Chicago Dermatological Society

November 2010
Monthly Educational Conference

Program Information
Continuing Medical Education Certification
and
Case Presentations

Wednesday, November 10, 2010

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

Venue Information

Registration, patient & slide viewing

Duchossois Center for Advanced Medicine (DCAM)
5758 S. Maryland Ave., Chicago
Dermatology Clinic - 3A

Lectures & Case Discussions

Wyler Children's Hospital
5841 S. Maryland Ave., Chicago
Billings Auditorium - Room P-117

(see enclosed map)

On-line CME Claims

To get your CME certificate for today's meeting, you need to complete a short on-line evaluation form. Once you answer the questions and click on the "submit" button, the system will automatically send your CME certificate by email in PDF format.

We have a link to the CME claim system on the Chicago Dermatological Society website: www.ChicagoDerm.org

Or you can go directly to the on-line CME system by visiting the website below. PLEASE NOTE that this web address is specific for the *November 2010* meeting. If you need to file a claim for other meetings, contact Rich Paul for instructions.

November CME Claim direct link –
http://www.yourcesource.com/eval/?act=461!11102010

Program

Committees & Registration

8:00 a.m.	Registration Opens for All Attendees *DCAM - Main Lobby*
9:00 a.m. - 10:00 a.m.	**Resident Lecture** – *Billings Auditorium, P-117* Wound Healing: How does it work? *Edward Maytin, MD, PhD*
9:30 a.m. - 11:00 a.m.	**Clinical Rounds** – Patient & Slide Viewing *Dermatology Clinic 3A, DCAM*
11:00 a.m. - 12:15 p.m.	**General Session** - *Billings Auditorium, P-117* LORINCZ LECTURE: "Shedding New Light on Old Diseases: New Approaches to Photodynamic Therapy" *Edward Maytin, MD, PhD*
12:15 p.m. - 12:45 p.m.	Box Lunches
12:45 p.m. - 1:00 p.m.	**CDS Business meeting** – *Billings Auditorium, P-117*
1:00 p.m. - 2:30 p.m.	**Case Discussions** – *Billings Auditorium, P-117*
2:30 p.m.	Meeting adjourns

Mark the Date!

Next CDS monthly meeting – Wednesday, December 8, 2010
at the University of Illinois at Chicago; Sewon Kang, MD from Johns Hopkins University

CDS coding seminar – Saturday, January 22, 2011 for members & staff. Registration materials will be in the mail shortly.

Please note the following date change . . .
The May monthly meeting sponsored by Rush University is now on Wednesday, May 11 at the Stephens Convention Center in Rosemont.

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

Guest Speaker

Edward V. Maytin, MD, PhD

Delivering the David Fretzin Lecture

Dr. Maytin is Section Head of Molecular Dermatology in the Department of Dermatology, and is a Staff Member in the Department of Biomedical Engineering at Cleveland Clinic's Main Campus. He also is an Assistant Professor of Chemistry and Biomedical Engineering at Cleveland State University and Assistant Professor, Department of Molecular Medicine at the Cleveland Clinic Lerner College of Medicine of Case Western Reserve University. Dr. Maytin earned his medical degree (1985) from the University of Rochester School of Medicine and Dentistry in Rochester, NY. He completed a residency (1990) in dermatology and fellowship in endocrinology through Harvard Medical School and Massachusetts General Hospital in Boston (1999). He is a Diplomate of the National Board of Medical Examiners, as well as the American Board of Dermatology.

Dr. Maytin is a member of several medical societies, and he has published a number of articles, reviews, chapters and editorials on various topics in dermatology.

Continuing Education Credit

Chicago Dermatological Society

"Chicago Dermatological Society Monthly Conference"

November 10, 2010 *Chicago, Illinois*

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:

http://www.yourcesource.com/eval/?act=461!11102010

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.

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:

1. List 3 diseases, in addition to actinic keratoses, for which photodynamic therapy may offer a superior treatment option in certain situations.
2. Discuss the two biochemical steps in the protoporphyrin synthesis pathway which are currently being investigated as potential targets to enhance the outcome of photodynamic therapy.
3. Describe how photodynamic therapy can be integrated in a dermatology practice successfully.

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.

Colorado Foundation for Medical Care designates this educational activity for a maximum of **5** ***AMA PRA Category 1 Credits™*****.** Physicians should only claim credit commensurate with the extent of their participation in the activity.

CFMC has no financial responsibility for this activity.

DISCLOSURE STATEMENTS

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, and also discloses discussions of off-label uses of drugs and devices before their presentation(s).**

TABLE OF CONTENTS

PRESENTERS
Shaily Patel, MD, Keyoumars Soltani, MD, Christopher R. Shea, MD, Aisha Sethi, MD

HISTORY OF PRESENT ILLNESS
A previously healthy 30-year-old pregnant female, gravida 2 para 1, at 10 ½ weeks gestation was admitted for a diffuse rash present for three weeks. She first noticed the rash on the trunk, and it subsequently spread to the upper extremities. It was extremely itchy, for which she tried calamine lotion and ibuprofen at home, without significant relief. About two weeks later, extensive blistering and painful erosions developed over the trunk and extremities. She was seen in the emergency room and treated with diphenhydramine and a single dose of vancomycin, and was admitted for further management.

PAST MEDICAL HISTORY
None

MEDICATIONS
Acetaminophen, diphenhydramine, morphine PRN, and vancomycin (single dose)

ALLERGIES
NKDA

PHYSICAL EXAMINATION
The patient was a well-appearing female in no acute distress. Vital signs were normal. On the trunk and upper extremities there were numerous tense and flaccid vesicles and bullae, some with hypopyon formation, and a few in an annular configuration. She also had widespread erosions, some with crusting, overlying diffusely erythematous, edematous plaques. There was focal sloughing of the epidermis, which showed with fine, cigarette-paper-like wrinkling. Approximately 40% of the total body surface area was involved. Examination of the mouth revealed a few shallow erosions on her tongue.

DERMATOPATHOLOGY
A 4-mm punch biopsy specimen obtained from a vesicle on the back showed epidermal spongiosis with focal acantholysis and dyskeratosis. There were numerous intraepidermal vesicles and pustules containing abundant neutrophils and eosinophils. In the dermis, there was a superficial and deep perivascular infiltrate of lymphocytes admixed with eosinophils. A second punch biopsy of peri-lesional skin was performed for direct immunofluorescence and demonstrated intercellular deposition of IgG.

LABORATORY DATA
Complete blood count and comprehensive metabolic panel were normal.

DIAGNOSIS
Pemphigus vulgaris in pregnancy

TREATMENT AND COURSE
The patient was started on prednisone (1 mg/kg/day). Mupirocin ointment was applied to the open erosions, which were then covered with petrolatum gauze and wrapped. She was maintained on prednisone (1 mg/kg/day) throughout her hospitalization and improved rapidly during her stay. One week after discharge there were no intact bullae or vesicles; only post-inflammatory hyperpigmentation was noted. Indirect immunofluorescence revealed a low titer of pemphigus antibodies, at 1:40. Therefore, given the extent of clinical improvement and low disease activity,

no additional steroid-sparing agents were initiated, and the patient was started on a slow prednisone taper. She remained clear both at her one month follow-up visit and upon the completion of her prednisone taper 6 weeks later.

Given the possibility of transplacental IgG antibody transfer to the fetus, she was followed in the high-risk pregnancy clinic. Unfortunately, intrauterine fetal demise occurred at eight months of gestation as the result of cord entanglement, thought to be unrelated to the patient's history of pemphigus vulgaris.

DISCUSSION

Pemphigus vulgaris is a rare, autoimmune blistering disorder that can affect the skin and mucous membranes. The prevalence in males and females is approximately equal, with the mean age of onset around 50 to 60 years of age. The pathogenic hallmark of the disease is the presence of IgG autoantibodies against desmogleins, which are cell-surface adhesion molecules of keratinocytes. Depending of the specific adhesion molecules targeted by the IgG autoantibodies, pemphigus vulgaris may have two varying clinical presentations. In the mucosal-dominant type, desmoglein 3 is targeted. In the mucocutaneous type, both desmoglein 1 and desmoglein 3 are targeted, and such patients typically present with numerous, usually flaccid, vesicles and bullae that easily rupture and result in widespread erosions and ulcerations.

Histopathologic evaluation reveals edema, acantholysis, and subsequent intraepidermal blister formation; these changes may extend down the adnexal structures. The blister cavity usually contains acantholytic cells. Eosinophils and neutrophils may also be present both in the blister cavity and in the perivascular dermal infiltrate. Direct and indirect immunofluorescence confirm the diagnosis, demonstrating IgG autoantibodies against keratinocytes in an intercellular pattern.

Pemphigus vulgaris in pregnancy is rare, with only about 40 cases reported in the literature. Of these, fewer than 10 had active disease during the first trimester. Due to transplacental transmission of maternally derived IgG antibodies, the fetus may develop clinical manifestations in up to 50% of cases. Of note, these lesions are self-limited, usually resolving within the first few weeks to months of life. Up to 10% of neonates born to affected mothers are stillborn; however, it remains unclear whether pemphigus vulgaris plays a causative role in fetal demise.

Management of pemphigus vulgaris in pregnancy revolves around systemic corticosteroids. Occasionally, additional immunosuppressive agents are necessary in order to decrease disease severity and allow tapering of systemic steroids. In pregnancy, both dapsone and azathioprine have been utilized with success. A number of other immunosuppressive agents, including cyclophosphamide, mycophenolate mofetil, cyclosporine, and methotrexate, are contraindicated in pregnancy due to fetal risk. Finally, some newer therapies that may safely be used in pregnancy include: plasmapheresis, IVIg, and biologic agents such as infliximab and rituximab.

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PRESENTERS
Edi Kaminska, MD, John Fox, MD, Sarah L. Stein, MD, Vesna Petronic-Rosic, MD, MSc

CASE A

HISTORY OF PRESENT ILLNESS
A 4 year old female presented with a greater than 1 year history of an asymptomatic lesion on her left cheek. The family recalled that it started as a small "pimple" that gradually increased in size. Previous treatments with cryotherapy and topical 5-fluorouracil reportedly resulted in no improvement. The last treatment was 4-6 months prior to presentation to our office.

PAST MEDICAL HISTORY
None

FAMILY HISTORY
Asthma, hypertension, and gastro-esophageal reflux disease.

SOCIAL HISTORY
The patient had traveled to a rural area of northern Pakistan in 2008.

MEDICATIONS
None

ALLERGIES
NKDA

PHYSICAL EXAMINATION
The patient was a well-appearing and well-developed 4 year old female in no distress. On her left cheek there was a firm, but non-tender 2 cm hyperkeratotic and yellowish verrucous nodule arising from a red brown indurated plaque. There was no lymphadenopathy detected. No other skin lesions were present.

DERMATOPATHOLOGY
A 3-mm punch biopsy specimen of the plaque revealed verruciform hyperplasia of the epidermis overlying a dermal infiltrate of lymphocytes, histiocytes, and multinucleated giant cells that formed non-caseating granulomas. The Ziehl Neelsen and Fite stains identified acid fast bacilli (AFB) within giant cells. The periodic acid-Schiff, Gomori methenamine silver, Gram and Giemsa stains were negative for organisms.

LABORATORY, RADIOLOGY, AND ANCILLARY DATA
A 3-mm punch biopsy specimen was sent for the following tests:
Gram Stain: Rare white blood cells, predominately mononuclear cells, no organisms seen.
Bacterial Culture: No growth.
Viral Culture: No virus isolated.
AFB Smear: No acid fast bacilli seen.
AFB Culture: No growth 56 days.
Fungal Smear: No fungi seen on direct smear.
Fungal Culture: No growth 28 days.

PCR: No AFB or mycobacterium tuberculosis complex detected.
Purified protein derivative (PPD): Negative.
Quantiferon Tuberculosis (TB) gold: Negative.
Chest X-Ray: Unremarkable.

DIAGNOSIS
Cutaneous mycobacterial infection

TREATMENT AND COURSE
The patient was treated with ciprofloxacin 250 mg po bid and clarithromycin 125 mg po bid. At the 2 month follow up, the plaque had clinically improved. The lesion measured 1.6 x 1.8 cm, and was a thin, pink-to-orange-brown plaque with fine papules but no deep induration. There was no overlying crust or scale. There was no lymphadenopathy appreciated. No other skin lesions were present. The antibiotic regimen was continued. At the 4 month follow up the patient continued to improve. The plaque was even thinner with subtle cribriform scarring and almost no papules. At this visit ciprofloxacin was discontinued.

CASE B

HISTORY OF PRESENT ILLNESS
A 43 year old female presented for evaluation of verrucous papules on her nose for greater than 2 years which had gradually increased in size and were causing a deviation of the nasal columella. The patient denied any pain or irritation at the site. She was previously prescribed Aldara for the lesion but did not fill the prescription.

PAST MEDICAL HISTORY
Deep venous thrombosis, asthma, chronic enlarged pelvic and retroperitoneal lymphadenopathy, positive PPD at age 25 treated with isoniazid for TB prophylaxis for 6 months, seborrheic dermatitis, and traction alopecia

FAMILY HISTORY/SOCIAL HISTORY
Non-contributory

MEDICATIONS
Warfarin, fluticasone/salmeterol, albuterol, mometasone ointment, ketoconazole shampoo

ALLERGIES
NKDA

PHYSICAL EXAMINATION
The patient was a well-appearing 43 year-old female in no distress. Within the right nare, including the columella and septum, verrucous papules coalesced into a plaque with depression and erosion of the septum; the mucosa was friable. There was no cervical lymphadenopathy and no other skin lesions were notable.

