trial. Meanwhile, he was regularly followed by his primary care doctor, who monitored his hemoglobin levels and provided blood transfusions as needed. Confirmation of the genetic defect was ultimately made by DNA analysis. However, he was lost to follow-up, and did not return to gastroenterology.

DISCUSSION

Ehlers-Danlos syndrome (EDS) is a group of hereditary disorders of connective tissue that feature hyperextensibility of the skin, hypermobility of the large joints, and easy bruising. In 1997, the previous numerical classification system was condensed from 11 to six disorders, and each was renamed according to its cardinal clinical symptom (see Table). The estimated prevalence for all EDS varies between 1/10,000 and 1/25,000.

Vascular EDS represents 5-10% of all EDS cases, and is recognized on the basis of four main clinical findings: arterial or internal organ rupture (intestine or uterus), characteristic facies, easy bruising, and translucent skin with visible veins. The striking facial appearance seen in vascular EDS includes thin lips and philtrum, small chin, thin nose, large eyes, and lobeless ears. While hyperextensibility of the skin and hypermobility of the large joints is a prominent feature of most types of EDS, it is unusual in vascular EDS. Diagnosis is typically suspected based on clinical signs and confirmed with genetic testing.

The vascular type of EDS is inherited in an autosomal dominant manner, and is caused by structural defects in the pro-α1 (III) chain of collagen type III encoded by the COL3A1 gene. Type III collagen is a homotrimeric molecule formed by the linking of three α1(III) chains to form a triple helix, the amino acid sequence of which is established by repeated glycine-X-Y sequences, where X and Y are often the amino acids proline and hydroxyproline, respectively. Vascular EDS can be caused by missense point mutations affecting the glycine residues of the triple helix, splicing mutations with exon skipping, small or large deletions, or haploinsuffiency.

Vascular EDS is a severe disease causing arterial dissections and ruptures that can lead to early death. Collagen III is a component of arterial, intestinal, and hollow organ walls (e.g. gravid uterus). Therefore, in vascular EDS these structures are the most vulnerable to dissection, aneurysm, and rupture. Arterial rupture can either follow aneurysms, fistulas, and dissections, or else occur spontaneously; although all anatomic sites may be affected, large and medium-diameter arteries are the most susceptible. Dissections of vertebral and carotid arteries and colonic perforations are typical. Recurrent pneumothoraces also may occur. These complications are rare during childhood, but increase with age, so that at least 25% of vascular EDS individuals experience one or more complications by 20 years of age, and at least 80% by 40 years. The most common cause of death is arterial rupture, as this catastrophic event is unpredictable

and inherent fragility of the arterial wall makes surgical repair difficult. Pregnant women with vascular EDS have a mortality rate of 15% due to vascular EDS-related complications during pregnancy.

Until recently there was no definitive treatment available for vascular EDS. A conservative approach, with practical avoidant behavior of trauma and elective procedures, was emphasized. Medical therapy rests on managing symptoms, trying to prevent complications, and emphasizing prophylactic measures to control blood pressure and reduce atherosclerotic risk factors. A recent article by Ong et al. suggested up to a threefold protective benefit in reduction of vascular complications with initiation of Celiprolol, a β1 receptor antagonist/β2 receptor agonist. Interestingly, this treatment effect was achieved without decreasing hemodynamic variables such as heart rate or systolic or diastolic pressures. Unfortunately, the study was designed prior to the recent advances in genetic testing of the disease and, as a result, mutational analysis was not performed. Patients were categorized based on clinical features using the Villefranche classification, which overlaps significantly with that of Loeys-Dietz syndrome (LDS), a disease due to mutation in TGFβ receptor subtypes. As a result, participants with COL3A1 mutations in the experimental and control groups differed in number and age distribution. This finding is significant, as individuals with clinical features of vascular EDS and a *TGFBR1/2* mutation typically have a much lower incidence of fatal complications from vascular surgery, despite the similarity to those of patients with *COL3A1* mutations.

Table: classification of Ehlers-Danlos syndromes

New	Former	OMIM	Pathogenesis	Inheritance
Classical type	Gravis (EDS, I)	130000	*COL5A1, COL5A2, TNXB,*	AD
	Mitis (EDS, II)	130010	*COL1A1* (rare)	AD
Hypermobility type	Hypermobile (EDS, III)	130020	*TNXB*/ tenascin-X	AD
Vascular type	Arterial-ecchymotic (EDS, IV)	130050 (225350) (225360)	*COL3A1*	AD
Kyphoscoliosis type	Ocular-scoliotic (EDS, VI)	225400	*PLOD1*/lysyl hydroxylase	AR
Arthrochalasia type	Arthrochalasis multiplex congenita (EDS, VIIA and VIIB)	130060	*COL1A1, COL1A2*	AD
Dermatosparaxis type	Human dermatosparaxis (EDS, VIIC)	225410	*ADAMTS2*/procollagen N-peptidase	AR
Other	X-linked EDS (EDS, V)	305200		XR
	Periodontitis (EDS, VIII)	130080		AD
	Fibronectin-deficient EDS (EDS, X)	225310		AR
	Familial hypermobility (EDS, XI)	147900		AD
	Progeroid EDS	130070	*B4GALT7*/galactosyl transferase-1	AR
	Unspecified forms			

REFERENCES

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PRESENTERS
Carlos Paz, MD, PhD, Aisha Sethi, MD, Vesna Petronic-Rosic, MD, MSc, Keyoumars Soltani, MD

UKNOWN CASE

PRESENTERS
Tunisia Finch, MD, Arlene Ruiz de Luzuriaga, MD, MPH, Vesna Petronic-Rosic, MD, MSc, Keyoumars Soltani, MD

HISTORY OF PRESENT ILLNESS
A 40 year old black male with a history of hypertension presented with a 2 month history of multiple enlarging verrucous plaques in bilateral axillae, spreading hyperkeratotic papules and nodules over the trunk and extremities, and pink erosions on the glans penis. The patient reported that the lesions would occasionally spontaneously resolve. He was applying Drysol and Zeasorb powder to the axillae with no improvement.

PAST MEDICAL HISTORY
Hypertension, osteoarthritis, arrythmia

MEDICATIONS
Hydralazine, hydrochlorothiazide, lisinopril, spironolactone

REVIEW OF SYSTEMS/FAMILY HISTORY/SOCIAL HISTORY
Review of systems was negative for systemic symptoms. The family history was significant for hypertension. The social history was negative for tobacco use, alcohol intake, and drug use.

ALLERGIES
No known drug allergies

PHYSICAL EXAMINATION
Multiple large coalescing verrucous papules and plaques on a background of velvety hyperpigmentation were present in the axillae. Over the trunk and extremities, there were multiple hyperkeratotic, violaceous papules and plaques. Erythematous plaques were present on the scrotum and in the inguinal creases. Superficial ovoid pink erosions on the glans penis were also apparent. No nail changes were appreciated.

HISTOPATHOLOGY
Shave biopsy of the left axilla shows prominent papillomatous hyperplasia, parakeratosis, and acanthosis of the epidermis, without significant atypia. Neutrophils are present in the stratum corneum. There is a superficial perivascular lymphocytic infiltrate. Prominent, thin walled dermal blood vessels approach close to the epidermis. The periodic acid-Schiff stain is negative for fungi or significant basement membrane thickening.

Punch biopsy of the left leg shows parakeratosis and acanthosis of the epidermis, without significant atypia. Neutrophils are present in the stratum corneum. There is a superficial perivascular lymphocytic infiltrate. Prominent, thin walled dermal blood vessels approach close to the epidermis. The periodic acid-Schiff stain is negative for fungi or significant basement membrane thickening.

Direct immunofluorescence showed no evidence of immunobullous disease.

