Chicago Dermatological Society

Monthly Educational Conference

Program Information
CME Certification
and
Case Presentations

Wednesday, December 7, 2016
Gleacher Center – Chicago, IL

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

Program

Host: University of Chicago

Conference Location

Gleacher Conference Center
450 N. Cityfront Plaza Dr., Chicago

All meeting activities take place on the 6th Floor of the Gleacher Center.

8:00 a.m.	**Registration & Continental Breakfast with Exhibitors** *6th Floor Lobby and Room 600*
8:30 a.m. - 10:00 a.m.	**Clinical Rounds** Posters – *Room 600/202/604 (available throughout the morning)* Slide viewing – *Room 608 (available throughout the morning)*
9:00 a.m. - 10:00 a.m.	**Resident/Basic Science - Medenica Lecture** – *Room 621* "Use of Special Studies in the Diagnosis of Melanocytic Lesions" *Victor G. Prieto, MD, PhD*
10:00 a.m. - 10:30 a.m.	**Break and Visit with Exhibitors** – *Room 600*
10:30 a.m. - 12:00 p.m.	**Resident Case Presentations & Discussion** *Room 621*
12:00 p.m. - 12:15 p.m.	**MOC Self-Assessment Questions** *Room 621*
12:15 p.m. - 12:45 p.m.	**Box Lunches & visit with exhibitors** *Room 600*
12:45 p.m. - 1:00 p.m.	**CDS Business Meeting** *Room 621*
1:00 p.m. - 2:00 p.m.	**General Session** – *Room 621* *LORINCZ LECTURE*: "Update of the AJCC/CAP Recommendation for Melanoma Reporting" *Victor G. Prieto, MD, PhD*
2:00 p.m.	**Meeting adjourns**

Mark the Date!
Next CDS monthly meeting – Wednesday, April 12, 2016 at the Gleacher Center
IDS Practice Management Workshop – Wednesday, February 15, 2017 in Rosemont
Watch for details on the Internat: www.ChicagoDerm.org and www.IllinoisDermSociety.org
Save time and money – consider registering online!

Guest Speaker

VICTOR G. PRIETO, MD PHD

Department Chair, Department of Pathology, Division of Pathology/Lab Medicine, The University of Texas MD Anderson Cancer Center; Houston, TX

Delivering the Allen Lorincz Lecture

Victor G. Prieto, MD, PhD, received his BA degree from the International School Lope de Vega, Benidorm, Spain. He earned his medical degree from the University of Alicante, Spain; and his Ph.D. from the University of Barcelona, Spain. He took residency training in Pathology at the Hospital del Mar in Barcelona and at the New York Hospital-Cornell Medical Center. He took Fellowship training in Oncologic Pathology at the Memorial Sloan Kettering Cancer Center and in Dermatopathology at the New York Hospital-Cornell Medical Center.

Dr. Prieto is a pathologist/dermatopathologist with special interest in melanoma. He has been the director of the dermatopathology section and the co-director of the melanoma tissue bank at MD Anderson Cancer Center for the last 10 years. During this time he has participated in multiple melanoma projects. In particular he examined the pattern of expression of iNOS, retinoid receptors, galectin-3, tyrosin kinases, and related molecules in primary and metastatic melanoma.

CME Information

This educational activity is jointly provided by AXIS Medical Education, Refine Me CE and the Chicago Dermatological Society

Overview

The Chicago Dermatological Society was established in 1903 and has strived to provide meaningful educational opportunities to dermatologists in the Chicago area for more than a century. Guest speakers from across the country share their expertise with CDS members, as well as residents in training medical students doing their dermatology rotation. CDS schedules six day-long meetings each year which are "hosted" by one of the dermatology residency programs in the city. In addition to two lectures given by the guest speaker, the residents of the host institution present cases which are offered for audience discussion. In addition, live patients, posters and microscopic slides prepared by the residents are made available during the "clinical rounds" portion of the meeting. CDS also offers a 15-minute session that qualifies for "Maintenance of Certification" self-assessment questions under the auspices of the American Board of Dermatology.

Target Audience

This activity has been designed to meet the educational needs of dermatologists. CDS members, residents in training and medical students engaged in their dermatology rotation are invited to attend.

Learning Objectives

At the conclusion of the 2016/17 series of meetings, the participant should be able to:

1. Discuss key factors in the diagnosis and treatment for viral diseases and bacterial infections.
2. Describe the manifestation of skin cancers and the efficacy of treatments available to the dermatologist.
3. List the therapeutic options available to the dermatologist for a variety of skin diseases, both medical and surgical, and discuss how new emerging treatments can be successfully incorporated into a dermatology practice.

Physician Accreditation Statement

This activity is planned and implemented by AXIS Medical Education, Refine Me CE and the Chicago Dermatological Society. AXIS Medical Education is accredited by the Accreditation Council for Continuing Medical Education (ACCME), the Accreditation Council for Pharmacy Education (ACPE), and the American Nurses Credentialing Center (ANCC) to provide continuing education for the healthcare team.

Credit Designation for Physicians – AXIS Medical Education designates this live activity for a maximum of 4.75 *AMA PRA Category 1 Credit(s)*™. Physicians should claim only the credit commensurate with the extent of their participation in the activity.

Attendees are required to submit a CME claim form upon departure from the conference. Please leave your form, along with the attached evaluation form, at the registration table when you leave the meeting. Thank you for your attention to this important item.

Disclosure of Conflicts of Interest

AXIS Medical Education requires instructors, planners, managers and other individuals and their spouse/life partner who are in a position to control the content of this activity to disclose any real or apparent conflict of interest they may have as related to the content of this activity. All identified conflicts of interest are thoroughly vetted by AXIS for fair balance, scientific objectivity of studies mentioned in the materials or used as the basis for content, and appropriateness of patient care recommendations. All speakers are expected to follow the "first slide" rule to repeat their conflict of interest disclosures during their talk.

Today's guest speaker, Victor Prieto, MD, PhD, has no conflicts of interest to disclose. Likewise, the following individuals also have no conflicts to disclose: Residents presenting cases at this meeting; planning committee members - Alix Charles, MD, program chair and CDS president; Julie Moore, MD, CDS past-president; Richard Paul, CDS Executive Director; Ronald Viggiani, MD and Dee Morgillo, MEd, MT(ASCP), CHCP, AXIS Medical Education.

AXIS Contact Information

For information about the physician accreditation of this program please contact AXIS at 954-281-7524 or info@axismeded.org.

Americans with Disabilities Act

In compliance with the Americans with Disabilities Act, we will make every reasonable effort to accommodate your request. For any special requests, please contact the CDS at: Rich@ChicagoDerm.org.

Disclaimer

Participants have an implied responsibility to use the newly acquired information to enhance patient outcomes and their own professional development. The information presented in this activity is not meant to serve as a guideline for patient management. Any procedures, medications, or other courses of diagnosis or treatment discussed in this activity should not be used by clinicians without evaluation of patient conditions and possible contraindications on dangers in use, review of any applicable manufacturer's product information, and comparison with recommendations of other authorities.

Dislosure of Unlabeled Use

This educational activity may contain discussion of published and/or investigational uses of agents that are not indicated by the FDA. The planners of this activity do not recommend the use of any agent outside of the labeled indications. The opinions expressed in the educational activity are those of the faculty and do not necessarily represent the views of the planners. Please refer to the official prescribing information for each product for discussion of approved indications, contraindications, and warnings.

THE UNIVERSITY OF CHICAGO

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CHICAGO DERMATOLOGICAL SOCIETY **Case #1**

Presented by Olga Radkevich-Brown, MD, PhD, Sarah Stein, MD
Section of Dermatology, Department of Medicine, University of Chicago

HISTORY OF PRESENT ILLNESS

A 4-month-old African American male infant was transferred from an outside hospital to the pediatric intensive care unit with lethargy, hypothermia, profound hypoglycemia, and hypotension. On day 5 of admission, Pediatric Dermatology was consulted for evaluation of a scaly rash on the forehead, lips, neck and upper chest, noticed after the patient was extubated. Nutritional history was notable for the finding that since about 2 weeks of age, the parents had been overdiluting the powdered formula. One month prior to admission, when the family noticed that the infant appeared underweight, he was switched to goats' milk formula, which was also inappropriately diluted.