DERMATOPATHOLOGY
A 4-mm punch biopsy specimen of the plaque revealed pseudoepitheliomatous hyperplasia overlying a dense dermal infiltrate of histiocytes, multinucleated giant cells, and lymphocytes. There were focal areas of caseous necrosis. The Ziehl Neelsen and Fite stains identified AFB within giant cells. The periodic acid-Schiff, Gomori methenamine silver, Gram and Giemsa stains were negative for organisms.

LABORATORY, RADIOLOGY, AND ANCILLARY DATA
A 4-mm punch biopsy specimen was sent for the following tests:
Bacterial Culture: coagulase negative Staphylococcus species.

AFB Smear: No acid fast bacilli seen.
AFB Culture: No growth 56 days.
Fungal Smear: No fungi seen on direct smear.
Fungal Culture: No growth 28 days.

PCR: No mycobacterium tuberculosis complex detected.
HIV Antibody: Negative.
PPD: Not performed.
Quantiferon TB gold: Not performed.
Chest X-Ray: Unremarkable, no significant pulmonary or pleural abnormalities, no active TB.

Note: PPD and quantiferon TB gold tests were not performed as these may remain positive after exposure to TB.

DIAGNOSIS
Cutaneous mycobacterial infection

TREATMENT AND COURSE
The patient was referred to the infectious disease clinic and was empirically started on therapy for a presumed cutaneous mycobacterial infection. Therapy included clarithromycin, ethambutol and rifabutin for a course of at least 6 months. The patient has currently completed 3 months of therapy and has since improved clinically. The verrucous plaques persist but appear to be less friable and the septum has started to regenerate.

DISCUSSION
Mycobacteria are acid fast bacilli that cause infections commonly associated with pulmonary disease and may be associated with skin and soft tissue infections. Innoculation is usually a result of hematogenous spread or direct extension from latent or active foci of infection, but may occur from direct trauma or injury. One of the major risks of infection is immunosuppression (such as patients with HIV or cancer on chemotherapy). Treatments in combination that are effective for tuberculous mycobacterial infections include: rifampin, isoniazid, ethambutol, and streptomycin. For non-tuberculous infections, effective treatments singly or in combination are tetracycline, minocycline, clarithromycin, ciprofloxacin, amikacin, rifabutin, and cefoxitin. Clarithromycin is often recommended as initial therapy.

Tests for the diagnosis of mycobacterial infections include fresh tissue AFB culture and smear, polymerase chain reaction (PCR), and histopathological examination with AFB special stains. Ancillary studies such as PPD placement, quantiferon TB gold test, sputum culture, and chest X-Ray are equally important. The exclusion of other entities such as bacterial, fungal, or viral infections are also warranted. Currently, culture is the gold standard for diagnosis. Limitations include time to diagnosis, low sensitivity (80-85%), difficulty to grow these organisms in culture, and failure to detect killed organisms. AFB smears of fresh tissue exudates for mycobacteria have demonstrated positivity rates of 5.8% -15.8%. These stains are less expensive compared to other techniques and easily performed. Sensitivity and specificity of PCR are 0.5%-100% and 73-100% respectively, which is highly variable based on bacterial load. Proposed limitations (i.e. false negative results) of PCR include: degradation of DNA in archival materials, difficulties extracting mycobacterial DNA, and decreased amplification as a result of formalin fixation. Special histopathology stains for cutaneous mycobacteria have demonstrated 11%-90% identification of AFB in patients depending on immune status and bacterial loads.

In the cases presented above, histopathology and special histopathology AFB stains demonstrated features of mycobacterial infection, although supplementary studies were negative for mycobacteria. Despite the negative culture and PCR results, when clinical evidence in

conjunction with laboratory data is compelling, the diagnosis should be considered highly likely and empiric therapy should be initiated even in the absence of speciation. Practioners with limited investigative facilities often make the diagnosis of mycobacterial infections based on therapeutic response to treatment. Our patients were treated with anti-mycobacterial drugs, each demonstrating clinical improvement.

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PRESENTERS
Ingrid Polcari, MD, Sarah L. Stein, MD

HISTORY OF PRESENT ILLNESS
A ten-year-old female with tuberous sclerosis presented to our pediatric dermatology clinic for routine evaluation and to establish care after a change in insurance. Her family reported that her condition is stable. The patient and the family seemed most concerned about the numerous facial angiofibromas which began to develop around four years of age and have become more prominent over time. In an effort to improve the facial appearance, the family had previously tried Elidel, Protopic, Differin and 1% Hydrocortisone cream without improvement. Additionally, the patient had undergone two treatment sessions with a pulsed-dye laser to decrease the facial erythema, also without satisfactory improvement. The family had consulted with a CO2 laser specialist but never pursued such treatment. The patient has also had shave excision of a few larger individual lesions.

PAST MEDICAL HISTORY
The patient was diagnosed with tuberous sclerosis at six months of age after macrocephaly and ash-leaf spots were noted. She had seizures in infancy and early childhood which necessitated the intermittent use of antiepileptics until age seven. She has kidney and cardiac involvement which are stable.

FAMILY HISTORY
No family history of tuberous sclerosis.

SOCIAL HISTORY
The patient is doing well in 4th grade and is active in extracurricular activities.

MEDICATIONS
None

ALLERGIES
NKDA

PHYSICAL EXAMINATION
In addition to other typical cutaneous findings of tuberous sclerosis, the patient had greater than 100 1-3 mm erythematous, dome-shaped shiny papules over the nose, bilateral cheeks, upper cutaneous lip and chin.

DIAGNOSIS
Extensive facial angiofibromas in the setting of tuberous sclerosis

TREATMENT AND COURSE
We recommended a trial of topical rapamycin 1% ointment applied to the facial angiofibromas once to twice daily. A local pharmacy compounded the medication in Dermabase. The treatment was initiated in early October.

DISCUSSION
Facial angiofibromas are one of the most common cutaneous manifestations of tuberous sclerosis, with up to 80% of affected individuals eventually developing these lesions. They may develop as early as the first two years of life and are usually present by adolescence. The prominent centrofacial location makes angiofibromas more disfiguring and distressing to patients than other cutaneous manifestations

of the disease. Furthermore, some patients' angiofibromas have prominent erythema instead of flesh-colored to brown coloration which makes these lesions even more noticeable.

Until recently, treatment options for facial angiofibromas have been limited to therapies such as dermabrasion, surgical excision, and CO2 or pulsed-dye laser therapy. Such therapies have limited effectiveness and have the potential for scarring.

Rapamycin is an mTOR (mammalian target of rapamycin) inhibitor. Widely used in renal transplantation patients as a systemic immunosuppressant, the antitumor properties of this medication are now being explored. A 2008 case report by Hofbauer, et al. described a patient with tuberous sclerosis who was receiving rapamycin for treatment of visceral angiomyolipomas and had incidental improvement of her facial angiofibromas. Such observations have led to the use of topical rapamycin, which is a new, promising treatment for facial angiofibromas that is not yet commercially available. A recent case report by Haemal, et al. detailed the response of a 16-year-old patient with tuberous sclerosis to a compounded topical rapamycin 1% ointment. After 6 and 12 weeks of twice daily application, the patient had a striking reduction in the number and size of facial angiofibromas.

While large-scale clinical trials are in the planning stages, pediatric dermatologists around the country have started using this topical therapy in select patients, with anectodal reports of improvement. Some have experienced difficulty in obtaining the ointment formulation, which has to be prepared by a compounding pharmacy able to crush the rapamycin tablets into a vehicle such as Dermabase. Therefore some dermatologists are prescribing rapamycin intravenous solution for topical use. While the ointment is generally well-tolerated, the solution is reportedly more irritating and has led some to prescribe mid-potency topical corticosteroids for concurrent use.

The potential of systemic absorption of topically applied rapamycin has been considered. Haemal, et al. tested rapamycin levels in their patient and found that serum levels remained under the limits of detection over the 3 month application course, which was to be expected given that application was confined to the face. Systemic use of rapamycin results in immunosuppression and a theoretical increased risk of infection. There have not been reports of systemic complications in patients using topical rapamycin preparations.

Many questions regarding the use of topical rapamycin have yet to be answered. It is unknown how long the effects of topical rapamycin will last and whether patients will need to use the medication on a long-term basis to have sustained improvement in their facial angiofibromas. Anecdotally, patients are so pleased with the response that they are hesitant to discontinue the medication. Large-scale clinical trials are necessary to further evaluate the long-term efficacy and safety of this exciting new treatment for facial angiofibromas.

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PRESENTERS
Brian E. Pucevich, MD, John C. Fox, MD, and Bernhard Ortel, MD

UNKNOWN

A 30-year-old male presented with a 4-week history of a pruritic scrotal eruption.

PRESENTERS
John C. Fox, MD, Vesna Petronic-Rosic, MD, MSc, Sarah L. Stein, MD

HISTORY OF PRESENT ILLNESS
An 11-month-old boy presented to the pediatric dermatology clinic for evaluation of numerous skin lesions that began at one month of age with a single lesion on the scalp. The parents described progressive acquisition of similar lesions on the trunk and extremities, with some lesions getting larger over time. There had been no bleeding or skin breakdown involving any of the lesions. The parents stated that the child was otherwise well.

PAST MEDICAL HISTORY
Failure to thrive evaluation at 3 months of age, including testing for cystic fibrosis—findings unrevealing. Catch-up weight gain documented subsequently.

FAMILY HISTORY
No skin disorders noted.

MEDICATIONS
None

ALLERGIES
NKDA

PHYSICAL EXAMINATION
Physical examination revealed an alert, but irritable 11-month-old male in no acute distress with pale skin; thin, sparse, fair hair; and a protuberant, tense abdomen with palpable liver edge. Inguinal and cervical lymphadenopathy was also detected. Two populations of cutaneous lesions were appreciated: numerous smooth, yellow-orange macules, and dome-shaped papules throughout the scalp, with rare similar lesions on the trunk and extremities, largest lesion measuring 1 cm in diameter; and smaller, pinpoint erythematous to violaceous excoriated papules on the lower face, abdomen, and medial thighs.

DERMATOPATHOLOGY
A punch biopsy specimen from a yellow-orange papule on the lower abdomen demonstrated a diffuse dermal infiltrate of monocytic cells with abundant amphohilic cytoplasm. These cells were positive for CD68 and negative for CD1a and S100.

LABORATORY DATA
Complete blood count: Leukocytes 60.8 K/μL (3.5-11), hemoglobin 8.2 g/dL (11.5-15.5), hematocrit 26.3 % (33-39), platelets 11 K/μL (150-450)
Differential: Neutrophils 47%, lymphocytes 18%, monocytes 14%, eosinophils 10%, metamyelocyte 2%, myelocyte 5%, blasts 4%
Comprehensive metabolic panel: Lactate dehydrogenase 676 U/L (116-245)
Bone marrow biopsy: hypercellular bone marrow consistent with juvenile chronic myelomonocytic leukemia (JMML); BRAF mutational analysis was negative for V600E.

DIAGNOSIS
"Benign" cephalic histiocytosis in the setting of juvenile myelomonocytic leukemia

TREATMENT AND COURSE

While preparing for stem cell transplantation, the patient received intrathecal chemotherapy with methotrexate, hydrocortisone, and cytosine arabinoside for two months, and has needed almost weekly transfusions of platelets and red blood cells. A matched unrelated donor has been identified; however, a lung nodule was discovered during pre-transplant screening that was subsequently biopsied to reveal caseating granulomas with numerous acid-fast bacilli. Tissue culture demonstrated *Mycobacterium avium-intracellulare* complex. Transplantation has been delayed, and the patient is being treated with clarithromycin, rifampin, isoniazid, and ethambutol.

DISCUSSION

Benign cephalic histiocytosis (BCH) is a rare non-Langerhans cell histiocytosis (NLCH) characterized by asymptomatic papules on the head and neck of infants and young children, with eventual spontaneous regression. Although lesions of BCH classically involve the head and neck, extension to the trunk and extremities may occur later in the course of the disease. Histologically, BCH is characterized by a well-circumscribed proliferation of histiocytic cells with abundant pale to amphophilic cytoplasm without cytoplasmic lipids. Immunochistochemistry reveals the neoplastic cells to be negative for the neuronal protein S100 and for the Langerhans cell marker, CD1a.

Recent reports and studies indicate that BCH may have overlapping clinical and histologic features with juvenile xanthogranuloma (JXG) and generalized eruptive histiocytoma (GEH), indicating BCH may lie within a spectrum of NLCH. Transformation of BCH into JXG has been reported in the literature, leading some to suggest that BCH represents an abortive form of JXG, or that BCH and JXG are different morphologic expressions of the same disease. GEH is histologically similar to BCH but classically afflicts adults, though there are rare reports in children. It has been suggested that BCH represents a limited form of GEH in children. Other primarily cutaneous NLCH include giant cell reticulohistiocytoma, papular xanthoma, progressive nodular histiocytoma, and indeterminate cell histiocytosis (ICH).

Juvenile myelomonocytic leukemia (JMML) classically presents between birth and 6 years of age, with a male predominance of at least 2.5:1. Presenting features include pallor, failure to thrive, irritability, protuberant abdomen secondary to hepatosplenomegaly, and lymphadenopathy. JMML is considered a myeloproliferative disorder, with nonspecific bone marrow findings, leukocytosis (median = 33,000/ μl), peripheral monocytosis, anemia, and thrombocytopenia. Abnormalities in the Ras signaling pathway exist in 70% of cases, and there exists a known association between JMML and both neurofibromatosis type 1 (NF1) and Noonan syndrome.

