Chicago Dermatological Society

November 2007
Monthly Educational Conference

Program Information
Continuing Medical Education Certification
and
Case Presentations

Wednesday, November 14, 2007

Conference Location:
University of Chicago Hospitals
Chicago, Illinois

Program

Committees & Registration

8:00 a.m. - 9:00 a.m.	IDS Board of Directors Room A-109
9:00 a.m. - 10:00 a.m.	CDS Plans & Policies Committee Room A-109

Program Activities

8:00 a.m.	Registration opens & continental breakfast Billings Auditorium Foyer - Room P-117
9:00 a.m. - 10:00 a.m.	Resident Lecture – *Billings Auditorium, Room P-117* TRENDS IN CUTANEOUS ANGIOGENESIS Jack L. Arbiser, MD, PhD
9:30 a.m. - 11:00 a.m.	Clinical Rounds *Duchossois Center for Advanced Medicine, 5758 S. Maryland Ave.* Patient Viewing – *Dermatology Clinic 6C* Slide Viewing – *Room 1402*
11:00 a.m. - 12:15 p.m.	General Session - *Billings Auditorium, Room P-117*
11:00 a.m.	CDS Business Meeting
11:15 a.m.	Guest Lecture – MELANOMA, MANY MUTATIONS, FEW PATHWAYS Jack L. Arbiser, MD, PhD
12:15 p.m. - 1:00 p.m.	Luncheon *Box lunches to be distributed in the basement of Billings Auditorium*
1:00 p.m. - 2:30 p.m.	Case Discussions – *Billings Auditorium, Room P-117*
2:30 p.m.	Meeting adjourns

CME Information

This activity is jointly sponsored by the Chicago Medical Society and the Chicago Dermatological Society.

This activity has been planned and implemented in accordance with the Essentials Areas and Policies of the Accreditation Council for Continuing Medical Education (ACCME) through the joint sponsorship of the Chicago Medical Society and the Chicago Dermatological Society. The Chicago Medical Society is accredited by the ACCME to provide continuing medical education for physicians. The Chicago Medical Society designates this educational activity for a maximum of four (4) *AMA PRA category 1 credits*™. Each physician should claim only those hours of credit that he/she actually spent in the educational activity.

Commercial Support: There are no educational grants associated with this meeting. One or more companies may pay a fee to be present as exhibitors. The program content is free from any commercial or corporate influence.

Guest Speaker

JACK L. ARBISER, MD, PHD; Associate Professor of Dermatology; Emory University School of Medicine; Atlanta – Dr. Arbiser joined the Dermatology Department at Emory after completing his PhD and medical school training, internship and residency at Harvard University. He also completed a 3-year Howard Hughes Fellowship and junior faculty position in the laboratory of Dr. Judah Folkman (Harvard Medical School). He was certified by the American Board of Dermatology in 1995. Dr. Arbiser's research focuses on the regulation of angiogenesis and tumorigenesis by signal transduction pathways

Speaker CME Disclosure of Financial Interests

Dr. Arbiser serves on the scientific advisory board of Johnson & Johnson; is a founder of Naturderm and Curry Pharmaceuticals; and is a shareholder in Genentech.

CME Credit Documentation

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

Evaluation Forms

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

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PRESENTERS
Bernhard Ortel, MD, Christiane Querfeld, MD, Vesna Petronic-Rosic, MD, MS, and Keyoumars Soltani, MD

HISTORY OF PRESENT ILLNESS
A 47-year-old Caucasian male presented for evaluation of plaques that had first appeared 6 years earlier on his scalp, face and trunk. In July 2005, three rapidly growing flat tumors were excised from the scalp yielding a histological diagnosis of perifolliculitis. The excision specimen of an additional lesion from the cheek two months later was diagnosed histologically as granuloma faciale. In 2007 the patient came to our outpatient clinic for an additional opinion and to discuss treatment options.

PAST MEDICAL HISTORY
Hypertension, diabetes mellitus type II, lower extremity cellulitis 2006

REVIEW OF SYSTEMS
Non-contributory

MEDICATIONS
Lisinopril, amlodipine, metformin, atorvastatin

ALLERGIES
No known drug allergies

FAMILY HISTORY
Non-contributory

SOCIAL HISTORY
Non-smoker, works late shifts

PHYSICAL EXAMINATION
On the scalp several thick light brown plaques with polycyclic borders were present. The surface was smooth and had accentuated follicular openings. Smaller round lesions with similar morphology were disseminated on the face, neck and trunk. The lesions were firm and non-tender and did not bother the patient except for their appearance.

LABORATORY DATA
Pending

DERMATOPATHOLOGY
Specimens from the scalp lesions shared the following features. The epidermis was acanthotic and the underlying papillary dermis showed fibrosis. The dermis contained an inflammatory cell infiltrate composed of neutrophils, eosinophils and plasma cells with occasional Russell bodies. The infiltrate showed a perivascular distribution with areas of leukocytoclasia and concentric perivascular fibrosis.

DIAGNOSIS
Fibrosing Leukocytoclastic Vasculitis – Erythema Elevatum Diutinum (EED) versus Granuloma Faciale (GF)

TREATMENT & COURSE

Several lesions had been excised in the past. Two persistent, fibrotic-appearing plaques on the scalp were planed using surgical shave technique. The specimens were submitted for histological evaluation, and the bases treated with the 595nm flashlamp pulsed dye laser. Because of the dense infiltrate with numerous neutrophils and eosinophils, a trial with dapsone is planned following the systemic work-up.

DISCUSSION

This patient presented with a clinical picture typical for neither EED nor GF. Multiple chronic plaques and tumors were localized first and predominantly on extra-facial areas including the trunk, while the extensor surfaces of the joints were spared. The individual red-brown lesions had a peau d'orange surface without visible scale. Histopathology showed leukocytoclastic vasculitis, perivascular fibrosis, and a mixed inflammatory infiltrate of neutrophils, eosinophils, and plasma cells. The acanthotic epidermis was separated from the cellular infiltrate by a fibrotic band of papillary dermis.

EED is considered a chronic leukocytoclastic vasculitis that most commonly affects middle-aged patients without gender bias or familial association. Multiple disease associations have been described, including those with hematological and autoimmune disorders, immune suppression and infections. Therefore, EED is included in the spectrum of neutrophilic dermatoses. The lesions are typically localized to joint extensor surfaces.

GF affects middle-aged men more than women with multiple lesions in less than 40%. Only a small group of patients have extrafacial plaques; even less both facial and extrafacial involvement. GF may be associated with eosinophilic angiocentric fibrosis, an idiopathic nasal mucous membrane inflammation with similar histologic features.

Due to shared features of both conditions, we consider this presentation a middle ground of the spectrum of fibrosing cutaneous neutrophilic vasculitides that spans from EED to GF. The treatment for both conditions may be frustrating. In EED dapsone may induce remission but its discontinuation leads to relapse. Recent success in the treatment of GF with calcineurin inhibitors is encouraging. Both conditions have been treated with a host of additional modalities with variable, mostly moderate success at best. Response to vascular-targeted laser treatment has been reported for GF as well as EED.

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PRESENTERS
Olga Ulitsky, MD and Sarah L. Stein, MD

HISTORY OF PRESENT ILLNESS
A 28 month-old male with a history of eczema was transferred to Comer Children's Hospital with a fever and new-onset blistering. He had had severe itching and redness on his hands and face for approximately four-five days and a fever of 39°C for two days prior to presentation. His mother noticed that blisters appeared first on the face and spread to areas where the eczema was most severe.

PAST MEDICAL HISTORY
Atopic dermatitis

MEDICATIONS
Acyclovir, clindamycin

ALLERGIES
No known drug allergies

FAMILY HISTORY
Father and brother with histories of atopic dermatitis, not active

SOCIAL HISTORY
The patient lives with his parents. Five days after admission, it was discovered that the patient's father was in the U. S. Army in Iraq and had visited his family for five days, two weeks prior to the patient's admission, and three weeks after receiving a smallpox vaccination.

PHYSICAL EXAMINATION
The patient presented with erythema over much of the face, with multiple areas of shallow erosions and small vesicles. The neck, upper chest, arms, and legs demonstrated thick, lichenified plaques with scattered vesicles, pustules, and erosions. Over the next three days, he developed more flesh-colored, umbilicated vesicles that spread over large areas of the face, trunk, and extremities.

LABORATORY DATA
Direct fluorescent antibody (DFA): (-) herpes simplex and varicella zoster virus.
Blood culture: methicillin-susceptible *Staph. aureus* (MSSA) and Group G *streptococcus*.
Wound culture: methicillin-resistant *Staph. aureus* (MRSA).
Polymerase chain reaction: vesicular scrapings and viral culture supernatant were (+) for non-variola orthopoxvirus, confirmed by vaccinia-specific PCR at the Centers for Disease Control (CDC).

DIAGNOSIS
Eczema Vaccinatum

TREATMENT & COURSE
Admission diagnosis was eczema herpeticum with bacterial superinfection. The patient was treated with acyclovir, clindamycin and topical care. Immediately upon confirmation of the diagnosis of eczema vaccinatum, Vaccinia Immune Globulin Intravenous (VIGIV) was delivered by the U.S. Department of Defense and Centers for Disease Control and administered. The patient was transferred to the pediatric intensive care unit for aggressive wound care, pain control,

and fluid and electrolyte management. The patient's condition continued to deteriorate requiring intubation. Ongoing viremia and continued spread of skin lesions prompted administration of cidofovir, a second line antiviral agent recommended in the management of vaccinia infection. In addition, ST-246, an investigational new agent with activity against multiple orthopoxvirus species, was also administered. By hospital day eight, there were no new skin lesions, by day 13 the existing lesions began to crust. Plastic surgery ultimately placed cadaveric allografts on limited areas of deeper dermal injury. The patient was discharged home on hospital day 48 and was functioning close to his baseline.

The patient's mother also reported a rash, which began on her face and then spread to her neck and fingers over the next five days. She also developed cervical lymphadenopathy, fatigue, and myalgias. Vaccinia infection was confirmed by virus specific PCR analysis, and she was admitted to the same hospital room as the child. After treatment with a single dose of VIGIV, her lesions began to scab, and systemic symptoms resolved.

DISCUSSION

Vaccination against smallpox with vaccinia virus was practiced throughout the 20th century until 1980 when the World Health Organization (WHO) announced the eradication of smallpox infection. In response to the possibility of intentional release of smallpox virus as a biological weapon, the U.S. government re-instituted immunization to select military and public health personnel most at risk for exposure in December 2002.

Eczema vaccinatum is a potentially life threatening illness that occurs in individuals with atopic dermatitis, who are exposed to vaccinia virus either through direct vaccination or contact with a recent vaccinee. Since restarting immunizations in 2002, no confirmed cases of eczema vaccinatum have been reported in the United States until now. Life threatening complications of smallpox also include encephalitis and progressive vaccinia. Other adverse reactions include inadvertent inoculation, generalized vaccinia, and erythema multiforme.

Current military pre-vaccination screening includes a history of atopic dermatitis in the vaccinee or in household contacts as a contraindication to receiving the smallpox vaccine. Under these criteria the patient's father should never have been vaccinated. The father's close contact with his son, as well as his own history of eczema likely contributed to prolonged viral shedding and increased likelihood of transmission.

Prior to the 1950s, there was no specific therapy for vaccinia infections. Since the increase in vaccinations in September 2001, research for new therapeutic agents has resumed. Several novel therapies from this research were used for the treatment of this patient, including VIGIV, cidofovir, and ST-246. Prior to immunoglobulin therapy, the reported mortality rate of eczema vaccinatum was between 30-40%.

This case illustrates the importance of careful pre-vaccination screening and the potential hazards of smallpox vaccination. A high index of suspicion is required to make this diagnosis. Further research is required to ensure safe vaccination and new therapeutic options as long as the threat of smallpox exists.

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PRESENTERS
Diana Bolotin, MD, PhD, Christopher R. Shea, MD, and Sarah L. Stein, MD

HISTORY OF PRESENT ILLNESS
The patient is a 13-year-old Hispanic boy presenting for evaluation of lesions on his arms and lower legs that have been present for the past 3 years. The lesions are asymptomatic but are increasing in number. The patient was previously treated for "folliculitis" with incision and drainage of one of the lesions in the emergency department and a 10-day course of oral clindamycin without improvement. The patient denied any preceding or associated illnesses.

REVIEW OF SYSTEMS
The patient denied muscle pain or weakness, joint pains, fever, or weight loss.

PAST MEDICAL HISTORY/ MEDICATIONS/ ALLERGIES
None

FAMILY HISTORY
Maternal uncle who lives in Mexico has reportedly similar nodules on the arms and no known diagnosis. No known autoimmune diseases or malignancy.

SOCIAL HISTORY
Patient was born in Mexico and travels there frequently, but lives with his parents in Chicago.

PHYSICAL EXAMINATION
There are scattered, firm, white, and hyperpigmented papules and medium-sized nodules on the extensor surfaces of bilateral forearms and shins. Additionally, there are indurated, pitted subcutaneous plaques palpable between and underlying the papules on the forearms.

DERMATOPATHOLOGY
A 4 mm punch biopsy specimen from a representative lesion on the patient's right arm was obtained under local anesthesia. The pathology revealed epidermal hyperplasia with transepidermal elimination of basophilic, granular deposits. The dermis also contained abundant amphophilic deposits of mineral material.