PAST MEDICAL HISTORY

Born at full term via spontaneous vaginal delivery, with no maternal or fetal complications during pregnancy, labor or delivery

FAMILY HISTORY

Mother and maternal grandmother with sickle cell trait

MEDICATIONS

Ceftazidime, metronidazole, vancomycin, levocarnitine, thiamine, parenteral nutrition, fat emulsion, dextrose 20% in water, esomeprazole, topical zinc oxide paste

ALLERGIES

None

PHYSICAL EXAMINATION

Weight 3.5 kg (7 lbs 11.5 oz, below 1st percentile weight-for-age and weight-for-height)
Height 56.5 cm (22 inches, below 1st percentile stature-for-age)
Head circumference 36.5 cm (14.4 inches, below 1st percentile head circumference-for-age)
Body mass index 11.4 (normalized BMI values are only available for ages 2 to 20 years)
On upper chest, extending into the neck fold, there were brown adherent scales similar in appearance to flaky paint. Similar scaling was noted on the forehead and around the eyes and nose. There were focal areas of desquamation revealing pink patches, but no erosions or ulcerations. Lips were dry and peeling, with fissuring and crusting at bilateral oral commissures. Buccal mucosa, gingiva and tongue were unremarkable; hard palate had a focal petechial plaque, consistent with intubation trauma. There was pronounced scrotal edema. Skin of the buttocks was erythematous, without desquamation or erosions. Nails were normal.

LABORATORY DATA

Comprehensive metabolic panel on initial presentation:

- ↓ glucose 10 mg/dL (reference range 60-109)
- ↓ Na, K, Cl, CO_2, Ca, creatinine
- ↑ blood urea nitrogen (BUN), alanine aminotransferase (ALT), aspartate aminotransferase (AST)
- ↓ alkaline phosphatase
- ↓ total protein 4.6 g/dL (6-8.3), albumin 3.4 g/dL (3.5-5.0), and pre-albumin 9 mg/dL (21-41)
- ↑ ammonia 77 μg/dL (20-70)
- Normal venous lactate 1.14 mmol/L (0.56-2.20), anion gap 15 mmol/L (6-15)

Complete blood count on initial presentation:

↓ hemoglobin 7.8 g/dL (9.3-13.2)

↓ mean corpuscular volume (MCV) 60.4 fL (73-107)

Normal leukocytes, platelets

Vitamin and micronutrient levels measured prior to supplementation:

Normal serum folate, vitamin B12 (cyanocobalamin), iron, zinc. 25-hydroxy vitamin D

Inborn errors of metabolism markers measured prior to supplementation:

↓ Amino acids, quantitative, blood: multiple amino acids were reduced, not indicative of specific disorder, but a dietary artifact secondary to low protein diet

↓ Carnitine: reduced total, free and acylcarnitine, no accumulation of esterified species

Normal urinary organic acids

Normal newborn screen

Vitamin and micronutrient levels measured after supplementation was initiated:

↓Vitamin B6 (pyridoxal 5 phosphate), vitamin C (ascorbic acid), vitamin E (α-tocopherol), selenium

Normal vitamin A (free retinol), vitamin B3 (niacin), copper, free fatty acids, triglycerides, free fatty acids

IMAGING

Abdominal ultrasound demonstrated moderate amount of ascites

DIAGNOSIS

"Flaky paint" dermatosis associated with kwashiorkor

TREATMENT AND COURSE

The patient required intensive care for hypovolemic shock, multiple electrolyte disturbances, and intubation for airway protection. His infectious workup was negative, but he received a course of vancomycin, ceftazidime and metronidazole for presumed gut bacterial translocation. Based on history of inappropriate formula mixing, very low weight and height for patient's age, and low albumin and pre-albumin, he was diagnosed with severe malnutrition. He was started empirically on carnitine supplementation, multivitamins and total parenteral nutrition with lipid supplementation. He had persistent hypoglycemia requiring high glucose infusion rates. Extensive metabolic workup demonstrated reduced levels of all carnitine species and reduced levels of multiple amino acids, consistent with severe malnutrition rather than an inborn error of metabolism, particularly in the setting of a normal newborn screen evaluation. Workup for specific vitamin and trace element deficiencies revealed low selenium and vitamin C, and borderline levels of vitamin B6 and E. He was eventually transitioned to oral amino acid-based formula and finally milk protein-based formula, and maintained appropriate glucose levels. After a three-week hospital stay, he was discharged to foster care. Petroleum jelly was recommended for the care of the nutritional dermatosis.

DISCUSSION

Protein-energy malnutrition describes a spectrum of malnutrition disorders, including marasmus, kwashiorkor, and an intermediate state between the two. Marasmus is an adaptation to chronic and global nutrient deficiency, while kwashiorkor is due to disproportionately increased carbohydrate intake or decreased protein intake, particularly seen during periods of stress. In marasmus, weight is usually less than 60% of ideal body weight, with no edema, while kwashiorkor has been traditionally characterized by less dramatic weight loss (60-80% of ideal body weight) due to edema in the setting of hypoproteinemia and hypoalbuminemia. These conditions are predominantly seen in developing countries, however, cases are reported in the US and developed countries as well.

Marasmus is rare in the US, except in cases of extreme malnutrition such as neglect. Patients demonstrate dry and wrinkled skin, with generalized loss of subcutaneous fat and muscle. Kwashiorkor has been reported more commonly and is attributable to nutritional ignorance, food faddism, presumed food allergy and/or specific food avoidance. The classic cutaneous findings of kwashiorkor are fine reddish-brown scales resembling flakes of peeling paint, and termed "flaky paint" dermatosis. Other cutaneous manifestations include erosions in the areas of friction, focal hyper- and hypopigmentation, and lightening of the hair, with alternating lighter and darker areas of hair pigmentation known as the "flag sign", which reflects states of inconsistent nutritional intake. Hair is dry, brittle and lusterless, and nails become thin, soft and separate easily from the nail bed.

The clinical picture of kwashiorkor is not always uniform, and differentiation from other nutritional dermatoses is not always straight-forward. In fact, dietary intake of several micronutrients, as well as macronutrients, can be absent at the same time. Acquired zinc deficiency, essential fatty acid, riboflavin (vitamin B2), niacin (vitamin B3) and pyridoxine (vitamin B6) deficiencies, cystic fibrosis, certain inherited immunodeficiencies, Langerhans cell histiocytosis, and inborn errors of metabolism, including hereditary acrodermatitis enteropathica, Hartnup's disease and multiple carboxylase deficiency, as well as atopic dermatitis, should be considered in the differential diagnosis of protein-energy malnutrition and generalized eczematous dermatitides.

Other etiologic considerations in kwashiorkor should include, but are not limited to, social and economic factors (lack of income, education, or access to healthcare), deliberate restriction of dietary intake (anorexia nervosa, perceived allergy, or medically indicated dietary restrictions), catabolic states (malignancy, liver disease), malabsorption (cystic fibrosis, celiac disease, inflammatory bowel disease), psychologic/neurologic diseases (food aversion, psychosocial deprivation), or acute decompensation in chronic borderline malnutrition, for example due to infection.

Initial diagnostic evaluation recommended by the World Health Organization consists of screening for hypoglycemia and anemia, and a comprehensive workup to rule out coexisting infectious disease. Additional laboratory testing includes a complete blood count, measurement of levels of total protein, albumin, zinc, sweat chloride, and biotinidase, and evaluation for HIV infection. Biopsy will demonstrate the histological features of malnutrition: epidermal pallor with overlying confluent parakeratosis. These findings are not specific for kwashiorkor, but will differentiate nutritional dermatosis from other dermatoses such as atopic dermatitis and Langerhans cell histiocytosis. Treatment of protein-energy malnutrition requires aggressive nutritional support, as well as management of concomitant conditions such as dehydration and infection. Oral refeeding is preferred over intravenous hyperalimentation, but the potential complications of rapid refeeding must be carefully managed.

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CHICAGO DERMATOLOGICAL SOCIETY **Case #2**

Presented by Carly Roman, MD, Haider Bangash, MD, Farah Abdulla, MD, Keyoumars Soltani, MD
Section of Dermatology, Department of Medicine, University of Chicago

HISTORY OF PRESENT ILLNESS

A 52-year-old Caucasian man presented for dermatologic evaluation of multiple facial papules. These lesions had been present for 15 years and were asymptomatic. Prior treatment by an outside dermatologist included electrodessication and curettage, which led to transient improvement, but the lesions eventually recurred. A prior biopsy was reportedly consistent with a benign "hair follicle growth". He was otherwise in good health with no systemic complaints.

PAST MEDICAL HISTORY

None

FAMILY HISTORY

Unknown; patient was adopted.

MEDICATIONS

None

ALLERGIES

None

PHYSICAL EXAMINATION

Numerous, monomorphic, 2-3 mm skin colored to slightly hypopigmented papules clustered on the face and superior chest.