LABORATORY AND RADIOLOGIC DATA
Complete Blood Cell Count: WBC 7.7 K/uL (3.5-11), Hgb 16.1 g/dL (13.5-15.5) Hct 49.1% (41-53), platelet 202 K/uL (150-450)
Complete Metabolic Panel: Glucose 89 mg/dL (60-109), Sodium 142 mEq/L (134-149), Potassium 3.8 (3.3-4.7), Chloride 103 mEq/L (95-108), CO2 28 mEq/L (23-30), BUN 13 mg/dL (7-20), Cr 1.3 mg/dL (0.5-1.4), Calcium 9.7 mg/dL (8.4-10.2), Total bilirubin 0.3 mg/dL (0.1-1.0), Total protein 7.6 g/dL (6.0-8.3), Albumin 4.5 g/dL (3.5-5.0), Alk Phos 47 U/L (30-20), AST 17 U/L (8-37), ALT 37 U/L (8-35)

Thyrotropin: 1.10 mcU/mL (0.30-4.00)
Lipid panel: Cholesterol 202 mg/dL (120-199), HDL cholesterol 36 (40-80), Triglycerides 107 (30-149), LDL cholesterol 145 (60-129)
Streptolysin O Ab: 400 IU/L (<100)
Rapid Plasma Reagin (RPR): nonreactive
Human immunodeficiency virus (HIV): nonreactive
Hepatitis panel: nonreactive

DIAGNOSIS

Verrucous psoriasis

TREATMENT AND COURSE

The patient was prescribed a 14 day course of cephalexin 500 mg BID for the elevated ASO titer. He was treated with triamcinolone 0.1% ointment, urea 20% cream, and betamethasone dipropionate 0.05% ointment which resulted in resolution of the axillary lesions. However, he continued to develop more lesions on the trunk and extremities. The patient declined treatment with phototherapy. Treatment with methrotrexate 22.5 mg weekly was initiated and titrated to 25 mg weekly; he noted moderate improvement with only a few eruptive papules occurring on the trunk. After 5 months of treatment, the patient opted to discontinue methotrexate. Calcipotriene 0.005% ointment was prescribed in attempt to transition to topicals only. The patient reported stable disease with no new lesions while off of methotrexate for 2 weeks.

DISCUSSION

Psoriasis is a common chronic, multisystem, inflammatory disorder with a range of clinical presentations and a relapsing course. Patients with psoriasis have a genetic predisposition for the illness, which most commonly affects extensor surfaces of the extremities, elbows, knees, scalp, lumbosacral areas, intergluteal clefts, and glans penis. Several distinct forms of psoriasis have been identified, with plaque-type psoriasis being the most common type. Other forms of the disease include guttate, pustular, and erythrodermic.

Hypertrophic or verrucous psoriasis (VP) is an under recognized and seldom described distinctive variant in which lesions show a wart-like appearance. The lesions usually develop in patients with established psoriasis; however, the condition can occur in individuals without a previous history of psoriasis. Histopathological examination shows overlapping features of both verruca and psoriasis. Tissue sections show hyperkeratosis, parakeratosis, Munro's microabscesses, thinning of the granular layer, and papillomatosis along with dermal vascular dilatation and perivascular lymphocyte infiltration. VP may present with dome-shaped papules or crater-like papules. In a series of 12 patients with VP, most of the lesions conformed to dome-shaped papules with some tendency to form plaques on the extremities. The lesions were fairly evenly distributed in regards to sex, race, and age. On histology, all of the cases lacked koilocytic change, hypergranulosis, clumping of keratohyaline granules, and HPV immunostaining was negative. VP may be confused with other lesions including verruca vulgaris, epidermal nevus, pemphigus vegetans, eczema, and fungal infection. Review of the literature revealed only a small number of reports on VP: an annular variant of VP, an erythrodermic variant of VP, VP after treatment with IFN-α treatment for hepatitis C, and VP in a Japanese male responding to oral etretinate. One report of verrucous plaques on the lower extremities that responded to acitretin is suspected to have been VP masquerading as verrucous carcinoma.

Little is known about the pathogenesis and treatment of VP. Kwazebart et al reported that diabetes mellitus may be a predisposing factor by way inducing microangiopathy and macroangiopathy. It has also been reported that disturbance of the peripheral circulation resulting in local anoxia might be responsible for the marked hyperkeratosis. It may be likely that this under recognized variant represents a

patterned response of the epithelium to repeated trauma/irritation in a person with pre-existing psoriasis or psoriasis diathesis. VP is extremely treatment resistant. Options for VP include treatments for other forms of psoriasis such as topical corticosteroids, vitamin D analogues, topical tar, topical salicylic acid, topical anthralin, phototherapy, retinoids, immunosuppressants, and biologics.

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PRESENTERS
Juliana Basko-Plluska, MD, Vesna Petronic-Rosic, MD, MSc, Ortel Bernhard, MD

HISTORY OF PRESENT ILLNESS
A 78 year old African American male presented with a five month history of asymptomatic, generalized hypopigmentation of the skin that started on the lower extremities, but gradually progressed to involve the upper extremities and the trunk. The dorsal aspects of the hands and the face were largely unaffected. The patient denied any preceding skin eruption or new medications prior to the hypopigmentation.

PAST MEDICAL HISTORY
Prostatic adenocarcinoma- diagnosed in 2005, status post radiation therapy to the whole pelvic area and anti-androgen therapy; hypertension, atrial fibrillation, pulmonary embolus

REVIEW OF SYSTEMS/ FAMILY HISTORY/ SOCIAL HISTORY
Review of systems was notable for fatigue and loss of libido.
Family and social history were non-contributory.

MEDICATIONS
Amlodipine, metoprolol, hydrochlorothiazide, valsartan, warfarin, atorvastatin, cetirizine and tadalafil

ALLERGIES
None

PHYSICAL EXAMINATION
Reticulated hypopigmented macules and patches were present on the lower extremities. The trunk and upper extremities had confluent patchy hypopigmentation. The dorsal aspects of the hands and the face were significantly darker than the rest of the body.

DERMATOPATHOLOGY
A punch biopsy specimen (labeled A) was obtained from a patch with relatively preserved pigment on the right lower leg. A second punch biopsy specimen (labeled B) was taken from an adjacent, uniformly hypopigmented patch on the right lower leg. H&E of both specimens showed no apparent abnormality. Fontana-Masson stain of specimen B demonstrated pigment loss at the basal layer relative to specimen A. Anti-Mel-5 antibody labeled occasional melanocytes at the basal layer in both specimens, whereas anti-MITF antibody demonstrated a slightly decreased number of melanocytes in specimen B relative to specimen A.

LABORATORY DATA
Normal: complete blood count, comprehensive metabolic panel, thyroid stimulating hormone, free T4, adrenocorticotropic hormone (ACTH), prolactin, prostate-specific antigen, selenium, copper, 25-hydroxy-vitamin D
Abnormal: free testosterone 0.6ng/dL (9-30), luteinizing hormone 13.6mIU/mL (2-6.8)

DIAGNOSIS
Acquired generalized hypopigmentation in the setting of testosterone deficiency

TREATMENT AND COURSE
The patient has not had any skin-directed therapies. Clinically, there has been of late no noticeable progression of the degree of hypopigmentation. The patient was referred to endocrinology for further endocrine workup given that generalized hypopigmentation is a rare cutaneous manifestation of testosterone deficiency.