IMAGING
Complete retroperitoneal ultrasound: normal
Skeletal survey: Extensive popcorn calcifications of the soft tissues of arms and legs and near the wrists and metacarpophalangeal joints. No hyperostosis.

DIAGNOSIS
Calcinosis cutis with perforation, possibly in the setting of Familial Tumoral Calcinosis

TREATMENT & COURSE
The patient underwent evaluation by pediatric nephrology, but no clear metabolic cause for his hyperphosphatemia was identified. Given the patient's unexplained hyperphosphatemia, extensive soft tissue calcification, and possible family history of similar subcutaneous lesions, familial tumoral calcinosis seems the most likely explanation for this constellation of findings. Optimal treatment is being considered.

DISCUSSION

Cutaneous calcification disorders have traditionally been divided into four categories: metastatic, dystrophic, iatrogenic and idiopathic. Metastatic calcinosis cutis generally refers to disorders involving metabolic dysfunction of calcium regulation such as secondary hyperparathyroidism and hyperphosphatemia of chronic renal insufficiency. Conversely, dystrophic cutaneous calcification occurs in the absence of metabolic abnormalities and is due to localized tissue damage that is most often seen in autoimmune connective tissue disease. In the pediatric population, calcinosis cutis is frequently due to dermatomyositis. Calcinosis cutis without definitive historical, clinical, or laboratory evidence of metabolic or rheumatologic disease tends to fall into the category of idiopathic cutaneous calcinosis.

Histologically, calcinosis cutis exhibits dark, basophilic deposits on hematoxylin and eosin staining of the skin. These may be surrounded by fibrosis or foreign-body reaction. Calcinosis cutis with transepidermal elimination has been reported in patients with renal disease.

Cutaneous calcinosis is a rare presentation of tumoral calcinosis. Since tumoral calcinosis encompasses a spectrum of pathologic processes, a reclassification scheme has been proposed and widely used for these disorders into primary normophosphatemic, primary hyperphosphatemic, and secondary tumoral calcinosis. Familial tumoral calcinosis falls into the primary hyperphosphatemic category and is a rare, idiopathic calcifying disorder that typically presents as soft tissue and skin calcification in patients in their teens. These deposits often accumulate to form tumoral masses in the periarticular and extensor regions of the extremities. Laboratory values characteristic of this disorder include elevated serum phosphate level and normal to elevated serum calcitriol but normal serum PTH, electrolytes and BUN/Cr.

Recently two genetic mutations have been identified in families with familial tumoral calcinosis. GALNT3 and FGF23 mutations are both thought to lead to a deficiency in circulating FGF23 signaling molecule. FGF23 is involved both in stimulating phosphate excretion and in down-regulating 25-hydroxyvitamin D1 hydroxylase. Thus lower levels of FGF23 lead both to increased phosphate reabsorption in the distal nephron (with resulting hyperphosphatemia) and upregulation of calcitriol production (with resulting high calcitriol relative to the level of hyperphosphatemia in these patients). Hyperphosphatemia leads to calcium phosphate crystal deposition in the soft tissues of patients with familial tumoral calcinosis.

Patients with familial tumoral calcinosis must be counseled to avoid trauma, which can lead to further calcifications. Treatment options for this condition include surgical excision and phosphate depletion therapy with acetazolamide, diet, and aluminum hydroxide.

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PRESENTERS
Christiane Querfeld, MD, Vesna Petronic-Rosic, MD, MS, Keyoumars Soltani, MD, Aisha Sethi, MD, and Christopher R. Shea, MD

PATIENT A

HISTORY OF PRESENT ILLNESS
This 62 year-old white man presented with a four-week history of a non-pruritic papulo-nodular eruption on the trunk and extremities. Histopathological evaluation of an outside biopsy was described as cutaneous involvement of CD56+ lymphoma with diffuse atypical mononuclear cells.

PAST MEDICAL HISTORY
Status post resection of left occipital lobe hemangioma in 2005, chronic meningeal infection secondary due to impaired brain barrier, rheumatoid arthritis previously treated with adalimumab and methotrexate, history of pneumonia with pleural effusion, benign prostatic hypertrophy, and attention deficit disorder.

MEDICATIONS
Naproxen, prednisone, hydroxychloroquine, tamsulosin, amphetamine-dextroamphetamine, modafinil, varenicline, co-trimoxazole

ALLERGIES
No known drug allergies

FAMILY HISTORY
Father died of prostate cancer; mother is alive with dementia and hypothyroidism.

SOCIAL HISTORY
He is a graphic designer does not currently smoke with a history of smoking one pack of cigarettes per day for 35 years; drinks four glasses of wine per week, denies illicit drugs.

PHYSICAL EXAMINATION
The exam showed numerous erythematous to violaceous papules and nodules distributed on the neck, trunk, and upper and lower extremities. There was palpable left axillary lymphadenopathy. No hepatosplenomegaly was noted.

LABORATORY DATA
White blood cell count slightly elevated at 11,400/uL, otherwise complete blood cell count with differential, comprehensive metabolic panel, uric acid, and LDH were all within normal limits.
Peripheral blood negative for FLT3 gene mutation.
Flow cytometry of left axillary lymph node: no significant CD56+ population.

HISTOPATHOLOGY
Left arm: Superficial and deep dense dermal infiltrate with sheets and cords of neoplastic cells involving appendageal structures. Neoplastic cells were intermediate in size with large, round to oval nuclei and prominent nucleoli. Numerous atypical mitotic figures were noted. There was a grenz zone sparing the epidermis. Tumor cells were positive for CD4, CD56, and CD123. The myeloperoxidase reaction was negative.

Bone marrow: hypercellular bone marrow with focal involvement of CD4+CD56+ cells. T-cell rearrangement studies: monoclonal.

IMAGING
8/23/2007 CT scan of chest, abdomen, and pelvis did not demonstrate significant adenopathy.

DIAGNOSIS
CD4+/CD56+ Hematodermic Neoplasm

TREATMENT & COURSE
The patient is being followed by hematology/oncology and dermatology. He underwent induction chemotherapy with high-dose cytarabine (HIDAC) and mitoxantrone leading to regression of his skin lesions after two cycles. Skin and bone marrow biopsies were negative for neoplastic cells. However, he relapsed shortly after his second course with new cutaneous nodules. Subsequent skin and bone marrow biopsy revealed recurrence of his hematodermic neoplasm. The patient otherwise feels well. His regimen was switched to high-dose IV methotrexate and the patient is currently being evaluated for an allogeneic bone marrow transplant.

PATIENT B
HISTORY OF PRESENT ILLNESS
This 70 year-old white man presented with a three-week history of a non-pruritic papulo-nodular eruption on his trunk and extremities. He complained of increased fatigue and shortness of breath. He had received a recent diagnosis of acute leukemia of ambiguous lineage confirmed by blood and bone marrow biopsies with cytogenetic analysis; the leukemia was initially thought to be a therapy-related acute myeloid leukemia (AML) secondary to therapy for large B-cell lymphoma of the left posterior chest wall in 2005. He underwent previous induction chemotherapy with HIDAC and daunarubicin for his acute leukemia followed by 2-chlorodeoxyadenosine (2-CdA) and was in remission prior to the onset of the rash.

PAST MEDICAL HISTORY
Acute leukemia of ambiguous lineage in 2006, large B-cell lymphoma in 2005, prostate-carcinoma status post prostatectomy, status post appendectomy, status post tonsillectomy, COPD/asthma, nephrolithiasis

MEDICATIONS
Fluticasone/salmeterol inhaler, albuterol inhaler, potassium citrate

ALLERGIES
No known drug allergies

FAMILY HISTORY
Mother is alive with history of breast cancer

SOCIAL HISTORY
He is single and lives with his mother and brother. He denies tobacco, alcohol, or illicit drugs.

PHYSICAL EXAMINATION
There were numerous skin-colored, erythematous to violaceous papules and nodules distributed on the trunk, upper and lower extremities. There were no cervical or axillary lymphadenopathy or hepatosplenomegaly noted.

LABORATORY DATA
Elevated white blood cell count at 22,600/uL with predominantly blasts (32%) and myeloid precursor cells, hematocrit 36.9%, platelets 98,000/uL, LDH 7565 U/L, SGOT 178 U/L, SGPT 85 U/L, glucose 146 mg/dL, otherwise normal comprehensive metabolic panel.
Peripheral blood negative for FLT3 gene mutation.
Flow cytometry of peripheral blood: 60-80% of large blast-like cells are CD4+CD56+ population.

HISTOPATHOLOGY
Left arm: dense dermal and subcutaneous infiltrate with diffuse and nodular aggregates of large atypical cells with large nuclei and prominent nucleoli. Numerous mitotic figures were present. There was a grenz zone sparing the epidermis. Tumor cells were positive for CD4 and CD123 and weakly positive for CD56. The myeloperoxidase reaction was negative.

Bone marrow: hypercellular bone marrow almost completely replaced by large blast-like CD4+CD56+ cells. T- and B-cell rearrangement studies: polyclonal for T-cells and monoclonal for B-cells.

IMAGING
1/6/2007 CT scan of chest with bilateral pleural effusions, large subcarinal calcified lymph node, calcified pulmonary granulomas

DIAGNOSIS
CD4+/CD56+ Hematodermic Neoplasm, Leukemic Phase

TREATMENT & COURSE
The patient is being followed by hematology/oncology and dermatology. He was restarted on 2-CdA as this regimen was well tolerated in the past and led to near-complete regression of his skin infiltrates after one course; however, significant tumor lysis syndrome and neutropenia necessitated discontinuation of his therapy. A second course with HIDAC and mitoxantrone was initiated one month later, however, the patient was found to have refractory leukemia/lymphoma with excess number of blasts (99%) on peripheral blood smear. Home hospice care was arranged.

DISCUSSION
The new revised WHO-EORTC consensus classification for cutaneous lymphomas categorizes CD4+CD56+ hematodermic neoplasm, formerly known as blastic CD56+ NK-cell lymphoma, as a precursor hematological neoplasm. It is a rare, highly aggressive tumor with poor prognosis that frequently presents in the skin followed by rapid nodal and bone marrow involvement and leukemic dissemination. Accordingly, early plasmacytoid dendritic cell leukemia/lymphoma has been proposed as a more appropriate term.

The blastic morphology and expression of CD4 and CD56 in the absence of lineage-specific markers of T-cells, B-cells, or myelomonocytic cells initially suggested an NK precursor origin. Further immunophenotyping studies have shown that these cells are characterized by plasmacytoid dendritic cell markers such as CD123 and T-cell leukemia/lymphoma 1 (TCL1), suggesting a plasmacytoid dendritic precursor origin. Cutaneous lymphocyte antigen (CLA) is usually expressed in CD56+ plasmacytoid cells and may explain their skin-homing property.

Patients usually present with erythematous to violaceous papules, plaques, or nodules of heterogeneous size, but a more ecchymosed type of presentation has also been observed. Approximately 50% of patients at initial presentation have bone marrow and/or nodal involvement. When performed, skin biopsies reveal histopathologic features of a dense dermal

infiltration of uniform blast-like cells with periappendageal involvement. Epidermotropism is usually absent.

The relationship of hematodermic CD4+CD56+ malignancies to myeloid leukemias has been described. CD4+CD56+ plasmacytoid cells share some features with blast cells of acute leukemia. CD56 can be expressed in 20% to 30% of AML with monocytic differentiation (French-American-British classification M4/M5) and is frequently associated with cutaneous presentation suggesting that CD4+CD56+ hematodermic neoplasms are conceptually similar to aleukemic leukemia cutis.

There is at present no curative treatment for CD4+CD56+ hematodermic neoplasms and overall prognosis is dismal. Adverse prognostic factors are advanced age and bone marrow involvement. Patients are best treated with regimens used in acute leukemias. Most patients respond favorably to induction chemotherapy with complete remission, but they relapse frequently to skin and extracutaneous sites, and undergo rapid leukemic dissemination and ultimately die of disease. The median survival is 12-14 months. No significant differences have been found between patients presenting with skin lesions with or without concurrent extracutaneous disease. However, a recent retrospective analysis from the Dutch Cutaneous Lymphoma Group found that patients presenting with solely cutaneous involvement had a better prognosis than those presenting with both cutaneous and extracutaneous disease, median survival was 21 months versus 12 months, respectively. Allogeneic hematopoietic stem cell transplantation has been shown to improve survival in single cases.

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PRESENTERS
David J. Mann, MD, Irene J. Vergilis, MD, Justin R. Wasserman, MD, Christopher R. Shea, MD, Aisha Sethi, MD, and Vesna Petronic-Rosic, MD, MS

PATIENT A

HISTORY OF PRESENT ILLNESS
This 64-year-old white woman with histologically confirmed (2006) genital lichen sclerosus et atrophicus (LSA) presented in March of 2007 with an inframammary rash and "red, itchy bumps" located in the bilateral axillae for four months. No previous treatment was applied to the extragenital lesions, although clobetasol had been prescribed by her gynecologist for the genital LSA.

Initially the patient was seen in 2004 for a "depression" in her right arm which was followed for several months. The patient refused a biopsy or MRI, and a presumptive diagnosis of lipoatrophy was made. Later that year, she began to experience additional pruritic spots on her neck, thigh, and shoulder.