HISTOPATHOLOGY

A 3mm punch biopsy of a representative lesion of the right mandible was taken. Histopathologic analysis showed thin epithelial strands emanating from follicular structures and from the overlying epithelium. Around the cords was a proliferation of loose connective tissue consistent with a fibrofolliculoma.

TREATMENT AND COURSE

Based on the clinical and histopathologic data, there was suspicion for Birt-Hogg-Dubé syndrome. Evaluation for visceral manifestations with a CT chest/abdomen/pelvis was recommended. The imaging revealed multiple bilateral pulmonary cysts, but was negative for pneumothoraces. Kidneys were grossly unremarkable.

Regular imaging to monitor for the development of renal neoplasms was recommended. Avoidance of high atmospheric pressure such as air travel and scuba diving was encouraged. Cosmetic treatment of the fibrofolliculomas was discussed but deferred.

DIAGNOSIS

Birt-Hogg-Dubé syndrome

DISCUSSION

Birt-Hogg-Dubé syndrome (BHDS) is an autosomal dominant disorder characterized by multiple fibrofolliculomas, trichodiscomas and acrochordon-like lesions as well as visceral manifestations. It is a rare syndrome occurring in approximately 1/200,000 people. It is caused by a mutation in the tumor suppressor gene FLCN (folliculin). The diagnostic criteria are as follows: Major criteria, 1) At least five

fibrofolliculomas or trichodiscomas with at least one of them confirmed histologically and occurring in adult onset, 2) Pathogenic FLCN germline mutation; Minor criteria, 1) Multiple bilateral and basilar lung cysts with no other apparent cause, with or without spontaneous primary pneumothorax, 2) Renal cancer, early onset (<50 years) or multifocal or bilateral renal cancer, or renal tumor composed of mixed chromophobe and oncocytic morphology, 3) A first-degree relative with BHDS. The diagnosis of BHDS is feasible when a patient meets one major or two minor criteria.

BHDS is characterized by the cutaneous triad of fibrofolliculomas, trichodiscomas, and acrochordons. Fibrofolliculomas and trichodiscomas are thought to be part of a morphological spectrum. These lesions typically appear after the age of 20 and present as numerous, small, dome-shaped whitish papules on the face, neck and upper torso. These lesions are benign and require no treatment. If treatment is desired for cosmesis, options include carbon dioxide laser ablation, superficial electrodessication or dermabrasion. Recurrence is likely following any of these therapies.

Pulmonary involvement is common in BHDS, manifesting as multiple basilar pulmonary cysts and the development of pneumothoraces. Pulmonary cysts are seen in >80% of patients and most commonly occur in the fourth to fifth decades. The cysts are typically asymptomatic until the development of a pneumothorax, which has an estimated incidence of 33-38%. The odds of this complication are 50 times more likely than in an unaffected individual and is correlated to the number, diameter and volume of the lung cysts. The surrounding lung parenchyma is largely normal, thus pulmonary function is only minimally impaired or normal. There has been no established lung cancer association. Baseline high-resolution chest CT is recommended to better characterize the extent of disease and facilitate patient education. Although no disease specific data exists, patients are advised to not smoke and avoid scuba diving as the change in ambient atmospheric pressure could predispose to development of a pneumothorax. There is a theoretical risk of air travel as the pressurized cabin may result in gas expansion within the pulmonary cysts and lead to the development of a pneumothorax, though in general air travel is thought to be safe. Pleurodesis is recommended after the first episode of pneumothorax.

The presence of renal tumors varies between 25% to 35% with a mean age at diagnosis of 50 years and a male predominance. They are frequently multiple, bilateral and slow growing. A variety of histological subtypes have been observed including hybrid oncocytic tumor, chromophobe RCC, oncocytoma, papillary RCC and clear cell RCC. Benign renal cysts have also been documented in patients with BHDS, but their exact prevalence compared to the general population is unknown. Renal tumors associated with BHDS generally follow a favorable clinical course as the clinical behavior of the hybrid oncocytic tumor, chromophobe RCC and oncocytoma are not usually aggressive. Regular screening is essential, although the optimal mode, timing and duration of surveillance are unclear. CT and MRI are more sensitive than ultrasound in detecting smaller lesions. There are no established guidelines, but the general recommendations include screening around age 20 with repeat imaging every 36 to 48 months. Other less common associations include colonic adenomas, medullary thyroid carcinoma, and tissue nevi.

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CHICAGO DERMATOLOGICAL SOCIETY **Case #3**

Presented by Ashley Jenkins, MD, Aisha Sethi, MD, and Vesna Petronic-Rosic, MD
Section of Dermatology, Department of Medicine, University of Chicago

UNKNOWN

A 32-year-old male presented with a new rash, eye redness, retro-orbital pain, fatigue, and generalized muscle aches.

CHICAGO DERMATOLOGICAL SOCIETY **Case #4**

Presented by Stephanie M. Kazantsev, MD, Ashley Jenkins, MD, Farah R. Abdulla, MD, Sarah L. Stein, MD
Section of Dermatology, Department of Medicine, University of Chicago

HISTORY OF PRESENT ILLNESS

Dermatology was consulted to evaluate a hospitalized five-week-old full term girl for "worsening diffuse mucosal and cutaneous hemangiomas." At birth, the infant was reported to have several tiny red spots on her skin that gradually enlarged. At 3 weeks of age, a red bump in the diaper region and one on the right cheek had developed surface breakdown. She was evaluated by hematology/oncology and topical timolol gel was initiated. Evaluations prior to admission included an abdominal ultrasound that showed multiple hypervascular hepatic lesions, consistent with hemangiomas, a chest x-ray that showed "large cardiac size", and a transthoracic echocardiogram (TTE) demonstrating hypofunction and mitral insufficiency.

PAST MEDICAL HISTORY

Born at 39 weeks via repeat c-section following an uncomplicated pregnancy with normal prenatal ultrasounds.

FAMILY HISTORY

Non-contributory

MEDICATIONS

Timolol 0.5% gel

ALLERGIES

NKDA

PHYSICAL EXAM

Well appearing, well developed five-week-old female. Pulse tachycardic with rate of 155. Cardiac exam demonstrated Grade II/VI systolic ejection murmur. Respiratory exam demonstrated normal effort and normal breath sounds. Abdominal exam notable for hepatomegaly with liver edge palpable 5cm below costal margin. Numerous (>50), red dome-shaped vascular papules scattered densely over the entire body, ranging in size from about 0.5 to 2cm. In the oropharynx, several red 1-2mm macules noted on the gingivae and floor of the mouth. No papules were ulcerated or eroded.

LABORATORY DATA

Complete blood count: within normal limits
Basic Metabolic panel: within normal limits
Liver Function test: notable for total bilirubin 1.9 mg/dL (0.1-1.0), AST 182 U/L (8-37), ALT 39 U/L (8-35)
Thyroid function tests: normal including TSH, T3 and free T4
N-terminal pro-brain natriuretic peptide (NT-proBNP): 657 pg/mL (<125)
Troponin: within normal limits
Coagulation studies: notable for PTT 38.3 s (24.0-34.0)

IMAGING

Abdominal Ultrasound: Multiple hypervascular hepatic lesions, consistent with hemangiomas.
MRI Liver: Innumerable T2 hyperintense enhacing hepatic high flow lesions, compatible with hemangiomas. Cardiomegaly, secondary to high flow.
Electrocardiogram: Normal sinus rhythm, right atrial enlargement, right axis deviation, right ventricular

hypertrophy, possible biventricular hypertrophy.
Transthoracic echocardiogram (TTE): Mild concentric left ventricular hypertrophy, mild left ventricular dilation. Left ventricular wall motion is mildly, globally reduced. Shortening fraction 30%. There is mild mitral regurgitation. Mild left atrial dilation. Single mitral regurgitation jet directed posteriorly. Patent foramen ovale. Left to right atrial shunt, small.
MRA brain, MRI brain and soft tissue neck: Several subcentimeter posterior fossa lesions likely represent a manifestation of diffuse hemangiomatosis.

DIAGNOSIS
Multifocal infantile hemangiomas with extracutaneous disease

TREATMENT AND COURSE
The patient was started on propranolol 0.65 mg/kg/day divided three times per day, with stepwise increase to 4.0 mg/kg/day divided three times per day. She was also started on furosemide at 3mg twice per day, with increase to 6mg twice per day. She has tolerated the medications and dosing changes well. Direct laryngoscopy and broncoscopy showed no airway involvement. Ophthalmologic exam revealed normal fundus and ocular exam.