DISCUSSION

Hypopigmentation can be due to loss of melanocytes or to their inability to produce melanin or transport melanosomes correctly. Acquired hypopigmentation disorders that arise in adulthood have been categorized according to the extent of lesions as localized, widespread or generalized[1]. Acquired generalized hypopigmentation is rare in adults. It may occur in the setting of nutritional deficiencies, such as of copper or selenium, and with endocrinopathies. Panhypopituitarism and, less frequently, hypogonadism, are two endocrine disorders that are associated with generalized hypopigmentation. In panhypopituitarism, the hypopigmentation is thought to occur due to decreased ACTH and melanocyte-stimulating hormones, which normally stimulate melanogenesis. In the setting of hypogonadism, the absence or decreased levels of sex hormones may account for the reduction of skin pigmentation. The first observation that sex hormones may play a role in skin pigmentation was made by Hamilton et al. in 1938. The authors reported that treatment with androgenic hormones caused darkening of the skin in a human male castrate. Subsequently, Edwards et al. described four cases of castrated human males who developed darkening of the skin after receiving intramuscular injections of testosterone propionate. A spectrophometric analysis of the skin of these individuals before, during and after treatment with testosterone revealed an increase in the amount of melanin during the treatment, with subsequent relapse to the hypopigmented condition when the androgenic medication was withdrawn.

The exact mechanism by which androgens may regulate skin pigmentation remains unclear. A series of *in vitro* studies have shown that human skin melanocytes are androgen-sensitive cells. They contain nuclear androgen receptors and high levels of type I 5α-reductase activity, the enzyme that converts testosterone to the more potent 5α-dihydrotestosterone. Tadokoro et. al. were able to show that incubation of human genital skin melanocytes with the potent synthetic androgen, methyltrienolone (R1881), stimulated the tyrosinase activity of melanocytes, but did not affect their cell growth or the expression of tyrosinase mRNA. On the contrary, incubation with cyproterone acetate, a compound which blocks the androgen receptor, antagonized this stimulatory effect of androgen, suggesting that the effect is likely to be mediated by the androgen receptor pathway. Thus far, an androgen responsive element has not been identified in the promoter region of the human tyrosinase gene, suggesting that the upregulation of tyrosinase activity by androgens may be determined by post-transcriptional events and/or by participation of other co-factors. Recently, the same authors proposed another pathway for the regulation of melanogenesis by androgens. They suggested that androgens may bind to the sex-hormone-binding globulin (SHBG)-SHBG receptor complex at the plasma membrane and decrease intracellular cAMP levels and tyrosinase activity. Contrary to what they had shown previously, this pathway inhibits melanogenesis. The contribution and significance of each pathway *in vivo* remains to be elucidated; however, the possible existence of these two conflicting pathways may help explain why not all male patients with low testosterone develop generalized hypopigmentation. Additional work is needed to elucidate the exact mechanism by which androgens contribute to melanogenesis; however, the data strongly suggest that androgens influence melanin production and, along with other factors, may contribute to the regulation of cutaneous pigmentation.

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PRESENTERS

Edidiong Kaminska, MD, Richard A. Larson, MD, Vesna Petronic-Rosic, MD, MSc

HISTORY OF PRESENT ILLNESS

A 38 year old man with an 11 year history of idiopathic autoimmune aplastic anemia that became refractory to multiple immunomodulatory medications (antithymocyte globulin, cyclosporine, methylprenisolone, and mycophenolate mofetil) and required frequent blood transfusions underwent an allogeneic hematopoietic stem cell transplant one year prior to presenting for evaluation of diffuse hair whitening and generalized anhidrosis. Twelve months earlier, he had received chemotherapy with fludarabine, alemtuzumab, and melphalan as preparation for a matched unrelated donor stem cell transplant. Shortly after chemotherapy his hair fell out, but it subsequently re-grew back to its original brown color. Three months later, his hair started to fall out again; 9 months after the transplant, he had diffuse re-growth of white hair, complete anhidrosis and excessively dry skin. He denied decreased tear or saliva production.

PAST MEDICAL HISTORY

Significant for asthma, chronic graft versus host disease (GvHD), gastrointestinal reflux disease, hypertension, hypothyroidism, and iron overload

REVIEW OF SYSTEMS / FAMILY HISTORY / SOCIAL HISTORY

Non-contributory

MEDICATIONS

Albuterol, dapsone, levothyroxine, multivitamin, nicotinamide, omeprazole, prednisone, tacrolimus, and valcyclovir

ALLERGIES

Trimethoprim/sulfamethoxazole causes a rash

PHYSICAL EXAMINATION

On physical examination there were depigmented hairs on the entire body surface and irregular thinning of scalp and facial hairs, including eyelashes. Wiry hairs were observed on the extremities and trunk. The skin appeared mildly erythematous, xerotic and devoid of pigment.

DERMATOPATHOLOGY

A 4-mm punch biopsy from the right arm showed vacuolization of the basal layer, spongiosis and individual cell necrosis in the epidermis. Ill-appearing eccrine glands with thick basement membranes and hair follicles surrounded by lymphocytes were also noted. Immunohistochemical staining with Melan A and microphthalmia-associated transcription factor demonstrated a specimen completely devoid of melanocytes.

LABORATORY DATA

Complete blood count: leukocytes 7.6 K/μL (3.5-11), hemoglobin 14.1 g/dL (13.5-17.6), platelets 199 K/μL (150-450)
Differential: neutrophils 92%, lymphocytes 5%, monocytes 3%, eosinophils 0%
Ferritin: 1957 ng/mL (20-300)
Thyrotropin: 1.62 mcμ/mL (0.30-4.00).

DIAGNOSIS

Amelanocytic anhidrotic alopecia areata

TREATMENT AND COURSE

The patient was treated for cutaneous GvHD with topical triamcinolone 0.1% ointment twice a day as needed; he was instructed the white hairs and depigmented skin were likely permanent. Additionally, he was advised that he must prevent himself from overheating because of the anhidrosis and wear sun protection regularly.

DISCUSSION

Diffuse alopecia areata or canities subita is a rare variant of alopecia areata in which hair loss may be associated with re-growth of white hairs and lightning of the skin. The pathophysiology is not completely understood, but a 2-step mechanism has been proposed. First, the pilar unit is transformed from one that produces pigmented hair to one that produces non-pigmented hair; the pigmented telogen hairs are shed and the new anagen hairs are depigmented. Next, the sudden whitening may be attributed to the retention of pre-existing white hairs and abrupt selective shedding of the pigmented hairs. Synchronous lengthening of the white hairs during re-growth provides the final appearance. Alopecia areata has demonstrated abnormal melanoblasts and melanogenesis, and the disease preferentially targets pigmented hairs while depigmented hairs are preserved within evolving patches. Preferential loss of pigmented hair in this immune-mediated disorder has led some experts to hypothesize that the autoimmune target in alopecia areata may be related to the melanin pigment system and/or the melanocytes.

Observations in mouse models indicate that the induction of T-cell-mediated immunity against hair follicle melanocytes causes alopecia areata and may be accompanied by vitiligo-like coat color change. Additionally, a decreased number of follicular melanocytes have been documented in patients with alopecia areata. The skin lightning phenomenon may also be a result of the proposed defect or destruction of the melanin pigment system and melanocytes; therefore diffuse alopecia areata may overlap with or include vitiligo in its disease course. c-kit tyrosine kinase inhibitors are a known cause of hair and skin depigmentation that is usually reversible upon cessation of the medication. However the patient did not have exposure to c-kit tyrosine kinase inhibitors, and the white hairs persist. Additionally, histopathology demonstrated a complete lack of epidermal and follicular melanocytes, further supporting the theory that melanocytes may be the autoimmune target in alopecia areata.

Acquired generalized anhidrosis has not been described with diffuse alopecia, but has been associated with autoimmune disease, cancer, GvHD, medications, or it is idiopathic. Drugs that induce hypohidrosis, or deficient sweating, include antimuscarinic anticholinergic agents, carbonic anhydrase inhibitors and tricyclic antidepressants. While a lymphocytic infiltrate surrounding the eccrine glands could be consistent with an autoimmune anhidrosis, a definitive etiology of the anhidrosis could not be confirmed in this patient.