PAST MEDICAL HISTORY
Atopic dermatitis, stasis dermatitis

MEDICATIONS
Clobetasol ointment, alendronate sodium, lisinopril

ALLERGIES
Aspirin, sulfa

FAMILY HISTORY
Unremarkable for any skin disorders or skin cancer

SOCIAL HISTORY
Middle-school teacher

PHYSICAL EXAMINATION
Involving the chest, axillae, and submammary regions there were numerous erythematous papules, several of which had collarettes of scale. Involving the lower abdomen, there were hyperpigmented, hyperkeratotic stuck-on papules. Varicosities and hyperpigmented patches were present on both lower extremities. The rest of the physical examination was unremarkable.

LABORATORY DATA/IMAGING
The following tests were performed: lipid panel, CBC with differential, hemoglobin A1c, thyrotropin, and a comprehensive metabolic panel. All results were within normal limits except for elevated triglycerides of 156 mg/dL (30-149), cholesterol of 246 mg/dL (120-199), LDL cholesterol 155 mg/dL (60-129).

DERMATOPATHOLOGY
Two shave biopsy specimens (axilla and chest) revealed an atrophic epidermis. The papillary dermis was edematous and sclerotic. There was a lymphocytic infiltrate in the dermis. The final pathologic diagnosis was consistent with lichen sclerosus et atrophicus.

DIAGNOSIS
Lichen Sclerosus et Atrophicus

TREATMENT & COURSE
The patient was started on tacrolimus ointment and was last seen on 10/30/2007 with intermittent flares of pruritus involving the same lesions. Tretinoin cream (0.025%), nystatin powder, and ammonium lactate cream were added to her treatment regimen.

PATIENT B:
HISTORY OF PRESENT ILLNESS
This 71-year-old African American woman presented for evaluation of a worsening rash in the form of pruritic white spots spreading over the chest, back, elbows, and legs. The patient had not been using any treatment for several years.

Initially, she was seen in September of 2004 for a burning spot on her right thigh after spilling iodine on that location one-month prior. The patient was subsequently diagnosed with lichen simplex chronicus and treated with topical triamcinolone and tacrolimus. At that time, she was found to have clusters of hypopigmented and depigmented macules on her back and left shoulder and depigmented flat papules on the lower extremity. The lesions were occasionally mildly itchy. In December 2004, a punch biopsy of the abdomen proved consistent with lichen sclerosus et atrophicus She was advised to use moisturizers only and subsequently was lost to follow up until October of 2007.

PAST MEDICAL HISTORY
Hypertension

MEDICATIONS
Hydrochlorathiazide, atorvastatin, irbesartan, amlodipine, aspirin, metformin

ALLERGIES
Penicillin

FAMILY HISTORY
Diabetes mellitus

SOCIAL HISTORY
The patient was a housewife for most of her adult life (worked in housekeeping for a hotel for 10 years). Denies tobacco products, rarely drank, denies illicit drugs.

PHYSICAL EXAMINATION
There were multiple perifollicular shiny white macules, some with slight scale located in a generalized distribution on the trunk and extremities. On the left shoulder and back, there was a shiny plaque with hypopigmented macules and follicular scale within it. The rest of the physical exam was unremarkable.

LABORATORY DATA/IMAGING
The patient had a recent CBC with differential, BMG, lipid panel, and hemoglobin A1c. All results were normal except for an elevated HDL of 101 mg/dL (40-80), serum glucose of 117 mg/dL (60-109), and carbon dioxide 34 mEq/L (23-30).

DERMATOPATHOLOGY
Two punch biopsy specimens (10/11/07 from the right back and 12/27/04 from the right abdomen) revealed that the epidermis was atrophic. The papillary dermis was edematous and

sclerotic. There was a lymphocytic infiltrate in the dermis. Final pathologic diagnosis: lichen sclerosus et atrophicus.

DIAGNOSIS
Lichen Sclerosus et Atrophicus

TREATMENT & COURSE
The patient was started on clobetasol ointment and scheduled to follow up in 2 months. Future management of the generalized LSA is being discussed.

DISCUSSION
Lichen sclerosus et atrophicus (LSA) is a chronic inflammatory, scarring dermatologic disease. Initially described clinically by Hallopeau in 1887 and then histologically by Darier in 1892, the etiology of the disease remains unknown. While it can be seen in all age groups, LSA affects women more commonly than men with a bimodal peak of incidence: the first occurring between eight and thirteen years of age and the second occurring between the fifth and sixth decade, both in women with physiologically low estrogen states.

Histologically, there is homogenization of papillary dermal collagen, extensive edema, a band-like lymphocytic infiltrate, and thinning of the overlying epidermis. Clinically, this results in atrophic or sclerotic white papules, which often coalesce into large plaques.

LSA has a predilection for the anogenital region, seen in 85% of cases in both sexes. Both of our cases presented with extragenital involvement. While15-20% of those with lichen sclerosus have extragenital lesions, neither the flexural nor generalized distribution ("white spot disease") is commonly written about in the literature and is thus less well understood.

Extragenital LSA is often asymptomatic, aside from dryness and itch. Typically, the lesions occur on the trunk and proximal extremities, often favoring the neck, shoulders, wrists, or other sites of increased trauma or sustained pressure. Occasionally, microguttate lesions have been reported. It is unusual for the disease to involve the periorbital area, scalp, palms, and soles. Early on, the white, sclerotic or atrophic papules are found between hair follicles and then often coalesce into larger plaques. Our second case is unusual given its folliculocentric nature and generalized distribution.

There are only a few studies outlining the various treatment options for LSA. First line agents include ultra-potent topical steroids and intralesional triamcinolone injections. One study found ALA-PDT to be effective in relieving the pruritus. Phototherapy has also been used for extragenital LSA. One study demonstrated a marked reduction or clearing after treatment with 40 sessions of UVA-1 (20J/cm2) in ten patients with extragenital lichen sclerosus without acute adverse effects. Other recent case reports proved successful therapy using thrice-weekly narrow band UVB. It is believed that both UVA-1 and narrow band UVB work by increasing matrix-metalloproteinase levels.

Vitamin D and A derivatives have also been reported in the treatment of LSA. One study demonstrated a marked reduction in the number of hypertrophic plaques within three weeks of beginning treatment with calcipotriol 0.005% ointment applied BID under occlusion. Systemic vitamin A has shown some success after several months of treatment. This is thought to work by inhibiting TGF-β, which decreases collagen synthesis by fibroblasts.

There is no evidence that topical testosterone or progesterone are of benefit. Likewise, earlier studies showed no benefit of using penicillin, other antibiotics, or penicillamine. Surgery is typically reserved for symptomatic patients who have failed multiple medical modalities. Recent research has focused on the use of topical tacrolimus for LSA.

A workup is being planned for autoimmune related diseases in our patients, as a 1981 study of 50 women with histologically confirmed LSA (36% of patients had extragenital involvement) showed that 37 were found to have tissue autoantibodies and 17 of 50 had at least one autoimmune disease. A second study in 1988 confirmed this finding, as 147 of 350 women with LSA (17.5% involving extragenital sites) had tissue autoantibodies, 74 of 350 women had one or more first-degree relatives with an autoimmune disease, and 75 of 350 women had one or more autoimmune disease (by history). However, no identifiable difference in clinical features was found in those women who developed autoimmune related phenomena, nor was it clear whether screening for such diseases was justifiable, as only a small percentage developed autoimmune diseases after the diagnosis of LSA.

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PRESENTERS
Justin Wasserman, MD, Vesna Petronic-Rosic, MD, MS, Keyoumars Soltani, MD, Aisha Sethi, MD, and Sarah L. Stein, MD

HISTORY OF PRESENT ILLNESS
A 9-month-old Caucasian male was transferred to Comer Children's Hospital on 5/19/07 for a spreading vesicular rash. The child had a 2-week history of a rash that began behind the ears and spread to the genital and perineal area. He was initially diagnosed with chicken pox. The lesions became more extensive, crusted and purulent. The child developed fever and was treated with clindamycin and acyclovir prior to transfer. There were no known sick contacts.

PERTINENT PMH, FH, SH
Full-term infant, uncomplicated pregnancy and delivery. Immunizations up to date. Does not attend daycare. One brother, 9 years old. One visiting young child, healthy.

MEDICATIONS
When admitted to Comer Children's Hospital on 5/19 – clindamycin and acyclovir

ALLERGIES
No known drug allergies

PHYSICAL EXAMINATION
Vital signs within normal limits. Well developed well nourished male sleeping soundly in no acute distress. Easily arousable, responded appropriately to stimulation. Multiple vesicles and bullae in various stages of development concentrated in the retroauricular and perineal area with lesions extending onto the trunk, extremities, face, and scalp. The posterior aspect was less involved than the anterior aspect, and the inguinal folds were spared. Bullae were arranged in a "crown of jewels" formation. There were focal areas of honey-colored crusting overlying eroded bullae.

LABORATORY DATA
Viral culture negative
DFA - negative for VZV, HSV
Quantitative G6PD - 13.4
CBC (5/30/07) – WBC: 10.8 H/H: 11.2/33.3 Plat: 653

DERMATOPATHOLOGY
H & E - Focal parakeratosis, scattered dyskeratinocytes, subepidermal blister formation filled with numerous neutrophils and scattered eosinophils. Adjacent papillary dermis is edematous with a superficial perivascular infiltrate composed of lymphocytes, a few neutrophils and eosinophils.

DIF - Linear deposition of IgA at the epidermal basement membrane zone.

DIAGNOSIS
Linear IgA Bullous Disease of Childhood

TREATMENT & COURSE
On admission to Comer Children's Hospital the patient was on acyclovir and clindamycin. After dermatology consultation the patient was immediately started on Orapred 15 mg per day (1.5 mg/kg dose) with a tapering regimen, and antimicrobials were discontinued. Gentle skin care

including warm soaks to crusted areas and emollients were started. After G6PD levels were tested and found to be normal the patient was started on dapsone 12.5 mg (1-1.5 mg/kg dose) daily. The patient was discharged from the hospital within 4 days with significant clearing of the rash. At follow up 1 week later, he had significant improvement in all areas with only a few new lesions. Subsequently, he has been weaned off of prednisone and continues on an increased dose of dapsone of 25 mg daily. He intermittently gets flares of a few lesions on the face or groin requiring short courses of low dose prednisone and antibiotics for secondary infection.

DISCUSSION

The exact epidemiology of LABD in the US is unknown but estimated to be about 0.6 : 100,000 in Utah. In adults the average age of onset is after 60, in children 4.5. Patients have been found to have circulating antibodies to specific basement membrane antigens. In the lamina lucida type of LABD, the antigen was found to be the 97kD ectodomain of BPAg2. In the sublamina densa cases of LABD, the antigen is thought to be type VII collagen. The pathophysiology of LABD is thought to be similar to that of dermatitis herpetiformis. Antibody deposition along the basement membrane leads to neutrophil chemotaxis which in turn leads to vesicle formation. There are some reports in the literature associating LABD with GI disorders, autoimmune disease, malignancies, and infection. However, there is no data to show the significance of these associations. Drug induced LABD has been reported in relation to certain antibiotics, but is not a common cause for disease in children.

Clinically the lesions appear as vesiculobullous lesions in a herpetiform arrangement on erythematous or normal appearing skin. In children the lesions usually affect the scalp, face, and flexural areas, especially the lower trunk, inner thighs and groin. The lesions are typically sausage-shaped blisters grouped in annular arrangements termed “crown of jewels” and “string of pearls.” Mucous membrane lesions occasionally occur.

On histopathology, LABD appears as a subepidermal blister with neutrophils predominant, eosinophils may be present. It can be difficult to distinguish from dermatitis herpetiformis on H&E, however linear distribution of neutrophils along the BMZ and at the tips of the papillae favors LABD. DIF will show linear IgA deposits along the lamina lucida most often, and rarely in the sublamina densa region of the BMZ.

Treatment is with dapsone and response is usually noted within 72 hours. Sometimes sulfapyridine or prednisone is used in addition to obtain adequate control. Reports of LABD being successfully treated with tetracycline, erythromycin, and dicloxacillin are in the literature, but no controlled studies have been conducted. More refractory cases have been successfully managed with mycophenolate mofetil. The natural course of the disease is to persist for several years and often spontaneously remit. Attempts to wean off systemic therapy should be pursued for this reason. In children LABD often remits within 2-4 years, and generally before the onset of puberty.

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PRESENTERS
Irene J. Vergilis-Kalner, MD, Vesna M. Petronic-Rosic, MD, MS, Christopher R. Shea, MD, and Sarah L. Stein, MD

PATIENT A

HISTORY OF PRESENT ILLNESS
This is a 7-year-old African American female who presented for evaluation of discolored patches that had been progressing for three months. Treatment with a topical antifungal medication reportedly had no effect. Patient denied any symptoms associated with these lesions or prior history of having similar lesions. Review of systems was unremarkable.

PAST MEDICAL HISTORY / MEDICATIONS / ALLERGIES
None

FAMILY HISTORY
Systemic lupus erythematosus – father

PHYSICAL EXAMINATION
On the face, neck, chest, back, arms and upper thighs, there were many well-defined hypopigmented patches ranging from 1 to 4 centimeters in diameter. Erythema and fine scale was appreciated in the patch on the right medial check. Some patches seemed to have a hyperpigmented rim. No lymphadenopathy was appreciated. Physical examination was otherwise unremarkable.