Although BCH is classically not associated with systemic disease, there have been reports in the literature of other NLCH associated with systemic diseases and with malignancies. Most well known of these is the triple association between JXG, JMML and NF1. ICH has been reported in association with acute myeloid and myeloblastic leukemias. Given the emerging notion of NLCH existing on a spectrum, it may be prudent to perform a baseline laboratory evaluation of patients in whom any NLCH is diagnosed, especially in the presence of other abnormal findings on physical examination.

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PRESENTERS
Shani Francis, MD, Brian Pucevich, MD, Aisha Sethi, MD

HISTORY OR PRESENT ILLNESS
A 24-year-old African American male presented to the dermatology clinic with a one year history of generalized alopecia. Per the patient the alopecia developed preceding his recent diagnosis of HIV by approximately four months. The alopecia was asymptomatic but of concern to the patient due to the physical appearance of the hair loss. The patient also noted that the alopecia seemed to be slowly resolving since starting on anti-retroviral therapy eight months ago.

PAST MEDICAL HISTORY
HIV-positive since April 2009, AIDS (defined at diagnosis with PCP pneumonia and CD 4 count of 2). Recent history of herpes zoster.

FAMILY HISTORY/SOCIAL HISTORY
Non-contributory. Patient denies any pertinent STD risk factors.

MEDICATIONS
Atripla (efavirenz/tenofovir/emtricitabine)

ALLERGIES
NKDA

PHYSICAL EXAMINATION
Diffuse patches of alopecia extensively involving parietal, temporal and frontal scalp, face, extremities, and the trunk. Few black vellus hairs present on the vertex and occipital scalp. Nail pitting noted in the left hand.

LABORATORY DATA
Comprehensive metabolic panel and thyroid function tests were within normal limits.
ANA was negative, at 1:80, speckled.
RPR was non-reactive.
CD4 counts: 2 (4/15/09); 153 (9/28/09); 239 (12/28/09); 850, by report (7/2010)

DIAGNOSIS
Alopecia universalis, resolving with recovered CD4 count

TREATMENT & COURSE
Patient was initially seen in Dermatology ten months after his HIV diagnosis and was already currently on HAART treatment for approximately eight months. At time of the first dermatology clinic visit, his most recent CD4 count was 239. Treatment with topical tacrolimus was considered, but unable to be initiated due to cost. Upon follow-up five months later, the patient demonstrated near complete re-growth of terminal hair on the scalp, face, trunk and extremities. CD 4 count at this visit was reportedly 850.

DISCUSSION
Alopecia universalis, a variant of alopecia areata (AA) is a chronic inflammatory condition causing non-scarring hair loss. AA predominantly involves focal areas on the scalp, but can also progress to include the entire scalp (alopecia totalis), or the entire body (alopecia universalis). The etiology is not fully understood, but thought to be a multifactorial interplay between genetics and autoimmunity. The diagnosis is typically clinical, although can be confirmed histologically, by demonstrating a peribulbar

CD4+ predominate lymphocytic infiltrate, which may appear in a characteristic "swarm of bees" pattern. A CD8+ infiltrate predominantly is observed intrafollicularly.

The normal hair cycle exhibits a tightly controlled balance of proliferation, differentiation, and apoptosis. However, in AA this process is disrupted, resulting in premature termination of anagen phase with subsequent apoptosis-mediated regression (catagen phase) and finally, a resting hair follicle (telogen phase). Hair follicles may then reenter the anagen phase, but in the presence of a lymphocytic infiltrate, anagen is again terminated prematurely, resulting in miniaturized hair follicles.

Diffuse alopecia occurs in almost 7% of HIV-1-infected patients, particularly those with CD4 counts <200 cells/⌈L. Telogen effluvium and alopecia areata/universalis mechanisms have been described. Although the mechanism is not well understood, human immunodeficiency virus (HIV) infection is thought to contribute to hair cycle disruption. The collapse of immune privilege is one possible explanation for this observation. Normal anagen hair follicle keratinocytes typically lack expression of class I and class II major histocompatibility (MHC) antigens, suggesting immunologic privilege of the human hair follicle bulb. In alopecia areata, immune privilege is lost, and human leukocyte antigens (HLA-A, -B, -C, -DR) become expressed by the hair follicle, allowing an interaction of cytotoxic T lymphocytes with hair matrix cells, resulting in apoptosis.

HIV infection, through a systemic CD4/CD8 ratio depression, induces a change in the balance between helper and suppressor cells, which may result in an aberrant cell-mediated immune effect around hair follicles. As the peripheral blood returns to a more normal ratio of CD4/CD8 cells, as can be seen following initiation of HAART therapy, the cutaneous influx of CD4-positive lymphocytes subsides, and hair regrowth is initiated. This case demonstrates HIV-associated alopecia universalis preceding HAART initiation and subsequent resolution corresponding to an increased CD4 count once the patient was started on HAART. It further highlights a unique perspective to understanding a therapeutically challenging problem and may advocate for earlier initiation of HAART for HIV-1 patients with generalized alopecia.

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PRESENTERS
Erica R. Aronson, MD; Carlos Paz, MD, PhD; David Mann, MD; Vesna Petronic-Rosic, MD, MSc; Christopher R. Shea, MD; and Bernhard Ortel, MD

HISTORY OF PRESENT ILLNESS
A 59-year-old African-American male with a history of congestive heart failure, recently admitted to the hospital for superior vena cava syndrome and extraction of his second implantable cardioverter-defibrillator device, presented with a 3-4 day history of lesions developing on the arms. The lesions were initially small erythematous papules that evolved over a three-day period into larger, tender, edematous plaques with vesicles and pustules. The patient returned to dermatology clinic one month later with new pustular plaques on the opposite forearm as well as pustules with surrounding erythema at the site of a recent venipuncture.

PAST MEDICAL HISTORY
Anterior uveitis, apthous stomatitis (3-4 episodes per year), erythema nodosum-like lesions, congestive heart failure, hypertension, atrial fibrillation, deep venous thrombosis, prostate adenocarcinoma (status-post robotic prostatectomy).

FAMILY HISTORY
Mother with diabetes mellitus and hypertension. Father with stroke.

MEDICATIONS
Fondaparinox, lisinopril, carvedilol, aspirin, spironolactone, steroid eye drops for episodic uveitis

ALLERGIES
Heparin (leading to heparin-induced thrombocytopenia), Pneumovax

PHYSICAL EXAMINATION
Generally well-appearing gentleman with marked edema of the left upper extremity. There were three coalescing erythematous plaques with vesicles and pustules on the left dorsal hand and forearm, each measuring 1.5-2 cm in diameter. The lesions were tender and focally covered with hemorrhagic crust.

DERMATOPATHOLOGY
Biopsy 1: Dermal blood vessels are injured. There is a perivascular infiltrate of neutrophils, karyorrhectic debris, and erythrocytes. Additionally, several blood vessels contain thrombi.
Biopsy 2: There is a dense predominantly neutrophilic dermal infiltrate with focal exocytosis of neutrophils into the epidermis and areas of superficial epidermal necrosis. There is prominent papillary edema and extravasation of red blood cells. The neutrophilic infiltrate surrounds follicular and adnexal structures with involvement of the subcutis. Focally, there is vasculitis.

LABORATORY DATA
Complete blood count: WBC 6.8 K/μL (3.5-11), hemoglobin 9.8 g/dL (11.5-15.5) , platelets 290 K/μL (150-450)
Differential: Neutrophils 71%, lymphocytes 19%, monocytes 8%, eosinophils 2%
ESR 54 MM/HR (nl 0-33 MM/HR)
CRP 40mg/L (nl <5mg/L)

DIAGNOSIS
Behçet Disease

TREATMENT AND COURSE

The patient was treated symptomatically with topical steroids, as well as a course of oral cephalexin. For coagulopathy, he remains on fondaparinox indefinitely. He is followed closely by his cardiologist, hematologist, rheumatologist, and ophthalmologist.

DISCUSSION

Behçet disease (BD) is a multisystem, polysymptomatic vasculitis of unknown etiology. As it can present in a multitude of ways, an international study group established diagnostic criteria in 1990 based on data from 914 patients in 7 different countries. The diagnosis of BD requires the presence of the major criterion of recurrent oral ulceration observed by physician or patient at least 3 times within a 12-month period, plus two minor criteria which may include: 1) recurrent genital ulceration, 2) eye lesions including anterior uveitis, 3) skin lesions including those resembling erythema nodosum, pseudofolliculitis, or papulopustular lesions, and 4) positive pathergy test at 24-48 hours.

Vasculitis in BD can affect numerous extracutaneous targets including the central nervous system, gastrointestinal tract, and large vessels. It is characterized by hyperfunction of neutrophils, vascular injury, and autoimmune responses. Although the etiology is unknown, there is a strong prevalence of HLA-B51 in patients with BD who live along the old Silk Road (Eastern Asia to Mediterranean basin), but less so among Western patients with the disease. An infectious etiology has also been proposed (HSV, parvovirus B19, hepatitis C virus) but no single infectious agent has been proven to cause the disease.

Histopathological evaluation will generally demonstrate a neutrophilic, angiocentric infiltrate with leukocytoclastic or lymphocytic vasculitis. The findings vary according to the origin and nature of the lesion. In pathergic lesions there is generally a heavy neutrophilic infiltrate, and the vessel walls may lack fibrinoid changes; in contrast, most other lesions in BD exhibit prominent features of vasculitis, namely leukocytoclasis and fibrinoid changes.

Our patient fulfills the criteria for BD by virtue of his history of aphthous ulcers, recurrent anterior uveitis, erythema nodosum-like lesions, and pathergy. In addition, he has coagulation abnormalities, also a characteristic of BD, which may be due in part to activated endothelial cells and platelets. Thrombotic events occur in 25% of patients and may explain this patient's development of deep venous thrombosis resulting in superior vena cava syndrome.

Treatment of BD is guided by the clinical manifestations. Twenty-five percent of patients with ocular involvement eventually become blind even with pharmacological intervention. Treatment is aimed at decreasing the frequency and severity of attacks. Topical corticosteroid and mydriatic agents are administered for anterior uveitis; colchicine can be used to prevent both anterior and posterior uveitis. Topical corticosteroids are generally used for oral and genital ulcers. Oral and intravenous corticosteroids are used for systemic manifestations of central nervous and gastrointestinal system involvement. Anticoagulants and antiplatelet agents are used to treat and prevent deep venous thrombosis.

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PRESENTERS
Tunisia Finch, MD, Bernhard Ortel, MD, Vesna Petronic-Rosic, MD, MSc

HISTORY OF PRESENT ILLNESS
A 56-year-old male presented with a 3-week history of multiple asymptomatic skin-colored papules that first appeared on the neck, arms, and trunk. The lesions became more erythematous over several days but remained stable in size. Oral diphenhydramine did not result in any improvement of the lesions. The patient reported a similar eruption which occurred one year prior and resolved spontaneously over several months.

PAST MEDICAL HISTORY
Hypercholesterolemia, cleft lip/palate, temporomandibular joint disorder, seasonal allergies, chronic ear infections, inguinal hernia, hyperbilirubinemia

FAMILY HISTORY
Sister with systemic lupus erythematosus and Addison's disease

SOCIAL HISTORY/REVIEW OF SYSTEMS
Non-contributory

MEDICATIONS
Fexofenadine, cyclobenzaprine

ALLERGIES
NKDA

PHYSICAL EXAMINATION
Multiple 1-4 mm skin-colored, smooth, firm papules on the neck, trunk and extremities with sparing of the face, palm, and soles.

HISTOPATHOLOGY
A punch biopsy of the right arm has an interstitial infiltrate of large cells with abundant eosinophilic cytoplasm and kidney-shaped nuclei. Numerous mitotic figures are seen. A background infiltrate of lymphocytes is present. Anti-CD1a, anti-CD68 and anti-CD14 strongly stain the neoplastic cells. Anti S-100 stains only rare cells within the infiltrate. Anti-Factor XIIIa weakly stains the histiocytic cells in the infiltrate. Langerin is negative within the dermal histiocytic infiltrate.

LABORATORY AND RADIOLOGIC DATA
Complete Blood Cell Count: WBC 6.4 (3.5-11 K/uL), Hgb 15.9 (11.5-15.5g/dL) Hct 43.9 (41-53%), platelet 217 (150-450 K/uL)
Lactate Dehydrogenase: 195 (116-245 K/L)
CT Chest: No evidence of interstitial or cystic lung disease, or other abnormality.
X-Ray Osseous Survey: Healed non-ossifying fibroma in the right tibia, otherwise no discrete lesions.
NM Bone Scan Whole Body: Nonspecific increased focal areas of uptake in the left posterior 10^{th} rib and left skull base that could represent trauma, suspected Langerhans cell histiocytosis, or benign tumor.

DIAGNOSIS
Indeterminate cell histiocytosis

TREATMENT AND COURSE

The patient was started on narrowband UVB therapy 2x/week which led to a reduced size and number of lesions. Subsequent reports of bone pain, jaw pain, and fatigue prompted a skeletal survey, bone scan, and chest CT. Nonspecific focal areas of increased uptake in the rib and skull base found on the bone scan will be reevaluated in 6 mos. The patient was recently hospitalized for viral meningitis; 4 weeks after the last UVB session, the lesions recurred.

