Chicago Dermatological Society

June 2010
Monthly Educational Conference

Program Information
Continuing Medical Education Certification
and
Case Presentations

Wednesday, June 9, 2010

Conference Host:
Division of Dermatology
Loyola University Medical Center
Maywood, Illinois

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Program

Committees & Registration

8:00 a.m. - 9:00 a.m.	CDS Plans & Policies Committee – *Room 150*

Program Activities

8:30 a.m.	Registration & Continental Breakfast Main Lobby - Cuneo Center; Stritch School of Medicine
9:00 a.m. - 10:00 a.m.	RESIDENT LECTURE "Skin and Soft Tissue Infections: Everything that you wanted to know but were afraid to ask" Mark Enzler, MD *Tobin Hall Room 190*
9:30 a.m. - 11:00 a.m.	Clinical Rounds • Patient Viewing – *Clinical Skill Center Room 330* • Slide Viewing – *Leischner Hall Room 390* • Posters – *Seminar Rooms 363, 364, 375*
11:00 a.m. - 12:15 p.m.	General Sessions *Tobin Hall Room 190*
11:00 a.m.	CDS Business Meeting
11:15 a.m.	"Skin Problems in Returned Travelers" Mark Enzler, MD
12:15 p.m. - 1:00 p.m.	Lunch *Main Lobby and Room 160*
1:00 p.m. - 2:30 p.m.	Case Discussions *Tobin Hall Room 190*
2:30 p.m.	Meeting adjourns

Mark the Date!

Next CDS monthly meeting – Wednesday, October 13, 2010
Northwestern University, Chicago; Gerald Lazarus, MD

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

Guest Speaker

Mark Enzler, MD

Assistant Professor of Medicine at the College of Medicine,
Mayo Clinic; consultant in the Division of Infectious Diseases at
the Mayo Clinic's Department of Internal Medicine
Rochester, MN

Dr. Enzler is a graduate of the Mayo Medical School having earned his medical degree in 1985. He completed a residency in Internal Medicine at Mayo in 1988 and a fellowship in infectious diseases from 1993 to 1995, also at Mayo. He is board certified in internal medicine and infectious diseases.

Dr. Enzler has a connection to Illinois, including having served in several positions with Evanston Northwestern Healthcare Division of Infectious Diseases, Department of Medicine, and as an Assistant Professor of Medicine at the Northwestern Feinberg School of Medicine, Chicago.

Clinical practice interests and accomplishments include skin and soft tissue infections; cardiovascular infections; travel/tropical medicine; hospital systems improvement and in-patient mortality review quality improvement. Research interests include infective endocarditis and medical education. Dr. Enzler is the author of a number of peer-reviewed articles, book chapters and abstracts.

Continuing Education Credit

Chicago Dermatological Society

"Chicago Dermatological Society Monthly Conference"

June 9, 2010 *Chicago, Illinois*

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

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

Link address to evaluation form:

http://www.yourcesource.com/eval/?act=429!06092010

JOINT SPONSOR STATEMENT

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

GOAL/PURPOSE

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

SESSION OBJECTIVES

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

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

1. Describe common and less usual skin problems in recent travelers.
2. Discuss diagnostic techniques and treatment options for skin conditions found in travelers.
3. Employ examination methods and diagnosis steps when patients who have recently traveled present in the clinical setting.

CREDIT STATEMENTS

CME CREDIT

This activity has been planned and implemented in accordance with the Essential Areas and policies of the Accreditation Council for Continuing Medical Education (ACCME) through joint sponsorship of the Colorado Foundation for Medical Care, Office of Continuing Education (CFMC OCE) and Chicago Dermatological Society. CFMC is accredited by the ACCME to provide continuing medical education for physicians.

Colorado Foundation for Medical Care designates this educational activity for a maximum of **4.75** ***AMA PRA Category 1 Credits™*****.** Physicians should only claim credit commensurate with the extent of their participation in the activity.

CFMC has no financial responsibility for this activity.

DISCLOSURE STATEMENTS

Members of the faculty and planning team have nothing to disclose nor do they have any vested interests or affiliations. **It is the policy of the Chicago Dermatological Society and Colorado Foundation for Medical Care (CFMC) that the faculty discloses real or apparent conflicts of interest relating to the topics of the educational activity, and also discloses discussions of off-label uses of drugs and devices before their presentation(s).**

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CHICAGO DERMATOLOGICAL SOCIETY **CASE # 1**

Presented by Aaron Pace, MD, David Eilers, MD, and Scott Wickless, DO
Division of Dermatology, Hines Veterans Administration Hospital

HISTORY OF PRESENT ILLNESS

This 78-year-old male presented with a 6-month history of tender lesions that began on the abdomen and spread to the legs. The patient reported a continual increase in lesion quantity and associated pain. Lesions failed to respond to treatment with triamcinolone 0.1% ointment. The patient also reported concomitant exacerbation of pain related to his peripheral neuropathy that had been attributed to his diabetes.

PAST MEDICAL HISTORY

Diabetes mellitus type 2
Atrial fibrillation
Hypertension
Osteoarthritis
Benign prostatic hyperplasia

MEDICATIONS

Warfarin
Niacin
Metformin
Tramadol
Furosemide
Finasteride
Tamsulosin

ALLERGIES

Penicillin

FAMILY HISTORY

Non-contributory

SOCIAL HISTORY

The patient is a non-smoker, uses occasional alcohol, and no drug use.

PHYSICAL EXAM

On the right abdomen and left lower back, reticulated slightly tender erythematous patches were seen. On the bilateral anterior and posterior lower extremities there were several violaceous to erythematous tender nodules. In addition, a livedo pattern was appreciable on the lower extremities. Scattered blue macules and papules were seen on the bilateral dorsal feet.

HISTOPATHOLOGY

A deep incisional biopsy from the leg revealed hyalinized and thrombosed medium size arteries with necrosis and hemorrhage. There was a mononuclear cell infiltrate in the vessel walls, with nuclear debris. The dermis showed a predominantly perivascular lymphohistiocytic infiltrate.

LABORATORY RESULTS

The following were normal, negative, or within normal limits: factor V Leiden, cryoglobulins, antiphospholipid antibodies, antithrombin III, protein S, Hepatitis B and C, antistreptolysin O,

PPD, ANA, P and C-ANCA, creatinine kinase, complete blood count, metabolic profile, and liver enzymes.

The following labs were abnormal. CRP was 2.5, ESR was 39, and protein C was low (attributed to warfarin use prior to testing). DEXA scan revealed osteopenia (-1.4 of the femoral necks).

DIAGNOSIS

Cutaneous polyarteritis nodosa

TREATMENT AND COURSE

The patient initially began aspirin 325 mg orally daily and triamcinolone 0.1% ointment applied to the affected areas twice a day. He continued to worsen on this regimen and pentoxifylline 400 mg orally three times per day was added, and the triamcinolone switched to betamethasone. The disease continued to worsen and methotrexate was added. He began taking 15 mg weekly with folic acid in addition to a 21-day oral prednisone taper. The patient had a brief respite at this point but again began to progress. He was started on dipyramidole orally three times daily and topical lidocaine jelly because his lower extremity pain had become severe. Dipyramidole did not help and the patient was started on a protracted course of oral prednisone 60mg orally per day and the methotrexate dose was increased to 20mg weekly. The patient began to have improvement and relief of pain after about 4 weeks of prednisone and was tapered off over 4 months. The patient has been maintained on methotrexate 20mg orally per week and pentoxifylline 400mg orally three times per day. The patient has persistent erythematous to violaceous reticulated patches on the lower extremities but is pain free and without nodularity.