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PRESENTERS
Monique Kamaria, MD; Ingrid Polcari, MD; Sarah L. Stein, MD

HISTORY OF PRESENT ILLNESS
An 8 day old female was referred to dermatology for evaluation of skin blistering since birth. The infant was born at term via cesarean section (repeat cesarean delivery for the mother); both pregnancy and delivery were uncomplicated. During the hospitalization, the infant was noted to develop blisters at sites of friction. Intravenous antibiotics were initiated until blood cultures were negative. The infant was discharged on day of life 2 and was noted to have blisters at sites of adhesive and where the hospital tags were attached.

PAST MEDICAL HISTORY
Full term infant, uncomplicated pregnancy and delivery via cesarean section. Birth weight 8 pounds 2 ounces.

FAMILY HISTORY
No history of blistering disorders. Parents deny consanguinity.

MEDICATIONS
Oral clindamycin

ALLERGIES
No known drug allergies

PHYSICAL EXAMINATION
Well appearing, vigorous 8 day old with strong cry, in no apparent distress. There are several erosions with evidence of a dried and crusted blister roof at sites where adhesives had been placed and at the ankles. Both hands and several toes demonstrate flaccid blisters. The diaper area is erythematous with a small erosion near the anus. There is no sign of blistering or irritation along the free edges of the diaper. There are no oral erosions. Finger and toenails are intact.

IMMUNOFLUORESCENT MAPPING STUDIES
A punch biopsy was performed after inducing a blister and submitted for immunomapping. Subepidermal clefting was observed. Primary IF mapping studies revealed types IV and VII collagen and keratin 14 in the roof of the cleft. Additional mapping revealed roof localization of laminin 332, alpha6 integrin, beta4 integrin, type XVII collagen and plectin. Notably, intracytoplasmic granular deposits of collagen VII were present in the cytoplasm of basilar and suprabasilar cells.

LABORATORY DATA
WBC: 20,000 with 50% granulocytes, 40% lymphocytes, and 4% monocytes
Hemoglobin 17.4
Hematocrit 51
Platelet 188,000
Culture of skin lesions negative

DIAGNOSIS
Transient bullous dermolysis of the newborn

TREATMENT AND COURSE
Oral clindamycin was discontinued. Extensive counseling was provided to the family regarding gentle skin care and avoidance of items and practices which could induce blistering. Vaseline impregnanted

gauze was recommended as a dressing to be applied to eroded sites.

At the one week follow up visit, no new vesicles or bullae were noted. Erosions were healing with re-epithelialization. At three months of age, the patient had no new vesicles or bullae. Areas of previous blisters healed with pigmentary changes but no scarring.

DISCUSSION

First described in 1985 by Hashimoto et al, transient bullous dermolysis of the newborn (TBDN) is a rare sporadic or inherited self-limited mechanobullous disorder observed at birth or shortly after birth. Clinically, the blistering can be widespread and has been reported to occasionally affect the mucous membranes and nails. The diagnostic criteria include: (1) primary vesiculobullous lesions present at birth or induced by friction (2) spontaneous recovery at a few months of age (3) absence of dystrophic scarring (4) subepidermal blisters beginning in the dermal papillae (5) ultrastructural findings of collagenolysis and damage to anchoring fibrils (6) significant dilatation of rough endoplasmic reticulum, with stellate body inclusions of type VII collagen.

The pathogenesis is believed to be related to a transient abnormality in secretion or transportation of type VII collagen along the dermoepidermal junction, resulting in lack of anchoring fibrils and subsequent mechanical fragility. In one family with TBDN in three generations, a transversion mutation in the gene encoding for type VII collagen (COL7AI) was identified, resulting in shortened collagen polypeptides.

Electron microscopy of TBDN will show sublamina densa cleavage and stellate body inclusions within dilated rough endoplasmic reticulum. Immunofluorescence antigenic mapping demonstrates type XVII collagen, laminin-1, and type IV collagen along the epidermal roof of microvesicles while type VII collagen is generally decreased in quantity and noted in granular deposits within intraepidermal keratinocytes.

The clinical improvement has been reflected by electron microscopic images demonstrating a gradual disappearance of stellate bodies of intraepidermal type VII collagen, increased secretion of type VII collagen from keratinocytes to the basement membrane zone, and restoration of anchoring fibril morphology. However, electron microscopy of skin biopsies of some individuals affected several years prior have demonstrated persistent abnormalities in type VII collagen despite clinical resolution. In general, there is clinical and histological resolution by a few months of age, however a few cases of recurrent blisters developing over years to decades have been reported. Milia formation and permanent nail dystrophy have been reported as sequelae.

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PRESENTERS
Edi Kaminska, MD, Diana Bolotin, MD, PhD

UKNOWN CASE

PRESENTERS
Brian E. Pucevich MD, Carlos Paz MD, PhD, Vesna Petronic-Rosic MD, MSc, Sarah L. Stein MD

HISTORY OF PRESENT ILLNESS
An 8 year old African American female presented to the outpatient dermatology clinic for evaluation of a recurrent hard painful nodule on her left shin. The family states that the lesion was noted 6-8 weeks prior to presentation as a warm and painful bump which was described as soft, but not fluctuant. The pediatrician prescribed a course of oral antibiotics to which there was no response. A subsequent short taper of oral corticosteroids resulted in decreased tenderness and flattening of the lesion. However, 3-4 weeks later the bump recurred, now as the hard nodule present at the time of our evaluation.

Of note, about 10 months prior to presentation, the patient had her first episode of painful swollen nodules on the left shin after enduring numerous insect bites while traveling in the southern US. The pediatrician recalls that two or three of the bite reactions persisted, then became fluctuant. Incision and drainage resulted in a large amount of purulent discharge; however cultures were negative for bacteria. An exuberant insect bite reaction was presumed and the lesions resolved after a short taper of oral corticosteroids.

PAST MEDICAL HISTORY
RSV viral infection at 6 months of age. Streptococcal pharyngitis x 2 during the winter of 2010-11. Mononucleosis in May 2011.

FAMILY HISTORY
History of prostate cancer in maternal grandfather. There is no history of leukemia or lymphoma.

SOCIAL HISTORY
The patient lives at home with her mother, she has no siblings and is an active soccer player.

REVIEW OF SYSTEMS
The patient had been complaining of an intermittent cough over the month preceding her presentation.

MEDICATIONS
None.

ALLERGIES
No known drug allergies

PHYSICAL EXAMINATION
Well appearing 8 year old in no distress. Vital signs are normal. There is a solitary 2x3 cm firm, deep-seated, non-fluctuant, ill-defined nodule on the left anterior tibia. The lesion is mildly tender to deep palpation. The overlying skin is hyperpigmented centrally with fine scaling. About 6cm proximal to the nodule there is a well healed scar at the site of the previous incision and drainage procedure. There is no palpable lymphadenopathy. There are no abdominal masses.

DERMATOPATHOLOGY
A 4mm punch biopsy from the left anterior tibia demonstrates a bottom heavy mononuclear cell infiltrate in dense confluent sheets extending into the subcutaneous fat and to the deep margin of the specimen. The infiltrate shows marked nuclear pleomorphism. Numerous mitotic figures are demonstrated. Immunohistochemical staining profile is positive for B-cell markers CD19, CD20, Pax-5, and CD79a and negative for CD3, CD30, CD10, CD33, CD34, CD56, CD117, CK20, myeloperoxidase, synaptophysin, CAM 5.2, and TdT. There is a high proliferation index with approximately 50% of the infiltrating cells

staining positive for Ki-67. Flow cytometric analysis confirmed a CD19, CD20 +, CD10- population of cells.

LABORATORY DATA

Complete blood count with differential was normal. Circulating blasts were not present on peripheral blood smear. Metabolic and hepatic function panels were normal. LDH was very mildly elevated to 246 U/L (116-245).

RADIOGRAPHIC STUDIES

CT Thorax/Abdomen/Pelvis: Notable for enlarged lymph nodes in the right hilum, left adnexa, and around the external iliac and femoral veins.