Since discharge, NT-proBNP has continued to decrease (657 at 7-weeks-old, 108 at 12-weeks-old) and repeat echocardiogram demonstrated improved cardiac output with left ventricular shortening fraction ~36%. Repeat abdominal ultrasounds at 7-weeks-old, 9-weeks-old, and 14-weeks-old demonstrated stable hepatic hemangiomas.The cutaneous hemangiomas are overall stable with some becoming lighter in color and flatter. No bleeding or ulceration has occurred.

Multidisciplinary care has included pediatric specialists from dermatology, hematology/oncology, surgery, cardiology, otolaryngology, ophthalmology, and neurology.

DISCUSSION
Infantile hemangiomas (IH) are estimated to affect 4-10% of all neonates and infants. They occur more frequently in girls, caucasians, premature or low birthweight infants, multiple gestation pregnancy, and infants born to older mothers. These lesions can be further classified as focal, multifocal, segmental, and indeterminate, affecting the skin in a superficial, deep or mixed manner.

Among affected infants, an estimated 15-30% have multiple hemangiomas. The presence of five or more cutaneous hemangiomas is associated with a higher incidence of extracutaneous hemangiomas, most commonly hepatic hemangiomas. The presence of multiple cutaneous hemangiomas without visceral involvement has been categorized as multifocal infantile hemangiomas without extracutaneous disease (previously benign neonatal hemangiomatosis). The presence of multiple hemangiomas affecting the skin and visceral organs has been termed multifocal infantile hemangiomas with extracutaneous disease (multifocal IH; previously diffuse neonatal hemangiomatosis). Complications of multifocal IH are often a result of hepatic hemangiomas (HH). A classification for HH has been proposed, including solitary, multifocal, and diffuse. Multifocal HH usually occur in the setting of multiple small skin hemangiomas. The HHs may be asymptomatic, but if they contain arteriovenous shunts then congestive heart failure can ensue. Diffuse HH is associated with massive hepatomegaly and hypothyroidism. The hypothyroidism is the result of type 3 iodothyronine deiodinase produced by the hemangioma.

Accurately differentiating multifocal IH from other multifocal vasular anomalies is vital for treatment and prognostic purposes. Other diagnoses to consider include multifocal lymphangioendotheliomatosis with thrombocytopenia (MLT), pyogenic granuloma, tufted angioma, Kaposiform hemangioendothelioma, glomuvenous malformation, mucocutaneus venous malformations, blue rubber bleb syndrome, and capillary malformation-arteriovenous malformation. Differentiating IH from other possible diagnoses can

usually be done clinically, however occasionally can be challenging. IH typically appear within a few weeks of birth, followed by a period of rapid growth over months, followed by gradual involution. Other organ systems may be involved, most commonly the liver, and rarely the gastrointestinal tract. IH demonstrate glucose transporter-1 (GLUT-1) positivity on immunohistochemical staining. Furthermore, while thrombocytopenia is associated with other diagnoses like MLT, tufted angioma, and Kaposiform hemangioendothelioma, it is not associated with IH. In contrast to IH, MLT is GLUT-1 negative, associated with severe thrombocytopenia, severe gastrointestial bleeding, and commonly involves the lungs and bone/synovium.

Treatments for complicated solitary and multifocal IH include beta blockers, systemic corticosteroids, interferon-alpha-2a, vincristine, cyclophosphamide, and carbon dioxide laser. Propranolol was first reported as an effective treatment for IH in 2008, and has since become the preferred systemic therapy for slowing or even stopping the growth of hemangiomas and promoting more rapid involution. It was approved by the US Food and Drug Administration for the treatment of IH in 2014. Multiple case studies have reported a rapid response of multifocal IH to propranolol therapy, including cases complicated by high-output cardiac failure.

This case highlights the clinical presentation, diagnosis and treatment of an infant with multifocal IH with extracutaneous disease.

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CHICAGO DERMATOLOGICAL SOCIETY **Case #5**

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HISTORY OF PRESENT ILLNESS

In July 2015, a 69-year-old woman presented to the University of Chicago Dermatology Clinic with a lesion on the helix of her left ear that had been present for roughly 3 weeks. On exam, an 8 mm light brown, scaly, thin papule with a 2mm black macule within it was noted on the patient's superior helical rim (primary lesion). The lesion was biopsied, and revealed an invasive malignant melanoma with ulceration, 2 mitotic figures per millimeter squared, and a Breslow depth of 1.6mm (Clark level IV). Ten days after the initial biopsy, the patient was treated with a wide resection and sentinel lymph node biopsy. The excised tissue showed no residual melanoma, and the margins were clear. A sentinel lymph node biopsy was performed of four sentinel nodes in the left tail of the parotid gland and was negative. A CT head and soft tissue neck were negative for discrete neck mass or significant cervical lymphadenopathy. Her staging at that time was T2bN0M0, corresponding to Stage IIA by the current American Joint Committee on Cancer (AJCC) staging criteria. She underwent a delayed reconstruction of the auricle in October 2015. The patient was subsequently followed with clinical exams every three months in Dermatology Clinic.

In late May 2016, the patient returned to clinic with a new 2mm dark brown papule (lesion A) on the left posterior auricle that she had noticed the previous morning. Biopsy of this lesion revealed an invasive malignant melanoma with Breslow depth of 0.93mm and Clark Level IV. One week later, the patient had another brown papule (lesion B) on the helix of the left ear biopsied. This lesion was within 2cm of the primary melanoma but outside the original scar, and biopsy was consistent with another invasive malignant melanoma.

PAST MEDICAL HISTORY

Actinic keratoses
Severely atypical compound nevus treated with complete excision on 9/23/2015
Psoriasis as a teenager
Osteoarthritis
Glaucoma
No prior history of skin cancers

FAMILY HISTORY

Negative for skin cancer

MEDICATIONS

Calcium citrate/vitamin D3 supplement daily
Nabumetone 750 mg PO BID

ALLERGIES

Sulfonamides

PHYSICAL EXAMINATION

Primary lesion, 7/20/15: 8mm light brown, scaly, thin papule with an eccentric 2mm black macule within it on the upper helical rim of the left ear (shave biopsy)

Lesion A, 5/24/16: 2mm dark brown papule on the left posterior auricle (4mm punch biopsy)

Lesion B, 6/1/16: 3mm brown, variegated macule on the helix of the left ear (4mm punch biopsy)

HISTOPATHOLOGY

Biopsy – primary lesion – 7/20/15
Left ear helix biopsy: Invasive malignant melanoma with nevoid features and Breslow depth of 1.6mm, Clark level IV. Ulceration was present, and 2 mitotic figures per millimeter squared were identified. Both radial and vertical growth phases were present.
Excision of primary melanoma – 7/30/15
Left ear helix excision: Auricular skin with solar damage and with no residual melanoma.
Sentinel Lymph Node pathology – 7/30/15
Four sentinel lymph nodes and nine non-sentinel lymph nodes were excised. All were negative for tumor.
Biopsy – lesion A – 5/24/16
Left posterior auricle biopsy: Invasive malignant melanoma with a Breslow depth of 0.93mm, Clark level IV. Three mitotic figures per millimeter squared were present. No ulceration was identified, and only vertical growth was present.
Biopsy – lesion B – 6/1/16
Left ear helix biopsy: Invasive malignant melanoma with a Breslow depth of 1.01mm. Fewer than 1 mitotic figure per millimeter squared was present. No ulceration was identified, and both radial and vertical growth phases were present.
Excision of lesion A and lesion B – 6/27/16
Left posterior auricle excision: Scarred skin with no residual melanoma. S-100 staining was negative.
Left ear helix excision: Scarred skin with no residual melanoma.

IMAGING

3 month Surveillance CT Head and Soft Tissue Neck with IV contrast – 9/29/15
Evidence of postsurgical changes in the left neck, with no discrete neck mass or significant cervical lymphadenopathy. There was no evidence of intracranial metastatic disease.
CT Soft Tissue Neck with IV contrast – 6/23/16
Evidence of postoperative findings in the left neck, with no significant cervical lymphadenopathy based on size criteria.
CT Chest, Abdomen, and Pelvis with IV contrast – 6/23/16
No specific evidence of metastatic disease in the chest, abdomen, or pelvis.

DIAGNOSIS

Epidermotropic metastatic malignant melanoma

TREATMENT AND COURSE

This patient was determined to have regional metastatic disease based on the current AJCC guidelines. These guidelines define melanomas that occur within 2cm of an original melanoma as satellite metastases, and those that are more than 2cm from the primary lesion but within the same nodal draining basin as in-transit. Based on these criteria, lesion A and lesion B are an in-transit and satellite metastasis, respectively. This highlights the important clarification that metastatic disease in this patient refers to in-transit and satellite lesions, which are regional metastases and not distant, widespread metastasis.