DISCUSSION

Cutaneous polyarteritis nodosa (PAN) is a skin limited, medium-sized vessel necrotizing vasculitis. The cutaneous form typically follows a more benign, relapsing remitting, but chronic course compared to the systemic form. Cutaneous disease can rarely progress to systemic involvement. The cutaneous only form comprises about 10% of the total cases.

The more common presentation of PAN is a multisystem systemic disease. Patients with the systemic form of the disease will have cutaneous disease in 25-60% of cases.

Clinically, the most common presentations in cutaneous PAN are nodules, purpura, livedo, ulceration, gangrene, necrosis or combinations of these. Cutaneous lesions in systemic disease are more frequently palpable purpura. Cutaneous disease is most frequently found on the lower extremities. Patients with cutaneous PAN may also have limited associated symptoms usually confined to the affected area. These include musculoskeletal, neurologic, and even constitutional symptoms like fatigue and fever, and may be present in as many as 64% of patients. Our patient had severe, painful peripheral neuropathy.

Diagnosis is based on the above clinical findings and a skin biopsy showing medium-sized vessel vasculitis with wall necrosis. Biopsies should be deep and incisional to ensure adequate sampling. The necrosis seen on path may result in microaneurysms. Smaller superficial vessels can demonstrate only leukocytoclastic vasculitis, underscoring the importance of a deep incisional biopsy when PAN is suspected. To confirm the diagnosis of cutaneous PAN, systemic organ involvement and other similar appearing conditions in the differential must be excluded. The differential, even with the above pathologic findings, includes cryoglobulinemic vasculitis, autoimmune connective tissue disease, microscopic polyangiitis, erythema induratum (nodular vasculitis), Wegener's granulomatosis, and Churg-

Strauss. Lab evaluation should include complete blood count, complete metabolic profile, hepatitis B and C (frequent causative factors), ESR, ANA (to check for the possibility of other active autoimmune disease), CRP, tuberculin skin test (to rule out erythema induratum and check for tuberculosis which is a known cause of PAN), HIV, antistreptolysin O titer (can be due to strep infection), and perinuclear and cytoplasmic antineutrophilic cytoplasmic antibodies (in rare cases may be positive but used in order to rule out other rheumatologic disease). In skin-limited disease, an elevated erythrocyte sedimentation rate may be the only lab abnormality.

There is debate as to whether the cutaneous form can progress to systemic. Therefore, treatment must be approached with this in mind. In a case series, Nakamura et al. showed that of 22 patients none of the patients with cutaneous polyarteritis nodosa progressed to systemic disease. Other studies have had similar results, but a few have demonstrated that patients may progress. Since only the rare patient progresses, treatment for cutaneous only disease should follow a conservative approach. Typical first-line treatments include intralesional steroids, non-steroidal anti-inflammatory agents, sulfapyridine, pentoxifylline, and aspirin. More aggressive treatment may include prednisone, clopidogrel, IVIG, and low dose methotrexate. It is also important to note that PAN has been associated with minocycline use and is p-ANCA positive in contrast to idiopathic PAN, which is rarely ANCA positive. Minocycline induced PAN often has a very high positive titer ANA again in contrast to idiopathic forms of the disease. Other causes and relationships include: streptococcal infection (in these cases the infection must be treated), Crohn disease, Takayasu's arteritis, relapsing polychondritis, tuberculosis, and hepatitis B.

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CHICAGO DERMATOLOGICAL SOCIETY **CASE # 2**

Presented by Joshua Mandrell, MD, Anthony Peterson, MD, Madu Dahiya, MD, and Patricia Kammeyer*
Division of Dermatology and Department of Pathology*, Loyola University Medical Center

HISTORY OF PRESENT ILLNESS

This 61-year-old female with a history of a heart transplant, chronic kidney disease on hemodialysis, anemia, and hypothyroidism initially presented to an outside hospital with weakness and shortness of breath. She was found to have a pulmonary infiltrate, leukopenia, and experienced worsening respiratory distress requiring intubation. She was subsequently transferred to our facility for continued medical care. Upon arrival, the patient was found to have pancytopenia, hypoxia, hypotension, and was determined to be in septic shock. Dermatology was consulted shortly after her arrival to evaluate an erythematous plaque on her left lower leg. The symptoms and duration of the lesion were unobtainable due to patient's intubation and sedation.

PAST MEDICAL HISTORY

Heart transplant (July 2000)
Chronic kidney disease on hemodialysis
Peripheral vascular disease
Myocardial infarction
Cardiomyopathy with defibrillator and pacemaker
Chronic CMV infection
Pulmonary embolism
Right femoral-popliteal bypass
Type II diabetes mellitus

MEDICATION

Amlodipine
Calcium and Vitamin D
Clonidine
Clopidogrel
Estradiol patch
Ezetimibe
Folic acid
Insulin (long and short-acting)
Isosorbide mononitrate
Labetalol
Levothyroxine
Lisinopril
Omeprazole
Simvastatin
Prednisone
Azathioprine
Tacrolimus
Azithromycin
Vancomycin
Aztreonam
Sulfamethoxazole and Trimethoprim
Fluconazole
Ganciclovir
Filgrastim
Methylprednisolone
Fentanyl/Midazolam
Norepinephrine

ALLERGIES

Cephalexin
Ciprofloxacin

FAMILY HISTORY

Unable to obtain

SOCIAL HISTORY
Unable to obtain

PHYSICAL EXAM
Focused exam of the bilateral lower extremities showed a 2 cm x 2 cm erythematous plaque on the left anterior lower leg. A one cm fibrinous and mildly purulent erosion was noted centrally.

HISTOPATHOLOGY
Punch biopsy of the left lower leg revealed marked acute and chronic inflammation throughout the reticular dermis, extending into the subcutis. Periodic acid-Schiff (PAS) stain showed a superficial and deep deposition of septated branching hyphae with rare ovoid conidia.

LABORATORY RESULTS
Culture from the left leg revealed a moderate number of colonies of *Pseudallescheria boydii* species complex.

RADIOLOGY
Chest x-ray revealed severe bilateral airspace consolidation.

DIAGNOSIS
Pseudallescheria boydii species complex infection

TREATMENT AND COURSE
Upon presentation, the patient's course was complicated by hypoxic respiratory failure, *Pneumocystis carinii* pneumonia (PCP), and pseudomonal pneumonia, which led to bacteremia, subsequent septic shock, and disseminated intravascular coagulation (DIC). Despite antibiotic therapy, her hypotension worsened, requiring multiple pressors and ultimately resulting in an episode of pulseless electrical activity. Bilateral pneumothoraces were found requiring video-assisted thoracoscopic surgery and mechanical pleurodesis. Further complications included multiple cerebrovascular accidents. Once the diagnosis of *Pseudallescheria boydii* species complex infection was made, the patient was started on voriconazole 250mg twice daily for 8 weeks and subsequently improved. She was discharged to a specialty ventilator-weaning hospital.