DISCUSSION

Histiocytic disorders are a heterogeneous group characterized by the proliferation of cells of the mononuclear-macrophage system or of dendritic cells derived from the mononuclear-macrophage lineage progenitor cells in the bone marrow. These conditions have been classified as X (Langerhans cell lineage), non-X (monocyte/macrophage lineage), and indeterminate cell histiocytoses (ICH). ICH is a rare neoplastic proliferation in which the predominant cells share morphologic and immunophenotypic features of X and non-X histiocytosis. Indeterminate cells (IC) are thought to be closely related to Langerhans cells (LC), histologically and immunocytochemically, but do not contain Birbeck granules. IC are positive for CD1a and variably positive for S-100 protein and CD68. Various hypotheses regarding the relationship between LC and IC have been reported: 1) ICs may represent precursors of Langerhans cells that acquire granules as they transit for dermal to epidermal sites, 2) LC are precursors of indeterminate cells exhibiting loss of granules, 3) or both are independent types of dendritic cells.

ICH is characterized by solitary or multiple asymptomatic papules and nodules in otherwise healthy individuals. Early skin-colored to yellowish lesions become reddish brown over time and typically involve the trunk and extremities. Extracutaneous lesions and systemic symptoms are rare; however, mucosal, bone, eye, and lymph node involvement have been reported. ICH has a variable clinical course ranging from stable disease to slow progression of skin lesions or spontaneous resolution. An association with hematological malignancies such as low-grade B-cell lymphomas, mast cell leukemia, myelomonocytic leukemia, and acute monocytic leukemia has been reported. The biological basis for the association of ICH and lymphoma/leukemia remains unknown. The malignancy may precede or succeed ICH; molecular studies have revealed identical molecular abnormalities in the lesional IC as in the malignancy. This association highlights the importance of hematological tests and clinical staging.

Anecdotal reports have proposed several treatments, including topical 5-fluorouracil cream, PUVA, UVB, cyclophosphamide, vinblastine, etoposide, thalidomide, and 2-chlorodeoxyadenosine. Chemotherapy may be necessary for aggressive forms involving over 50% BSA and lasting at least 6 months with no evidence of spontaneous resolution. In ICH associated with malignancy, many patients received antineoplastic drugs prior to the development of ICH; therefore a causal relationship cannot be excluded. Consequently, it may be wise to limit chemotherapy to advanced ICH with diffuse disfiguring lesions and visceral involvement.

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PRESENTERS
Juliana Basko-Plluska, MD, Carlos Paz, MD, Christopher R. Shea, MD, and Sarah L. Stein, MD

HISTORY OF PRESENT ILLNESS
An eight-year-old male was referred by rheumatology for evaluation of asymptomatic discoloration on the arms and legs for 12 months. The patient had been seen by rheumatology for a several-month history of increasing fatigue, intermittent low-grade fevers, joint pains involving hands and feet, and a 12-lb weight loss. The working diagnosis by rheumatology was "vasculitis."

PAST MEDICAL HISTORY
Seasonal allergies, Sickle cell trait

MEDICATIONS
Motrin, Allegra

ALLERGIES
NKDA

PHYSICAL EXAMINATION
Linear hyperpigmented patches were noted overlying the superficial venous system of the lower and upper extremities. No nodules, induration or point tenderness were appreciated.

LABORATORY DATA AND IMAGING
Normal lab values
White blood count, platelets, comprehensive metabolic panel, TSH/TT4, IgM level
Thyroglobulin and thyroid peroxidase antibodies, anti-DNA double stranded antibody, anti-cardiolipin antibodies and Vascular ANCA IFA were negative.
Abnormal lab values
Hemoglobin 9.4 g/dL (11.3-15.2), Mean Corpuscular Volume 65.9 fL (76-94), Total Protein 9.5 g/dL (6.0-8.3), CRP 85 mg/L (<5), ESR 118 MM/HR (0-15), PT 15.6 (12.1-14.9), ANA (speckled pattern) 320 titer (0-80), tissue transglutaminase IgA antibody 26 units (<20), C3 184 mg/dL (60-180), C4 56 mg/dL (7-41), IgA 495 mg/dL (74-260), IgG 2288 mg/dL (730-1410), ASCA IgA 37.8 EU/mL (<20).
Lower Extremity Doppler Studies: reportedly normal

DERMATOPATHOLOGY
A 4 mm punch biopsy specimen of the right leg demonstrated a sparse perivascular lymphocytic infiltrate, without evidence of panniculitis or vasculitis. Direct immunofluorescence findings were negative. Specifically, there was no evidence of immune-mediated vasculitis.

DIAGNOSIS
Supravenous hyperpigmentation

TREATMENT AND COURSE
The patient was not prescribed any topical medications for the skin findings. Given the weight loss, iron-deficiency anemia, elevated inflammatory markers and positive IBD-7 panel, a further work-up for inflammatory bowel and celiac disease was undertaken by gastroenterology. Esophagogastroduodenoscopy showed a normal esophagus, stomach and duodenum. Lower endoscopy showed mild edema in the cecum and transverse colon. Biopsies of the cecum, right and left colon, transverse colon, sigmoid colon and rectum were negative.

The family has moved out of the Chicago area and is planning further follow up locally. The mother reported by phone that the patient's weight has been stable recently, the joint pain is less severe and the skin changes are stable. He continues to have low-grade fevers occasionally.

DISCUSSION

Serpentine supravenous hyperpigmentation was first described by Hrushesky et al. in 1976, referring to the development of increased linear pigmentation above the venous network used for 5-fluorouracil infusion. Subsequently, there have been additional reports of patients developing supravenous hyperpigmentation while undergoing chemotherapy. 5-fluorouracil is the most frequently associated chemotherapeutic agent. Other classes of culprit antineoplastic drugs include alkylating agents, antimicrobials, anti-microtubule agents and proteasome inhibitors. Chemotherapy-associated supravenous hyperpigmentation has been described more frequently in males with solid organ tumors. The hyperpigmentation is asymptomatic, may become progressively darker with each infusion, but it usually resolves with discontinuation of the drug. There are no signs of venous thrombosis or soft tissue infiltration of the inducing agents.

Supravenous hyperpigmentation has been also reported in association with underlying connective tissue diseases. The first observation was made by Jawitz et al. in 1984. The authors described pigment retention over the superficial vascular network in an area of depigmentation in three patients with progressive systemic sclerosis. In 1993, Werth et al. reported linear hyperpigmentation along the superficial veins in two patients with connective tissue disease. Case 1 was that of a 29-year-old African American male with a history of systemic lupus erythematosus who developed asymptomatic hyperpigmentation overlying veins on the legs and forearms. Case 2 was that of a 58-year-old African American male with rheumatoid arthritis who developed increased pigmentation along the distribution of veins on the lower extremities. Both patients had no history of minocycline or antimalarial drug use. The authors suggested that the circulating immune complexes present in patients with collagen vascular disease may play a role.

The pathogenesis of supravenous hyperpigmentation remains unknown. Several hypotheses have been proposed including: (1) direct stimulation of melanin synthesis or depletion of tyrosinase inhibitors, (2) depletion of reduced thioredoxin leading to tyrosinase stimulation, and (3) hyperthermia-related changes in the associated melanocytes, including decreased cytokine production and/or increased melanocyte-stimulating hormone receptor expression. Recently, the possibility of an immune-mediated alteration of cytokines has been suggested, especially in patients with underlying collagen vascular diseases. Histopathology shows increased basal melanin with a normal number of melanocytes, melanin incontinence into the dermis and/or a sparse perivascular lymphocytic infiltrate.

There are no specific treatments to expedite the resolution of supravenous hyperpigmentation. Topical hydroquinone therapy could accelerate the pigment clearing; although, there are no reports to demonstrate this. Photoprotection is recommended to minimize darkening. In the event of chemotherapy-associated supravenous hyperpigmentation, modifying the course of therapy based on skin findings alone is not advised, as the reaction is benign and self-limiting.

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PRESENTERS
Carlos Paz, MD, PhD, Vesna Petronic-Rosic, MD, Keyomours Soltani, MD

HISTORY OF PRESENT ILLNESS
A 44-year-old Caucasian man with a history of acute myelogenous leukemia presented twenty-two days after an allogeneic stem cell transplant with pruritic, perifollicular, erythematous macules on the trunk, extremities, scalp, and face. In the days that followed, the erythematous macules coalesced into confluent erythrema and the patient developed diffuse vesicles and bullae, which ultimately lead to widespread skin sloughing. The patient's palms and soles also had blisters and his mucous membranes exhibited some hemorrhagic crust. Review of systems was significant for a low-grade fever, nausea and vomiting, diarrhea, and jaundice

PAST MEDICAL HISTORY
Acute myelogenous leukemia, epidural hematoma

FAMILY HISTORY/SOCIAL HISTORY
Non-contributory

MEDICATIONS
Esomeprazole, fluconazole, tacrolimus, benazapril, levetiracetam, metoprolol

ALLERGIES
NKDA

PHYSICAL EXAMINATION
A physical examination revealed large areas of confluent erythema, vesicles and bullae, and sloughed skin on the head and neck, trunk, and extremities. Less involved areas exhibited erythema surrounding hair follicles. His mucosal surfaces had some hemorrorhagic crust.

LABORATORY DATA
A complete blood cell count and comprehensive metabolic panel were initially within normal limits. During his hospital stay, the patient developed significant electrolyte abnormalities, elevated liver enzymes, and bilirubinemia.

PATHOLOGY
A liver biopsy specimen showed damaged bile duct epithelium with apoptotic bodies and a sparse lymphocytic infiltration. The lobular parenchyma was notable for marked hepatocellular and canicular cholestasis and bile infarcts. Lymphocytes and neutrophils were scattered throughout the parenchyma.

DERMATOPATHOLOGY
Two 4-mm punch biopsy specimens showed vacuolization of the epidermal basal layer, individual cell necrosis with surrounding lymphocytes ("satellite cell necrosis") within the epidermis and adnexal epithelium, and scattered lymphocytes throughout the dermis.

Direct immunofluorescence showed no specific evidence of an immune-mediated dermatosis.

DIAGNOSIS
Stage IV acute graft versus host disease

TREATMENT AND COURSE

Within several days of admission, the patient was transferred to the burn unit with an evolving rash. Multiple skin biopsy specimens confirmed the diagnosis of graft versus host disease and the patient was started on methylprednisolone in addition to continuing post-transplant immunosuppression. Despite aggressive immunosuppresion, the patient continued to have electrolyte abnormalities, elevated liver enzymes, and bilirubinemia. Thirty five days into his hospital stay, the patient developed an overwhelming infection and expired.

DISCUSSION

Graft versus host disease (GVHD) occurs when immunologically competent cells are introduced into an immunoincompetent host and the immunocompetent cells recognize the host tissues as being foreign; in this setting, the ensuing inflammatory response leads to apoptosis of the target tissues. Death occurs in 15-40% of patients with GVHD, usually from overwhelming sepsis. GVHD is divided into acute and chronic forms based primarily on the onset of the condition, though there are significant differences between the clinical presentation of acute and chronic GVHD. Acute GVHD occurs within 40 days of transplantation and consists of the triad of dermatitis, enteritis, and hepatitis. Chronic GVHD occurs more than 100 days after transplantation and is characterized by lichen planus-like lesions and sclerodermatous skin changes.

Acute GVHD eruptions begin as faint erythematous macules on any part of the body, though palms and soles are usually affected first. When the trunk is involved, the erythema has a predilection for hair follicles. As the disease progresses, the erythematous macules may coalesce into confluent erythema. In severe cases, diffuse subepidermal blisters and skin sloughing may occur. There are four stages of acute GVHD. In Stage 1, <25% of the body surface exhibits cutaneous features of GVHD. In Stage 2, 25-50% of the body surface is involved. Stage 3 has 50-100% of body surface involvement while Stage 4 is characterized by the presence of vesicles and bullae. Extensive cases of Stage 4 GVHD can look like toxic epidermal necrolysis (TEN).

Clinical and histologic criteria help distinguish Stage 4 GVHD from TEN. TEN initially presents with irregularly-shaped erythematous macules while GVHD presents with erythema surrounding hair follicles. In both GVHD and TEN, extensive cutaneous involvement can lead to confluent erythema and skin sloughing. Hemorrhagic crust on mucosal surfaces, a feature typically reserved for TEN, can also be seen in GVHD, while diarrhea and jaundice are more common in GVHD. Histologically, TEN is characterized by full thickness epidermal necrosis. GVHD, on the other hand, is characterized by basal vacuolization and satellite cell necrosis in the epidermis and epithelium of adnexal structures. In severe cases of GVHD, however, a subepidermal split with full thickness epidermal necrosis can be seen, making Stage 4 GVHD difficult to distinguish from TEN. Complicating matters is that GVHD has been reported to cause TEN. While the aforementioned clinical and histological characteristics alone are not sufficient to diagnosis GVHD or TEN, in combination they can help guide the clinician make the correct diagnosis. In the future, molecular analysis may help distinguish GVHD from TEN, as the pathogenesis of the two conditions is different.

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PRESENTERS
John C. Fox, MD, Christopher R. Shea, MD, Maria L. Tsoukas, MD, PhD

HISTORY OF PRESENT ILLNESS
A 22-year-old male with a history of relapsed acute myelogenous leukemia (AML) presented 12 days following allogeneic stem cell transplant (SCT) with a tender skin eruption involving the face, trunk, extremities, palms, and soles for 4 days. The onset of skin changes was associated with tender swelling and redness of the left wrist.

PAST MEDICAL HISTORY
AML status post SCT in 2008, with relapse of disease in 2009 and SCT 12 days prior to presentation

MEDICATIONS
Acyclovir, imipenim/cilastatin, micafungin, tacrolimus, chlorhexidine gluconate rinse, metoprolol, ursodiol, chlorpromazine, phytonadione, esomeprazole

ALLERGIES
Cefepime

PHYSICAL EXAMINATION
Physical examination revealed generalized, discrete, non-follicular, necrotic papulovesicles on a violaceous base. Some lesions had a non-blanching, purpuric component. The palms and soles were involved, and an ill-defined, erythematous, edematous, tender plaque involving the skin overlying the left wrist and first metacarpophalangeal joint was also present.