DERMATOPATHOLOGY
Lesional skin: The stratum corneum had focal hyperkeratosis and parakeratosis. There was prominent epidermotropism of lymphocytes into the basilar epidermis forming small collections reminiscent of Pautrier microabscesses. The epidermotropic lymphocytes had large, hyperchromatic, convoluted and folded nuclei, and prominent pericellular halos. Only mild spongiosis and rare necrotic keratinocytes were noted. There was a patchy lichenoid infiltrate involving the epidermal-dermal interface. The papillary dermis was fibrotic. A perivascular lymphocytic infiltrate with mixed histiocytes and some plasma cells was predominantly superficial.
Immunohistochemical studies:
- Anti-CD3 labeled approximately 70% of dermal and intraepidermal lymphocytes.
- Anti-CD20 labeled scattered B-cells in dermis and dermal-epidermal junction.
- T Cells: 60% CD8 (+) and 40% CD4 (+).
- Anti-CD7 showed no loss of expression
- Anti-CD30 stained <5% of the cells.
- Mel-5 labeled greatly diminished numbers of melanocytes in the basal layer and scattered cells in the dermis.

Perilesional skin: Pigment was detected throughout the basal layer. There was a complete absence of melanocytes as indicated by the staining with Mel-5 and Melan A.

DIAGNOSIS
Hypopigmented Mycosis Fungoides

TREATMENT & CLINICAL COURSE
Treatment with narrow-band ultraviolet B therapy three times per week was initiated with great improvement in both the size and the pigmentation of the lesions.

PATIENT B

HISTORY OF PRESENT ILLNESS

This is a 9-year-old Hispanic male who first presented two years ago for evaluation of itchy lesions on the abdomen that began four months prior. Previous treatment with Benadryl and topical miconazole was unsuccessful. Patient denied any prior history of having similar lesions. Review of systems was unremarkable. Patient presented for follow up in July, 2007, at which time mother reported worsening areas of discoloration.

PAST MEDICAL HISTORY

Asthma and eczema as a child

FAMILY HISTORY / MEDICATIONS / ALLERGIES

None

PHYSICAL EXAMINATION

On the chest, abdomen, back, groin, buttocks and legs, there were many well-defined hypopigmented oval patches ranging from 0.5 to 2 centimeters in diameter. Erythematous scaly papules were appreciated in one of the patches on the left abdomen. Some of the other patches had mild central erythema, telangiectasia, and scaling. No lymphadenopathy was appreciated. Remainder of the physical exam was unremarkable.

LABORATORY DATA

The following were negative or within normal limits: complete blood count and complete metabolic panel.

The following were abnormal: LDH 275-292 U/L (normal range 116-245 U/L), SGOT 38-53 U/L (normal range 8-37 U/L), SGPT 75-99 U/L (normal range 8-35 U/L).

DERMATOPATHOLOGY

Biopsy 11/05: There were mounds of parakeratosis overlying an irregularly acanthotic epidermis with extensive exocytosis of lymphocytes. Some lymphocytes lined up along the dermal-epidermal junction. There was vacuolation of the basal layer. Within the dermis, there was a moderately dense perivascular and interstitial lymphocytic infiltrate, along with a number of extravasated red blood cells and melanophages.

Immunohistochemistry studies:

- Anti-CD2 and anti-CD3 labeled practically all of the infiltrating cells within the lower layers of the epidermis and in the papillary dermis.
- Anti-CD4 (+) 50% of cells within the dermis, <5% of cells within the epidermis.
- Anti-CD8 (+) 30% of cells within the dermis, ~1% of cells within the epidermis.
- Anti-CD5 (+) >90% of cells within both the dermis and the epidermis.

Biopsy 06/07: There were focal parakeratosis, mild acanthosis, and epidermotropism of atypical lymphocytes. Some lymphocytes were arranged linearly along the basal layer. Atypical lymphocytes showed irregular or folded nuclear contours. Some had a cerebriform appearance. In the dermis, there was a lichenoid infiltrate, with some lymphocytes exhibiting similar cytologic atypia described above. Extravasated erythrocytes were also seen in the dermis. Papillary dermis appeared fibrotic.

Immunohistochemistry studies:

- Anti-CD3 (+) >90% of cells in dermis and many cells in epidermis.
- Anti-CD4 (+) 50-60% of cells in dermis and scattered cells in epidermis.

- Anti-CD8 (+) many enlarged single lymphocytes and collections of such cells in epidermis. Within dermis, 40-50% of lymphocytes CD8 (+).
- Anti-CD30 (+) <5% of cells in dermis.
- Anti-PAX5 labeled rare B cells in dermis.

Molecular gene rearrangement studies are pending.

DIAGNOSIS

Based on the biopsy performed in 2005, patient was diagnosed with pityriasis lichenoides chronica with atypia, but on biopsy performed in 2007, the pathology evolved to a more definitive diagnosis of hypopigmented mycosis fungoides (cutaneous T-cell lymphoma).

TREATMENT & CLINICAL COURSE

Initial management in 2005 was with topical corticosteroid preparations and oral erythromycin for several months. The patient's mother reported initial improvement on this regimen and stabilization, but recent worsening of the condition prompted the return to clinic. Based on the recent biopsy diagnosis, treatment with narrow-band ultraviolet B therapy three times per week was initiated in July, 2007 with significant improvement within three months in the pruritus, as well as in the size, color, and number of lesions.

DISCUSSION

Mycosis fungoides (MF) is the most common type of primary cutaneous T-cell lymphoma. The cutaneous lesions of MF typically progress through three stages including early, erythematous, scaly patch stage with eczematous features, followed by infiltrated plaque stage, and then tumor stage. Amongst the reported clinicomorphologic types of MF is the hypopigmented MF, a rare variant most often observed in darker-skinned patients (skin types V-VI), but isolated cases have been reported in skin types I-IV. Unlike classic MF, which usually presents between 40 and 60 years of age, the hypopigmented variant seems to be more frequent in children: while childhood MF constitutes 4-11% of all MF cases, hypopigmented MF makes up 17-89% of all cases of childhood MF. In addition, in contrast to the male predominance reported in classical MF, there is almost an equal male to female ratio among patients with hypopigmented MF.

Hypopigmented MF typically presents as hypopigmented patches and plaques in otherwise healthy individuals; erythematous patches, plaques, or tumors may rarely accompany the hypopigmented lesions. Lesions are usually asymptomatic (or mildly pruritic), eutrophic, smooth, and have normal sensation. The differential diagnosis includes leprosy, pityriasis versicolor, vitiligo, pityriasis alba, pityriasis lichenoides chronica, halo nevus, hypomelanosis of Ito, and idiopathic guttate hypomelanosis.

MF is characterized by an atypical epidermotropic infiltrate containing numerous lymphocytes with highly irregular, darkly stained, cerebriform nuclei, sometimes forming Pautrier microabscesses. The malignant cells in classic MF are CD2+, CD3+, CD4+, CD8-, CD30-, CD45RO+, and CD56-, and there may be loss of CD7. However, some CD56+ cases have been reported for both classical and hypopigmented types of MF. Hypopigmented MF often shows predominance of CD8-positive suppressor cytotoxic T-lymphocytes infiltrating the epidermis, with some cases reporting an equivalent helper: suppressor T cell ratio in the dermal infiltrate. It has been postulated that these CD8-positive melanosomal-antigen-specific T-suppressor lymphocytes may exhibit a cytotoxic effect on the melanocytes, causing melanocyte degeneration, abnormal melanogenesis, or defective melanosome transfer, all of which might lead to dysfunction and/or loss of epidermal melanocytes and resulting hypopigmentation. In addition, expression of CD117 by epidermal melanocytes is decreased in hypopigmented as compared with

the classical MF, suggesting a possible correlation between the decreased expression of CD117 and the decreased number of melanocytes.

Hypopigmented childhood-onset MF generally has an excellent prognosis. Conservative therapy with topical emollients, potent topical steroids, phototherapy with narrow-band or broad-band ultraviolet B (UVB) or photochemotherapy with systemic psoralen plus ultraviolet A (PUVA) or topical PUVA often suffices to induce prolonged disease control and long-term survival. Other treatments that have been reported in the literature include topical nitrogen mustard or topical carmustine, local radiotherapy or whole-body electron beam therapy, extracorporeal photophoresis, methotrexate, acitretin, bexarotene, subcutaneous interferon-α and systemic chemotherapy with agents such as cyclophosphamide, doxorubicin, vincristine, and prednisolone.

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PRESENTERS
Elaine F. Kung, MD, Christopher R. Shea, MD, and Maria M. Tsoukas, MD, PhD

HISTORY OF PRESENT ILLNESS
A 61-year-old African-American man reported recurrent oral hemorrhagic bullae and erosions for several months, resulting in a 30-pound weight loss. Because the clinical presentation and initial histologic evaluation were worrisome for paraneoplastic pemphigus, an investigation for internal malignancy was initiated. Multiple myeloma was diagnosed based on monoclonal gammopathy, osteolytic lesions resulting in hypercalcemia, and a hypercellular bone marrow. The patient was treated with dexamethasone and thalidomide for four months, followed by autologous hematopoietic stem cell transplantation (HSCT). Two weeks after HSCT, dermatology was consulted to evaluate the recurrent oral lesions as well as periocular and perinasal hemorrhagic bullae and purpuric plaques that followed bouts of coughing or rubbing. He also complained of recurrent bloody diarrhea and numbness of both arms and both legs.

PAST MEDICAL HISTORY
Hypertension treated with diltiazem 100 mg daily, atenolol 100 mg daily, furosemide 20 mg daily; diabetes mellitus treated with glipizide 2.5 mg daily; benign prostate hypertrophy treated with tamsulosin hydrochloride 0.4 mg at bedtime.

PHYSICAL EXAMINATION
He had waxy purpuric periocular plaques resembling “raccoon’s eyes,” perinasal hemorrhagic nodules, and lateral tongue bulla.

LABORATORY DATA
Laboratory tests revealed elevated calcium and creatinine, depressed serum IgA, IgG, and IgM levels, monoclonal free kappa light chain with immunofixation of urine and serum protein electrophoresis, and a hypercellular bone marrow. A skeletal survey demonstrated an osteolytic lesion at the left ilium. Colonoscopy revealed friable and ulcerated mucosa in the distal descending and sigmoid colon, without evidence of cytomegalovirus infection or masses.

PATHOLOGY
Hematoxylin-eosin stained biopsy specimens of the medial canthus, perinasal skin, and tongue demonstrated dermal amphophilic amorphous deposits containing clefts. Congo Red staining of the medial canthal, perinasal, lingual, and colonic biopsy specimens highlighted the amorphous deposits.

DIAGNOSIS
Myeloma-associated Bullous Mucocutaneous Amyloidosis

TREATMENT & COURSE
One month after HSCT, the patient’s bone marrow had erythroid and megakaryocytic lineage hyperplasia, with no evidence of myeloma. He experienced dramatic resolution of the purpuric plaques and no recurrence of oral bullae or bloody diarrhea two months after HSCT.

DISCUSSION
Bullae containing extravasated red blood cells, as observed in our patient, can represent a rare manifestation of systemic amyloidosis, termed bullous amyloidosis (BA). Bullae and erosions typically occur at sites prone to friction or trauma, such as extremities or intertriginous areas. The pathologic hallmark of amyloidosis associated with multiple myeloma (MM) is deposition of extracellular fibrillar protein comprised of immunoglobulin lambda or kappa light chains.

Electron microscopy of bullae due to amyloidosis reveals deposition under the lamina densa in perilesional skin and within intercellular spaces between keratinocytes. These results suggest that skin fragility from BA may be due to engulfment or transepidermal elimination of amyloid deposits, disrupting the basal keratinocytes and basement membrane zone. Friction or trauma acts as local precipitants for blister formation. Histologic examination of BA lesions demonstrates both an intra- and/or sub-epidermal split. Clinically, they may mimic other vesiculobullous diseases such as paraneoplastic pemphigus, bullous pemphigoid, porphyria cutanea tarda, pseudoporphyria, bullous drug eruption, bullous lupus erythematosus, or epidermolysis bullosa. However, the presence of amorphous eosinophilic depositions helps in clarifying this differential diagnosis. Of note, direct immunofluorescence of BA lesions in two published cases demonstrated non-specific C3 and IgG deposition, a finding also seen in our patient's tongue biopsy specimen taken two weeks after HSCT.

Typical oral manifestation of systemic amyloidosis has been well documented as macroglossia causing difficulty in chewing or speaking and occasionally airway obstruction. Dental indentations of the tongue due to molding pressure against the teeth. In the absence of clinical symptoms, oral mucosa biopsy in the gingiva, parotid gland, minor salivary glands is advocated to detect amyloid deposition. Rarely, as in our patient, the tongue surface may contain hemorrhagic papules, bullae, or erosions. Oral BA, which has been described in only a few case reports, clinically mimics other vesiculobullous or hematologic diseases that affect the mucosa such as cicatricial pemphigoid, pemphigus vulgaris, paraneoplastic pemphigus, bullous lichen planus, epidermolysis bullosa, dermatitis herpetiformis, linear IgA disease, and thrombocytopenia.