BONE MARROW BIOPSY

The marrow was hypocellular with approximately 16.4% blasts. Flow cytometry of marrow showed strong expression of CD19, CD22, cytoplasmic CD79a and partial expression of CD10, CD20, and TdT. FISH analysis showed *MLL* gene rearrangement with concomitant loss of *MLL* and *TEL* gene expression in 29% of bone marrow cells.

DIAGNOSIS

Pro-B-cell lymphoblastic lymphoma with cutaneous presentation

TREATMENT AND COURSE

The patient was admitted to Comer children's hospital for induction chemotherapy. Because of the tumor's *MLL* gene rearrangement and partial loss of expression, she was begun on the high risk protocol. Treatment was initiated with vincristine, decadron, PEG-asparaginase, and intrathecal cytarabine and methotrexate. Shortly after beginning chemotherapy the cutaneous tumor clinically resolved, leaving overlying hyperpigmentation. Subsequent bone marrow biopsy after completion of induction chemotherapy showed no evidence of any residual pro-B-cell lymphoblastic process. The patient has been admitted on several occasions for diarrhea and neutropenic fever but is otherwise doing well.

DISCUSSION

Cutaneous involvement in pediatric patients with hematologic malignancies occurs most often in the setting of childhood acute myeloid leukemia and CD-30 positive anaplastic large cell lymphoma. Cutaneous lesions at presentation of acute lymphoblastic leukemia and lymphoma are rare. In one cohort of 1359 patients, only 24 (1.7%) had cutaneous lesions at the time of diagnosis. Of these 24 patients, 15 (62.5%) were diagnosed with acute lymphoblastic leukemia and 9 (37.5%) were diagnosed with acute lymphoblastic lymphoma. The appearance of those skin lesions ranged from within a day to as long as 8 months before the diagnosis of leukemia/lymphoma.

The location of the skin involvement in these cases has also been investigated. Of the 24 patients with skin involvement, 21 had lesions on the face or scalp. Thirteen patients had a single skin lesion (8 on the scalp and 2 on the face) while the rest of the patients had multiple lesions. Lesions were also observed on the trunk and thigh and in the axilla. Seven patients were noted to have diffuse cutaneous lesions; all of whom had advanced disease with hepatosplenomegaly, leukocytosis and overt leukemia with circulating blasts.

Acute lymphoblastic lymphoma comprises 20% of neoplastic proliferations of lymphoblasts while acute lymphoblastic leukemia comprises the other 80%. Determination of the leukemic variant is based upon >25% bone marrow involvement with lymphoblasts, the presence of circulating lymphoblasts, or the presence of prominent hepatosplenomegaly, all features which our patient lacked. Most lymphoblastic lymphomas are of T-cell origin. A B-cell origin accounts for less than 20%. In contrast to T-cell

lymphoblastic lymphomas, B-cell lymphoblastic lymphomas are more commonly seen in young females, have a tendency to have cutaneous and long bone involvement, and lack the prominent mediastinal lymphadenopathy seen in the T-cell counterpart.

Immunohistochemical profile of acute B cell lymphoblastic lymphoma is usually of the pre-B cell phenotype and most commonly stains positively for CD-79a, CD-19 and CD-10. The pro-B cell phenotype similarly will express CD79a and CD19, but lacks expression of CD10. The common B cell marker CD20 is less reliably positive in lymphoblastic leukemia/lymphoma.

Genetic analysis of hematologic malignancies is pursued in an effort to better understand the tumor subtypes and more precisely stratify risk. The *MLL* gene rearrangement has been shown to be a poor prognostic indicator in lymphoblastic leukemia/lymphoma. Studies have estimated *MLL* gene rearrangement occurs in 5.7% of patients and is associated with hyperleukocytosis, a young age at diagnosis, lack of CD10 expression, and a poor clinical outcome. Four-year event-free survival has been documented at 10% in patients with the *MLL* gene rearrangement, while 4-year event-free survival is 64% in patients without the *MLL* gene rearrangement. Identification of genetic prognostic markers and the subsequent development of risk stratification algorithms allow patients with the greatest chance of treatment failure and relapse to receive the most aggressive treatment protocols.

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PRESENTERS

Adaobi I. Nwaneshiudu, MD, PhD, Monique Kamaria, MD, Lawrence Levine, MD, Keyoumars Soltani, MD, Christopher R. Shea, MD

HISTORY OF PRESENT ILLNESS

A 61-year old white man presented with multiple, asymptomatic lesions on his upper back, first noticed in March 2011. The lesions had increased in size and number. He reported no fevers, chills, unintended weight loss, history of recent travel, or recent changes in his medications. A biopsy of one lesion on the mid-back was interpreted as a granulomatous inflammation by an outside facility. The patient was treated with topical desoximetasone, without improvement. He also reported persistent dry eyes and mouth for the past 2 years.

PAST MEDICAL HISTORY

Mantle cell lymphoma (stage IV), diagnosed in August 2000, treated with cytoxan/etoposide, and autologous stem cell transplantation; graft-versus-host disease; sicca syndrome; shingles, hypothyroidism, obstructive sleep apnea

REVIEW OF SYSTEMS / FAMILY HISTORY / SOCIAL HISTORY

Review of systems was notable for persistent dry, red eyes, dry mouth, and depression.
Family history was notable for mother with lung cancer. Social history is noncontributory.

MEDICATIONS

Levothyroxine, gabapentin, testosterone transdermal patch, valacyclovir, zolpidem, lorazepam, folate, vardenafil, desoximetasone

ALLERGIES

Ceftriaxone causes a rash

PHYSICAL EXAMINATION

Multiple, violaceous, non-tender, nodules were noted on the upper back and the right anterior shoulder. The surrounding skin was normal. The palpebral conjunctivae were injected bilaterally.

DERMATOPATHOLOGY

A 4-mm punch biopsy specimen from a lesion on the left upper back showed an interstitial infiltrate composed of macrophages with associated lymphocytes and numerous plasma cells, dissecting among eosinophilic, swollen, and degenerated collagen bundles. There was no nuclear atypia. Colloidal iron stain showed normal amounts of dermal mucin. Anti-*Treponema pallidum* was negative. The biopsy from the lesion on the mid-back was internally reviewed and showed similar findings.

LABORATORY DATA

RPR: non-reactive. HIV screen: non-reactive. ACE level: 26 U/L (12-68)

DIAGNOSIS

Atypical clinical presentation of necrobiosis lipoidica

TREATMENT AND COURSE

The lesions are flattening, and not progressing in number or symptoms. He was offered the option of intralesional steroid injections to the lesions that persist. The patient also may undergo corneal transplants for his severe ocular inflammatory disease.

DISCUSSION

Necrobiosis lipoidica (necrobiosis lipoidica diabeticorum, NLD) is a disease of unknown etiology. About 80% of NLD patients have insulin resistance, frank diabetes mellitus (DM), or a family history of DM. NLD may precede diagnosis of DM by an average of two years. Theories to explain NLD pathogenesis include: 1) DM microangiopathic damage, resulting in collagen degeneration and dermal inflammation; 2) primary collagen abnormality, evidenced by anti-collagen antibodies in NLD patients, with secondary inflammation; and 3) immune-complex-mediated vascular damage.

Clinically, NLD lesions typically begin as small, non-tender, firm, red-brown papules that then enlarge, resulting in a well-circumscribed, glazed plaque with an atrophic center, yellowish hue, and prominent telangiectasia. The classic site (~85%) for NLD is the lower extremities, particularly the shins. The lesions are prone to ulcerate, especially after minor trauma or infection, and heal with scarring. NLD lesions presenting in other body sites may lack the classic appearance. Erythematous, annular or arcuate plaques have been observed on the face and scalp. Ulcerative erythematous plaques on the penis have also been described. In addition, NLD lesions have been observed on the nipple and upper back.