DERMATOPATHOLOGY
A punch biopsy specimen demonstrated epidermal necrosis with dermal-epidermal separation. Dermal blood vessels exhibited congestion and focal thrombosis with intravascular and intramural fungal organisms. A perivascular and periadnexal inflammatory infiltrate of lymphocytes and neutrophils was also present. PAS and GMS stains confirmed the presence of fungal organisms within vessels and the interstitial dermis, and further highlighted septate hyphae and bulbous, vacuolated structures morphologically consistent with *Fusarium* species.

LABORATORY DATA
Complete blood count: Leukocytes <0.1 K/μL (3.5-11), hemoglobin 9.2 g/dL (11.5-15.5), platelets 16 K/μL (150-450) Differential: Neutrophils 65%, lymphocytes 10%, monocytes 25%
Comprehensive metabolic panel: Serum glucose 111 mg/dL (60-109), sodium 128 mEq/L (139-149), chloride 93 mEq/L (95-108), total bilirubin 3.0 mg/dL (0.1-1), conjugated bilirubin 1.6 mg/dL (0.0-0.3), unconjugated bilirubin 1.4 mg/dL (0.1-1)
Tissue culture: Fungal culture was positive for *Fusarium* species with sensitivity to voriconazole, posaconazole, and amphotericin B (University of Texas San Antonio Laboratory). Tissue culture was negative for bacteria and acid-fast bacilli.
Imaging: MRI: small abscess collections involving muscle and tendons of the left wrist with no extension to bone or osteomyelitis

DIAGNOSIS
Disseminated fusariosis

TREATMENT AND COURSE
Following identification of fungal organisms on the biopsy specimen, liposomal amphotericin B and posaconazole were administered. The cutaneous lesions and soft tissue swelling of the left wrist

quickly resolved with residual post-inflammatory hyperpigmentation. The patient's hospital course was complicated further by medication-induced acute renal failure with concomitant metabolic encephalopathy requiring intermittent dialysis, and BK (polyomavirus) viremia, viruria, and cystitis treated with intravesical cidofovir. Ultimately, the patient was discharged 12 weeks after admission on tacrolimus 1 mg p.o. BID, prednisone 10 mg daily, acyclovir 500 mg p.o. TID, atovaquone 1500 mg po daily, and voriconazole 300 mg po BID. One month following discharge, the patient was found to have significant peripheral blasts and relapse of his disease. As he was no longer a candidate for SCT, the patient, his family, and the oncologist decided to pursue palliative care. Within two months, the patient presented to the ambulatory dermatology clinic with numerous cutaneous lesions as described above, which were also determined through biopsy and tissue culture to be *Fusarium*. The patient was subsequently admitted to an outside hospital where he died from complications of refractory AML.

DISCUSSION

Fusarium species are important plant pathogens causing various diseases including crown rot and head blight. In humans, *Fusarium* species may cause superficial, locally invasive, or disseminated infections. *Fusarium solani* is the most frequent species to cause human infection, followed by *F. oxysporum*, *F. verticilliodes*, and *F. moniliforme*. Among immunocompetent hosts, keratitis and onychomycosis are the most common infections, although less frequently, the infection may occur as a result of skin breakdown from burns or wounds. Contact lenses have been linked to outbreaks of fusarial keratitis, and fusarial peritonitis has been described in patients receiving ambulatory peritoneal dialysis. Disseminated fusariosis almost exclusively affects severely immunocompromised patients, predominantly those with prolonged and profound neutropenia and/or severe T-cell immunodeficiency. In the allogeneic HSCT population, infection with *Fusarium* shows a trimodal distribution with a peak in the neutropenic early post-transplant period, a second peak at 70 days following transplant among patients with acute graft-versus-host disease (GvHD) receiving corticosteroids, and a third peak one year after transplant during treatment for chronic GvHD.

The prognosis of fusariosis in the immunocompromised host is directly related to immune status, with high death rates seen in patients with persistent immunodeficiency. Among patients with hematologic diseases, survival rates at 30 and 90 days after diagnosis are 50% and 21%, respectively. Persistent neutropenia and recent corticosteroid therapy are associated with poor outcome, and the actual survival of patients was 0% for patients with both these factors, and 4% for patients with only persistent neutropenia.

Treatment of localized infection is usually surgical debridement; disseminated infection requires the use of systemic agents and immunotherapy directed at restoring host immunity, when possible. *Fusarium* spp. are typically resistant to most antifungal agents; however, different species may have different patterns of susceptibility. *F. solani* and *F. verticillioides* are usually azole-resistant and require high-dose amphotericin B, while *F. oxyspoum* and *F. moniliforme* may be susceptible to voriconazole and posaconazole. Treatment for disseminated fusariosis is evolving as more data become available.

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

HISTORY OF PRESENT ILLNESS
A 42 year-old immunosuppressed black female presented with a 2-year history of multiple asymptomatic keratotic papules on the nose and a 7 month history of similar papules affecting the lower extremities. The lesions spontaneously healed with hyperpigmentation; however, new ones occured at different sites. A hard central core could be extruded from the papules by squeezing them. She was applying only cetaphil wash and lotion to her face.

PAST MEDICAL HISTORY
Hypertension, end-stage renal disease with renal transplant 2005, anemia, depression, hyperparathyroidism

FAMILY HISTORY/SOCIAL HISTORY
Non-contributory

MEDICATIONS
Prednisone, tacrolimus, mycofenolate mofetil, amlodipine, valsartan, tromethoprim-sulfamethoxazole, cinacalcet, multivitamin

ALLERGIES
Ace-inhibitors

PHYSICAL EXAMINATION
Multiple 1-2 mm, skin colored keratotic papules on the nose and thighs. Scattered hyperpigmented macules were present on the thighs.

HISTOPATHOLOGY
A punch biopsy of the right thigh shows skin with massively dilated follicles and proliferation of the inner root sheath cells containing large trichohyaline granules. The hair shafts have abrupt cornification with several layers of outer root sheath epithelium present in the upper half of the affected hair bulbs but absent in the lower half of the bulb. The follicular structure was no longer present on the otherwise unremarkable PAS stained sections.

LABORATORY AND RADIOLOGIC DATA
None

DIAGNOSIS
Trichodysplasia of immunosuppression

TREATMENT AND COURSE
The patient was prescribed topical adapalene 0.1% cream daily and topical azelaic acid 15% gel daily; however, she was unable to purchase the medications due to the cost. She recently noticed a reduction in skin lesions after repeatedly forgetting to take her evening dose of mycofenolate mofetil during a time period when a family member was hospitalized.

DISCUSSION
Trichodysplasia of immunosuppression (TOI) is a rare newly described clinicopathologic entity. Case reports identified as trichodysplasia spinulosa, viral-associated trichodysplasia spinulosa, pilomatrix dysplasia, and cyclosporine-induced folliculitis are likely the same condition. The first report of TOI

in 1995 was in the context of drug-induced immunosuppression in the setting of organ transplantation. It has since been described in non-transplant patients with pre-B cell leukemia, acute and chronic lymphocytic leukemia, and low-grade follicular-type non-Hodgkin's lymphoma. The pathogenesis is controversial; however, evidence suggests that chronic immunosuppression is the predisposing factor to a folliculotropic papovavirus that alters follicular differentiation.

TOI is an eruption characterized by asymptomatic or pruritic flesh-colored to erythematous follicular papules concentrated in the central part of the face. Growth of the lesions may ultimately result in a leonine facies. Spine like concretions replace hairs in the eyebrows, eyelashes and other hair-bearing areas of the face resulting in alopecia. Lesions often progress to involve the trunk and extremities. The duration of immunosuppression at the time of development of the eruption ranges from 8-48 months and lesions tend to persist in patients with ongoing immunosuppression.

The histological features are distinctive often demonstrating markedly dilated follicles, with proliferation of the inner root sheath cells containing large trichohyaline granules. The inner root sheath cells cornify abruptly with several layers of outer root sheath present only in the upper half of the bulb. The upper segment of the follicle may show a dilated, hyperkeratotic, and shaftless infundibulum. Electron microscopy performed on several biopsy specimens reveals intranuclear, icosahedral viral particles approximately 40 nm in diameter consistent with papovavirus infection. More recently, in pursuit of this unknown virus, DNA from the keratotic spines in TOI was isolated, amplified, cloned, and identified through several experiments. Genome analysis confirmed the presence of a new polyoma virus called the trichodysplasia spinulosa-associated polyomavirus (TSV). TSV shares several properties with other polyomaviruses and circulates in the human population; future studies are needed to gain insight on how TSV spreads and how it causes disease.

Treatment options remain limited. Topical cidofivir and oral valganciciclovir target the proposed causative agent. Reduction of immunosuppression is an alternative strategy. Topical keratolytics and tazarotene 0.5% gel have been found variably effective, as well. With an ever increasing number of patients receiving transplants and immunosuppressive treatment regimens, clinicians should be aware of the clinical and histopathologic characteristics of this condition.

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PRESENTERS
Shaily Patel, MD, Ingrid Polcari, MD, Vesna Petronic-Rosic, MD, MSc, Aisha Sethi, MD, Sarah L. Stein, MD

PATIENT A

HISTORY OF PRESENT ILLNESS
A 49-year-old African American female was seen for a right lower extremity cellulitis, and started on clindamycin at an outside hospital. She was also taking ibuprofen at that time as needed for pain, and denied taking any other medications. Over the next 3 to 5 days, she developed a rapidly progressing generalized skin rash in addition to acute renal failure and respiratory failure, necessitating intubation. The clindamycin was discontinued, and she was given a one time dose of vancomycin, piperacillin/tazobactam, and methylprednisolone. She was subsequently transferred to our institution for further management.

PAST MEDICAL HISTORY
Systemic lupus erythematosus, deep venous thrombosis, hypertension and migraines

FAMILY HISTORY/SOCIAL HISTORY
Non-contributory

MEDICATIONS
Vancomycin, mupirocin ointment, heparin sulfate, ferrous sulfate, midazolam, fentanyl, multivitamin, ascorbic acid, vitamin A, zinc sulfate, famotidine and lactated ringers solution

ALLERGIES
NKDA

PHYSICAL EXAMINATION
The patient was an ill-appearing woman who was intubated and sedated. Her vital signs were significant for a tachycardia, with a pulse of 115, and she was febrile to 102.9°F. She was erythrodermic with over 90% of her total body surface area involved. She had significant generalized edema, which was markedly pronounced periorally and periorbitally. Of note, her conjuctiva and mucous membranes were not involved. Over the trunk and extremities, there were numerous vesicles and flaccid bullae, some of which were turbid, along with coalescing pustules and edematous, erythematous papules. There was significant superficial desquamation of the epidermis with a fine cigarette-paper-like wrinkling. The palms and soles were clear.

DERMATOPATHOLOGY
A 4-mm punch biopsy was performed from a turbid vesicle on the left leg. This showed a subcorneal split with epidermal spongiosis and severe papillary dermal edema, leading to focal formation of subepidermal blisters. Neutrophils were found within the epidermis and in the dermal perivascular infiltrate along with some eosinophils and lymphocytes. Gram stain, periodic acid-Schiff and Gomori methenamine silver stains were negative for microorganisms.

LABORATORY DATA
Complete blood count: Leukocytes 20.8 K/µL (3.5-11), hemoglobin 9.3 g/dL (11.5-15.5), platelets 109 K/µL (150-450)
Differential: Neutrophils 93%, lymphocytes 2%, monocytes 3%, eosinophils 1%
Comprehensive metabolic panel (abnormal): Blood urea nitrogen 42 mg/dL (7-20), creatinine 3.1 mg/dL (0.5-1.4), calcium 6.6 mg/dL (8.2-10.2), total protein: 4.3 g/dL (6.0-8.3), albumin: 2.3 g/dL

Lactic acid 2.5 mEq/L (0.7-2.1), creatinine kinase 271 U/L (9-185), c-reative protien 200 mg/L (<5)
Normal: Liver transminases, hepatitis panel, amylase, lipase, RPR, and HIV 1/2 antibody
Urinalysis: 2+ proteinuria and 2+ hematuria
Urine and blood culture: No growth

DIAGNOSIS
Atypical acute generalized exanthematous pustulosis

TREATMENT AND COURSE
The patient was admitted to the burn intensive care unit for meticulous skin care and daily dressing changes. Mupirocin ointment was applied to open erosions, and covered in petrolatum gauze. Acticoat dressings (silver coated, high-density polyethylene mesh) were used on the trunk and extremities and subsequently wrapped in gauze. Over the course of two weeks, her skin dramatically improved with complete resolution.

Her hospital course was complicated by septic shock, for which she was treated with broad-sprectrum antibiotics including: vancomycin, imipenem/cilastatin, linezolid, metronidazole and micafungin. She was maintained on systemic corticosteroids throughout her stay, which were slowly tapered off over the course of a month. For her acute renal failure, she required hemodialysis, but eventually regained normal renal function. She also developed acute respiratory distress syndrome (ARDS), necessitating ventilation for the majority of her hospitalization; however, she was successfully extubated by the end of her stay. She was transferred to a rehabilitation facility almost one month after admission, and subsequently discharged home. Clindamycin was presumed to be the causative medication.