Hemorrhagic bullous colitis is another rare manifestation of systemic amyloidosis. Besides inflammatory bowel diseases, bloody diarrhea due to BA mimic infectious colitis and gastrointestinal neoplasm, both of which were concerns since our patient was immunosuppressed. In BA, colonic hemorrhage may follow Valsalva maneuver because of amyloid deposition in the lamina propria and muscularis as well as colonic vessels, as we demonstrated by Congo Red staining of this patient's colonic biopsy.

Between 12 and 30% of patients with MM have coexistent amyloidopathy. This is often overlooked during the HSCT induction, which may include agents that can further damage organs compromised by amyloid deposition. While occult amyloidosis appears to have no impact on the toxicity and outcome of HSCT (median overall survival = 59 to 66 months), the presence of symptomatic amyloidopathy lowers the survival to 38 months. It is recommended to proceed to HSCT without induction if there are <10% plasma cells in the bone marrow. If induction chemotherapy is to be administered, cardiotoxic, neurotoxic, and nephrotoxic drugs such as doxorubicin, vincristine, thalidomide, and bortezomib should be avoided and a short course of pulsed dexamethasone should be given, followed by melphalan (with dose adjustment if patient has end-organ damage). Fortunately, our patient's signs and symptoms of amyloidopathy have disappeared and have not recurred after one year of HSCT for MM.

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PRESENTERS
Jessica S. Maddox, MD and Vesna Petronic-Rosic, MD, MS

UNKNOWN CASE

PRESENTERS
Vishakha Sharma, MD, Jessica S. Maddox, MD, Justin Wasserman, MD, Maria Tsoukas, MD, PhD, and Vesna Petronic-Rosic, MD, MS

Patient A

HISTORY OF PRESENT ILLNESS
This 43-year-old male with a twenty-nine year history of Friedreich's ataxia presented to the emergency room for a three to four week history of progressive left-sided eye pain, headache, and altered mental status. He also presented with a six-week history of an asymptomatic skin eruption involving the palms and soles. Review of systems was positive for diarrhea of one year's duration. Prior to admission, his eye pain had been diagnosed as anterior uveitis and treated by Ophthalmology with prednisone 20 mg daily. His cutaneous eruption had been managed in Primary Care with a topical antifungal medication without any improvement.

PAST MEDICAL HISTORY
Friedreich's ataxia; scoliosis; diabetes mellitus

MEDICATIONS
Prednisone 20 mg daily; prednisone ophthalmic solution; nystatin powder; escitalopram oxalate, hydrocodone bitartrate/acetaminophen

ALLERGIES
No known drug allergies

FAMILY HISTORY/ SOCIAL HISTORY
The patient was adopted, and family history was unknown. He lived part-time on his own and part-time with his mother. There was no history of tobacco, alcohol, or illicit drug use. Sexual history was positive for multiple unprotected sexual encounters in the months prior to admission.

PHYSICAL EXAMINATION
Physical exam revealed a wheelchair-bound kyphoscoliotic male in no apparent distress. Neurological exam was significant for anisocoria, increased flexor tone with 4/5 strength in bilateral upper extremities, and muscle atrophy with 1/5 muscle strength of bilateral lower extremities. Mental status was impaired, and he had slight dysarthria. Skin examination revealed several thin erythematous plaques with peripheral scale on the palms and soles as well as two discrete ulcers on the ventral aspect of the penile shaft.

LABORATORY DATA
The following laboratory data were positive or abnormal: HIV +; viral load 704,000 copies/mL; CRP 145; ESR 52; RPR reactive with a titer of 1:64; Serum Treponemal IFA reactive; CSF with pleocytosis, reactive lymphoid cells, and VDRL reactive with a titer of 8; CSF Treponemal IFA reactive.

HSV cultures from ulcers on penile shaft were negative.

DERMATOPATHOLOGY
A punch biopsy specimen from a representative lesion on the left palm revealed hyperkeratosis and irregular hyperplasia of the epidermis with a patchy lichenoid dermal infiltrate composed of lymphocytes, histiocytes, and numerous plasma cells. The Warthin-Starry stain highlighted rare spirochetes within the papillary dermis.

DIAGNOSIS
Primary, Secondary, and Neurosyphilis in a Patient with Concurrent HIV infection

TREATMENT & COURSE
Pathology results and pertinent laboratory data confirmed the diagnosis of syphilis. A lumbar puncture and subsequent laboratory data additionally confirmed neurosyphilis and revealed a new diagnosis of HIV. The patient was summarily started on a fourteen-day course of three million units of intravenous penicillin G every eight hours. His hospital course was complicated by a urinary tract infection and aspiration pneumonia, which were treated with intravenous piperacillin/tazobactam. His mental status, neurological and ocular symptoms, and rash improved dramatically with the initiation of penicillin, and he was discharged to a skilled nursing facility to complete his course of intravenous antibiotics.

PATIENT B
HISTORY OF PRESENT ILLNESS
This 49-year-old Caucasian male with a past medical history of hypertension and an episode of Guillain-Barre syndrome ten years prior presented with a two-month history of an asymptomatic rash over his entire body. A skin biopsy from an outside hospital was suspicious for lymphoma cutis, prompting treatment with prednisone and a referral to our hematology/oncology clinic. Due to the extent of the patient's cutaneous findings, he was referred to our clinic for further assessment.

PAST MEDICAL HISTORY
Guillain-Barre syndrome; hypertension

MEDICATIONS
Prednisone, losartan, latanoprost ophthalmic

ALLERGIES
No known drug allergies

FAMILY HISTORY/ SOCIAL HISTORY
Family history noncontributory; social history significant for occasional alcohol; no tobacco or intravenous drug use

PHYSICAL EXAMINATION
Physical exam revealed a healthy, well-appearing male with trunk and extremities notable for diffusely distributed monomorphous, smooth, thin erythematous plaques. The face, palms, and soles were spared.

LABORATORY DATA
The following laboratory data were positive or abnormal: Treponemal IFA reactive; RPR reactive with a titer of 1:512; ANA 1:640

The following were negative or normal: HIV nonreactive; Lyme Ab IgM negative; Anti-dsDNA <10; SPEP with mild polyclonal hypergammaglobulinemia

PATHOLOGY
Outside histopathology report: Suspicious for lymphoma cutis.
Internal reading from Hematopathology of same epidermal specimen: Reactive mixed lymphoid infiltrate; gene rearrangement study with no evidence of a clonal T or B cell population.
Flow cytometry on peripheral blood: Reactive B and T cells.

DERMATOPATHOLOGY
A punch biopsy specimen from a representative lesion on the posterior aspect of the neck revealed irregular hyperplasia of the epidermis with a dense, lichenoid, perivascular mixed inflammatory cell infiltrate rich with plasma cells. The Warthin-Starry stain revealed spirochetes within the papillary dermis.

DIAGNOSIS
Secondary Syphilis

TREATMENT & COURSE
The patient was treated with a single dose of 2.4 million units of IM benzathine penicillin with resolution of clinical findings. An HIV test was performed and was found to be negative.

DISCUSSION
These two cases highlight several important issues salient to medicine in today's world. The first is the notorious comeback of syphilis. Highly prevalent in the early twentieth century, syphilis died down in the late 1940s's due in large part to the advent of penicillin therapy and an aggressive public health campaign. While the rates of syphilis had generally remained low, there has been a resurgence over the last several years.

The second pressing point is that sexual history should always be addressed. In the case of Patient A, most other medical professionals caring for him never thought to ask his sexual history. They just assumed he was not sexually active because of his wheelchair-bound state. This phenomenon of delayed diagnosis occurs in senior citizens and nursing home residents for much the same reason.

Patient A is also interesting because of the simultaneous presence of features of primary and secondary syphilis. While this usually does not occur, this phenomenon has been noted in patients with both syphilis and HIV. A large study looking at patients seen with newly diagnosed primary, secondary, or early latent syphilis found that HIV-infected patients were more likely to present in the secondary stage. In addition, HIV-infected patients with secondary syphilis were more likely to have chancres in addition to the cutaneous manifestations of secondary syphilis as compared to the HIV negative population. Additionally, it is known that HIV transmission is facilitated by genital ulcer disease. Studies have cited an up to 9-fold increased risk of HIV transmission in patients with syphilis. Patient A also had neurosyphilis. While neurosyphilis can occur at any stage of syphilis infection, it is unusual for it to have presented so early (while the primary chancre is still present). This phenomenon of early presentation of neurosyphilis has been reported in HIV positive patients. Also important to note is that while our patient's CSF VDRL was positive, this test can be negative initially in HIV-infected patients. It is now recommended to check CSF treponemal antigens or, if unavailable, to treat presumptively for neurosyphilis based on positive serologic tests and symptoms consistent with neurosyphilis in an HIV positive patient. Common presenting symptoms of neurosyphilis include headache, mental status change, and cranial nerve abnormalities. The classic symptoms of tabes dorsalis and Argyll Robertson pupil (accommodation in the absence of reaction to light) occur in the much later stages of meningovascular syphilis. Less discussed manifestations of neurosyphilis are the

ocular and otologic abnormalities. Uveitis, as was seen in our patient, is one of the most common ocular findings, particularly in patients with concurrent HIV infection.

Patient B is interesting because of the original misdiagnosis of lymphoma cutis, due largely in part to a low suspicion for syphilis and the absence of typical palmoplantar lesions of secondary syphilis. The original biopsy contained a plasma cell-rich infiltrate. Special stains were performed for mycobacteria and fungi but not for spirochetes. Syphilis has long been known as the "great mimicker." This case highlights how this can be true both clinically and histologically.

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PRESENTERS
Bernhard Ortel, MD, Jessica S. Maddox, MD, Arlene Ruiz de Luzuriaga, MD, Aisha Sethi, MD, and Christopher R. Shea, MD

PATIENT A

HISTORY OF PRESENT ILLNESS
A 40-year-old white woman presented for evaluation of ectatic vessels that first appeared on her legs at least six years earlier during pregnancy. Because of pulmonary embolism the patient was treated with enoxaparin around the time of their appearance. She also was on fluoxetine when the patient first noticed the telangiectasias.

PAST MEDICAL HISTORY
The patient had a history of hypothyroidism for six years. She had four Caesarean sections and a pulmonary embolism with her last pregnancy in 2000. She had a tubal ligation in 2001.

REVIEW OF SYSTEMS
No history of gastrointestinal or respiratory symptoms

MEDICATIONS
Levothyroxine and liothyronine

ALLERGIES
Cutaneous reaction to morphine

FAMILY HISTORY
Non-contributory

SOCIAL HISTORY
The patient stopped smoking 14 months ago.

PHYSICAL EXAMINATION
On the all four extremities there were telangiectatic macules and patches that blanched upon pressure. On the lower legs these were associated with mottled hyperpigmentation.

LABORATORY DATA
The following were negative or within normal limits: CBC, platelets and differential blood count, ANA, anti-doublestranded DNA antibodies, estradiol, leukocyte alkaline phosphatase, 24-hour urine for 11 beta-prostaglandin F2 alpha, serum tryptase.
The following tests were abnormal: D-dimer was increased on several occasions to above 1.0 mg/ml (normal < 0.42)

DERMATOPATHOLOGY
A punch biopsy specimen of lesional skin on the thigh showed normal epidermis and ectatic small vessels in the superficial dermis. The vessels were surrounded by a moderate perivascular infiltrate composed of lymphocytes and mast cells. The subcutaneous tissue was unremarkable. Immunohistochemical staining with an antibody directed against mast cell tryptase highlighted epithelioid and spindle–shaped mast cells around vessels at an average density of 40 cells per high power field.

DIAGNOSIS
Telangiectasia Macularis Eruptiva Perstans (TMEP)

TREATMENT & COURSE
The patient used make-up to conceal the lower leg lesions. She received pulsed dye laser therapy more than two years ago with some improvement. At present she has resumed therapy using the 595nm flashlamp pumped dye laser.

An evaluation by hematology is scheduled for persistent elevation of the D-dimer test.

PATIENT B
HISTORY OF PRESENT ILLNESS
A 46-year-old white man presented for follow-up of long-standing, widespread, stable vascular lesions that had first appeared about 20 years ago. At the time of follow-up he was most concerned with increasing dryness and scaling on his lower extremities. Antihistamines have been successful in preventing itching and skin swelling. Nothing appears to trigger itching or skin swelling, including dietary factors, occasional alcoholic drinks, and a variety of non-steroidal anti-inflammatory agents that the he has taken on occasion.

PAST MEDICAL HISTORY
In January, 2007 a malignant melanoma was removed from the abdomen (Clark level at least III, Breslow thickness at least 0.93 mm) with sentinel lymph node biopsy negative for regional spread. Two scaly plaques on the back were biopsied at the same time; one was diagnosed as actinic keratosis and one as flat wart. In all these specimens, histologic features of TMEP were present. In February, 2007 two small adenomatous polyps were removed during a routine colonoscopy.

REVIEW OF SYSTEMS
No history of respiratory or gastrointestinal symptoms

MEDICATIONS
Cetirizine hydrochloride, topical 12% lactic acid

ALLERGIES
No known drug allergies

FAMILY HISTORY
Non-contributory

SOCIAL HISTORY
Non-smoker with moderate alcohol consumption

PHYSICAL EXAMINATION
Widespread violaceous-brown macules and papules covered legs, arms, and trunk and coalescing into large patches and plaques. There was relative sparing of intertriginous skin. In the affected areas of the lower extremities, scaling was an additional feature.