Histopathology demonstrates a superficial and deep, predominantly interstitial inflammatory infiltrate of macrophages including multinucleate giant cells, lymphocytes, and plasma cells, involving the entire reticular dermis. There are layered palisading granulomas with pale pink degenerated collagen and no increased mucin. The major histopathological differential diagnosis is granuloma annulare (GA), which tends to have fewer plasma cells, increased mucin within granulomas, and a lesser degree of collagen degeneration. GA has also been reported in association with various malignancies, including gastrointestinal stromal tumor, non-Hodgkin lymphoma, and adult T-cell lymphoma/leukemia.

NLD has been associated with inflammatory eye disease, similar to several other inflammatory conditions including sarcoidosis and rheumatoid arthritis. One report described a patient without a history of DM, presenting with lesions on both shins typical of NLD. The patient had concomitant bilateral intermediate uveitis, and later developed bilateral obliterative peripheral retinal vasculitis. Worsening of this patient's skin lesions coincided with exacerbations of ocular disease. Patients with NLD may therefore require in-depth assessment of ocular symptoms.

Treatment for NLD includes intralesional steroids injected into the erythematous border, and not the center, to avoid risk of further atrophy and ulceration. Other published treatments showing some efficacy include PUVA, clofazime, tacrolimus, TNF-inhibitors (including use of intralesional infliximab), and antiplatelet therapy such as dipyridamole.

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PRESENTERS
Brian E. Pucevich, MD, Christopher R. Shea, MD, Vesna Petronic-Rosic, MD, MSc

HISTORY OF PRESENT ILLNESS
A 56-year-old man with hepatitis C, status post liver transplant in 2002 presented with an 8-month history of a slowly worsening rash on the feet. He complained of difficulty walking, severe itching and burning of the feet. He wears sandals because closed-toe shoes and sweating exacerbate the discomfort. He has used over-the-counter antifungal cream and hydrocortisone 1% cream, with little improvement. His primary-care physician diagnosed cellulitis felt to be secondary to scratching; treatment with oral clindamycin improved the cellulitis but not the rash.

PAST MEDICAL HISTORY
Hepatitis C leading to cirrhosis and liver transplantation in 2002; diabetes mellitus.

REVIEW OF SYSTEMS/FAMILY HISTORY/SOCIAL HISTORY
Non-contributory

MEDICATIONS
Tacrolimus, mycophenolate mofetil, gabapentin, insulin glargine, insulin aspart, vitamin C, B-complex vitamins, and multivitamin supplements

ALLERGIES
Penicillin

PHYSICAL EXAMINATION
There are well demarcated, dusky-red, confluent, erythematous patches and plaques with focal scale on the dorsal and lateral surface of both feet, extending over the ankles and shins. Several macerated-appearing white papules and plaques are noted posterior and inferior to the left lateral malleolus. There is no associated tenderness, warmth, or pitting edema. His skin is xerotic.

DERMATOPATHOLOGY
There is psoriasiform hyperplasia and hydropic degeneration with necrosis of the epidermis. Parakeratosis underlies compact orthokeratosis. A sparse superficial perivascular lymphocytic infiltrate surrounds dilated capillary loops and there is papillary dermal edema. The methamine silver stain is negative for fungi.

LABORATORY DATA
Hepatic function: AST 242 U/L (8-37), ALT 208 U/L (8-35), ALP 185 (30-120)
Serum zinc: 0.68 mcg/mL (0.66-1.1)
Serum glucagon: 145 pg/mL (<80)
Hepatitis C viral load by PCR: 4,745,080 IU/mL

DIAGNOSIS
Necrolytic Acral Erythema

TREATMENT AND COURSE
The patient was given fluocinonide ointment 0.05% and oral supplementation with zinc 220 mg daily. Treatment with interferon-α was considered, in consultation with hepatology. The patient was unable to tolerate previous interferon treatment due to nausea, vomiting and flu like symptoms and his viral load did not respond, either. If he does not improve the possibility of interferon and antiviral therapy will be reconsidered.

DISCUSSION

Necrolytic acral erythema (NAE) was first described in 1996 in Egypt in association with active viral hepatitis C infection. It is characterized by stable, well demarcated, erythematous, dusky, smooth, confluent patches and plaques with flaccid vesicles and bullae. In chronic stages the disease exhibits prominent hyperkeratosis in the affected areas, typically with a rim of dusky erythema surrounding the individual plaques. Patients often complain of pruritus and burning pain. In the first seven patients reported, the dorsal aspects of the feet were exclusively involved; subsequently involvement of the palms, soles, and dorsal hands as well as extension onto the forearms and tibial surfaces has been reported.

NAE has been the presenting sign leading to the diagnosis of hepatitis C in some patients and has occurred following diagnosis of the viral hepatitis in others. While described almost exclusively in association with hepatitis C, NAE has rarely been reported in its absence. Deficiencies of amino acids, and of both serum and cutaneous zinc have been described. NAE tends to run a chronic relapsing/remitting course. Pruritus and burning pain can be persistent and intractable, preventing wearing of shoes and impeding daily activities, as in our patient.

Histopathologic findings vary depending on the stage of the lesion. Early on there is variable acanthosis and spongiosis with a superficial perivascular infiltrate. Fully developed lesions have prominent psoriasiform hyperplasia and hyperkeratosis with dyskeratosis, vacuolar degeneration, and necrosis of the upper epidermis leading to blistering. Papillary dermal edema and dilatation of papillary dermal capillary loops can be seen. Frank necrosis is often absent.

Management involves identification and treatment of underlying viral hepatitis and other metabolic and/or vitamin deficiencies. Acute exacerbations may occur with deterioration of hepatic function and elevation of the viral load. Improvement has been associated with effective treatment of viral hepatitis with interferon-α, or interferon-α and ribavirin combination. Correction of zinc and amino acid deficiencies with oral zinc supplementation or intravenous/oral amino acid supplementation has produced improvement in some patients. However, not all patients respond reliably. Malabsorption may play a role, as improvement seen with intravenous amino acid replacement may be followed by relapse when oral therapy is substituted.

NAE shares many clinical and histopathologic characteristics with necrolytic migratory erythema, acrodermatitis eneteropathica, and pellagra. Distinctive features include its fixed anatomic involvement, predilection for acral surfaces, strong association with hepatitis C, and inconsistent demonstration of amino acid, zinc, niacin, or biotin deficiencies. Differentiation from psoriasis is based on histopathology and lack of response to topical steroids. This diagnosis, while rare, should be strongly considered in any patient with hepatitis C presenting with a new acral eruption not responsive to topical steroid therapy, and should prompt investigation for viral hepatitis.

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PRESENTERS
Shani Francis, MD, Keyoumars Soltani, MD, Christopher R. Shea, MD

HISTORY OF PRESENT ILLNESS
A 42-year-old man with a past history of HIV/AIDS presented with a three-year history of pruritic, recalcitrant genital growths, beginning two years after successful achievement of healthy CD4 counts and undetectable viral loads. These lesions were pruritic, but frequently bled. The patient felt otherwise well and denied any other active medical complaints.

PAST MEDICAL HISTORY
HIV-positive since May 2005, AIDS (defined at diagnosis with MAC pneumonia and CD4 count of 5). Recalcitrant verruca vulgaris, bronchitis, and history of polydactyly status post surgical correction

FAMILY HISTORY
Non-contributory

SOCIAL HISTORY
Remote history of alcohol abuse. Patient denies any pertinent STD risk factors.

MEDICATIONS
Atripla (efavirenz tenofovir emtricitabine), lidocaine cream

ALLERGIES
None

PHYSICAL EXAMINATION
The scrotum is covered with numerous, non-tender, discrete, monomorphic, hyperpigmented, verrucous, dome-shaped papules, ranging in size from 3-7 mm. Inguinal lymphadenopathy was not appreciated.