PATIENT B

HISTORY OF PRESENT ILLNESS
A 13-year old previously healthy African American female was treated for an abscess and cellulitis of her left shin with cephelexin and trimethoprim-sulfamethoxazole at an outside hospital. After three days, she developed myalgias, headaches, nausea, diarrhea and weakness and so discontinued the antibiotics. Her constitutional symptoms resolved over the course of one week and she resumed the antibiotics to complete the prescribed course. Five days later she developed significant swelling, most notable on her face, and a rash on her trunk and upper extremities. She was seen at an outside hospital and was given ceftriaxone, vancomycin, methylprednisolone, and diphenhydramine and transferred to our institution for further evaluation and management.

PAST MEDICAL HISTORY
None

FAMILY HISTORY/SOCIAL HISTORY
Non-contributory

MEDICATIONS
Diphenhydramine, acetaminophen, hydroxyzine, aquaphor ointment, and trimacinolone 0.1% ointment

ALLERGIES
NKDA

PHYSICAL EXAMINATION
The patient was in no acute distress with normal vital signs. She had diffuse edema, most notable periorbitally and on her face. There was no involvement of her conjuctiva or other mucous

membranes. She was erythrodermic and had numerous confluent vesicles and tense bullae, particularly over her extremites. Some pustules were noted on her face, along with turbid vesicles on her trunk and extremities. Superficial desquamation was also present on the trunk.

DERMATOPATHOLOGY

A 4-mm punch biopsy was performed from a vesicle on her right arm that revealed extensive epidermal spongiosis with neutrophils. There was increased papillary dermal edema with focal subepidermal blisters. The dermis had a superficial and deep perivascular infiltrate of neutrophils and lymphocytes. Two additional 4-mm punch biopsies were obtained for immunofluorescence and tissue culture, both of which were negative. A second 4-mm punch biopsy obtained 9 days later from the left thigh demonstrated subcorneal collections of neutrophils with epidermal spongiosis. The dermis had a superficial perivascular and interstitial infiltrate of lymphocytes and occasional eosinophils.

LABORATORY DATA

Complete blood count: Leukocytes 28.3 K/μL (3.5-11), hemoglobin 11.4 g/dL (11.5-15.5), platelets 184 K/μL (150-450)
Differential: Neutrophils 48%, lymphocytes 35%, monocytes 8%
Comprehensive metabolic panel (abnormal): Calcium 7.6 mg/dL (8.4-10.2), total protein 5.4 g/dL (6-8.3), albumin 2.5 g/dL (3.5-5), AST 85 U/L (8-37), ALT 68 U/L (8-35), alkaline phosphatase 45 U/L (100-390)
Antinuclear antibody titer: 2560, speckled (0-80), C-reative protien 10 mg/L (<5)
Normal: Anti-DNA doublestranded antibody, Ss-A/ Ss-B antibodies, complement, rheumatoid factor
Blood culture: No growth

DIAGNOSIS

Atypical acute generalized exanthematous pustulosis

TREATMENT AND COURSE

The patient's rash evolved over the first few days, with increased bullae and some new pustule formation on the thighs. Her skin was treated with Aquaphor ointment and petrolatum gauze dressings. The rash improved and the patient was discharged after 8 days. However, she returned to the emergency room 4 days later with increased skin weeping and pain. She was taking diphenhydramine and acetaminophen as needed at home. Given the extent of skin involvement, she was admitted to the burn intensive care unit. In addition, she was started on prednisone (1mg/kg/day) for 5 days, which was followed by a slow taper over 4 weeks. Her skin improved dramatically during her hospitalization with complete resolution of bullae and pustules upon discharge. Based on the time course and medication history, acetaminophen was presumed to be the causative agent, rather than the antibiotics.

DISCUSSION

Acute generalized exanthematous pustulosis is a rare and severe acute febrile hypersensitivity reaction, attributed to medications over 90% of the time. Typically, the time between drug administration and onset of the eruption is short, within 1-2 days, suggesting an immunologic recall phenomenon in patients with prior sensitization.

Clinically, patients present with a high fever, and an eruption that begins on the face and intertriginous zones, with subsequent dissemination to the trunk and extremities within hours. Classically, there are numerous non-follicular, sterile, <5 mm pustules arising within areas of edematous erythema. Significant edema of the face and hands, purpura, vesicles, bullae, erythema multiforme-like lesions and mucous membrane involvment have also been described in a fraction of the cases.

Histologically, there are subcorneal collections of neutrophils in the epidermis along with papillary dermal edema. Usually there is a perivascular mixed infiltrate of neutrophils, lymphocytes and eosinophils in the dermis. Laboratory work-up may reveal a marked leukocytosis with elevated neutrophils. Additionally, eosinophilia, transient renal dysfunction and hypocalcemia may be seen.

Antibiotics are most commonly implicated, with beta-lactam antibiotics and macrolides the most frequently reported. Rarely, clindamycin and acetaminophen have been reported as causative agents in a handful of cases, as was presumed to be the case in the above patients, respectively.

As the eruption tends to be self-limiting, and typically resolves with generalized desquamation within 1-2 weeks, withdrawal of the causative agent along with supportive care is the mainstay of therapy. Systemic corticosteroids have been used; however, in small retrospective case studies, it was not shown to be statistically significant in impacting the course or duration of the disease.

We describe the cases above to highlight the atypical presentation of acute generalized exanthematous pustulosis. Both cases have a more prolonged time frame from medication exposure to rash evolution of around 5 to 10 days. In addition, rather than presenting with the classic non-follicular sterile pustular eruption, both presented with extensive edema, erythroderma, bullae, and epidermal sloughing, reminiscent of toxic epidermal necrolysis or staphylococcal scalded skin syndrome. Histopathologic evaluation revealed many parallels between these two cases with marked papillary dermal edema leading to subepidermal vesicle formation, rather than multiple subcorneal collections of neutrophils as is characteristically described. Interestingly, patient A had a known history of lupus and patient B had a significantly elevated antinuclear antibody titer at 1:2560, perhaps suggesting an underlying role of autoimmune disorders and a predisposition to developing a severe drug hypersensitivity reaction. Thus, even with atypical presentations, acute generalized exanthematous pustulosis should be considered in the differential diagnosis for an acute febrile drug eruption.

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PRESENTERS
Edi Kaminska, MD, Carloz Paz, MD, PhD, Christopher R. Shea, MD, Aisha Sethi, MD

HISTORY OF PRESENT ILLNESS
A 19-year-old female college student presented for evaluation of ulcers on the back of the right leg for 1-2 months. The lesion started as an itchy papule followed by small blisters that burst and released a purulent fluid, then later crusted over and became painful and itchy. She was treated with topical clindamycin solution and mupirocin with no improvement. She reported recent travel to Senegal for three weeks, where she slept outdoors and bathed in a well. She denied any history of an animal or insect bite.

PAST MEDICAL HISTORY
Migraines

SOCIAL HISTORY
College student who traveled frequently.

MEDICATIONS
Clindamycin, mupirocin, sumatriptan (intermittently), OFF insect spray

ALLERGIES
NKDA

REVIEW OF SYSTEMS
Fever for 1-2 days and mild nausea.

PHYSICAL EXAMINATION
The patient was a well-appearing 19-year-old female in no distress. On the posterior right leg there were multiple crusted erosions with surrounding erythema, and one intact vesicle. There was no palpable cervical or axillary lymphadenopathy. The patient declined a total body skin exam. At follow up seven days later, there was a large bulla at the biopsy site and an adjacent erythematous, serpiginous plaque that was 2-3 mm wide and 3-4 cm long.

DERMATOPATHOLOGY
A 4-mm punch biopsy specimen of the lesion revealed surface crust and parakeratosis including fibrin deposits. The papillary dermis was edematous. There was a superficial and deep perivascular infiltrate of lymphocytes and numerous eosinophils throughout the dermis, with focal extension into the superficial subcutaneous tissue. The periodic acid-Schiff stain was negative for fungi or significant basement membrane thickening. The Gram stain was negative for bacteria.

LABORATORY AND ANCILLARY DATA
A 4-mm punch biopsy specimen was sent for the following tests:
Gram Stain: Rare white blood cells; sparse unidentifiable debris; no organisms seen.
Bacterial Culture: No growth.
Fungal Smear: No fungi seen on direct smear.
Fungal Culture: No growth at 28 days.
AFB Smear: No acid-fast bacilli seen.
AFB Culture: No growth at 56 days.
Parasitic Culture (leishmaniasis): No parasites seen.

DIAGNOSIS
Cutaneous larva migrans

TREATMENT AND COURSE

The patient was treated with a single dose of ivermectin 12 mg po, along with topical mupirocin and xeroform gauze bid. Two weeks later, the patient reported that the pain and pruritus had resolved. Exam was significant for a serpiginous arrangement of scales and few crusted erosions with surrounding erythema. The patient was instructed to apply polysporin ointment to the area daily for one week and to follow-up as needed.

DISCUSSION

Cutaneous larva migrans (CLM, "creeping eruption") is a parasitosis caused by penetration and migration of the larvae of dog or cat hookworms, most commonly *Ancylostoma canium* and *Ancylostoma braziliense*. It is one of the most frequent skin diseases aquired by travelers returning from the tropics. Initially, the classic presentation is that of a papule appearing hours after penetration, followed 4-6 days later by an erythematous, 2-4 mm wide, migratory, serpiginous plaque. However, atypical manifestations such as folliculitis, tinea pedis, hives, impetigo, and vesiculobullous reactions may occur. Interestingly, untreated the condition can last for up to two years, and incubation periods up to seven months prior to any symptoms have been reported. Although the disease is usually self-limited and lesions spontaneously resolve within weeks to months, patients report severe pruritus and complications may occur such as secondary bacterial infections, erythema multiforme, and Löffler syndrome.

The life cycle of the nematode involves egg, larval, and adult stages. The adult parasite lays eggs in the gastrointestinal tract of the dog or cat host. The eggs pass through the feces and the larvae hatch and become infective in the soil (filiform larvae). Access to a definitive host is commonly through skin penetration. Humans are not the normal host of the parasites and although the larvae are able to enter the epidermis, they are usually unable to penetrate the dermoepidermal junction and move deeper. The larvae migrate millimeters to centimeters daily, causing the characteristic eruption, until they die or are eradicated by medical therapy. The least invasive and most efficacious treatments for CLM are either oral thiabendazole (50 mg/kg, not to exceed 3 g/day for 3-4 days), albendazole (400 mg/day for 3-5 days), or ivermectin (12 mg in adults or 150 microg/kg in children, administered as a single dose).

CLM is a common dermatosis in tropical countries and should be suspected with patients presenting with severely pruritic lesions and a recent history of travel to the tropics. As exemplified in our case, an atypical presentation does not exclude CLM because classic lesions may have a delayed onset. A thorough history, physical examination, and appropriate follow-up are essential for establishing the diagnosis.

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PRESENTERS
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PATIENT A

HISTORY OF PRESENT ILLNESS
A 33-year-old white female with metastatic colon cancer presented with a one-month history of a firm, painful, tender, intermittently bleeding nodule on the scalp.

PAST MEDICAL HISTORY
Colon cancer metastatic to ovaries, treated with sigmoidectomy, total abdominal hysterectomy and salpingo-oöphorectomy, chemotherapy, and radiation therapy.

FAMILY HISTORY
Father with celiac disease, maternal grandfather with colon cancer

MEDICATIONS
Conjugated estrogens, metaxalone, metoprolol, doxycycline, multivitamin, zolpidem

PHYSICAL EXAMINATION
Well-appearing female with a 2.5 x 2.5 cm firm nodule with overlying central crust on posterior scalp.

DERMATOPATHOLOGY
Sections are of skin with epidermal hyperplasia and erosion. Within the dermis there are numerous glandular structures composed of cuboidal and many columnar cells, with central necrosis. Mitotic figures and high-grade cytologic atypia are evident. The stroma is densely fibrotic.

LABORATORY DATA
Complete blood count: Leukocytes 4.6 K/μL (3.5-11), hemoglobin 12.2 g/dL (11.5-15.5g/dL), platelets 116 K/μL (150-450)
Differential: Neutrophils 68%, lymphocytes 20%, monocytes 10%, eosinophils 1%, bands 1%

DIAGNOSIS
Metastatic Colonic Carcinoma

TREATMENT AND COURSE
The patient was treated with topical mupirocin and oral cephalexin. She received radiation therapy to her scalp and lungs for multiple metastases and received sunitinib and cilengitide in a clinical trial.

PATIENT B

HISTORY OF PRESENT ILLNESS
A 67-year-old white male with a history of prostate cancer presented with a plaque of the right medial thigh present for months.

PAST MEDICAL HISTORY
Metastatic, castration-resistant prostate cancer

FAMILY HISTORY
Uncle with testicular cancer, paternal grandfather with prostate cancer

MEDICATIONS
Oxacillin, nystatin, ondansetron, ergocalciferol, acetaminophen.

ALLERGIES
Sulfa

PHYSICAL EXAMINATION
Fatigued-appearing man with a large, exophytic plaque on the right lower extremity, composed of confluent, firm, pink papules with yellow crust.

DERMATOPATHOLOGY
Outside hospital report- pathology consistent with metastatic prostatic carcinoma

DIAGNOSIS
Metastatic Prostatic Carcinoma

TREATMENT AND COURSE
The patient had already received radiation therapy to this lesion without resolution. He was treated for methicillin-sensitive *Staphylococcus aureus* bacteremia with intraveneous antibiotics and discharged to a rehabilitation facility, where he died soon thereafter.

PATIENT C

HISTORY OF PRESENT ILLNESS
A 22-year-old female with metastatic poorly differentiated ovarian carcinoma presented with new nodules on her scalp.