LABORATORY DATA
The following were negative or within normal limits: CBC, platelets and differential blood count, HIV1/HIV2 antibodies, PSA.
The following tests were abnormal: urine N-methyl histamine 514 mg/g/24 hrs (30-200), serum tryptase 147.0 ng/mL (<11.5).

DERMATOPATHOLOGY

The epidermis showed psoriasiform hyperplasia and hyperkeratosis. A superficial and interstitial dermal infiltrate consisted of cells with round to elongated nuclei and an eosinophilic to amphophilic granular cytoplasm. Nuclear atypia was not prominent. There were some melanophages and eosinophilic granulocytes present. The papillary dermis appeared fibrotic. Mast cell tryptase immunostaining confirmed the infiltrating cells as mast cells.

DIAGNOSIS

Cutaneous Mastocytosis with Features of TMEP

TREATMENT & COURSE

The patient has a decades-long history of stable disease. In the eighties he was treated with antihistamines that prevented itch but caused drowsiness. He currently uses cetirizine hydrochloride to his satisfaction, and moderate compression (20-30 mmHg) on his legs. He also uses 0.1 % triamcinolone ointment and a 12% lactic acid preparation for scaly areas on the legs. A repeat evaluation by hematology is planned to rule out systemic involvement.

DISCUSSION

Cutaneous mastocytosis most often presents early in life as urticaria pigmentosa or isolated mastocytoma. In contrast, telangiectasia macularis eruptive perstans (TMEP) is a form of mastocytosis that occurs mainly in adults. This clinical presentation features prominent vascular changes and is generally not associated with systemic mastocytosis. The physical test for the Darier sign is most often negative. We present these two patients as examples of adult cutaneous mastocytosis with telangiectasia representing both ends of a spectrum of mast cell infiltration and persistent vascular response.

Laboratory findings in cutaneous mastocytosis may include increased plasma levels of histamine and tryptase. The urine can be tested for the histamine metabolites N-methyl histamine and N-methyl imidazole acetic acid, as well as prostaglandin D2 metabolites. Only Patient B had increased metabolite levels.

Symptomatic treatment of urticaria pigmentosa is approached with antihistamines, preferably those with reduced sedation, different forms of phototherapy, and corticosteroids. TMEP also has been treated successfully with the flashlamp-pumped dye laser (PDL). However, the vascular lesions may recur. Patient A had some success in the past and has resumed laser therapy recently.

While Patient A presents the features of TMEP as most often described in the literature with predominantly telangiectatic cutaneous lesions and no increase in plasma or urine levels of mast cell product metabolites, Patient B has clinical features of TMEP but histopathological features of urticaria pigmentosa as well as elevated levels of plasma tryptase and urine histamine metabolites.

Patient A had some success in the past and has resumed laser therapy recently. In Patient B current management is with a non-sedating antihistamine and compression stockings. With the history of melanoma he is not eligible for phototherapy but may also receive some benefit from flashlamp-pumped dye laser treatments.

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PRESENTERS
Olga Ulitsky, MD, Christopher R. Shea, MD, and Aisha Sethi, MD

HISTORY OF PRESENT ILLNESS
A 53-year-old woman presented with a two-month history of numerous, painful nodules and plaques over the left breast. The nodules had been increasing in size and number. She reported significant pruritus and intermittent pain of the left breast. Patient denied any nipple discharge. She denied history of varicella infection or pain prior to onset of her skin lesions. For a month, her primary care physician treated her with diphenhydramine and acetaminophen with codeine for "shingles." The patient lived with her granddaughter, who is well and did not have any skin conditions. Patient has not traveled in the past year. She has never had a mammogram.

PAST MEDICAL HISTORY
Hypertension, diabetes mellitus, congestive heart failure, osteoarthritis, hyperlipidemia

MEDICATIONS
Metoprolol, enalapril, nifedipine, hydralazine, furosemide, metformin, glipizide, rosiglitazone, gemfibrazil, potassium chloride, simvastatin, ranitidine, hydrocodone, tramadol

ALLERGIES
No known drug allergies

FAMILY HISTORY
Sister with head and neck cancer, mother with rectal cancer

SOCIAL HISTORY
The patient has smoked one pack per day for many years and denies alcohol or drug use.

PHYSICAL EXAMINATION
There are numerous, erythematous and light brown, firm nodules 0.5-1.0 cm over the left breast, and erythematous scaly plaques over the left scapula distributed in a T4 dermatomal pattern. There is significant non-pitting edema, warmth, and tenderness of the left breast. There is a palpable lymph node in the left axilla. No nipple discharge or retraction are noted.

LABORATORY DATA
01/07: Ultrasound and mammogram of right and left breasts: Tests were limited due to underlying edema. 4.1 x 2.5 cm lymph node was noted in left axilla
02/07: CT of head, chest, abdomen, pelvis for metastatic work-up: unable to perform due to body habitus

The following were negative or within normal limits: HIV, BMP, CBC, LFTs

DERMATOPATHOLOGY
01/07: A skin biopsy revealed epidermal atrophy and numerous intradermal aggregates of atypical epithelial cells with mitotic figures, focal lumen formation, and central comedo-type necrosis. PAS, methenamine silver, Gram, and Fite stains were negative for microorganisms.
04/07: Tissue biopsy revealed high grade in situ and infiltrating ductal carcinoma; estrogen/progesterone receptor negative. Immunohistochemistry was negative for HER-2/neu

DIAGNOSIS
Zosteriform Metastatic Mammary Carcinoma.

TREATMENT & COURSE

Patient was given a course of cephalexin and triamcinolone ointment for pruritus and referred to hematology/oncology. She was started on cyclophosphamide, doxorubicin, and 5-fluorouracil for six cycles. Eight months after her first presentation to dermatology, patient was admitted to the hospital secondary to her fall and chest pain. She subsequently developed rhabdomyolysis and acute renal failure, became bradycardic, and was pronounced dead 48 hours after admission.

DISCUSSION

Cancer metastases represent the most devastating aspect of malignancy since mortality is usually directly correlated with the metastatic potential of the primary neoplasm. In women, excluding melanoma, the most common tumor to metastasize to skin is breast cancer.

Cutaneous involvement from breast carcinoma usually occurs in the skin overlying the primary cancer by direct extension of skin via lymphatic vessels. There are different manifestations of lymphatic involvement, including nodular, inflammatory or erysipeloides carcinoma, telangiectatic, and "en-cuirasse" carcinoma. Inflammatory skin metastases may be difficult to distinguish from erysipelas but, in contrast to that infection, there is no fever, chills, or leukocytosis and the bacterial cultures are negative. A zosteriform pattern of metastasis, as observed in our patient, results from perineural involvement of the lymphatics. This pattern may pose a diagnostic challenge in differentiating this condition from herpes zoster. However, the presence of malignant cells on biopsy, and the negative viral PCR allows one to make a diagnosis of cutaneous metastases. Metastatic breast may also present as a reddish nodule on the tip of the nose ("clown nose"). Also, metastatic breast cancer has been reported in the eyelid and presented as a painless swelling and nodule formation. In that setting it must be distinguished from primary signet ring carcinoma of the eyelid.

Immunohistochemical studies can help identify the site of primary tumor. Cells from breast carcinoma stain positively with antibodies to a variety of epithelial markers including cytokeratins, epithelial membrane antigen, and carcinoembryonic antigen. Also, they may express estrogen and progesterone receptors and gross cystic disease fluid protein-15 (GCDFP-15), a glycoprotein expressed in apocrine epithelial cells.

The prognosis for patients with cutaneous metastasis depends on the type of the primary tumor and its response to treatment. Skin metastasis from breast carcinoma is associated with advanced stages of the disease and therefore may represent a poor prognostic sign.

Chemotherapy is the modality used most commonly in treatment of breast cancer; however, the specific protocol usually depends on the histopathologic subtype. In addition, surgical excision, radiotherapy, and immunotherapy are options for palliative treatment of the underlying disease and the cutaneous metastases.

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PRESENTERS
Diana Bolotin, MD, PhD, Jessica S. Maddox, MD, Vesna Petronic-Rosic, MD, MS, and Sarah L. Stein MD

HISTORY OF PRESENT ILLNESS
The patient is a 12 year-old African American male who presented with a new onset pruritic rash on his trunk and extremities in September, 2006. He was treated empirically with mometasone furoate ointment without improvement. A clinical diagnosis of lichen planus was entertained and a biopsy at this time showed lichenoid dermatitis. A 10-week tapering course of oral prednisone did not induce significant improvement. He was subsequently started on narrow band UVB light therapy three times per week. At a follow up visit in May 2007, the patient reported that his skin was now less red and itchy, but rather rough and bumpy in appearance.

REVIEW OF SYSTEMS
Pt denied changes in vision or GI symptoms, and was feeling well with no complaints.

PAST MEDICAL HISTORY
None

MEDICATIONS
May 2007:
Mometasone furoate ointment , hydroxyzine prn
Narrow Band UVB 3x week (1/26/07 to 5/23/07; max dose 1400mJ/cm2)

ALLERGIES
No known drug allergies.

FAMILY HISTORY
Reportedly father with psoriasis.

SOCIAL HISTORY
Noncontributory

PHYSICAL EXAMINATION
On examination, groups of folliculocentric coalescing skin colored papules with central horny hyperkeratotic spines were present extensively over the trunk and extremities.

LABORATORY DATA
CBC – Hgb 13.1 MCV 90.9[NL 13.5-17.5]
Vitamin E level - normal.
Free retinol (vitamin A) level – normal.

DERMATOPATHOLOGY
9/2006:
A 4mm punch biopsy of skin was obtained from the patient's right calf. Histopathology showed skin with hyperkeratosis, parakeratosis, wedge-shaped hypergranulosis and saw-toothing hyperplasia of the epidermis. There was exocytosis of lymphocytes. The dermis contained a dense lichenoid infiltrate with lymphocytes, melanophages and eosinophils. This infiltrate extended deep into the dermis and subcutaneous fat in a periadnexal and perivascular fashion. The findings were found to be most consistent with a lichenoid dermatitis.

5/2007:
A 4mm punch biopsy of skin was obtained from a representative lesion on the patient's right thigh. Histopathology revealed a dilated follicular infundibulum plugged with a compact orthokeratotic column of corneocytes that protruded above the surface of the epidermis. The specimen also showed a moderately dense lichenoid as well as perivascular lymphohistiocytic cell infiltrate with melanophages. Some fibrosis of the papillary dermis was noted.

DIAGNOSIS
Lichen spinulosus evolving during treatment of lichenoid dermatitis

TREATMENT & COURSE
The patient's NB-UVB therapy was discontinued. He was started on 12% lactic acid cream (Amlactin) with no response. The patient was then switched to a regimen of Salicylic acid 6% in hydrocortisone 2.5% base. With this treatment, the patient's condition continues to improve, especially in areas readily accessible to application of the topical medication.

DISCUSSION
Lichen spinulosus is a benign skin disorder that is most often seen in the pediatric rather than adult population and is frequently associated with atopy. Clinically, it presents as grouped follicular papules with a hyperkeratotic core on the neck, trunk, and extensor surfaces of the extremities. The vast majority of cases reported are benign and self-limited; however, there have been reports of this condition associated with Crohn's disease and HIV.

Histopathologically, lichen spinulosus is similar to keratosis pilaris and phrynoderma (vitamin A deficiency) and features infundibular follicular plugging, orthokeratosis and a perifollicular infiltrate. Other features that may or may not be present include dilation of sweat ducts, absence of a granular layer, and atrophy or absence of sebaceous glands. Diagnosis of this disorder requires correlation between clinical observations, laboratory testing, and histologic findings. Overall, lichen spinulosus falls into a spectrum of disorders of follicular keratinization which includes keratosis pilaris and phrynoderma.

The etiology of lichen spinulosus remains unclear as does its relationship to keratosis pilaris. To date, there have been no reports of lichen spinulosus developing during or after local UVB therapy, though it has been reported to follow administration of thallium, gold and omeprazole.

Treatment for lichen spinulosus includes keratolytic therapy and emollients. Interestingly, a recent case report showed complete clearing of lichen spinulosus with topical tretinoin treatment.

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PRESENTERS
Christiane Querfeld, MD, Elaine F. Kung, MD, Christopher R. Shea, MD, and Aisha Sethi, MD

HISTORY OF PRESENT ILLNESS
This 54 year-old Caucasian man presented with a 6-week history of a pruritic and painful skin eruption on his trunk and extremities following one week of systemic clindamycin therapy for left cervical adenopathy. His lymphadenopathy resolved clinically. His skin lesions tended to wax and wane, but overall progressed. Over the course of 4 weeks he was evaluated by multiple physicians. He was initially started on oral low-dose prednisone and eventually increased to 60 mg per day without much improvement. Outside skin biopsies were suggestive of an angiocentric lymphoma.

PAST MEDICAL HISTORY
Hepatitis C, hypertension, diabetes mellitus, erectile dysfunction, status post skin burn

MEDICATIONS
Lisinopril, glipizide, tadalafil, zolpidem, prednisone, cetirizine, mupirocin ointment, ketoconazole cream

ALLERGIES
No known drug allergies

FAMILY HISTORY
Maternal grandfather with leukemia; father died of unknown cause at young age; mother is alive and healthy.