DISCUSSION
Pseudallescheria boydii species complex are ubiquitous fungi seen in soil, water, and sewage. This infection is commonly seen in immunocompromised patients, especially solid-organ transplant patients. In one study, the overall incidence of infection with *Pseudallescheria* was 1 per 1,000 of solid organ transplant patients, with a higher incidence in lung transplant patients. Incidence of infection continues to increase, likely secondary to the increase in immunocompromised patients and solid-organ transplantation. In immunocompetent patients, the typical presentation is traumatic injury resulting in mycetomas. Other presentations, especially in the immunocompromised, include soft-tissue and wound infections, osteomyelitis, otomycosis, sinusitis, pulmonary infection, central nervous system disease (often from near-drowning incidents), keratitis and endophthalmitis, intravascular infection, vascular graft infection, endocarditis, prostatitis, and disseminated infection. *Pseudallescheria boydii* species complex are often colonizers of the lung in cystic fibrosis patients, rarely causing disseminated disease. Clinical morphologies include papules, plaques, nodules, and ulcers, occasionally in a sporotrichoid pattern.

The ascomycte *Pseudallesheria boydii* has gone through many taxonomic changes in recent years, much due to molecular techniques. Currently, the *Pseudallescheria boydii* species complex (or *Pseudallescheria boydii sensu lato*) includes seven species in the sexual genus *Pseudallescheria* (which have asexual states in the genus *Scedosporium* and often another asexual state in the genus *Graphium*) and two species of *Scedosporium* (*S. dehoogii* and *S. aurantiacum*) with no known sexual state. The seven currently accepted species of *Pseudallescheria are P. angusta, P. boydii, P. desertorum, P. ellipsoidea, P. fusoidea, P. minutispora,* and the newest accepted species *P. apiosperma*.

Until recently, it was thought that *P. boydii* was the sexual state of *S. apiospermum*, but in 2008, the two were found to be distinct species with *P. boydii* being the sexual state of *S. boydii* and in 2010, *P. apiosperma* was discovered to be the sexual state of *S. apiospermum.* Currently, all species of the genus *Pseudallescheria*, except *P. apioperma* are homothallic, meaning they are self-mating, and, under the right conditions, the sexual state will form. *P. apiosperma* has been found to be heterothallic (needing a mating type to form the sexual state), which may explain why many clinical isolates in the United States have not been found to produce a sexual state in the clinical laboratory. *S. apiospermum* appears to be the most common species in the complex found in clinical cases, although more studies need to be done to prove this hypothesis. *S. prolificans*, an important human pathogen, is an asexual fungus with no known sexual state, but is molecularly linked to the sexual genus *Petriella*.

Clinically and histopathologically, *Pseudallescheria boydii* species complex is similar to *Fusarium* and *Aspergillus* species which are also fungi that commonly present in the immunocompromised. Like *Aspergillus*, *Pseudallescheria* species complex and *Fusarium* species can also colonize the sinuses and the airways, particularly in patients with underlying pulmonary diseases. Making an early and accurate diagnosis is essential given the mortality associated with *Pseudallescheria boydii* species complex, especially in the immunocompromised.

Given the similarities, mycology is essential in distinguishing between *Aspergillus, Pseudallescheria,* and *Fusarium* species. Most species within the *Pseudallescheria boydii* species complex reproduce sexually. The genus *Aspergillus* contains some species which can sexually reproduce and others which are purely asexual. Most *Fusarium* species are heterothallic, needing a mating type to reproduce sexually, however most clinical isolates appear in their asexual state in the clinical laboratory. All three genera are ascomycetes, and appear as narrow, septate, often dichotomously branching hyaline (or clear) hyphae in tissue and have affinities for blood vessels (angioinvasive). The hyphae stain poorly with hematoxylin and eosin, and are best seen with PAS or Gomori methenamine silver (GMS) stains. Fungal culture or genetic sequencing is needed to accurately identify the genus involved in the disease process. All three genera grow on most fungal media although *Pseudallescheria* species often also grow on cyclohexamide-containing media and *Aspergillus* and *Fusarium* usually do not. Colonies of *Pseudallescheria boydii* species complex are initially white on most media, becoming “house-mouse” gray with a velutinous to downy surface with age. Conidial production (sporulation) is often produced on primary isolation media within a few days of incubation at 30 degrees Celsius. Conidia of all species of *Pseudallescheria boydii* species complex are oval to cylindrical, subhyaline, one-celled and are produced singly or in small groups on elongate conidiophores or laterally on hyphae.

Because many of the new species within the *Pseudallescheria boydii* species complex are recently described, it is still not clear how clinically important certain species will be. In one study evaluating the comparative virulence of *P. boydii sensu stricto, P. minutispora, S. apiospermum, S. aurantiacum,* and *S. dehoogii* in a murine model, *S. aurantiacum* and *S.*

dehoogii appeared to be extremely virulent killing 80% and 70% of the immunocompetent mice, respectively. The other species killed 0-20% of the animals.

While most species of *Aspergillus* are susceptible to amphotericin B and 5-flucytosine, *Pseudallescheria* species are usually resistant. In most studies, treatment with the newer triazoles has been most effective. However, some species, clinically and in vitro, have been resistant. The newer speciation within the *Pseudallescheria boydii* species complex likely explains the difference in sensitivity to various antifungals. Voriconazole and posaconazole tend to be the most active drugs. However, *S. aurantiacum* is the species most resistant to voriconazole, and *S. aurantiacum* and *P. fusoidea* tend to be resistant to posaconazole. Since it appears there are in vitro antifungal differences between species and strains within the *Pseudallescheria boydii* species complex, it is recommended that antifungal testing be performed on any clinical isolate from patients needing antifungal treatment. Surgical treatments may be employed, either as monotherapy or in combination with antifungals. The best outcome is achieved with combination therapy, especially in the immunocompromised.

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CHICAGO DERMATOLOGICAL SOCIETY **CASE # 3**

Presented by L Julia Kamalpour, MD, Anthony Peterson, MD, and Madhu Dahiya, MD
Division of Dermatology, Loyola University Medical Center
Division of Dermatology, Hines Veterans Administration Hospital

HISTORY OF PRESENT ILLNESS

This 48-year-old African American male with a history of cocaine abuse was transferred from an outside hospital (OSH) for workup of purpuric plaques and microcytic anemia. The patient reported that six months prior to presentation, he developed intermittent pain and swelling of his right ear with subsequent black discoloration of the affected area. He went on to develop similar lesions over his left ear, legs, feet, and most recently, arms and cheeks. Upon admission to the OSH, the patient had been started on anticoagulation and intravenous (IV) steroids with subsequent improvement in his pain. The patient denied any history of abnormal bleeding or blood clots, recent travel, sick contacts, or new medications prior to onset of his lesions. He did however admit to daily cocaine use for several months prior to onset of rash, with most recent use being just before admission to the OSH. He correlated the worsening of his rash and associated pain with cocaine use. Review of systems was significant for weakness, fatigue, and subjective fevers.