PAST MEDICAL HISTORY
Ovarian cancer that had metastasized to the brain, spine and lungs, treated with total abdominal hysterectomy and salpingo-oöphorectomy, chemotherapy and radiation therapy.

FAMILY HISTORY
Paternal and maternal grandfather with prostate cancer, grandmother with melanoma.

MEDICATIONS
Conjugated estrogens, acyclovir, dexamethasone, fentanyl, fluconazole, hydromorphone, pregabalin, topiramate

ALLERGIES
Cefaclor, morphine, celecoxib

PHYSICAL EXAMINATION
Comfortable appearing young woman with multiple, firm, pink nodules with overlying telangiectases and serous central crust on the scalp and chest.

DERMATOPATHOLOGY
Sections are of skin with focal epidermal erosion. Within the dermis is an extensive infiltration by atypical epithelial-type cells in cords and strands. Lumen formation is noted. High-grade cytologic atypia and mitotic figures are identified. There is extensive necrosis in the lower portion of the specimen. This biopsy shows a similar histologic pattern when compared to the previously diagnosed poorly differentiated carcinoma of müllerian origin from the same patient.

LABORATORY DATA
Complete blood count: Leukocytes 6.7 K/μL (3.5-11), hemoglobin 12.1 g/dL (11.5-15.5g/dL), platelets 78 K/μL (150-450)
Differential: Neutrophils 95%, lymphocytes 2%, monocytes 2%, 1% myelocytes
Ca-125 = 72U/ml (nl <35U/ml)

DIAGNOSIS
Metastatic Poorly Differentiated Ovarian Carcinoma of Müllerian origin

TREATMENT AND COURSE
The patient had undergone multiple surgeries and rounds of chemotherapy and radiation therapy. She died shortly after confirmation of cutaneous metastases.

PATIENT D

HISTORY OF PRESENT ILLNESS
58-year-old male with a history of leiomyosarcoma of left kidney presented with nodules on the scalp.

PAST MEDICAL HISTORY
Leiomyosarcoma
Chronic myeloid leukemia

FAMILY HISTORY
Father with prostate and colon cancer
Sister with breast cancer

MEDICATIONS
Imatinib, gemcitabine

PHYSICAL EXAMINATION
Well-appearing man with four firm, smooth, mobile nodules on the posterior scalp measuring 1-2 cm in diameter.

DERMATOPATHOLOGY
Sections show fascicles of atypical spindle cells with nuclear pleomorphism and numerous mitotic figures.

LABORATORY DATA
Complete blood count: Leukocytes 4.1 K/μL (3.5-11), hemoglobin 11.3 g/dL (13.5-17.5g/dL), platelets 419 K/μL (150-450)
Differential: Neutrophils 61%, lymphocytes 13%, monocytes 24%, eosinophils 1%, basophils 1%

DIAGNOSIS
Metastatic Leiomyosarcoma

TREATMENT AND COURSE
The patient was continued on imatinib and gemcitabine but died of the cancer.

DISCUSSION
Cutaneous metastases from internal malignancies are rare. The published data on rates of metastasis to the skin are limited and come mainly from retrospective studies based on autopsies. The reported

rates of cutaneous metastases in patients with known metastatic disease range from 0.7 to 10% though a recent meta-analysis places the number closer to 5% after excluding melanoma, leukemia, and lymphoma.

Cutaneous manifestations of visceral malignancy often occur late in the disease process and confer a poor prognosis. Survival from the time of identification of skin metastases averages 3 to 12 months. In some cases, however, skin lesions can be the first sign of underlying cancer. Metastases may occur by three routes: hematogenous, lymphatic, and direct extension. They are most often located in the anatomic vicinity of the primary cancer, though some malignancies may metastasize to distant cutaneous sites. Metastases to the skin do not have a unique clinical appearance, but are often firm, cutaneous or subcutaneous nodules, flesh-colored to violaceous, and may ulcerate.

Breast cancer is the most common internal malignancy to metastasize to the skin in women, with a reported incidence as high as 30% of cases of cutaneous metastases. Lung cancers make up the majority of non-melanoma cutaneous metastases in men. The most common sites of metastasis include chest and abdominal wall whereas the least common areas are the face and scalp. Colorectal and ovarian cancer both account for ~ 4% of skin metastases. Prostate cancer, although very prevalent in the population, makes up only 0.7% of cases of cutaneous metastatic disease. Sarcomas make up 2-3% of the cutaneous metastases observed; however only 16 cases of leiomyosarcoma metastasizing to the skin have been reported in the literature.

In our series of patients, we have included four cases of malignancy that are rarely reported to metastasize to the skin: colon cancer, ovarian cancer, prostate cancer and leiomyosarcoma. Of note, in three of our four cases the scalp was the site of metastasis; however metastasis to the scalp is generally an uncommon event, representing only about 7% of reported cutaneous metastases. The cancers most often reported to metastasize to the scalp are lung, breast, and renal carcinomas.

Cutaneous lesions may be the first clue that a patient has an underlying metastatic malignancy. Identifying these lesions early by completing a thorough examination of the skin, including the scalp, may prompt more aggressive therapy and potentially lead to prolonged life expectancy.

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PRESENTERS
Brian E. Pucevich, MD, John Fox, MD, Sarah L. Stein, MD

HISTORY OF PRESENT ILLNESS
A 2 year old female presented for evaluation of abnormal toenails. The parents recall that since shortly after birth the left 4th toenail has seemed to curve under the toe. They also feel that all of the toenails of the right foot are "abnormal". The patient's mother states that she thinks she has similar abnormalities of her toenails.

PAST MEDICAL HISTORY
Patient was born at term via normal spontaneous vaginal delivery.

FAMILY HISTORY
Abnormal curvature of toenails in patient's mother, maternal aunt and one female cousin.

SOCIAL HISTORY
Non-contributory

MEDICATIONS
None

ALLERGIES
NKDA

PHYSICAL EXAMINATION
Accentuated dorsal to plantar curvature of several toenails. Changes most notable on 2nd, 3rd, and 4th digits bilaterally. Hypoplasia of the pulp of the distal 4th phalanges with firm, non-tender, subungual projections on the 4th digits of both feet. There were no noted abnormalities of the fingernails. Examination of the mother's feet demonstrated similar curvature of the toenails as well as a shortening of her 2nd right toe.

RADIOLOGY
Hypoplasia of the distal phalanges is noted bilaterally. No bone destruction or exostosis is present.

DIAGNOSIS
Congenital curved nail of the fourth toe

TREATMENT AND COURSE
Carmol 40 cream was recommended to soften the nails and surrounding skin and to facilitate nail trimming.

DISCUSSION
Congenital curvature of the fourth toe (OMIM 219070) is a rare condition observed and documented in both the dermatology and plastic surgery literature. It is believed to be expressed in an autosomal recessive fashion and as of yet not associated with any underlying abnormality or other disorders.

The first case was reported in 1977 by Egawa. Egawa described two siblings, one of whom had bilateral deformity of the fourth toes with decrease in soft tissue of the distal phalanges and curving of the overlying nails, these changes were most pronounced on the 4th toe but present on the 2nd and 3rd toes as well. The other sibling in Egawa's report had changes of the fifth finger bilaterally. These changes included shortening of the digits and loss of soft tissue of the distal phalanges. The fifth

fingernails were described as horizontally curved in a tubular fashion. No underlying or associated abnormalities were noted. Subsequent reports have demonstrated a uniform phenotype of hypoplasia of the distal phalanx of the toe with curving of the overlying nail plate towards the plantar surface, typically occurring in a bilateral fashion. Additional anomalies have been reported rarely and include duplication of the right thumb in one case, and a cleft lip and palate in a second case. Radiographic findings have ranged from no underlying abnormality to the presence of bony symphalangism (fusion of the distal two phalangeal bones of the affected digit. Chromosomal analysis when performed failed to exhibit any identifiable abnormality.

In Egawa's original cases surgery was performed for cosmesis. Incision and advancement of the normal volar surface of the affected distal phalanx to achieve approximation with the hyponychium was followed by full-thickness skin grafting to cover the proximal defect. More recent management recommendations have ranged from observation to conservative use of humectants such as 40% urea in an attempt to soften the keratotic plaque which tethers the affected nail.

Several diagnoses may be considered when evaluating curved nails. Pterygium inversum unguis is generally considered to involve the fingernails, but has been rarely described affecting toenails. Reports of this entity suggest very similar features as congenital curved nail of the 4th toe. It is characterized by hyperplasia of the hyponychium which anchors the distal nail plate causing increased ventral curvature of the nail. A case originally published as pterygium inversum of the toes by Nogita et. al in 1991, described a 6 year old girl with involvement of both 4th toenails since birth with similar finding in the patient's mother. This case may be better classified as congenital curved nail of the 4th toe as Iwasawa described in his paper, also published in 1991. Congenital claw-like fingers and toes is a condition in which the curvature of the nails is secondary to the loss of tissue of the distal digits. Parrot beak nail is a condition where only the distal free margin of the nails exhibits over curvature. This curvature improves with soaking of the nails. Acquired curvature of the nails can be the result of repetitive trauma or prior surgical manipulation.

The clinical and radiological features of our case are consistent with previous descriptions of this rare entity termed congenital curved nail of the fourth toe. The inheritance in this family suggests an autosomal dominant variant. The finding of the shortened 2nd toe observed in our patient's mother, in conjunction with the characteristic changes in the 4th toe, has not been previously described.

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PRESENTERS
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HISTORY OF PRESENT ILLNESS
A 70-year-old African American female with no significant past medical history, presented with a two-year history of a pruritic facial rash, which had started on the nose, then spread to both cheeks. The patient reported intermittent shortness of breath during the previous two years, which had significantly improved by the time of this visit. She also complained of swelling of both wrists, without associated pain or morning stiffness.

PAST MEDICAL HISTORY
None

MEDICATIONS
None

ALLERGIES
NKDA

PHYSICAL EXAMINATION
A well-demarcated, violaceous, indurated plaque extended across the bridge of the nose to both cheeks. A similar, 3 x 4 cm, well-circumscribed plaque was noted on the right forehead. A 0.8 x 1 cm, solitary, violaceous, dome-shaped papule was noted on the right distal nasal ala. Swelling of both wrists and several fingers was noted, without overlying skin changes.

DERMATOPATHOLOGY
A 4 mm punch biopsy specimen from the right cheek was obtained for histopathology and mycobacterial culture. H&E revealed abundant epithelioid histiocytes and multinucleated giant cells with a sparse lymphocytic infiltrate in the dermis. Observation with polarized light was negative for birefringent foreign material. The GMS, AFB and Fite stains were negative for microorganisms.

LABORATORY DATA AND IMAGING
Complete blood count: normal
Comprehensive metabolic panel: carbon dioxide 31 mEq/L (23-30), otherwise normal
Angiotensin converting enzyme level**:** 67.5 U/L (8-52)
Pulmonary function tests: decreased diffusing capacity (68% predicted); otherwise normal.
Microbiology: Mycobacterial culture was negative

Chest X-Ray PA/Lateral**:** Minimal left hilar prominence. No significant pulmonary or pleural abnormality.
XR of right hand and wrist: Lacelike erosion of the distal ulna extending from the styloid process approximately 6-7 cm into the diaphysis, with associated soft tissue swelling; lacelike trabeculation in the middle phalanx of the ring finger and proximal phalanx of the fifth finger with soft tissue swelling, and focal lucency in the soft tissues of the tip of the thumb, suggestive of a small ulceration.
XR of left hand and wrist: Lacelike erosion of the distal ulna extending from the styloid process proximally 5-6 cm into the diaphysis, with associated soft tissue swelling. No lesions were seen within the bones of the hands.

DIAGNOSIS
Cutaneous sarcoidosis with osteitis cystoides multiplex Jüngling

TREATMENT AND COURSE

The patient was prescribed Lidex 0.05% cream and Protopic 0.1% ointment to apply to her face. Several attempts to place a PPD were unsuccessful since the patient could not come back in time for a PPD reading. The patient was referred to rheumatology for further evaluation given the radiographic evidence of osseous sarcoidosis, and to pulmonology given the slightly abnormal PFT findings. In consultation with rheumatology, the decision was made to pursue a symptom-directed therapy. Plaquenil 200 mg daily was recommended to control the cutaneous sarcoidal granulomas; however, the patient opted to use topical medications only. Skin lesions improved within 2 weeks of starting topical therapy.

DISCUSSION

Sarcoidosis results in non-caseating granulomas in multiple organ systems, including the lungs, skin, lymph nodes, liver, musculoskeletal system and CNS. Cutaneous sarcoidosis affects anywhere from 9 to 37% of patients with sarcoidosis. The two most distinctive cutaneous manifestations of sarcoidosis are erythema nodosum and lupus pernio. Erythema nodosum, the hallmark of acute sarcoidosis, is characterized by tender, erythematous nodules, predominatly on the anterior aspect of the lower extremities, which resolve without significant scarring. Lupus pernio, the hallmark of chronic sarcoidosis, is characterized by violaceous papules and nodules that tend to coalesce to plaques, distributed primarily on nasal alae, cheeks, lips and ears. These are typically associated with a prolonged course and scarring.

Osseous sarcoidosis occurs in about 5% of patients with sarcoidosis. The prevalence of sarcoid bone involvement is as high as 50% in patients with concurrent chronic cutaneous sarcoidosis. Osseous sarcoidosis affects mainly the hands and feet, but rarely can affect the axial skeleton. In the hands, the middle and distal phalanges are more frequently involved than the proximal phalanges or metacarpals. The characteristic radiographic features are an abnormal trabecular lace-like pattern of destruction, lytic lesions of the cortex or larger punched-out defects of both cortex and medulla which take the appearance of cysts when they heal, hence the term osteitis cystoides multiplex Jüngling. If the wrist is involved, cystic changes and lytic lesions may be present. Periosteum is preserved and periosteal reaction is uncommon. Occasionally, there may be soft tissue swelling. Extraosseous calcification is absent and joint spaces are usually spared.