SOCIAL HISTORY
He is a manager of a truck company, does not currently smoke, but has a history of smoking one pack per day for 30 years; recently quit alcohol, used to drink six-pack of beer per day, denies illicit drugs.

PHYSICAL EXAMINATION
The exam showed numerous painful erythematous to violaceous papules and plaques with scaling, ulceration and/or overlying hemorrhagic crusts distributed on the trunk, upper and lower extremities. There were scattered subcutaneous nodules on further examination. No oral ulcerations were seen. There was palpable left axillary lymphadenopathy. There was no cervical or axillary lymphadenopathy present. No hepatosplenomegaly was noted.

LABORATORY DATA
CBC with differential, platelets, basic metabolic panel, LDH, immunoglobulin levels, beta-2 microglobulin, hepatic panel except for SGPT 43U/Lwere all within normal limits.
Negative RPR and HIV1/2 test.

DERMATOPATHOLOGY
Left arm: epidermis with focal exocytosis of small lymphocytes. Superficial and deep perivascular dermal and subcutaneous infiltrate of atypical lymphoid cells, arranged around and infiltrating into dermal blood vessels. Fibrin deposits within several vessel lumina are seen.

Right abdomen: epidermis with reactive hyperplasia with parakeratosis and some hemorrhagic crust. Superficial and deep perivascular and interstitial infiltrate of atypical lymphocytes involving vessel walls. There are focal areas of macrophages forming small granulomas. Atypical

cells were positive for CD2, CD3 and negative for CD56. The ratio for CD4 and CD8 in CD3-positive T-cells was 2:1. In-situ hybridization for EBV-encoded RNA was negative. T-cell rearrangement studies: clonal proliferation of γ/δ T-cell receptor.

Bone marrow: hypercellular bone marrow without clear morphologic or immunophenotypic evidence of involvement by T-cell lymphoma. T-cell rearrangement studies: clonal proliferation of γ/δ T-cell receptor.

IMAGING
12/22/2006: CT scan of neck, chest, abdomen, and pelvis showed small lymph nodes in the neck and axillary areas.

DIAGNOSIS
Peripheral T-cell Lymphoma, Unclassified

TREATMENT & COURSE
The patient is being followed by hematology/oncology, hepatology and dermatology. He eventually was tapered off oral prednisone. Clobetasol 0.05% ointment was initiated. The patient has continued doing well on this regimen with waxing and waning of his skin lesions. He is currently being evaluated for his liver disease and is being considered for a combined regimen of pegylated interferon-α 2b and ribavirin for one year.

DISCUSSION
On repeated histological examination and by molecular biology work-up, the diagnosis of an unclassifiable peripheral T-cell lymphoma could eventually be established. The diagnosis of cutaneous angiocentric lymphoma has been suggested, which is histologically similar to the nasal T/NK-cell lymphoma that often presents with destruction of midline facial features (lethal midline granuloma). In our case, histologic findings of a preferential concentration of atypical lymphocytes around blood vessels with only focal infiltration, but no frank destruction of vessel walls were not sufficient for the designation of an angiocentric process. Furthermore, the presence of EBV-genome has not been demonstrated.

The histologic diagnosis of peripheral T-cell lymphoma (PTCL) may also presents a challenge because of variations in the degree of cellular infiltrate and cellular atypia. PTCLs, unspecified, in the WHO-EORTC classification represent a heterogeneous group of T-cell lymphomas that do not fit into other categories of better defined subtypes of T-cell lymphoma/leukemia. Prognosis and outcome is largely unknown and the optimal treatment is not well-defined due to disease rarity and biological heterogeneity. In the majority of cases, prognosis remains poor with a 5-year overall survival of less than 30%.

The patient was recently diagnosed with hepatitis C. Hepatitis C has been reported to be associated with vasculopathies and low-grade lymphoproliferative disease of B-cell lineage. At present, it is not clear whether the patient's underlying hepatitis C may contribute to his lymphoproliferative process.

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PRESENTERS
Vishakha M. Sharma, MD, Christopher R. Shea, MD, and Sarah L. Stein, MD

HISTORY OF PRESENT ILLNESS
This 15-month-old male was transferred to Comer Children's Hospital for treatment of a left-sided Group A Streptococcal empyema. Upon transfer, the patient was taken to the operating room for a video-assisted thoracoscopic surgical (VATS) procedure. He was then taken to the pediatric intensive care unit for further care, during which time he was noted to have a new rash on his left arm at the site of a peripheral IV. The site had been covered by tape.

PAST MEDICAL HISTORY/ MEDICATIONS/ ALLERGIES
The patient had no previous hospitalizations or surgeries.
No medications. No known drug allergies. No known history of allergy to tape or adhesives.

FAMILY HISTORY/ SOCIAL HISTORY
Family history negative for any skin conditions. Patient lives with his mother.

PHYSICAL EXAMINATION
Multiple small hemorrhagic, crusted papules and vesicles were distributed focally on the left forearm. All of the lesions were confined to a well-demarcated rectangular shape that seemed to correspond with the area of skin that had been occluded by tape. The remainder of the skin exam was unremarkable.

LABORATORY DATA/ IMAGING STUDIES
The following were positive or abnormal: Chest CT: large left pleural effusion with stranding and loculation; nasopharyngeal aspirate: Influenza A virus; left pleural space fluid: *S. pyogenes*; tissue fungal culture: many *Rhizopus* species; IgA 321 (high); IgG 1843 (high); IgM 241 (high).

The following were negative or normal: Lymphocyte subsets; hepatitis viral panel.

DERMATOPATHOLOGY
A punch biopsy specimen from a representative lesion on the left arm showed subcorneal pustulosis and spongiosis. Numerous large fungal hyphae with ninety-degree angle branching were noted both in the epidermis and the dermis. Some organisms appeared to be located within dermal and subcutaneous vessels with associated thrombosis.

DIAGNOSIS
Cutaneous Zygomycosis (*Rhizopus* species)

TREATMENT & COURSE
The patient was promptly started on amphotericin B. A work-up for immunodeficiency was performed and found to be negative. A noticeable improvement was noted within days of treatment. The patient was continued as an outpatient on amphotericin B and then later switched to oral posaconazole. A repeat biopsy six months later showed no residual infection.

DISCUSSION
The term zygomycosis includes infections caused by pathogens from the classes Mucorales and Entomophthorales. The most common causes are *Rhizopus* spp. and *Mucor* spp. Rhizopus is an environmental inhabitant of soil, dung, and decaying vegetative matter. Infection is usually via the upper respiratory tract through inhalation of airborne spores. However, disease can also be contracted through a gastrointestinal source (contaminated foodstuffs). In adults, the most

common manifestations are pulmonary or rhinocerebral infection. Cutaneous disease can be seen in the setting of disseminated pulmonary disease. Although less common in the adult population, primary mucocutaneous infection can occur via traumatic breaks in the skin and mucous membranes. In children, the most common presentation is a primary cutaneous infection. In general, those at highest risk for zygomycosis include patients with neutropenia, stem-cell transplants, hematological malignancies, poorly controlled diabetes, and history of recent surgery, burns, or trauma. Situations unique to pediatrics that also portend a higher risk for zygomycosis include prematurity, high-risk newborns, and patients with congenital metabolic aciduria.

The distinctive characteristics of zygomycotic infections are vascular invasion and subsequent tissue necrosis. This can lead clinically to ecthyma-like lesions, black eschar, and discharge. As in our patient, cutaneous zygomycosis can also clinically present as hemorrhagic, crusted vesicles.

Although most patients with zygomycosis are immunocompromised, some have no known risk factors (up to 14% in one large pediatric review). This includes those cases of "epidemic" cutaneous Rhizopus infection associated with contaminated elasticized adhesive bandages and wooden tongue depressors. There have also been reports of infection associated with contaminated karaya (nonsterile plant-based adhesive) ostomy bags.

Treatment for cutaneous zygomycosis infection includes a combination of medical and surgical therapy. Of the various systemic antifungal medications, amphotericin B appears to have the greatest activity against Rhizopus. In general, the azoles have very little efficacy, with posaconazole as the sole exception. This recently approved broad-spectrum triazole has a success rate of 60-70% and is available for oral use. As there are very few data with using this medication in children, amphotericin B remains the mainstay of treatment. The rate of cure is significantly higher when medical therapy is combined with surgical debridement of devitalized tissue. However, this consideration pertains more to immunosuppressed patients or those with disseminated disease. In some cases, as in our patient, medical therapy alone is enough if the infection is an isolated cutaneous infection that is caught early.

Even with combined treatment modalities, the prognosis for disseminated zygomycosis is poor, especially in premature babies with gastrointestinal zygomycosis. Fortunately, mortality from cutaneous zygomycosis is low, especially when treatment is begun promptly. This case highlights the importance of including a fungal infection in the differential diagnosis for hemorrhagic or vesicular eruptions, even in an immunocompetent patient.

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PRESENTERS
Justin Wasserman, MD, Vesna Petronic-Rosic, MD, MS, and Sarah L. Stein, MD

HISTORY OF PRESENT ILLNESS
An 11-year-old healthy African-American male presented for evaluation of a lesion on the back. His mother reported that the lesion was present since birth. She said that the child's grandmother believed it had developed due to trauma during delivery via forceps extraction. The lesion had gradually grown in size, occasionally swelling or bleeding after trauma, but otherwise was asymptomatic. According to the patient, it had recently become more "bumpy" at the edges after being bumped.

PMH, FH, SH
Otherwise healthy male with no pertinent medical, family, or social history

MEDICATIONS
None

ALLERGIES
No known drug allergies

PHYSICAL EXAM
Healthy well appearing male in no distress. Over the scapula on the left upper back, there was a well defined violaceous to dull red plaque with nodules and areas of atrophy. The lesion was not tender to palpation. No lymphadenopathy was detected.

HISTOPATHOLOGY
H & E - Skin biopsy reveals a proliferation of spindle-shaped cells forming fascicles within the dermis in a storiform pattern of varying density throughout the neoplasm. Some of the neoplastic cells are enlarged, with hyperchromatic nuclei, and multiple nucleoli. Adnexal structures are preserved; a thin layer of surrounding normal dermis separates some of them from the neoplasm.
Immunohistochemistry - Diffusely positive CD34 staining in all neoplastic cells. Factor XIIIa stains many dermal dendrocytes within the normal dermis as well as dendritic cells dispersed throughout the proliferation. Neoplastic cells did not stain for S-100 or desmin.
Molecular studies - Molecular cytogenetic studies are positive for a chromosomal translocation t(17;22)(q21.3;q13.1) (COL1A1-PDGFβ fusion) in 89% of the interface cells.

DIAGNOSIS
Congenital Dermatofibrosarcoma Protuberans

TREATMENT & COURSE
The patient was referred to plastic surgery for complete excision of the lesion.

DISCUSSION
Dermatofibrosarcoma protuberans (DFSP) is a low grade cutaneous malignancy long thought to affect almost exclusively adults, in whom the tumor typically presents as a firm nodular growth with an infiltrative pattern. Classic histopathology is of a dermal mass of CD34 positive spindle-shaped cells in a storiform pattern. Information on DFSP in children is not as prevalent and only about 30 cases of congenital DFSP are reported in the literature. It is possible that many cases of DFSP from birth and early childhood are not diagnosed until young adult age, leading to an underestimation of the frequency in children, as well as delay in treatment. In children, DFSP can have a clinically varied appearance and can mimic other common entities such as morphea,

neurofibromas, angiomas, mastocytomas, or benign fibrohistiocytic growths, as well as the more classical appearance of adult DFSP. The most common locations in both adults and children are the trunk and proximal extremities.

Histopathologically, DFSP can be confused with other neoplasms, such as fibrous hamartoma of infancy, fibromatosis, neurofibroma, or congenital fibrosarcoma. Immunohistochemical analysis of DFSP is positive for CD34 and negative for Factor XIIIa, S100, and Desmin. A valuable confirmatory tool in the diagnosis of DFSP or its variants, Bednar tumor (BT) and giant cell fibroblastoma (GCF), is cytogenetic analysis by FISH or RT-PCR for a chromosomal translocation t(17;22) resulting in a COL1A1-PDGFβ fusion. According to Maire et al, the genetic alteration in children is an unbalanced translocation, whereas in adults it occurs as a ring chromosome. It is unclear whether the translocation transforms into a ring chromosome as the patient ages. Perhaps such a genetic transformation can lead to the alteration in clinical appearance seen in adults.

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PRESENTERS
Irene J. Vergilis-Kalner, MD, Christopher R. Shea, MD, and Aisha Sethi, MD

HISTORY OF PRESENT ILLNESS
This 59-year-old African-American woman presented to the Dermatology clinic in July of 2006 for evaluation of the pruritic lesions on the left arm and left thigh, present for seven months. She had a ten-year history of cancer of the left breast, with metastasis in 2003 to the liver, vertebrae, and skull. The patient first noticed the skin lesions after undergoing radiation therapy to the left breast and left thigh. She denied a prior history of a similar eruption or a personal history of any other skin diseases. Patient also denied exposure to any toxins or new medications. .