PAST MEDICAL HISTORY

Non-contributory

MEDICATIONS

None

ALLERGIES

No known drug allergies

FAMILY HISTORY

Aunt with systemic lupus erythematosus and possible bleeding disorder

SOCIAL HISTORY

Tobacco use: 45 pack-year history
Illicit drug use: admits to daily cocaine use (smokes cocaine), denies history of IV drug use
Alcohol use: quit 6 months prior to presentation
Positive history of tattoos
Patient is divorced, lives with friends, and works in construction

PHYSICAL EXAM

Physical exam revealed palpable purpuric plaques over bilateral helices with soft tissue loss over the left helix. Symmetrically distributed stellate-shaped palpable purpuric plaques with brightly erythematous borders were seen over the bilateral cheeks, arms, chest, abdomen, lower legs, and thighs. Numerous plaques were studded with large bullae.

HISTOPATHOLOGY

Punch biopsy of the left thigh revealed mixed features of cutaneous vasculopathy and vasculitis. Intraluminal thrombi (predominantly of venules or capillaries) were seen along with small vessels with associated fibrinoid necrosis and leukocytoclasis (leukocytoclastic vasculitis). The overlying epidermis was unremarkable.

LABORATORY RESULTS
The following were abnormal:
CBC (Hgb 9.2, Hct 28.7, MCV 76.8)
CMP (BUN 26, Cr 1.44 with unknown baseline)
ESR 110
UA (large blood, trace glucose, 1+protein, 88 RBCs)
ANA (positive 1:160 with mixed pattern)
Anti-neutrophil cytoplasmic antibodies (positive with p-ANCA pattern)
Anti-myeloperoxidase antibodies (positive, 251)
Lupus anticoagulant (positive)
dsDNA (positive, 96)
Mixing studies (noncorrecting)

The following were normal or negative:
Complement titers, rheumatoid factor, cryoglobulin screen, cryofibrinogen screen, anti-smith Ab, HIV, hepatitis panels, iron panel

RADIOLOGY
The following were normal: chest X-ray, transthoracic echocardiogram (EF 55-65%)

DIAGNOSIS
Presumptive levamisole-induced vasculitis

TREATMENT AND COURSE
Upon transfer to Loyola, the patient was continued on IV steroids with Solumedrol 100mg every 8 hours. Rheumatology was consulted, and he was started on IV Cytoxan for suspected microscopic polyangitis (MPA). The patient's hospital course was complicated by impetiginization of foot lesion for which he was treated with clindamycin. The patient did not develop any new lesions during hospital stay and had significant improvement in all cutaneous lesions. He was discharged home on an oral prednisone taper.

DISCUSSION
Our patient's retiform purpura, histopathologic findings, anemia, lupus anticoagulant positivity and p-ANCA positivity, along with temporal association with daily cocaine use are strongly suggestive of levamisole-induced vasculitis. Physicians should be aware of the ubiquitous contamination of cocaine with levamisole and the potentially dangerous clinical manifestations of levamisole exposure.

Levamisole is believed to be a contaminant in over 70% of the United States cocaine supply. Prior studies have shown it to be a cause of agranulocytosis as well as purpuric eruptions in association with lupus anticoagulant positivity and/or c- or p-ANCA positivity. Similarly, levamisole-adulterated cocaine has been recently associated with life-threatening agranulocytosis and a positive lupus anticoagulant. Our patient had microcytic anemia of unknown etiology and a positive lupus anticoagulant antibody. Although his neutrophil count was not low, this may have been secondary to a steroid-induced leukocytosis as he was started on steroids at the OSH.

In patients with levamisole-associated vasculitis, clinical resolution of skin lesions generally occurs within 2 to 3 weeks of stopping levamisole use and serologies normalize within 2 to 14 months of medication cessation. Skin biopsy specimens from purpuric plaques in children who were given levamisole for nephrotic syndrome revealed thrombotic vasculitis, leukocytoclastic vasculitis, and/or vascular occlusion. The presence of both leukocytoclastic vasculitis and

vascular occlusion was noted upon exam of our patient's skin biopsy, corresponding to the prior histopathologic findings identified in patients exposed to levamisole.

We acknowledge that our suspicion of levamisole contamination was retrospective. However, detection of levamisole is challenging, as the drug's half-life is very short (5.6 hours) and only 2% to 5% of the parent drug is detected in urine. In addition, the sensitivity of available testing is low.

It is not known why pharmaceutically active agents are added to the cocaine supply. It is likely that cocaine producers believe that certain pharmaceutical agents may enhance the drug's effects or decrease associated side effects. Cocaine's psychoactive effects are achieved via increased dopamine concentrations in the euphoric centers of the brain. Animal studies have found that levamisole also increases dopamine levels in these regions. It is thus hypothesized that levamisole may potentiate the euphoric effects of cocaine by further increasing brain dopamine levels.

Despite our suspicion that the patient likely had levamisole contaminated cocaine-induced vasculitis, he was given the diagnosis of MPA by his primary team. Consequently, he was treated with Cytoxan for possible MPA-induced glomerulonephritis despite a paucity of lab results in support of progressive renal failure and a lack of histologic confirmation of the crescentic glomerulonephritis that is classically seen in MPA.

MPA is characterized by involvement of small-sized vessels with a rapidly progressive glomerulonephritis along with frequent pulmonary involvement leading to alveolar hemorrhage. Over 90% of MPA patients exhibit renal involvement with varying degrees of extra-renal vasculitis. The diagnosis is often made following a prodromal phase of several months duration of constitutional symptoms, including polymyalgia. MPA may occur either as a primary disease or secondary to an underlying disease process. Anti-neutrophil cytoplasmic antibodies (ANCAs) are seen in approximately one-half of MPA patients and usually exhibit a perinuclear staining pattern and myeloperoxidase activity.

This case underscores the diagnostic dilemma posed by ANCA-associated vasculitides. Levamisole-induced vasculitis is likely an under-recognized entity and should be considered in the differential diagnosis for any patient presenting with retiform purpura in the setting of chronic levamisole contaminated cocaine abuse.

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CHICAGO DERMATOLOGICAL SOCIETY **CASE # 4**

Presented by Linda Sheu, MD, Anthony Peterson, MD, Darryl Oble, MD, and Maria Picken-Mrozowicz, MD, PHD
Division of Dermatology, Loyola University Medical Center

HISTORY OF PRESENT ILLNESS

This 47-year-old African American female with history of systemic lupus and poor compliance, was admitted with shortness of breath, chest pain and altered mental status. She was found to have congestive heart failure secondary to a large pericardial effusion, lupus nephritis and a lupus cerebritis, indicating a severe systemic lupus flare. Dermatology was consulted on her second day of hospitalization when she developed multiple hemorrhagic bullae.

PAST MEDICAL HISTORY

Systemic lupus erythematosus diagnosed 1995

MEDICATIONS

Aspirin
Carvedilol
Heparin
Hydroxychloroquine

ALLERGIES

Morphine

FAMILY HISTORY

No history of systemic lupus or other connective tissue disease

SOCIAL HISTORY

Non-contributory

PHYSICAL EXAM

Examination revealed dorsal and palmar hands with tense, hemorrhagic bullae ranging from five millimeters to two centimeters. The right antecubital fossa and lower extremities were remarkable for erosions ranging from four to five centimeters, and several smaller, tense bullae ranging five millimeters to one centimeter. Hemorrhagic crusting was noted on her oral mucosa.