In late June 2016, the patient underwent wide local excision of metastatic malignant melanomas (lesions A and B). The margins on these excisions were clear. She has been seen by Hematology-Oncology and discussed at Melanoma Tumor Board; the recommendations from this conference were to pursue imaging studies, which were negative for discrete mass or lymphadenopathy. These recommendations were based on repeat clinical staging done after metastatic melanoma occurred that put her at Stage IIIC disease

(T2bN2cM0) based on AJCC guidelines. The presence of in-transit and satellite metastases automatically elevates her nodal staging to N2c. She does not have distant systemic metastases, which limits her M staging to M0. Current National Comprehensive Cancer Network (NCCN) guidelines recommend imaging work up and allow for close observation of patients with Stage IIIC disease that has been completely resected and who have negative imaging. Adjuvant therapy is a suggested consideration in these patients. Our patient and her multidisciplinary care team had a conversation regarding the risks and benefits of adjuvant therapy compared to the risks and benefits of local resection with close observation, and the latter was the preferred treatment route. She continues to be followed closely in Dermatology Clinic with complete skin and clinical lymph node exams every 3 months.

DISCUSSION

This patient was diagnosed with epidermotropic metastatic malignant melanoma (EMMM) of the left ear, and is considered to have Stage IIIC disease. EMMM is a type of malignant melanoma in which the invasive metastatic malignant cells involve the epidermis. Typically, metastatic melanoma to the skin involves the subcutis and the dermis, and spares the epidermis. In rare cases, metastatic melanoma involves the epidermis, resulting in the histopathological feature of epidermotropism, as is demonstrated in this case. In cases with EMMM, epidermotropic metastases tend to closely mimic primary malignant melanoma (MM), making the diagnostic distinction challenging. Staging and subsequent treatment for these two types of melanoma are different, so making this distinction is crucial.

There are three potential ways to consider this case. The first is that the patient developed three independent, primary malignant melanomas in close proximity to each other. Multiple localized primary melanomas have been described, but these are typically associated with trauma, irritation, immunodeficiency, or other predisposing factors, and our patient had no known risk for developing multiple primary melanomas in one location. The second possibility is that this patient experienced numerous local, non-metastatic recurrences of her malignant melanoma. We feel this is unlikely given that the margins were clear on the excised cutaneous lesions, the sentinel lymph nodes were negative, and the patient's recurrences were outside of her original scar. The third option is that the two subsequent lesions represent cutaneous epidermotropic metastases of the original invasive melanoma of the helical rim.

We feel that the third option, EMMM, is the most clinically and pathologically consistent scenario in this patient's case. Historically, the distinction between EMMM and primary MM has been established by a set of criteria outlined by Kornberg et al in 1978. These authors found that certain cases of clinically metastatic melanoma show histopathologic features such as involvement of the epidermis that until then were attributed to primary melanoma. Classic criteria for EMMM include dermal involvement greater than or equal to epidermal involvement, junctional epidermal involvement not extending beyond the edge of the dermal component, atypical melanocytes filling the papillary dermis with thinning of the epidermis, widening of the papillae with formation of an epithelial collarette, and identification of atypical melanocytes in vascular lymphatic spaces. Until recently, these criteria were widely accepted; however subsequent reports have described cases of EMMM that do not fit into this definition, calling these criteria into question. For example, the findings of small size, extensive pagetoid scatter, symmetry, extension of the intraepidermal component beyond the dermal component, epidermal-only involvement, and involvement of adnexal epithelium have been described in EMMM.

Our own case exhibits the classic findings of EMMM, as well as features more recently described in the primary literature. For example, lesion A demonstrated effacement of the epidermis and inward turning of the rete ridges surrounding the dermal melanocytic proliferation, which are classic features of EMMM. Some more recently described findings were appreciated in this melanoma as well, such as involvement of the adnexal epithelium and epidermal involvement that is greater than the dermal component.

Clearly, malignant melanoma with involvement of the epidermis creates an extremely challenging diagnostic puzzle. In this case, identifying her disease as EMMM rather than multiple primary lesions elevates her staging to IIIC. The 5-year survival rate for Stage IIIC melanoma is estimated at roughly 40%. The overall incidence of in-transit metastases in melanoma is 4%, and in-transit metastases are seen more often in tumors >1mm thick. It is well known that in-transit lesions are likely to recur, but currently, the consensus is that the morbidity associated with multiple resections of individual in-transit lesions is more desirable than the morbidity associated with adjuvant therapies. The utility of repeating a SLN biopsy in patients with multiple in-transit disease is not known. For such cases, the standard of care is a multidisciplinary approach to consider whether a difference in staging that could occur based on SLN results, would potentially change management. Presently, no randomized controlled trials exist to study the value of adjuvant therapy in patients with in-transit disease who are declared disease-free following surgical treatment. A recent randomized, double-blind, phase III clinical trial showed statistically significant higher rates of recurrence-free, overall, and distant metastasis-free survival in patients with Stage III melanoma treated with ipilimumab, compared to placebo. Notably, this study excluded patients with in-transit disease.

Patients diagnosed with EMMM are expected to have a poor prognosis due to the nature of metastatic disease, and case reports describe distant metastatic disease at the time of diagnosis, or within one year; however there appears to be a subset of patients who have slow expansion of their disease burden and do much better than anticipated. Given the rare occurrence of EMMM, no large studies have been done to evaluate this possibility.

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CHICAGO DERMATOLOGICAL SOCIETY **Case #6**

Presented by Laura Buford, MD, Christopher R. Shea, MD
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HISTORY OF PRESENT ILLNESS

A 37-year-old Caucasian female presented to clinic complaining of excessive sweating of the face and scalp. This condition began approximately 15 years prior and has been progressively worsening for the past two years. Initially, she experienced flushing and mild sweating of the face occurring while eating. Over time, the condition progressed from seemingly inconsequential prandial perspiration to life-altering drenching sweating of the face and scalp in response to any gustatory stimuli such as going to the grocery store, seeing food on television, or making lunch for her kids. Her attempts to avoid triggers are interfering with all aspects of her life. She is unable to complete basic activities of daily living, and personal and professional relationships are affected. She sought help specifically from a dermatologist at the urging of her family.

PAST MEDICAL HISTORY

Type I diabetes mellitus (DM) complicated by diabetic retinopathy, neuropathy, and nephropathy; cholelithiasis, and thyroid goiter

PAST SURGICAL HISTORY

Wisdom tooth extraction, cholecystectomy, and thyroidectomy

FAMILY HISTORY

There is no family history of hyperhidrosis or autonomic dysfunction.

SOCIAL HISTORY

The patient lives at home with her family. She is a current tobacco user. She denies past or current recreational drug use.

MEDICATIONS

Insulin

ALLERGIES

No known medical allergies

REVIEW OF SYSTEMS

HEENT: blurry vision
GI: inadequate food intake
GU: diabetic nephropathy
Neuro: diabetic neuropathy
Endocrine: DM, weight loss
Skin: dryness in distal lower extremities
Psychiatric: significant impairment of quality of life and inability to carry out activities of daily living

PHYSICAL EXAMINATION

Physical examination revealed an underweight woman. The hair of the scalp was slightly damp and of normal density. A transverse surgical scar was present on the anterior neck just cranial to the sternal notch, but no other primary skin findings of the affected area were appreciated. The bilateral lower extremities were dry with slightly decreased hair density in a stocking distribution. Sensory deficits to soft touch and temperature discrimination were noted in the same distribution.

DIAGNOSIS
Diabetic gustatory hyperhidrosis

TREATMENT AND COURSE
The patient was started on glycopyrrolate 1 mg by mouth twice daily with excellent results at one month follow up. She had resumed all activities of daily living, and her quality of life has been restored. She experienced mild xerostomia, which is reportedly well-controlled with gum or sugar-free candy. She has maintained regular follow up with ophthalmology as recommended, and no changes in vision have been noted.

DISCUSSION
Secondary hyperhidrosis is defined as excessive sweating due to or associated with an underlying systemic disorder. It is not as common as primary hyperhidrosis and can be caused by a variety of conditions. The diagnosis of secondary hyperhidrosis is typically clinical, so a detailed history and physical exam are paramount in making the correct diagnosis. Past medical history, surgical history, and medication history must be thoroughly evaluated, and a complete review of systems is imperative in identifying secondary causes. Laboratory testing and radiographic imaging are occasionally necessary.