PAST MEDICAL HISTORY
Hypertension, supraventricular tachycardia, metastatic breast cancer

FAMILY HISTORY
Non-contributory

MEDICATIONS
Valsartan, hydrochlorothiazide, indomethacin

ALLERGIES
Penicillin

PHYSICAL EXAMINATION
On the left arm and left thigh there were many, well-defined, hyperpigmented to violaceous, shiny, reticulated plaques ranging from 0.5 to 2 cm in diameter. These lesions were confined to radiation treatment sites, had surrounding erythema, and appeared to follow lines of Blaschko. Examination of the palms, soles, mucous membranes, and nails did not reveal any involvement.

LABORATORY DATA
The following were negative or within normal limits:
Hepatitis B and C serologies, comprehensive metabolic panel, magnesium, inorganic phosphate, unconjugated bilirubin, cholesterol, triglycerides, white blood cell count, coagulation studies.

The following were abnormal:
Lactic dehydrogenase 246-277 U/L (normal 116-245 U/L), albumin 2.4-2.9 g/dl (normal 3.5-5.0 g/dl), bilirubin total 2.8-14.4 mg/dl (normal 0.1-1.0 mg/dl), bilirubin conjugated 1.9-3.2 mg/dl (normal 0.0-0.3 mg/dl), alkaline phosphatase 637-974 U/L (normal 30-120 U/L), SGOT 231-462 U/L (normal 8-37 U/L), SGPT 69-145 U/L (normal 8-35 U/L), calcium 7.3-7.9 mg/dl (normal 8.4-10.2 mg/dl), hemoglobin 8.7-9.6 g/dl (normal 11.5-15.5 g/dl), hematocrit 24.9-28.0% (normal 36-47%), platelet count 96-149 K/ul (normal 150-450 K/ul).

Ultrasonography of the abdomen: hepatomegaly and diffuse hepatic metastasis.
Computed tomography of the chest / abdomen / pelvis: left breast mass, liver metastases, diffuse bony metastases in ribs, thoracic and lumbar vertebral bodies, pelvis, proximal femurs, and right humerus, and metastases to right axillary and subcarinal lymph nodes.

DERMATOPATHOLOGY
Punch biopsies of representative plaques on the left arm and left thigh showed orthohyperkeratosis and hypergranulosis. Interface dermatitis was noted, with vacuolar changes of the basal layer and a scant, superficial, perivascular lymphocytic infiltrate. In addition, there

were many dyskeratotic keratinocytes with satellite cell necrosis, colloid bodies, and pigment incontinence in the papillary dermis.

DIAGNOSIS
Lichen Planus

TREATMENT & CLINICAL COURSE
The patient was treated topically with triamcinolone 0.1% ointment twice a day with mild improvement in both pruritus and in appearance of the lesions, prior to her death six months ago.

DISCUSSION
Lichen planus is an inflammatory disease of the skin and mucous membranes that is characterized by pruritic, violaceous papules that favor the extremities. Under light microscopy, lesions of lichen planus usually exhibit orthohyperkeratosis, hypergranulosis, irregular acanthosis, and a "sawtooth" pattern of the rete ridges. The principal dermal feature of lichen planus is a bandlike lymphohistiocytic infiltrate that "hugs" and obscures the basal layer.

Although its etiology and pathogenesis of lichen planus are not fully understood an immunologic disturbance is believed to precipitate both humoral and cellular attacks on the dermoepidermal junction. Lichen planus has been associated with viral infections such as hepatitis C, autoimmune diseases, or trauma (as part of Koebner's isomorphic phenomenon). There have also been four cases reported in the English literature of cutaneous lichen planus arising post-radiation therapy.

We believe that this case represents an interesting example of lichen planus restricted to skin traumatized by radiation therapy. This occurrence of lichen planus could be attributed to what has been previously described as an isoradiotopic response, a term proposed to describe the phenomenon of secondary dermatoses arising in radiation fields. This isoradiotopic response could represent a response to localized radiation-induced injury, which would be a specialized form of the isomorphic response of Koebner, with Koebnerization being a well-known phenomenon of lichen planus and other inflammatory dermatoses that usually develop in areas subjected to trauma.

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PRESENTERS
Elaine F. Kung, MD, Vesna Petronic-Rosic, MD, MS, and Maria M. Tsoukas, MD, PhD

HISTORY OF PRESENT ILLNESS
A 65 year-old white man, with an 80-pack year smoking history and squamous cell carcinoma of the tongue had been treated by 5 cycles of paclitaxel, 5-fluorouracil, and hydroxyurea as well as radiation followed by 3 rounds of sunitinib for metastatic disease to the liver and abdominal lymph nodes. He complained of a blister on his left thumb and two abrasions on his dorsal right hand after gardening and experiencing a "sunburn" feeling. Those injuries developed into larger, tender, partly ulcerated hemorrhagic blisters over 3 weeks. He denied preceding fevers or chills. His primary care doctor treated him with a one-week course of cephalexin after which his oncologist hospitalized him for intravenous ampicillin and sulbactam.

PAST MEDICAL HISTORY
Cerebrovascular accident, coronary artery disease, hypertension, spondylolysis with stenosis

MEDICATIONS
Clopidogrel bisulfate, aspirin, lisinopril, hydrocodone elixir

PHYSICAL EXAMINATION
On his left thumb and dorsal right hand, he had 2 to 3 cm hemorrhagic bullae with central superficial ulceration. The ulcers did not have undermined borders, necrotic bases, or purulent discharge.

LABORATORY DATA
Only mild anemia was notable with blood tests; there were no leukocytosis, neutrophilia, or electrolyte abnormalities. Bacterial, mycobacterial, and fungal tissue cultures did not grow microorganisms.

DERMATOPATHOLOGY
Biopsy of the right dorsal hand demonstrated epidermal spongiosis, extensive papillary dermal edema, a dense predominantly neutrophilic infiltrate, abundant leukocytoclasia and extravasation of red blood cells. GMS, PAS, Fite, and gram stains were negative for microorganisms.

DIAGNOSIS
Neutrophilic Dermatosis of the Dorsal Hands - a Variant of Localized Sweet Syndrome

TREATMENT & COURSE
His lesions improved with the initiation of prednisone at 60mg per day with a slow taper and topical clobetasol ointment. His wound care included an oxidized regenerated cellulose and collagen dressing (Promogran, Johnson & Johnson Advanced Wound Care), a non-stick dressing (Telfa, The Kendall Company Ltd.), and gauze changed daily to every other day. Unfortunately, two months later, our patient died from a pulmonary fungal infection resulting in septic shock.

DISCUSSION
1n 1964, Dr Robert Douglas Sweet described acute febrile neutrophilic dermatosis, also known as Sweet syndrome (SS), with features of pyrexia, elevated neutrophil counts, painful red plaques, and a predominantly mature neutrophilic dermal infiltrate. In 1998, cases were reported without fever but associated with metastatic carcinoma. Since then dermatologic literature has embraced the association with malignancies and/or medications and descriptions of histopathologic variants or overlaps. Localized SS on the dorsal hands has often been misdiagnosed as cutaneous infection

since it occurs in those with an occult or previously diagnosed malignancy (acute myelogenous leukemia, chronic myelogenous leukemia, myelodysplastic syndrome, metastatic carcinomas), with a systemic inflammatory syndrome (connective tissue or inflammatory bowel diseases), and or with upper respiratory or gastrointestinal infections. Drug-induced SS has been reported with all-trans retinoic acid, carbamazepine, trimethoprim-sulfamethoxazole, granulocyte colony-stimulating factor, lenalidomide, and imatinib mesylate.

Neutrophilic dermatosis on the palmar aspect tends to be erythematous and edematous, whereas those on the dorsal hands tend to have a pustular or bullous appearance. The histopathologic features of neutrophilic dermatosis of the hands include predominantly neutrophilic infiltrate, papillary dermal edema, leukocytoclasia with consequent extravasation of red blood cells throughout the dermis extending to the subcutaneous fat. This condition, similar to classic presentations of SS, responds well to corticosteroids but has also reportedly improved with colchicine, dapsone, tetracyclines, and indomethacin.

When SS, pyoderma gangrenosum (PG), or pustular vasculitis occur on the hands, they are often clinically indistinguishable, but they can sometimes be separated histologically by the presence of papillary dermal edema (SS), ulceration and necrosis (PG), or vasculitis (pustular vasculitis). Initially termed pustular vasculitis of the hands, the localized variant of SS has recently been renamed neutrophilic dermatosis of the (dorsal) hands (NDDH) since vasculitis is an inconsistent finding, found in only 14 of 52 reported cases. Since older lesions tend to have vasculitis and recent ones may have leukocytoclasia, the vascular damage is considered an epiphenomenon of the intense neutrophilic infiltrate. Although ulceration is more characteristic of PG, it is not uncommon in NDDH, and was present in 27 of 52 reported cases. While NDDH is distinct from classic PG, a deep ulcer with undermined borders on the lower extremities, it resembles vesiculobullous or atypical PG. Similar to bullous SS, atypical PG presents as hemorrhagic bullae with superficial ulcerations commonly found on the dorsal hands. Hence, the distinctions between these three conditions may be arbitrary, and may reflect differences in the course and degree of inflammation at the time of biopsy. Thus, bullous SS, atypical PG, and pustular vasculitis of the dorsal hands are probably along the spectrum of a single disease entity most appropriately termed NDDH.

Morphologic and histologic features of our patient's dermatologic lesions support a bullous variant of SS termed NDDH. Although not anteceded by fever or infection, our patient had an underlying metastatic squamous cell carcinoma of the tongue treated by sunitinib, an epidermal growth factor inhibitor, both of which may have been contributing factors to NDDH. In addition, NDDH appeared after abrasions from gardening and sun exposure, which may also be inciting pathergic factors in this case.

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PRESENTERS
Jessica S. Maddox, MD, Maria M. Tsoukas, MD, PhD, Robert Chen, MD, and Christopher R. Shea, MD

HISTORY OF PRESENT ILLNESS
A 60-year-old white man was admitted to the hospital for chemotherapy for high-grade osteosarcoma of the right proximal tibia. Five weeks prior to this admission he underwent excision of the primary skeletal mass, and his right lower extremity was placed in a cast post-operatively. No further cutaneous findings were present at the time of surgery. Upon removal of the cast five weeks post-operatively, he presented with an asymptomatic nodule at the right lower extremity, anteriorly and medially to the primary tumor and on the opposite side of the incision wound. Further imaging studies included CT scans, which revealed multiple new masses on the ipsilateral leg, as well as numerous densities in both lungs.

MEDICATIONS
Etoposide, mesna, hexadrol, granulocyte-colony stimulating factor

PAST MEDICAL HISTORY
Hypertension

ALLERGIES
None

PHYSICAL EXAMINATION
At the proximal right lower leg, anterior medial aspect, there was a firm, bright-red to violaceous nodule two cm in diameter. The nodule was non-tender, not blanchable, and immobile. The right lower leg had 3+ pitting edema. No other cutaneous findings were of note.

DERMATOPATHOLOGY
Biopsy revealed a poorly-differentiated spindled and epithelioid cellular proliferation arranged in nodules and cords throughout the dermis. There was notable nuclear hyperchromasia, pleomorphism, and prominent mitotic figures including atypical forms.

DIAGNOSIS
Cutaneous Metastasis of Osteosarcoma

DISCUSSION
Osteosarcoma is the most common cancer of the bone, accounting for more than one-third of primary bony malignancies. It commonly appears at the metaphyses of long bones near growth plates, and approximately 50-80% arises around the knee in the distal femur or proximal tibia. The sarcoma often presents with pain, noted especially during activity.

Osteosarcoma is the third most common malignancy of children, and is less common in the elderly. While previous radiation is a risk factor for all ages, Paget's disease is a known precipitating entity in adults. Syndromes such as Rothmund-Thompson, Li-Fraumeni, and mutations in the *retinoblastoma 1* gene contribute to a very small number of all diagnosed cases of osteosarcoma.

The prognosis depends upon stage and cellular subtype. Stage I osteosarcoma is rare and includes periosteal osteosarcoma or low-grade central osteosarcoma. It has an excellent prognosis (>90% survival) with wide resection. The five year survival rate for stage II disease ranges from

50-70% and depends on whether the tumor is contained in the cortex or has penetrated to become intramedullary. Presence of distant metastases defines stage III disease. The prognosis of patients with lung metastases depends on the resectability of the primary tumor and lung nodules, degree of necrosis of the primary tumor, and the number of metastases. Overall five-year survival is estimated to be 15-30%. Patients with multiple bone tumors have an even poorer prognosis.

Osteosarcoma frequently metastasizes, with lungs the most commonly involved. However, cutaneous metastases of this cancer are extraordinarily rare, with only ten reported cases in literature. The mechanism by which osteosarcoma metastasizes to a distant cutaneous site is not well delineated. It may be related to the tendency of osteosarcoma to disseminate hematogenously, rather than via lymphatics as is the case with most carcinomas and melanomas.

Virtually all reported cases of osteosarcomas that metastasized to the skin occurred in the elderly, usually with concurrent distant spread to other organs such as the lungs. Hence, metastatic spread to the skin should alert the clinician to the likely possibility of an advanced cancer necessitating careful workup and close follow-up.

This case supports that osteosarcoma metastatic to the skin, while rare, must be considered in the differential diagnosis of spindle-cell tumors of the dermis, along with primary cutaneous sarcomas and malignant melanoma.

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