HISTOPATHOLOGY

A biopsy from the right knee demonstrated a lymphocytic and leukocytoclastic vasculitis with incipient sub-epidermal bullae containing fibrin and mixed inflammatory, predominantly neutrophilic infiltrate. Periodic acid-Schiff stain was negative for fungi or significant basement-membrane thickening. A colloidal iron stain demonstrated a mild increase in dermal mucin. The direct immunoflourescence was positive for IgG, kappa and lambda light chain and C3 along the basement membrane zone, consistent with cutaneous lupus.

LABORATORY RESULTS

The following were abnormal or positive:
Tissue culture of skin specimen revealed few colonies of *Mucor* species. Sequencing demonstrated *Mucor ramosissimus*.
WBC 17, HGB 8.7, HCT 25.1, MCV 82.1, RDW 18.9
BUN 101, Cr 4.55
Albumin 1.5, AST 43

PT 15, PTT 41.7
C3 51, C4 12
ANA: 1:1280; homogenous pattern

DIAGNOSIS
Systemic lupus, including lupus nephritis, lupus cerebritis, pericardial effusion and cutaneous bullous lupus

TREATMENT AND COURSE
After being found to have lupus cerebritis and pericardial effusion consistent with a flare of systemic lupus, the patient was started on hydroxychloroquine and methylprednisolone. When lupus nephritis was confirmed by biopsy, mycophenolate mofetil, and Cytoxan were instituted. She had rapid improvement over the ensuing two weeks. She developed no new blisters. Her cutaneous erosions and bullae began to heal. After a three-week hospital course, she was discharged home on hydroxychloroquine and has continued to do well.

DISCUSSION
The development of bullae is a rare but well-documented cutaneous manifestation of systemic lupus erythematosus. It was first described in 1973 by Pedro and Dahl. Since then, several cases have been reported with similar features. Many have been observed in young, black women in the second through fourth decades of life. Bullous lupus generally develops after the diagnosis of systemic lupus has been made, often occurring during a systemic flare and often in conjunction with renal disease.

There are no pathognomonic clinical features of bullous systemic lupus erythematosus (BSLE) but it commonly occurs as a sudden, generalized eruption of tense vesicles and bullae arising on previously uninvolved skin. The trunk and flexural areas are most commonly involved, though vesicles and bullae confined to the face have also been described. Not uncommonly, mucocutaneous surfaces including oral, nasal, pharyngeal and vulvar membranes are affected.

Patients with BSLE have demonstrated antibodies against the major anchoring fibril, type VII collagen. The antigenic domains are within the noncollagenous NC1 domain, identical to the domains recognized by antibodies from patients with epidermolysis bullosa acquisita (EBA). BSLE lesions do not leave scars and milia as seen in EBA.

BSLE responds well to medical therapy and treatment with dapsone is particularly effective. Response is dramatic with cessation of new blister formation within days to weeks, and rapid healing of existing lesions. Dapsone at low doses of 25-50 mg is often effective. Though rapid recurrence may occur upon withdrawal, remission within one year is usual. Prednisone may be effective for those who do not respond to dapsone, cannot tolerate dapsone, or require treatment of concurrent systemic disease. Methotrexate, azathioprine, and mycophenolate mofetil represent additional therapeutic options, particularly for treatment of concurrent systemic lupus.

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CHICAGO DERMATOLOGICAL SOCIETY **CASE # 5**

Presented by Anita Satyaprakash, MD, Anthony Peterson, MD, Guilz Barkan, MD, and Razan Massarani, MD
Division of Dermatology, Loyola University Medical Center

PATIENT A

HISTORY OF PRESENT ILLNESS

This 67-year-old male with a history of basal cell carcinoma on the right thigh in 2004 as well as severe plaque psoriasis and psoriatic arthritis for over 30 years presented to clinic for routine follow-up of biologic therapy. Prior treatments for his psoriasis included topicals, phototherapy, and acitretin. Etanercept 50 mg weekly had been started in 2005, with good control of his cutaneous symptoms and improvement of his arthritis. The patient noted a one-year history of right lower extremity swelling. More recently, he had been having recurrent episodes of cellulitis in this extremity, requiring multiple courses of oral antibiotics.

PAST MEDICAL HISTORY

Basal cell carcinoma of the right thigh (clinically measuring 2.9 cm x 3.0 cm), status post Mohs surgery in 2004, recurrent lymphedema and cellulitis of right leg, psoriasis, hyperlipidemia, hypertension, atrial fibrillation, coronary artery disease

MEDICATIONS

Aspirin
Ezetimibe
Lisinopril
Amlodipine-benazepril
Clopidogrel
Pravastatin
Warfarin
Metroprolol succinate
Hydrochlorothiazide

ALLERGIES

No known drug allergies

FAMILY HISTORY

No family history of skin cancer

SOCIAL HISTORY

The patient used tanning beds in his youth. He denied use of alcohol, tobacco, or illicit drugs.

PHYSICAL EXAM

Physical exam revealed scattered, thin, well-demarcated erythematous plaques with silvery scale on the left lower leg, left thigh, buttocks, lower back, and bilateral elbows, covering 5% of the body surface area. A well-healed linear surgical scar was present on the right medial thigh. The right inguinal fold was notable for a 1.5 cm non-tender subcutaneous nodule, and the right lower extremity was remarkable for 2+ pitting edema extending up to the lower thigh.

HISTOPATHOLOGY

Fine needle aspiration of the right inguinal nodule showed cohesive groups of atypical-appearing epithelioid cells with a high nuclear-to-cytoplasmic ratio and irregular nuclear contour, in a background of benign lymphocytes and adipose tissue. Immunohistochemical stain of the tumor cells was positive for pankeratin.

Excisional biopsy of the right inguinal nodule showed fibroadipose tissue with an infiltrative tumor composed of large and small nests, cords, and strands of atypical basaloid epithelial cells. Focal necrosis was seen, as well as retraction of the tumor from the fibrotic stroma. Keratin cyst-like structures containing whorls of laminated keratin were present within some tumor nests. Immunohistochemical stains were positive for CK7 and chromogranin and negative for CK20, uroplakin, and thrombomodulin. No lymph node parenchyma was present.

Core biopsies of the left inguinal lymph node were negative.

RADIOLOGY

A PET scan showed hypermetabolic lymph nodes in both inguinal regions (three in the right, one in the left) and subcutaneous edema in the right thigh.

DIAGNOSIS

Metastatic basal cell carcinoma while on etanercept

TREATMENT AND COURSE

Etanercept was discontinued after the clinical finding of a right inguinal nodule. The patient underwent excision of the nodule and was considered for both full right inguinal lymph node dissection and inclusion in a clinical trial of GDC-0449, a sonic hedgehog pathway inhibitor being evaluated for use in advanced basal cell carcinoma. However, as follow-up full-body PET scan showed no other areas of involvement, the patient's oncologist felt that his disease was in remission and required no further treatment. The patient's psoriasis and psoriatic arthritis flared after discontinuation of etanercept. Although he was considered for acitretin therapy, he was subsequently seen by Rheumatology and started on methotrexate 12.5 mg weekly along with prednisone 10 mg daily in order to quickly control his arthritis.