The treatment of osteitis cystoides multiplex remains controversial. It responds poorly to corticosteroids and other drugs used in treating sarcoidosis. Corticosteroids decrease pain and soft tissue swelling, but do not completely normalize bone abnormalities. Furthermore, they increase the risk of osteoporosis, fractures and avascular necrosis. Colchicine, indomethacin and other NSAIDs may be used for symptomatic relief.

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PRESENTERS
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HISTORY OF PRESENT ILLNESS
A 45-year-old Caucasian female presented with an exophytic, macerated, red tumor on the right heel. The lesion had been steadily growing in size over the past three years and was exquisitely tender. Biopsy of this tumor at an outside institution had established a diagnosis of clear cell acanthoma. The patient was treating the lesion with a topical antibiotic without effect. On review of systems, the patient denied fevers, chills, or weight-loss.

PAST MEDICAL HISTORY
Bronchiolitis obliterans organizing pneumonia, idiopathic CD4 lymphopenia, vulvar cancer, thyroidectomy

FAMILY HISTORY/SOCIAL HISTORY
Non-contributory

MEDICATIONS
Prednisone, trimethoprim and sulfamethoxazole, fluconazole, valacyclovir, levothyroxine, inhaled mometasone, and inhaled albuterol.

ALLERGIES
Vancomycin

PHYSICAL EXAMINATION
On the right heel, there was a well-circumscribed, macerated, red, exophytic tumor approximately 4cm in diameter

LABORATORY STUDIES
A complete blood cell count and comprehensive metabolic panel were within normal limits.

DERMATOPATHOLOGY
Within a hyperplastic epidermis were increased numbers of basaloid cuboidal cells and eccrine-type ductules. There was cytologic atypia with numerous mitotic figures throughout the neoplasm. No vascular or perineural invasion was noted and the lesion was completely excised.

IMAGING STUDIES
CT scan of the chest, abdomen and pelvis was unremarkable. There was no evidence of metastatic disease.

DIAGNOSIS
Porocarcinoma

TREATMENT AND COURSE
The lesion was excised with 0.5 cm margins and the wound allowed to heal by second intention. A CT scan of the chest, abdomen and pelvis, to evaluate for lymphandenopathy and metastases, was unremarkable.

DISCUSSION
First described in 1963 by Pinkus and Mehregen, eccrine porocarcinoma is a rare malignant neoplasm arising from the intraepidermal portion of the eccrine duct. Porocarcinomas present as moist, red,

exophytic tumors usually on the lower extremities (50%), head and neck (20%), and rarely on the palms and soles. Porocarcinomas have no gender predilection. As is the case for most carcinomas, the elderly are more often affected, with an average age of diagnosis between 50 and 80 years. The average size of the tumor at presentation is typically 2-3 cm and up to four years may elapse between lesion onset and treatment. This interval between onset and treatment probably stems from the insidious nature of the condition and/or its development from preexisting lesions. Porocarinomas can arise de novo or in association with benign adnexal neoplasms (usually eccrine poromas) and typically manifest as an increase in size and tenderness. Porocarcinomas have metastatic rates of up to 20%. Once metastasized, prognosis is poor with a mortality rates reaching 80%. If clinically indicated, imaging to rule out metastases is generally recommended.

Histologically, porocarcinomas have nests and/or chords of neoplastic cells showing squamous, basaloid, or mixed features. Acrosyringeal differentiation is a prominent feature, characterized by the presence of multiple lumina with a cuticular border. However, because porocarcinomas can display a wide variety of histologic patterns, diagnostic error is a concern. In a large case series, mitoses, lymphovascular invasion, tumor depth >7mm emerged as important prognostic indicators. The presence of necrosis and clinical tumor diameter had no significant relationship to prognosis while an "infiltrative" tumor margin had a dramatic influence on tumor recurrence. Thus, it is generally recommended that the aforementioned parameters be evaluated when examining these tumors. There are no strict management criteria. In most cases, conservative excision with follow-up to monitor for recurrence is appropriate.

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PRESENTERS
Ingrid Polcari, MD, Christopher R. Shea, MD, and Sarah L. Stein, MD

HISTORY OF PRESENT ILLNESS
A three-week-old healthy female infant presented with a one-week history of a lesion on her scalp. It was first felt by the parents as a hard "knot" under the skin and was not visible. A few days later the parents noted crusting and some drainage over the bump. The infant did not seem bothered by this lesion. She had been afebrile and feeding well. Her pediatrician had seen her five days prior, sent a bacterial culture, and given an empiric 10-day course of cephalexin.

PAST MEDICAL HISTORY
The infant was born at 39 weeks via vaginal delivery. An external version procedure was performed prior to delivery due to breech positioning. Extraction at delivery was somewhat complicated but instrumentation was not necessary. Apgar scores were 8 and 9.

FAMILY HISTORY/SOCIAL HISTORY
Non-contributory

MEDICATIONS
Cephalexin

PHYSICAL EXAMINATION
The left occipital scalp had a three-cm, brown, crusted plaque with overlying yellow, moist exudate. Debridement revealed an ulcer with rolled borders, granulation tissue at the base, and white debris. There was no lymphadenopathy and the remainder of the skin examination was unremarkable.

DERMATOPATHOLOGY
A punch biopsy of the plaque and the underlying ulcer showed extensive coagulative necrosis of the epidermis, dermis, and subcutaneous tissue, including cutaneous adnexa. Within the superficial and deep dermis and extending through the subcutaneous tissue, adipocytes contained crystalline cleft-like structures. Many of the structures were surrounded and engulfed by multinucleated giant cells. Infiltrates of lymphocytes, neutrophils, eosinophils, and plasma cells were present.

DIAGNOSIS
Ulcerated subcutaneous fat necrosis of the newborn

LABORATORY DATA
Wound drainage culture: mixed flora
Tissue culture (bacterial): many coagulase-negative *Staphylococci* and many *Enterobacter cloacae*
7/22 Ionized calcium: 5.51 mg/dL (4.6-5.4)
8/3 Ionized calcium: 5.72 mg/dL, calcium 10.4 mg/dL (8.4-10.2)
8/9 Ionized calcium 5.85 mg/dL, calcium 11.4 mg/dL; albumin 4.2 g/dL (3.5-5)
9/8 Ionized calcium 5.74 mg/dL, calcium 10.8 mg/dL; albumin 4.2 g/dL

TREATMENT AND COURSE
After tissue culture results were received, gentamicin ointment was used twice daily on the base of the ulcer along with gauze dressings. At follow-up appointments one and three weeks later, the ulcer was noted to be getting progressively smaller in diameter and to be healing in from the base.
Calcium levels were drawn at the time of diagnosis and were noted to be elevated. Dietary calcium restriction was not possible given that the infant was exclusively formula-fed, so she was monitored closely by the parents and the pediatrician for signs and symptoms of hypercalcemia. The infant has

remained vigorous and without irritability or lethargy. We plan to monitor calcium levels until they return to normal.

DISCUSSION

Subcutaneous fat necrosis of the newborn (SCFN) is a rare type of panniculitis that occurs in full-term infants during the first few days or weeks of life. Typical lesions consist of variably erythematous to violaceous indurated plaques or subcutaneous nodules. The back, shoulders, arms, buttocks, thighs, and cheeks are classically affected. Scalp involvement is uncommon. Diagnosis is confirmed by the histopathologic finding of necrotic fat lobules with needle-shaped clefts. The etiology of SCFN is unknown but often a perinatal complication, ranging from trauma during labor to perinatal asphyxia, is present in affected patients. A leading theory is that "cold stress" as a result of ischemic injury, hypoxia or hypothermia is the common factor, resulting in solidification and crystallization of neonatal fat. The greater ratio of saturated to unsaturated fats in infancy translates to a higher melting point and an increased tendency for fat to crystallize.

Unlike other types of panniculitis (infectious, alpha-1-antitrypsin, pancreatic, etc.) SCFN does not typically ulcerate. There are only two reports of ulcerated SCFN in the literature. Both of these cases describe patients who had ulcers on the extremities noted from birth

SCFN, whether ulcerated or not, carries a risk of associated metabolic complications, in particular hypercalcemia. Various hypotheses have been offered for the mechanism of hypercalcemia in this condition. The most widely accepted explanation is that macrophages in the necrotic fat lobules produce 1,25-dihydroxy-vitamin D3, which increases intestinal calcium uptake. Mild hypercalcemia is asymptomatic, whereas severe hypercalcemia puts children at risk for cardiac arrest and renal failure in the short term, and visceral and cerebral calcifications and failure to thrive in the long term. The onset of hypercalcemia is often delayed and corresponds to the resolution phase of the lesions. In our patient the peak of hypercalcemia was present about one month after diagnosis and calcium levels were still elevated one month later. This highlights the importance of monitoring calcium levels for several months after diagnosis.

Management of hypercalcemia typically includes instruction to limit dietary intake of calcium. Since most infants are fed exclusively on breast milk or formula until at least four months of age, dietary reduction of calcium is not possible in this population. The dilution of milk or formula is strongly discouraged due to the risk of hyponatremia. Therefore, in cases of mild hypercalcemia clinicians must educate parents to observe their infant for lethargy, irritability, hypotonia, polyuria, and polydypsia, which could indicate a rising calcium level and need for intervention. In critical cases of hypercalcemia, treatments may include administration of intravenous fluids and calcium-wasting diuretics in an inpatient setting.

Treatment of typical SCFN lesions is usually not required since they resolve spontaneously over several weeks. However, if ulceration is present, surgical intervention with grafts or flaps may be necessary. Our patient was successfully managed conservatively with local wound care.

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PRESENTERS
Shani Francis, MD, Vivek Iyengar, MD

HISTORY OR PRESENT ILLNESS
A 56-year-old African-American woman presented to clinic with a one month history of peeling hands and feet. This scaly eruption was gradual in onset and associated with occasional 10/10 pain, worse with applying pressure, unrelieved with twice daily application of Betamethasone valerate 0.1% cream. She denied any constitutional symptoms

PAST MEDICAL HISTORY
Diabetes, hypertension, GERD, obstructive sleep apnea, asthma, obesity

FAMILY HISTORY
Negative for psoriasis. Positive for colon cancer, maternal grandmother and rheumatoid arthritis, mother.

SOCIAL HISTORY
Positive for tobacco and alcohol. She denies the use of illicit drugs.

MEDICATIONS
Advair, metformin, glipizide, pantoprazole, montelukast, atenolol, celecoxib, albuterol, prn

ALLERGIES
Aspirin, penicillin

REVIEW OF SYSTEMS
Bilateral knee, hand, and elbow arthralgias.

PHYSICAL EXAMINATION
Bilateral palms and soles demonstrated well demarcated erythematous plaques with thickened hyperkeratotic scale and scattered fissures.

LABORATORY DATA
Complete blood count, comprehensive metabolic panel, liver function tests, and lipid panel were unremarkable. Serologies for syphilis, gonorrhea, and chlamydia were negative.

IMAGING
Notable for osteoarthritis. No radiographic evidence of erosive or psoriatic arthritis demonstrated in plain films of bilateral feet, hands, and knees.

DIAGNOSIS
Palmoplantar psoriasis

TREATMENT & COURSE
Initially, we planned to start an oral retinoid and keratolytic topical emollient. However, the patient had significant insurance and financial limitations and was unable to obtain the medications. Alternatively, we treated with a more affordable solution of 40% urea mixed with vaseline in 1:1 ratio, BID and with nightly occlusion. At one month follow-up, the patient significantly improved with no appreciable scale on palms, nearly 50-75% clearance on soles, and completely resolved fissures and pain. There was residual asymptomatic erythema of both palms and soles. Smoking cessation was emphasized.

DISCUSSION

Palmoplantar Psoriasis (PP) occurs in less than 20% of all cases of psoriasis. The diagnosis is typically based on its clinical appearance of well demarcated erythematous plaques with overlying scale, occasionally accompanied by deep painful fissures. Treatment of psoriasis is determined by the severity and location of the psoriasis as well as medication side effects, patient preferences, and financial constraints. While the palms and soles represent a relatively small body surface area, their involvement may lead to severe disease. Patients with palmoplantar psoriasis often experience significant morbidity due to difficulty and discomfort using their hands and feet for daily activities.

Urea, one of the natural moisturizing factors (NMFs) of the stratum corneum, plays an important role in maintaining epidermal water via corneolytic activity, thus further enhancing moisturization and maintenance of intact barrier function in skin. The proteolytic action of urea, promotes degradation of the intercellular matrix, thus facilitating desquamation. In psoriatic skin, urea is diminished by 40%. Topical treatment with urea in psoriasis has been shown to reduce epidermal hyperproliferation and induce differentiation. Traditionally, urea has only been used in psoriatic therapy as a keratolytic adjunct to salicylic acid, particularly when there is a significant scale load, thus allowing enhanced penetration of topical medications.

PP is often resistant to even potent topical treatment, likely due in part to the thickness of the skin in these areas and frequently requires the use of systemic therapies such as acitretin, and/or phototherapy. In addition to traditional systemic agents and biologic agents, many medications have been used off label, including colchicine. The challenging management of palmoplantar psoriasis has been well established, and many utilize systemic medications as first-line therapy. This case demonstrates that with good patient compliance, a simple, economic solution can significantly reduce overall morbidity and improve quality of life.

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