Secondary hyperhidroses are subcategorized into five groups based on the source of aberrant neural impulse: cortical, hypothalamic, medullary (or gustatory), spinal cord, and local. Medullary or gustatory hyperhidrosis results from afferent nerve impulses to the nuclei in the medulla oblongata, and can be further classified as physiologic or pathologic. In physiologic gustatory hyperhidrosis, taste receptors provide afferent stimuli that travel through the glossopharyngeal nerve to the medullary nuclei resulting in erythema of the cheeks and sweating on the upper cutaneous lip. This is common after ingestion of spicy foods. Pathologic gustatory hyperhidrosis results when disrupted parasympathetic secretomotor fibers heal with aberrant nerve connections to adjacent sympathetic sudomotor fibers as seen in auriculotemporal syndrome (Frey syndrome) and chorda tympani syndrome.

Diabetic gustatory hyperhidrosis is highly characteristic of diabetic autonomic neuropathy, but the pathophysiology is not completely understood. It has been hypothesized to be either a compensatory response to anhidrosis or hypohidrosis of the bilateral lower extremities or a pathologic medullary hyperhidrosis caused by aberrant connection of sympathetic sudomotor afferent fibers and parasympathetic secretomotor fibers. The gustatory nature and characteristic distribution on the head, face, and scalp suggest that both physiologic and pathologic mechanisms play a role in the genesis of this condition.

Sweating abnormalities are common in poorly-controlled DM and are thought to arise as a consequence of autonomic dysfunction, microangiopathy, and neuropathy. Diabetic gustatory sweating typically occurs in patients with diabetic nephropathy, and the onset may be sudden. It typically persists indefinitely; although, unexplained resolution after renal transplantation has been described. The severity ranges from mild to debilitating. Anticholinergic drugs are highly effective if tolerated. Glycopyrrolate is available in both systemic and topical preparations. Care should be taken to counsel patients on side effects and regular follow up with ophthalmology should be emphasized. Case reports of successful treatment with botulinum toxin as well as the topical application of aluminum chloride 20% solution have been reported. While mild cases often do not require treatment, treatment of severe cases can be life changing.

This case of diabetic gustatory hyperhidrosis was presented for clinical interest.

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CHICAGO DERMATOLOGICAL SOCIETY **Case #7**

Presented by Rebecca Kaiser, MD, Keyoumars Soltani, MD, Vesna Petronic-Rosic, MD, MSc, Christopher R. Shea, MD
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PATIENT A

HISTORY OF PRESENT ILLNESS
A 43-year-old, African American female presented for evaluation of exquisitely painful, expanding, lesions of the bilateral thighs and buttocks. She reported onset two weeks previously with bullae, which rapidly evolved to retiform, purpuric plaques. She endorsed nausea and fatigue but denied fever and chills.

PAST MEDICAL HISTORY
Alcoholic cirrhosis, complicated by renal failure (hemodialysis initiated one month earlier), chronic anemia, neuropathy, and protein-calorie malnutrition

FAMILY HISTORY
Non-contributory

MEDICATIONS
Lactulose, rifaximin, sulfamethoxazole-trimethoprim, sevelamer carbonate, midodrine, pantoprazole, zinc sulfate

ALLERGIES
Ceftriazone, ciprofloxacin

PHYSICAL EXAMINATION
Examination revealed a well-nourished, tearful African American woman. On the bilateral thighs and buttocks were retiform purpuric plaques with surrounding, indurated rims of erythema that were exquisitely tender to touch. Flaccid bullae and serous drainage were located at the periphery of select purpuric plaques, and one plaque was centrally ulcerated. Her lower extremities were grossly edematous. No lymphadenopathy was appreciated.

HISTOPATHOLOGY
Punch biopsy of the left thigh was obtained for histopathologic analysis, which demonstrated amphophilic granular deposits in the blood vessel walls and free in the subcutaneous adipose tissue. These deposits were highlighted by the von Kossa stain. There were additional areas of vessel wall necrosis with leukocytoclasis, and extravasated red blood cells. Staining with periodic acid-Schiff and Gram stains was negative for organisms.

LABORATORY DATA
Complete Blood Count: Grossly abnormal with leukocyte count of 13.7x10^3/μL (3.5 – 11.0), hemoglobin of 7.0 g/dL (11.4 – 14.4), and platelet count of 130x10^3/μL (150 – 450)
Comprehensive metabolic panel: within normal limits except for elevated creatinine of 2.9 mg/dL (0.5 – 1.4), albumin of 3.3 g/dL (3.5 – 5.0), total bilirubin of 4.5 mg/dL (0.1 – 1.0), unconjugated bilirubin of 2.2 mg/dL (0.1 – 1.0), and serum alkaline phosphatase of 141 U/L (30 – 120)
Mineral Balance: Calcium (corrected for albumin), inorganic phosphate, and magnesium were within normal limits.
Parathyroid Hormone: 39 pg/mL (15 – 75)

Coagulation Studies: PT 21.8 s (12.0 – 14.7), INR 1.9 (0.9 – 1.1), and PTT 47.6 s (24.0 – 34.0)

DIAGNOSIS
Calciphylaxis with concurrent leukocytoclastic vasculitis

CLINICAL COURSE
The patient was admitted for pain control and shortly thereafter discharged to a subacute rehabilitation center. Sodium thiosulfate was started after histologic-confirmation of calciphylaxis diagnosis. She was readmitted two weeks later with profound anemia, leukocytosis, progression of ulcerations, and worsening pain. Plastic surgery recommended against debridement. Wound cultures grew Pseudomonas aeruginosa and Enterococcus faecalis. After initial treatment with vancomycin and piperacillin/tazobactam, infectious disease specialists recommended the discontinuation of antibiotics, attributing bacterial growth to colonization rather than acute infection. The patient was maintained on sodium thiosulfate and discharged to a subacute rehabilitation center. She died soon thereafter—six weeks following her tissue diagnosis of calciphylaxis and leukocytoclastic vasculitis.

PATIENT B

HISTORY OF PRESENT ILLNESS
A 50-year-old Caucasian female was admitted to the hospital from an outpatient hepatology visit with erythematous to violaceous, exquisitely painful lesions on her thighs. The patient stated that she developed nodules on her thighs three weeks previously, which subsequently became erythematous, warm, and tender. She reported two admissions at an outside hospital for pain control.

PAST MEDICAL HISTORY
Alcoholic cirrhosis complicated by end-stage renal disease (hemodialysis initiated three months earlier), type 2 diabetes mellitus, and depression

PAST SURGICAL HISTORY
Transjugular intrahepatic portosystemic shunt placement with multiple revisions

FAMILY HISTORY
Non-contributory

MEDICATIONS
Insulin (regular human; glargine), lactulose, rifaximin, midodrine, sodium bicarbonate, zinc sulfate, ferrous sulfate, alprazolam, doxepin, duloxetine, gabapentin, famotidine

ALLERGIES
No known drug allergies

PHYSICAL EXAMINATION
Examination revealed a well-nourished, comfortable-appearing, Caucasian female. On the right buttock and bilateral thighs were large, 10 – 30 cm erythematous to violaceous, indurated, retiform plaques, some with central duskiness, ulceration, and black eschar.

HISTOPATHOLOGY
Punch biopsy of the right thigh was obtained for histopathologic analysis, which demonstrated amphophilic granular deposits in the blood vessel walls and free in the subcutaneous adipose tissue. The von Kossa stain confirmed calcium in the vessels and soft tissue. A deep blood vessel demonstrated focal

fibrinoid necrosis of its wall and karyorrhexis of neutrophils, as well as focal thrombosis. Staining with periodic acid-Schiff, methenamine silver, and Fite stains were negative for organisms.

LABORATORY DATA

Complete Blood Count: notable for leukocyte count of 11.9*10^3/μL (3.5 – 11.0), hemoglobin of 7.3 g/dL (11.4 – 14.4)
Comprehensive metabolic panel: within normal limits except for elevated creatinine of 5.2 mg/dL (0.5 – 1.4), albumin of 2.2 g/dL (3.5 – 5.0), conjugated bilirubin of 0.5 mg/dL (0.0 – 0.3), and serum alkaline phosphatase of 240 U/L (30 – 120)
Mineral Balance: calcium (corrected for albumin) and magnesium were within normal limits. Inorganic phosphate 5.5 mg/dL (2.5 – 4.4 mg/dL), 15-Hydroxy-Vitamin D < 7 ng/mL (10 – 52)
Parathyroid Hormone: 255 pg/mL (15 – 75)
Coagulation Studies: PT 15.8 s (12.0 – 14.7), INR 1.3 (0.9 – 1.1), and PTT 47.6 s (24.0 – 34.0)
Auto-antibodies/Serology: ANA, C3, C4, cryoglobulin, anti-dsDNA, and RF all within normal limits

DIAGNOSIS

Calciphylaxis with concurrent leukocytoclastic vasculitis

CLINICAL COURSE

The patient was started on sodium thiosulfate by nephrology. Her hospital course was complicated by the development of acute abdominal pain, with CT scan revealing pneumoperitoneum. Exploratory laparotomy revealed a gastric perforation. The patient was transferred to the surgical ICU, where her postoperative course was complicated by persistent hypotension (requiring vasopressor support), pain, and clotting of multiple central lines. Her condition stabilized prior to development of a rectovaginal fistula, which was repaired surgically. She decompensated shortly following this surgical procedure with respiratory failure and profound hypotension requiring ventilation and vasopressor support. Her family decided to withdraw care, and she died thirteen weeks following her tissue diagnosis of calciphylaxis and leukocytoclastic vasculitis.