DERMATOPATHOLOGY
The epidermis is acanthotic. The dermis contains prominent, thin-walled blood vessels that approach very close to the epidermis. Masson' s change (papillary endothelial vascular hyperplasia) and focal thrombosis are present. The Warthin-Starry stain is negative for bacteria or spirochetes. Anti-HPV-1 and anti-Kaposi sarcoma virus (HHV-8) are negative.

LABORATORY DATA
Complete blood count: WBC 9.5K/µL (3.5-11), Hb 12.6g/dL (13.5-17.5), platelets 158K/µL (150-450)
Differential: Neutrophils 67%, lymphocytes 22%, monocytes 8%, eosinophils 2%, basophils 1%

The following tests are negative: Toxoplasmosis IgG antibody, RPR, hepatitis A antigen, hepatitis B surface antigen, hepatitis B surface antibody, hepatitis B core antibody, hepatitis C antibody
HIV viral load: <50 copies (12/02/08, 11/10/09, 02/01/10)

CD4 counts: 5 (5/2/05); 225 (12/14/05); 535 (10/03/06); 372 (09/25/07); 692 (01/09/08); 804 (12/02/08); 540 (11/10/09); 507 (02/01/10)

DIAGNOSIS
Angiokeratoma of Fordyce in a patient with HIV/AIDS

TREATMENT AND COURSE
After multiple treatments with topical imiquimod and cryosurgery for presumed condylomata accuminata,

a biopsy was performed. Topical hydrocortisone, pramoxine, methol-camphor, and lidocaine creams failed to control the pruritus. Individual lesion electrodesiccation, scissor excision, and pulsed dye laser irradiation were initiated. Adequate analgesia could not be achieved with topical lidocaine cream. Due to uncontrollable pain and severe reactive hypertension during these treatments (blood pressure peaked at 202/98), additional treatments with destructive modalities were not pursued. The patient continues to follow-up intermittently and has recently begun topical rapamycin.

DISCUSSION

Clinically, the term *angiokeratoma* includes several unrelated disorders presenting with hyperkeratotic, vascular papules, including solitary, linear, acral, genital, or generalized subtypes of various etiologies (see Table). While generalized subtypes are usually associated with inborn errors of metabolism, no systemic disease can be attributed to the localized forms. Histopathology confirms superficial dermal vascular ectasia with overlying epidermal hyperplasia. These lesions are not true angiomas (vascular neoplasms) but rather telangiectasias of preexisting vessels. The basic pathological process is dilatation of the papillary capillaries with secondary epidermal changes of hyperkeratosis and acanthosis.

Angiokeratomas of Fordyce are typically asymptomatic, 2-5 mm, blue-to-red, scaly papules on the scrotum, shaft of penis, labia majora, vulva, inner thigh, or lower abdomen. Uncommon complaints may include soreness, burning, pain, pruritus, swelling, ulceration, and bleeding. Confluence of lesions may lead to discoloration, with a red scrotum or strawberry glans penis. The pathogenesis of this condition can be attributed to increased venous pressure, as derangements of the genitourinary system (e.g., varicocele, inguinal hernia, prostatitis, lymphogranuloma venereum, epididymal tumor, urinary system tumor, and thrombophlebitis) are well established associations; however, underlying venous hypertension can be demonstrated in only approximately half of all cases. Other proposed causes include congenital venular defects and local injury to capillaries from direct trauma.

Angiokeratoma of Fordyce is usually treated because of cosmetic concerns or bleeding, and can be challenging when lesions are numerous. Treatments include surgery or locally destructive treatment modalities such as electrocoagulation, cryotherapy, and various vascular laser systems; these include 578-nm copper, 578-nm argon, 532-nm potassium-titanyl-phosphate, and 1064-nm long-pulse neodymium-doped yttrium aluminum garnet, and pulsed-dye. Recently, success with sclerotherapy has been described. Analgesia can usually be achieved with various topical anesthetic preparations.

To date, there has been only one report of angiokeratoma in an HIV patient. That patient presented with a large, hypertrophic, solitary lesion on the plantar foot. Hypertrophy of angiokeratomas in HIV patients may be related to the pro-inflammatory endothelial milieu of HIV infection. Many clinical and laboratory studies have found that HIV infection causes profound functional alterations of the endothelium. The virus and its viral proteins are able to induce expression of several adhesion molecules and inflammatory cytokines such as ICAM-1, VCAM-1, E-selectin, TNF-a, and IL-6. A hypercoagulable state is often induced and depends on plasma HIV load. HIV and its viral proteins can also induce endothelial apoptosis and increase endothelial permeability. These effects could significantly contribute to vascular disease formation, and perhaps point to a potential mechanism by which angiokeratomas may become hypertrophic in HIV patients. The molecular mechanisms underlying HIV-associated vascular diseases and endothelial injury are not completely understood, but could represent a unique approach to clarifying the pathogenesis of angiokeratomas of Fordyce and, potentially, expand therapeutic options.

Table: Clinical entities with angiokeratomas

	Localization/distribution	Age of onset	Sex	Inheritance	Pathogenesis
Localized angiokeratomas					
Solitary	Lower extremities	3rd-4th decade	M>F	None	Chronic trauma
Fordyce	Scrotum/vulva	5th decade	M>F	None	Venous pressure
Circumscriptum neviforme	Zosteriform	Infancy	M=F	None	Vascular malformation
Mibelli	Dorsa of hands/feet	Early adulthood	F>M	Possible	Chillblains
Angiokeratoma corporis diffusum					
Fabry-Anderson	Bathing trunk area / generalized	Prepuberty	M>F	XR	Alpha-galactosidase deficiency
Fucosidosis	Bathing trunk area / generalized	Early childhood	M=F	AR	Alpha-fucosidase deficiency
Sialidosis	Bathing trunk area / generalized	1-2 years old	M=F	?	Alpha-neuraminidase deficiency
Kanzaki disease	Axilla, breast/generalized	Adult		AR	Alpha-N-aspartylgalactos-aminidase deficiency
Without enzymatic defects, familial	Limbs/trunk	Late infancy		AD	Arteriovenous fistula
", sporadic	Bathing trunk area / generalized	Infancy/adult	M=F	None	Unknown

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PRESENTERS
Tunisia Finch, MD, Vesna Petronic-Rosic, MD, MSc, Sarah L. Stein, MD

HISTORY OF PRESENT ILLNESS
A 4 year old male with a history of idiopathic neutropenia managed with subcutaneous injections of G-CSF presented with a 2-3 day history of swelling of the right superior helix and left dorsal hand, and a few additional red papules over the bilateral upper extremities. At the time of consultation, he was hospitalized and being treated for presumed cellulitis. The patient had a 1.5 year history of recurrent episodes of skin swellings affecting the head, trunk, and extremities that often began abruptly as flat "red dots" that would gradually enlarge and persist for several days. These lesions were mildly tender and itchy, and were typically treated with oral antibiotics for presumed cellulitis before resolving and leaving dark discoloration. There was never any associated blistering or drainage. An episode occurred every 4-6 months with lesions developing in various locations.

PAST MEDICAL HISTORY
Full term infant born by Cesarean-section secondary to gestational diabetes. Idiopathic neutropenia (suspected autoimmune), asthma, heart murmur, atopic dermatitis, MRSA furunculosis

MEDICATIONS
Filgrastim (G-CSF) (1 year), acetaminophen, albuterol, aztreonam, vancomycin, diphenhydramine, montelukast

REVIEW OF SYSTEMS/FAMILY HISTORY/SOCIAL HISTORY
Review of systems on admission was notable for fevers at home, malaise and poor appetite. Family history was negative for autoimmunity and immunodeficiency. Social history was non-contributory.