PATIENT B

HISTORY OF PRESENT ILLNESS

This 49-year-old female with a history of invasive breast cancer, diagnosed in 2004 and status post lumpectomy, axillary lymph node dissection, and subsequent chemotherapy, presented for a routine visit for her severe plaque psoriasis and psoriatic arthritis, diagnosed over 30 years prior with initial involvement of 10 percent of her body surface area. Her psoriasis had been refractory to topical treatments; she was unable to tolerate phototherapy due to a history of photosensitivity and unable to take acitretin or methotrexate due to a history of fatty liver disease. After clearance from her oncologist, the patient was started on etanercept 50 mg twice weekly in May 2008. At the time of inception of etanercept therapy, she was warned of the theoretical increased risk of malignancy, both new and recurrent, with biologic therapy, and gave her informed consent. At this visit, her psoriasis was well-controlled with etanercept. Routine chest X-ray and CT scans had initially been negative since her diagnosis and treatment; however, she had been recently diagnosed with an enlarging left lung nodule.

PAST MEDICAL HISTORY

Invasive ductal carcinoma of the right breast, stage IIIA grade II, diagnosed in 2004, with tumor staging T2N2M0, and tumor positive for estrogen receptor (ER), progesterone receptor (PR), and human epidermal growth factor Receptor 2 (HER2), with subsequent lumpectomy, right axillary lymph node dissection, and chemotherapy.

The patient also has a history of psoriasis, osteoarthritis, fibromyalgia, migraines, nephrolithiasis, hyperparathyroidism, hypothyroidism, asthma, and fatty liver.

MEDICATIONS

Albuterol
Benadryl
Etanercept
Exemestane
Ezetimibe
Fluticasone-salmeterol
Lansoprazole
Levothyroxine
Nortriptyline
Topiramate
Zolpidem

ALLERGIES

Latex, shellfish, cephalexin, hydromorphone, sumatriptan, tramadol, pontacaine

FAMILY HISTORY

No family history of breast or ovarian cancer.

SOCIAL HISTORY

The patient denies use of tobacco, alcohol, or illicit drugs.

PHYSICAL EXAM

Physical exam reveals a well-demarcated erythematous plaque with silvery scale on the left abdomen. No lymphadenopathy was noted.

HISTOPATHOLOGY

A resection of the left upper lobe of the lung showed moderately differentiated adenocarcinoma consistent with metastasis from a breast primary tumor. The tumor was positive for CK7, mammoglobin, HER2, ER, and PR and negative for CK20 and TTF1.

LABORATORY RESULTS

The following laboratory results were normal: CBC and CMP.

RADIOLOGY

In January 2009, routine chest x-ray showed a new 4 mm nodule in the left upper lobe of the lung. Chest CT in September 2009 showed enlargement of this nodule to 7mm; no lymphadenopathy was noted. Subsequent PET scan showed increased metabolic activity in the left upper lobe lung nodule and in the right axilla, likely corresponding to a lymph node.

DIAGNOSIS

Metastatic breast adenocarcinoma while on etanercept

TREATMENT AND COURSE

Etanercept was discontinued in October 2009, after which the patient's psoriasis flared considerably. The patient underwent surgical resection of the lung nodule. PET scan done after surgery showed stable increased uptake in the right axilla. She is currently undergoing chemotherapy with trastuzumab and letrozole, and due to the metastatic nature of her disease, she has been given a poor prognosis. She elected to restart etanercept in order to be comfortable. After discussion with the patient's oncologist, she was restarted on etanercept 25 mg twice weekly along with acitretin 25 mg daily.

DISCUSSION

TNF-α antagonists such as etanercept, adalimumab, and infliximab have been proven to be efficacious treatments in moderate to severe psoriasis and psoriatic arthritis. Whether treatment with TNF-α antagonists increases the risk of malignancy is controversial, as several

large scale cohort studies and meta analyses, in both psoriasis and rheumatoid arthritis patients, have shown a somewhat higher rate of malignancy in the groups treated with biologic agents, but this increased rate has often been shown to be statistically insignificant. Even without biologic treatment, patients with moderate to severe psoriasis or psoriatic arthritis have been shown to carry a baseline higher risk for certain cancers, especially non-melanoma skin cancer (NMSC) and lymphoproliferative disorders, due to the abnormal immune activation and chronic inflammation inherent in psoriasis.

Many anecdotal reports have seemed to show a temporal and presumed causal relationship between initiation of therapy with a TNF-α antagonist and the onset of malignant conditions such as lymphoma, NMSC, melanoma, and both *de novo* and recurrent solid tumors. The combination of TNF-α antagonists with other immunosuppressants has also been reported to increase the risk of lymphoma in these patients. In certain cases, withdrawal of the TNF-α antagonist medication has led to clinical regression of the malignancy.

The World Health Organization's International Pharmacovigilance program has reported 74 case of leukemia reported in connection with infliximab therapy, 39 with etanercept, and 12 with adalimumab; of these 121 reports, most occurred in patients with rheumatoid arthritis or Crohn's disease, and 54 patients were simultaneously using other immunosuppressants. A meta-analysis of 18 randomized controlled trials with a total of 8808 patients with rheumatoid arthritis treated with TNF-α antagonists at recommended doses showed no increase in lymphoma, NMSC, melanoma, or other cancers in trials with up to a one-year follow-up. Another meta-analysis of nine trials including 3316 rheumatoid arthritis patients, 2244 who received etanercept and 1072 who received control therapy revealed a higher estimated incidence of malignancies in etanercept compared with placebo, but found that their results were not statistically significant. An earlier meta-analysis of nine trials including 5005 rheumatoid arthritis patients, 3493 patients who received infliximab or adalimumab and 1512 patients who received placebo, showed a dose-dependent increased risk of malignancy in patients treated with the TNF-α antagonists.

At this time, all TNF-α antagonists carry black box warnings regarding the increased risk of malignancies in children and adolescents using the medications, especially lymphoma and other malignancies most often seen in immunosuppressed patients. Published guidelines concerning the use of TNF-α antagonists generally contraindicate their use in patients with proven malignancy or pre-malignancy states, excluding adequately treated NMSC and malignancies diagnosed and treated more than 20 years prior (due to the high probability of definitive cure). Patients should be screened for hematologic malignancy prior to initiation of TNF-α antagonists by a complete blood count and differential, with further workup if indicated. In addition, consideration should be given for age-appropriate malignancy screening prior to initiation of these therapies, especially in patients with a pertinent family history.

This patient series is being presented to remind clinicians of the possible risks of use of TNF-α antagonists in patients with prior malignancies, even NMSC, and to maintain a high level of clinical suspicion of *de novo* or metastatic malignancy in patients with new clinical complaints.

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CHICAGO DERMATOLOGICAL SOCIETY **CASE # 6**

Presented by L Julia Kamalpour, MD, and David Eilers, MD
Division of Dermatology, Hines Veterans Administration Hospital

UNKNOWN

CHICAGO DERMATOLOGICAL SOCIETY **CASE # 7**

Presented by Tricia Hultgren, MD, Elaine Kung, MD, and Darryl Oble, MD
Division of Dermatology, Loyola University Medical Center

HISTORY OF PRESENT ILLNESS

This 20-year-old female of Hispanic and European descent presented to our clinic for evaluation of new onset genital ulceration. She first noted a non-healing, painful lesion on the labia minora three days prior to evaluation. She also reported mild dysuria. She had never been sexually active and denied history of genital lesions in the past. Upon further questioning, she reported history of recurrent oral aphthous ulcerations, approximately four times per month, since childhood. She denied arthralgias, vision changes, or other skin problems.