DISCUSSION

Calciphylaxis, also known as calcific uremic arteriopathy, is a devastating and uncommon disease, causing significant morbidity and associated with a one-year mortality rate of 45 – 80%. Calciphylaxis predominantly affects patients with chronic kidney failure treated with dialysis. It has also been described in patients with normal kidney function, most commonly those with primary hyperparathyroidism, malignancy, alcoholic liver disease, coagulopathies, and connective tissue diseases. Incidence peaks in the fifth decade of life. Caucasian patients are more commonly affected, as are females. Among patients on hemodialysis, high-risk comorbid conditions include diabetes mellitus, obesity, autoimmune conditions, hypercoagulable states, prolonged treatment with dialysis, and hypoalbuminemia.

The first clinical diagnosis of calciphylaxis was by Bryant and White in 1898, who described it in a six-month-old child with hydronephrosis. The term “calciphylaxis” was coined by Selye, *et al.* in 1961 to describe an induced systemic hypersensitivity reaction producing cutaneous calcinosis in rats. This inducible calcification resulted from exposure of rats to calcifying “sensitizers,” such as vitamin D compounds, parathyroid hormones, and sodium sulfathiazole, and subsequent “challengers,” such as metallic salts and albumin. Although an imperfect recapitulation of human disease, this rat model shaped the conception of calciphylaxis as resulting from dysregulation of calcium, phosphate, and parathyroid hormone levels. Subsequent research has begun to unravel the complex nature of this disease, but the exact pathogenesis remains elusive.

The lesions of calciphylaxis start out as livedoid erythema and subsequently evolve to retiform purpura, indurated plaques, nodules, and ulcerations, all of which are extremely painful. Palpable calcification and

bullae have been noted. A distal pattern of involvement is associated with favorable outcomes whereas involvement of the thighs, buttocks, or abdomen portends a grave prognosis . Involvement of the face and upper extremities is rare. Although cutaneous lesions are most common, vascular calcification within internal organs has been reported. Sepsis is the most common cause of death.

Biopsy is required to definitively diagnosis calciphylaxis. The hallmark histopathologic feature is intravascular calcium deposition in the media of dermal and subcutaneous arterioles. Calcium deposition can be highlighted with von Kossa or Alizarin red stains. Thrombi, fibrointimal hyperplasia, panniculitis, and cutaneous necrosis can also be seen. Multiple sources note a characteristic absence of vasculitis.

The treatment of calciphylaxis requires a multi-disciplinary approach. Wound care, including use of hyperbaric oxygen and sterile maggot therapy, aims to facilitate wound healing, avoid buildup of devitalized tissue, and prevent infection . Surgical debridement remains controversial due to the risk of infection. Regulation of calcium, phosphate, and parathyroid hormone levels is recommended. Multiple systemic treatment options exist, the mainstay of which is intravenous sodium thiosulfate. Its exact mechanism of action is unknown, but it is thought to act as an antioxidant, vasodilator, and chelator of calcium salts. Small studies have shown potential benefits of bisphosphonates as well as cinacalcet (a calcimimetic suppressor of parathyroid hormone secretion). The use of systemic corticosteroids remains controversial although growing evidence suggests inferior outcomes in patients treated with corticosteroids and other immuno-suppressants due to an increased risk of sepsis. Nutritional optimization, pain management, and aggressive dialysis are also important.

The implications of the histopathologic findings of leukocytoclastic vasculitis with calciphylaxis are unclear and, to our knowledge, have not been described previously. Leukocytoclastic vasculitis (LCV) is an immune complex-mediated, small vessel vasculitis with characteristic histopathologic features of vessel wall neutrophilic infiltration with leukocytoclasis, endothelial cell damage, fibrinoid necrosis, and extravasation of red blood cells. Infectious, autoimmune, drug, and malignant etiologies have been described, though the majority of LCV cases are idiopathic. LCV is often isolated to cutaneous vasculature but also can be seen with systemic vasculitis.

Incidental vasculitis, resulting from vascular injury in areas of trauma or ulceration, has been described. Though both of our patients had ulcers, incidental vasculitis is focally restricted to areas of ulceration and necrosis, the features of which were not noted in our tissue cuts. Alternatively, these histopathologic findings could demonstrate a previously undescribed population of calciphylaxis patients. Both patients described in this series shared certain clinical features - hepatorenal syndrome, calciphylaxis diagnosis rapidly following initiation of dialysis, and precipitous clinical decline. More cases and research will be required to determine what, if any, implications—prognostic, therapeutic, or otherwise--these concurrent histopathologic features possess.

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CHICAGO DERMATOLOGICAL SOCIETY **Case #8**

Presented by Larry A Napolitano Jr, MD, Christopher R. Shea MD, Arlene Ruiz de Luzuriaga MD,MPH
Section of Dermatology, Department of Medicine, University of Chicago

HISTORY OF PRESENT ILLNESS

A 47-year-old Caucasian male, recently diagnosed with HLA-DQ2 and anti-tissue transglutaminase antibody-positive celiac disease was referred to dermatology by his gastroenterologist for evaluation and treatment of a pruritic blistering rash of the extensor elbows, knees, and buttocks. The gastrointestinal symptoms, abdominal pain and diarrhea, and cutaneous symptoms started two years prior to presentation and had taken a waxing and waning course. The rash initially improved with a gluten-free diet, but subsequent flares led the patient to present to an outside dermatologist, who obtained biopsies, which led to the diagnosis of dermatitis herpetiformis. He was prescribed mometasone 0.1% ointment for use twice daily during flares, but with inadequate response.

PAST MEDICAL HISTORY

Gastroesophageal reflux disease
Celiac disease

FAMILY HISTORY

Family history of colon cancer in mother and thyroid disease in father

MEDICATIONS

Mometasone 0.1% ointment twice daily during flares, omeprasole 40 mg twice daily

ALLERGIES

No known drug allergies

PHYSICAL EXAMINATION

Clusters of well-demarcated, 3-5 mm, pink papules, a few having erosive centers, scattered over extensor knees, extensor elbows, and superior buttocks bilaterally. Intact vesicles were not observed.

LABORATORY DATA

Thyroid-stimulating hormone 2.08 (0.3-4.00 mcU/mL)
HLA-DQ2-positive, HLA DQ8-negative
Anti-tissue transglutaminase IgA antibody 21 Units (negative= <20 U, weak positive 20-30 U, positive =>30 U)
Anti-gliadin IgG antibody 18 U (negative <20 U, weak positive 20-30 U, positive =>30 U)
Glucose-6-phosphate dehydrogenase (G6PD) 10.0 U/g Hb (8.8-13.4)

HISTOPATHOLOGY

Slides from punch biopsy of the left buttock were reviewed at the University of Chicago. There were microabscesses in the dermal papillae, composed mainly of neutrophils and a few eosinophils. Subepidermal vesicles were noted. The dermis had a superficial and deep perivascular infiltrate of lymphocytes and eosinophils.

DIAGNOSIS

Dermatitis herpetiformis

TREATMENT AND COURSE

Upon presentation to the University of Chicago dermatology practice, his gluten free diet was continued, and he was started on dapsone 50 mg by mouth daily for one month with good control. This dose was subsequently decreased to 25 mg by mouth daily without recurrence of the rash for two months. Due to patient's concerns about recent increase in headaches and relationship to medications, dapsone was subsequently discontinued. Pruritic vesicles occurred within 48 hours. Dapsone was restarted at 25 mg by mouth daily with stable control of dermatitis herpetiformis for six months. While on 25 mg of dapsone, the patient developed nausea, right upper quadrant abdominal pain, and headaches. Gastrointestinal work-up was negative and gastroenterology attributed symptoms to dapsone. The patient discontinued his oral dapsone with subsequent cutaneous DH flare within three days. However, his gastrointestinal symptoms resolved within five days of stopping oral dapsone. A trial of triamcinolone 0.1% ointment and flurandrenolide 0.05% lotion did not improve his cutaneous symptoms. The patient restarted dapsone at his maximum tolerated dose of 6.75 to 12.5mg by mouth three times a week with persistent, but stable, cutaneous manifestations. Given poor tolerance of oral dapsone, this medication was discontinued and topical dapsone 5% gel initiated with twice daily application to affected areas. The patient reported initial resolution and subsequent stable control with topical-only regimen. The patient restarted pral dapsone (12.5 mg by mouth three times a week) of his own volition, without gastrointestinal upset. Patient is now 6months out, with well controlled DH, and intermittent diarrhea.