ALLERGIES
Ceftriaxone

PHYSICAL EXAMINATION
There was erythema and edema of the right superior helix. The dorsal left hand was diffusely erythematous, edematous and warm to palpation. A small erosion was present over a warm erythematous plaque on the right upper arm. On the left upper arm there was a small erythematous papule.

HISTOPATHOLOGY
A punch biopsy of the left dorsal hand shows skin with abundant eosinophils in the superficial and deep dermis. There is epidermal spongiosis. In the dermis there is marked edema and masses of histiocytes and eosinophils adhering to cores of collagen bundles with eosinophilic debris (flame figures). The periodic acid-Schiff stain is negative for fungi or significant basement membrane thickening. The methenamine silver stain is negative for fungi. The Gram stain is negative for bacteria.

LABORATORY AND RADIOLOGIC DATA
Complete Blood Cell Count: WBC 5.2 K/uL (4.0-13.8), Hgb 11.8 g/dL (11.2-13.8) Hct 33.3% (34-40), platelets 202 K/uL (150-450), eosinophils 3%, monocytes 10%, lymphocytes 72%, granulocytes 15%
Erythrocyte sedimentation rate: 10 sec (0-15)
C-reactive protein: 8 (<5)
ANA: 1:80 (0-80)

DIAGNOSIS
Wells Syndrome (eosinophilic cellulitis) in association with autoimmune neutropenia

TREATMENT AND COURSE

At the one week follow-up, the lesions were noted to have resolved leaving residual hyperpigmentation. Betamethasone dipropionate ointment was prescribed for future recurrences.

DISCUSSION

Eosinophilic cellulitis (WS) is a rare condition reported in approximately 80 cases since its initial description by Wells in 1971 as a "recurrent granulomatous dermatitis with eosinophilia". WS is most commonly seen in adults, and only 28 pediatric cases of WS have been reported. WS is characterized by recurrent cutaneous swellings which resemble acute bacterial cellulitis and by distinctive histopathological changes. Patients typically present with mildly pruritic or tender erythematous plaques, sometimes with associated bullae that evolve rapidly over 2-3 days. The clinical presentation can vary and may include annular plaques, urticaria, edema, and papules or nodules that can occur anywhere on the skin. These lesions resolve spontaneously over 2-8 weeks, leaving behind hyperpigmentation and minimal scarring. Systemic symptoms, including wheezing, arthralgia, lymphadenopathy, and fever, rarely occur. Associated laboratory findings include an elevated white blood cell count and peripheral eosinophilia in 50% of cases.

The histopathologic findings are quite specific and are characterized by edema, flame figures, and a marked infiltrate of eosinophils in the dermis. Although the histopathologic findings of eosinophilia, histiocytes, and flame figures are typical of WS, they may also be seen to a lesser degree in other conditions, including bullous pemphigoid, eczema, dermatophyte infection, and arthropod assault reactions. The diagnosis of WS should be reserved for cases with consistent clinical and histological findings and a recurrent course.

The etiology of WS is unknown; one hypothesis is that it represents a hypersensitivity reaction triggered by various infections, drugs, and solid organ and hematological malignancies. Concurrence of WS and hematological diseases such as hypereosinophilic syndrome, non-Hodgkin lymphoma, myelosclerosis, polycythemia vera, and leukemia have been reported. Prior to our patient's presentation, he was diagnosed with idiopathic neutropenia of suspected autoimmune etiology. Other autoimmune disorders rarely reported in association with WS include Churg–Strauss syndrome, ulcerative colitis, and systemic lupus erythematosus. Many drugs have been associated with Wells syndrome including penicillin, tetracycline, anticholinergic agents, anesthetics, and acetyl salicylic acid. One report described a case of WS occuring in association with adalimumab for rheumatoid arthritis. No reports have been published involving G-CSF in the etiology of the syndrome. Our patient's mother noted the onset of skin lesions approximately 5 months prior to the initiation of G-CSF.

Treatment options suggested in the literature include topical corticosteroids, griseofulvin, antihistamines, cyclosporine, minocycline, antimalarials, dapsone, systemic corticosteroids, and phototherapy. Treatment for WS is often unnecessary because cases frequently resolve spontaneously. Identification and treatment of the underlying precipitating factor is essential.

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PRESENTERS
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HISTORY OF PRESENT ILLNESS
An 82-year-old African American woman presented in 2009 complaining of new growths on the left posterior thigh and left forearm. Both were very sensitive to touch and frequently irritated by rubbing but stable in size. These lesions were biopsied. The patient was noted to continue to develop additional similar growths on the arms and the trunk at subsequent visits.

PAST MEDICAL HISTORY
Hypertension; breast cancer (1999) treated with chemotherapy and modified radical mastectomy; vertigo; seborrheic keratoses; xerosis cutis

MEDICATIONS
Amlodipine, atenolol, hydrochlorothiazide, ammonium lactate, multivitamin, vitamin D supplements, and vitamin B6

ALLERGIES
Penicillin (rash)

FAMILY HISTORY
No family history of skin cancer or significant dermatologic illness.

PHYSICAL EXAM
In 2009 the left arm showed a 6 mm flesh-colored pedunculated papule and the left posterior thigh had an 8 mm erythematous pedunculated papule. In 2011, several scattered pink-red sessile and pedunculated papules are present on the trunk and upper extremities.

HISTOPATHOLOGY
The epidermis is acanthotic, with an increased number of basaloid cuboidal cells. Eccrine-type ductules are present. Significant atypia is not identified.

DIAGNOSIS
Eccrine Poromatosis

TREATMENT AND FOLLOW UP
In the office lesions were removed using shave technique and sent to pathology. Photos were taken at each visit to monitor the remaining individual lesions clinically.

DISCUSSION
Eccrine poromas are rare, benign adnexal tumors derived from the acrosyringium. First reported by Pinkus et al. in 1956, eccrine poromas are believed to constitute ~10 percent of all sweat gland tumors. Generally they occur in the middle-aged and elderly and are seldom seen in childhood. The finding of multiple lesions (eccrine poromatosis) is very rare and some reported cases may instead be examples of acrosyringeal nevus. Among published cases of eccrine poromatosis, in one patient the lesions arose in an area of chronic radiation dermatitis. Another patient developed multiple poromas following total body irradiation and immunosuppression for bone marrow transplantation as part of treatment for acute lymphocytic leukemia.

Clinical diagnosis of eccrine poromas may be challenging due to their variable appearance, sometimes resembling pyogenic granulomas, skin tags, warts, cysts or other adnexal tumors. They are usually

solitary, slow-growing, skin-colored or red papules or nodules preferentially located on acral surfaces. They have also been seen in healed burn sites. Pigmented variants have been reported. Surface erosion or ulceration, presumably secondary to trauma, may occur.

Histopathologically, poromas consist of solid masses of uniform, cuboidal epithelial cells with ample cytoplasm and focal ductal differentiation. The cells are smaller than those of the contiguous epidermis and tend to be arranged in cords and broad columns. Keratins 1 and 10 are expressed in the tumor nests. Rarely, divergent adnexal differentiation is noted in eccrine poromas, with focal sebaceous, pilar, and even apocrine differentiation. Due to the common embryological origin of follicular, sebaceous and apocrine structures, it has been suggested that some poromas may be of apocrine origin.

Reports of dysplasia and malignant change in benign variants of eccrine poroma support theories that they can evolve from benign poromas to malignant porocarcinomas. Eccrine porocarcinoma has been reported in limited number of patients most commonly in the sixth to seventh decade of life. Approximately 50% of eccrine porocarcinomas appear first in the lower limbs and more than 40% occur below the knees. Eccrine porocarcinomas are documented to have long clinical histories, with a mean duration of 8.5 years, followed by a rapid growth phase. The pathogenesis and role of premalignant precursors of this lesion is still unknown. The upper portion of the dermal eccrine duct may have a role in oncogenesis. More recently, the p53 gene involved in tumor suppression was also implicated in porocarcinoma oncogenesis.

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