PAST MEDICAL HISTORY

Iron-deficiency anemia

MEDICATION

Ibuprofen as needed

ALLERGIES

None

FAMILY HISTORY

No family history of autoimmune conditions

SOCIAL HISTORY

The patient denied tobacco use and admitted to occasional alcohol and marijuana use.

PHYSICAL EXAM

There were well-demarcated, ovoid ulcerations with an overlying whitish pseudomembrane on the midline tongue and upper lip mucosa. A punched out ulceration with purulent drainage and surrounding induration was present on the right labia minora and a similar but smaller lesion was seen on the right perineum. The patient had scattered acneiform papules on the cheeks.

HISTOPATHOLOGY

Punch biopsy of the right perineum revealed a spongiotic dermatitis and a mixed neutrophilic and lymphocytic small vessel vasculitis.

LABORATORY RESULTS

The following tests were negative or normal: RPR, HIV, ESR, viral culture, aerobic culture, pathergy test. Eye exam by an ophthalmologist showed astigmatism without evidence of uveitis or retinal vasculitis.

The following tests were positive or abnormal:

Hemoglobin	11.4 g/dL	(12.0-16.0 gm/dL)
MCV	77.9 Fl	(85-95 Fl)
Plt	145 k/uL	(150-400 k/uL)
Lymph	9%	(20-45%)
Gran	83%	(45-70%)

HLA Sub-typing revealed serologic equivalents to be B62 and B57, with further allelic results showing B5701

DIAGNOSIS
Evolving Behçet's disease

TREATMENT AND COURSE
The patient's genital ulcerations were treated symptomatically with topical lidocaine cream. An oral suspension consisting of viscous lidocaine, hydrocortisone, Orasweet and tetracycline was used to treat the oral aphthae. After biopsy results were obtained, a short course of prednisone was prescribed along with methotrexate. Both the oral and genital ulcerations healed rapidly. The patient is currently maintained on 10 mg of methotrexate weekly. She reports a decrease in number and severity of oral aphthae since starting methotrexate and denies new genital ulcerations.

DISCUSSION
Behçet's disease (BD) was first described by Hippocrates in the 5th century BC and further characterized in 1937 by the Turkish dermatologist Behçet, who identified the 3 cardinal signs: recurrent oral aphthae, genital ulcerations and recurrent hypopyon uveitis. The condition has the potential to affect nearly all organ systems with vascular, neurologic, gastrointestinal, pulmonary and articular involvement.

Also known as the Old Silk Route disease, BD most commonly occurs in Asian and Eurasian populations in an area that was once an ancient commercial trading route traversing the Mediterranean, Middle East and Far East. The prevalence ranges from 80-420/100,000 in Turkey to 0.12-0.64/100,000 in Northern Europe and the U.S. This prominent geographic variance is likely secondary to both genetic and environmental factors. BD is slightly more common and follows a more severe clinical course in men. Onset is typically in the third to fourth decade, with a worse prognosis seen in patients that manifest symptoms at an early age.

Although the exact etiology has yet to be defined, the clinical findings in BD are believed to result from an autoimmune reaction to an infectious or environmental agent in genetically predisposed individuals. The HLA-B51 allele on chromosome 6 has been identified as the strongest risk factor for BD in the Old Silk Route region, but is less common in Caucasians with BD. A recent study by Ahmad et al. identified HLA-B5701 as a risk factor for BD in Caucasians from the United Kingdom. In this study, HLA-B5701 carried a relative risk of disease that was equivalent to that of HLA-B51 (present in 18% of BD patients versus 6.8% in controls).

Microbial pathogens may play a role in disease pathogenesis. It is believed that certain microbial peptides share sequence homology with human proteins resulting in cross-reactivity and an autoimmune response causing the TH-1 inflammatory reaction seen in BD. Neutrophils are also hyperactive in BD, exhibiting increased chemotaxis, phagocytosis, superoxide and myeloperoxidase production. Circulating immune complexes and neutrophils appear to mediate tissue damage in mucocutaneous lesions. Histologically, a vasculopathy is seen ranging from neutrophilic infiltrate with leukocytoclasia in early lesions to angiocentric lymphocytic inflammation in older lesions. Acneiform lesions exhibit a sterile neutrophilic vasculopathy.

Oral ulcerations are the cardinal feature and often the first manifestation of BD (47-86% of patients). Lesions appear identical to common aphthous ulcers and heal without scarring. Ulcerations most commonly occur on the gingival and buccal mucosa, tongue and lips. Genital ulcerations are similar to oral lesions in clinical appearance, but are often larger and deeper with irregular borders. Common locations include the penis and scrotum in men and the vulva in women. Additional cutaneous findings include papulopustular lesions, which may appear acneiform but are not folliculocentric and are often more widespread, affecting the face, limbs, trunk and buttocks. Erythema nodosum is frequent, affecting 15-78% of patients. Lesions are more common in women and predominantly affect the lower legs. Pyoderma gangrenosum-like lesions have also been reported. In addition to mucocutaneous findings, pathergy can be seen in BD and is one of the diagnostic criteria. Pathergy results vary by geographic region, being positive in 60% of Middle Eastern patients but only 5% of Caucasian patients.

Ocular disease is often bilateral and generally occurs 2-3 years after the onset of symptoms. . Anterior uveitis is the most frequent presentation, but posterior and pan-uveitis may occur. Additional findings may include hypopyon, retinal vasculitis, keratitis, episcleritis, and optic neuritis. Ocular complications may lead to blindness in up to 25% of patients.

The vasculitis seen in BD can involve virtually every organ system. Neurologic disease affects 5-10% of patients and most often affects the brainstem or basal ganglia. Symptoms include cranial nerve palsies, extrapyramidal signs, pyramidal signs, hemiparesis, behavioral changes or headache. Dural sinus thrombosis and arterial vasculitis can also occur. Articular involvement affects 45-60% of patients and is characterized by a non-erosive, non-deforming arthritis. Involvement is usually monoarticular but may also present as asymmetric polyarthritis. Vascular system manifestations include deep vein thrombosis in 30-40% of patients. Gastrointestinal manifestations include mucosal inflammation and ulcerations, most commonly in the ileocecal region. Cardiac involvement may cause pericarditis, myocarditis, endocarditis and valvular lesions.

As no pathognomonic clinical or laboratory findings exist, several diagnostic criteria have been developed to aid in the diagnosis of BD. The most commonly used criteria was developed in 1985 by the International Study Group (ISG) for Behçet's disease. Diagnosis is made when recurrent oral ulcerations and two additional features are present (see table 1).

Treatment of BD is aimed at preventing irreversible organ damage. A recent review by Alpsoy et al. recommends following a treatment algorithm dictated by specific organ involvement. In purely mucocutaneous disease, topical medications such as corticosteroids, tetracycline suspension, viscous lidocaine and topical tacrolimus may decrease pain and accelerate healing, but should almost always be paired with systemic therapy. Colchicine is considered first line systemic treatment, with dapsone, methotrexate and thalidomide reserved for more severe mucocutaneous involvement. Immunosuppressants remain the mainstay of therapy for systemic disease. Corticosteroids, azathioprine, cyclosporine, cyclophosamide and thalidomide have all shown efficacy in clinical studies. Recently, anti-TNF agents including infliximab, etanercept and adalimumab have shown promising results. Three prospective studies using infliximab for ocular disease reported rapid improvement. The first randomized, double-blind placebo-controlled study using etanercept (25mg twice weekly for 4 weeks) demonstrated significant decreases in the number of oral ulcerations and improvement in papulopustular lesions. A recent review on anti-TNF agents for BD recommends that these medications be reserved for cases recalcitrant to traditional immunosuppressant agents due to the cost and potential side-effects.