DISCUSSION

Dermatitis herpetiformis (DH) was initially described by Louis Duhring in 1884. It is a rare dermatologic condition with an estimated prevalence of 11.2 per 100,000 people, affecting mostly patients of Northern European descent and with a male to female ration ranging from 1.5:1 to 2:1. DH is multifactorial disease with strong genetic and autoimmune influences, including a clear immunologic relationship to celiac disease. DH is a polymorphic pruritic skin disease typically characterized by grouped, 1-to 3-mm papules, seropapules, vesicles, crusted erosions, and/or excoriations. Diagnosis of DH can be done via serologic testing, genetic testing or direct immunofluorescence studies. Anti-endomysial and anti-tissue transglutaminase antibodies can be detected through serology, each found to be highly specific with moderate sensitivity for DH. The absence of human leukocyte antigen (HLA) DQ2 or DQ8 has high negative predictive value for DH, such that patients lacking these alleles are very unlikely to have the disease. On direct immunofluorescence, granular deposits of IgA at the tips of dermal papillae are pathognomonic of DH. Proper management of DH includes a strict gluten-free diet (GFD). A consultation with a dietician can be helpful, as a GFD can be difficult to maintain. Sulfone medications, such as dapsone, are often necessary for rapid control of symptoms. Oral dapsone is usually well tolerated, with hematologic abnormalities being the most notable side effect. However, neurological and GI symptoms, including headaches, neuropathy, abdominal pain, nausea, vomiting, and pancreatitis are not uncommon. Prior to starting oral dapsone a screening of glucose-6-phosphate dehydrogenase deficiency is warranted to prevent severe dapsone-mediated hemolysis.

Topical dapsone is a well-tolerated medication with mild side effects including local dryness, rash and sunburn. Topical dapsone was initially introduced in 2004 for the topical treatment of acne vulgaris. It is considered safe to use in patients with glucose-6-phosphate dehydrogenase deficiency and those with sulfonamide allergies, giving a possible treatment option for those with contraindication to oral dapsone. A review of the literature revealed two case reports of methemoglobinemia due to topical dapsone.

There have been two reports in the literature of successful treatment of DH with topical dapsone 5% gel. The first was in a 14 year old male with direct immunofluorescence confirmed DH, with recalcitrant disease on oral dapsone at 25mg daily. A split-body trial of topical dapsone was performed for four weeks with subsequent blinded examination by two dermatologists finding relative improvement of the skin treated with topical dapsone. The second case involved a 66-year-old female, who was started on topical dapsone while awaiting lab work to start oral dapsone. She experienced dramatic improvement in her DH

within two weeks of starting therapy and had lasting control at one year of follow up on GFD and topical dapsone only. Our case demonstrates short term disease control with twice daily topical dapsone 5% gel and a typically subtherapeutic dose of oral dapsone (12.5 mg three times weekly) in a patient unable to tolerate therapeutic doses of oral dapsone.

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CHICAGO DERMATOLOGICAL SOCIETY **Case #9**

Presented by Haider K. Bangash, MD, Vesna Petronic-Rosic, MD, MSc, Arlene Ruiz de Luzuriaga, MD, MPH
Section of Dermatology, Department of Medicine, University of Chicago

UNKNOWN

A 51-year-old African American male presented with a 3-year history of recurrent pruritic nodule on right cheek.

CHICAGO DERMATOLOGICAL SOCIETY **Case #10**

Presented by Juliana Gao, MD[1], Vera Tesic, MD[2], Vesna Petronic-Rosic, MD, MSc[1]
[1]Section of Dermatology, Department of Medicine, University of Chicago
[2]Department of Pathology, University of Chicago

HISTORY OF PRESENT ILLNESS

An 85-year-old Caucasian female presented to dermatology clinic for evaluation of a growing painful nodule on the scalp. It had recently become crusted. She also complained of intermittent associated stabbing and shooting pain. The lesion was thought to be a cyst, and she was scheduled for excision.

Prior to the onset of symptoms, the patient had traveled to India and Belize, returning to the United States just a few weeks prior to presentation.

PAST MEDICAL HISTORY

Squamous cell carcinoma in-situ
Basal cell carcinoma

FAMILY HISTORY

Non-contributory

MEDICATIONS

Atovaquone-proguanil
Calcium carbonate
Econazole cream

ALLERGIES

No known drug allergies

PHYSICAL EXAMINATION

Initial examination in clinic showed a 1 cm subcutaneous nodule with overlying linear erosion and hemorrhagic crust. Examination in procedure clinic 4 weeks later showed a 2.5 cm subcutaneous nodule with central 1 mm “punched-out” opening.

INTRAOPERATIVE FINDINGS

After the area was prepped and anesthetized, a standard fusiform incision was made over the subcutaneous nodule. Upon removal of the overlying skin, a 1.2 cm yellow striated larva was identified. The larva was alive and moving at the time. The specimen was then sent to microbiology for further identification.

HISTOPATHOLOGY

Histopathology of the overlying skin showed dense, chronic inflammation, with neovascularization and edema associated with tunneling epithelium, consistent with granulation tissue and overlying fistula tract.

LABORATORY DATA

The larva was identified as *Dermatobia hominis*

DIAGNOSIS

Furuncular botfly myiasis

TREATMENT AND COURSE

The patient was empirically started on cephalexin 500 mg twice a day for a total of ten days. A head CT was obtained and did not show evidence of skull or sinus involvement. At one week follow up, she was healing well and reported resolution of the stabbing and shooting pain over the area.

DISCUSSION

Geographic locations of cutaneous myiasis are usually limited to the tropical and subtropical areas, including countries in Central America, South America, Africa and the Caribbean Islands. It is very uncommon within the United States, and the majority of patients had recent travel to topical areas. Most commonly, the botfly causes furuncular myiasis, but patients with open wounds can also develop wound myiasis. Cavitary myiasis occurs when the botfly larva is deposited near facial orifices, where it can then burrow deeper to involve the nearby sinuses.

Dermatobia hominis (human botfly) is one of the most common flies that cause human infestation worldwide, and one of the two frequent causes of furuncular myiasis. The life cycle of a botfly involves a blood-sucking arthropod as well as a warm-blooded host (mammal or avian). The adults of *D. hominis* are free living. During breeding, they lay eggs on the bodies of mosquitos, where they are cemented via a glue-like substance. Larvae develop within the eggs and remain there until the arthropod comes in contact with a warm-blooded host during feeding. Once in contact with the host, the larva penetrates into the skin and remains in a subdermal cavity for the next 5 to 10 weeks where it feeds on the host as it matures. Typically, these present as boil-like lesions with a central punctum which functions as a breathing hole for the larva. Once the larva matures, it burrows through the breathing hole and drops to the ground where it pupates and becomes a free-living botfly.

During their course of maturation, botfly myiasis usually does not pose any danger to the host. Patients may experience pruritus, sensations of movement and lancinating pain, which may be explained by rotational movement of the larvae and its rows of hooklets. Secondary bacterial infections with *Staphylococcus* and Group B S*treptococcus* have been reported. Overall, furuncular myiasis is a self-limited infestation as the larvae will eventually leave the host; however, leaving the parasite to perform its natural cycle is generally not recommended.

There are several methods used for the extractions of the botfly larvae. Traditional folk remedy calls for a strip of bacon over the central punctum to suffocate the larvae, which forces it to surface for air over the course of several hours, at which point the larva can then be gently extracted with a forceps. This can also be accomplished using petroleum jelly, liquid paraffin, beeswax, or even nail polish. Other authors have advocated the use of 1% lidocaine to paralyze the parasite, and liquid nitrogen to stiffen the larvae for easier extraction. In most cases, surgical excisions and extractions are unnecessary, but can be done under local anesthesia if other methods of extractions are unsuccessful. Antibiotics are recommended if there are signs or symptoms of secondary bacterial infection.

We present this case of furuncular myiasis for clinical interest, and to highlight the importance of travel history in the diagnosis of cutaneous parasitic infections.

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