Table 1. ISG criteria for the diagnosis of Behçet's disease

Recurrent oral ulceration	Minor/major aphthous or herpetiform ulcers observed by the physician or patient, which have recurred at least 3 times over a 12-month period
Plus any 2 of the following:	
Recurrent genital ulcerations	Aphthous ulcerations or scarring observed by the physician or patient
Eye lesions	Anterior/posterior uveitis, or cells in the vitreous on slit lamp examination, or retinal vasculitis detected by an ophthalmologist
Skin lesions	Erythema nodosum, pseudofolliculitis or papulopustular lesions; or acneiform nodules in a post adolescent patient who is not receiving corticosteroids
Positive pathergy test	Test interpreted as positive by the physician at 24-48 h

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CHICAGO DERMATOLOGICAL SOCIETY **CASE # 8**

Presented by Krisanne Sisto, MD, and Anthony Peterson, MD
Division of Dermatology, Loyola University Medical Center

HISTORY OF PRESENT ILLNESS

This 69-year-old female with a history of multiple non-melanoma skin cancers presented for evaluation of a painful eruption on the central chest. Two weeks prior to presentation she had undergone photodynamic therapy (PDT) to the face and central chest for the treatment of actinic keratoses. During PDT, 5-aminolevulinic acid was applied to target areas with a 75-minute incubation period on the face and a 120-minute incubation period on the chest. This was followed by a 15-minute irradiation with the Blu-U blue light illuminator at a wavelength of 417 nm (DUSA Pharmaceuticals, Inc.). The patient had previously undergone two prior PDT treatments to the face and ears without complication. The patient did not have a history of herpes zoster. She received the herpes zoster vaccine in 2000.

PAST MEDICAL HISTORY

Actinic keratoses
Hypertension
Multiple basal cell skin cancers
Osteoporosis
Diverticulosis

MEDICATIONS

Alendronate
Aspirin
Calcium + Vitamin D
Nifedipine
Pravastain
Ramipril

ALLERGIES

No known drug allergies

FAMILY HISTORY

Non-contributory

SOCIAL HISTORY

Non-contributory

PHYSICAL EXAM

On physical examination the patient's central chest was diffusely erythematous and notable for extensive small erosions with notched borders; many of the erosions had become confluent. The patient's conjunctiva were injected bilaterally.

HISTOPATHOLOGY

Not applicable

LABORATORY RESULTS

Direct immunofluorescence assay was positive for varicella zoster virus.

DIAGNOSIS

Bilateral herpes zoster following photodynamic therapy

TREATMENT AND COURSE

The patient was immediately sent to ophthalmology for evaluation of herpetic keratitis and was not found to have eye involvement. She was treated with valacyclovir 1 gram three-times-a-day for seven days. Within one month of the outbreak all lesions had healed without scarring or post-herpetic neuralgia sequelae.

DISCUSSION

Herpes zoster results from reactivation of the varicella zoster virus (VZV). VZV is acquired during primary varicella infection and normally lies dormant in neurons of sensory dorsal root ganglia. Cell-mediated immunity is the primary defense against VZV reactivation.

The precise triggers of viral reactivation are not well understood but are probably multifactorial. Within the general population, advancing age is the most important risk factor for the development of zoster. This is thought to be due to immune senescence, a progressive decline in immune function that occurs as individuals age. In addition, VZV immunity in the elderly tends to be less robust simply because older individuals are further from primary varicella exposure. Immunosuppression, independent of age, is another well-documented risk factor for the development of herpes zoster, and immunosuppressed patients are much more likely to develop disseminated disease. Less well documented is the relationship between zoster and exposure to sunlight, however several studies have linked VZV reactivation to ultraviolet radiation. Ultraviolet radiation is known to cause localized immunosuppression which may explain the relationship between zoster and sun exposure. Other studies have reported an increased incidence of zoster localized to sites of recent trauma and have lead to the theory that trauma, surgical or otherwise, may lead to zoster reactivation.

The zoster vaccine is a strain of live attenuated VZV. It decreases the incidence of zoster by about half in vaccine recipients and significantly reduces post herpetic neuralgia in vaccinated patients who go on to develop zoster. The vaccine is recommended for individuals over the age of 60. It is important to note that a previous episode of zoster does not appear to be immunoprotective.

Direct immunofluorescence assay uses fluorescein-conjugated monoclonal antibodies to detect varicella zoster virus. It is a highly sensitive and specific diagnostic test.

Photodynamic therapy (PDT) is a highly-effective treatment for actinic keratoses. PDT relies on the interaction between visible light, a photosensitizer and oxygen to eliminate neoplastic cells. During the treatment process the photosensitizer 5-aminolevulinic acid (5-ALA) is applied topically. It is preferentially taken up by neoplastic cells and undergoes intracellular conversion to protoporphyrin IX. Protoporphyrin IX absorbs light; maximal absorption occurs at wavelengths of 400-410 nm (blue) and to a lesser extent at wavelengths of 500 nm (green) and 540-630 nm (red). As light is absorbed by protoporphyrin IX energy is transferred to oxygen molecules and oxygen free radicals are formed. This reactive oxygen species then goes on to cause cell damage and ultimately results in death of neoplastic cells. Acute pain during the procedure and subsequent erythema are common side effects of PDT. Edema, crusting and scaling frequently occur. Rarely there may be blistering.

To date there has been one other report of PDT-induced herpes zoster. This occurred in a patient who underwent endoscopic PDT for the treatment of mucosal adenocarcinoma and subsequently developed zoster of the thoracic wall in a T8 distribution. A literature search revealed no reports of herpes zoster occurring after PDT for the treatment of a dermatological condition.

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CHICAGO DERMATOLOGICAL SOCIETY **CASE #9**

Presented by Anita Satyaprakash, MD and David Eilers, MD
Division of Dermatology, Hines Veterans Administration Hospital

HISTORY OF PRESENT ILLNESS

This 69-year-old African-American male presented initially with a 4-year history of worsening pruritic, occasionally painful, bumps on the scalp. Another doctor had treated him for folliculitis with clindamycin 1% topical solution without improvement. At that time, his exam was suggestive of folliculitis of the scalp. The lesions were cultured and he was started on oral doxycycline along with Hibiclens wash. Topical clindamycin was continued. His lesions continued to worsen in clinical appearance, so he was reevaluated with a biopsy 2 months later.

PAST MEDICAL HISTORY

Coronary artery disease
Hypertension
Hyperlipidemia
Diabetes mellitus type 2
Glaucoma
Depression
Migraine
Traumatic arthritis of cervical and thoracic spine

MEDICATIONS

Amlodipine
Aspirin
Clopidogrel
Dorzolamide-timolol eyedrops
Fluoxetine
Hydrochlorothiazide
Insulin NPH
Isosorbide dinitrate
Losartan
Metoprolol tartrate
Omeprazole
Simvastatin
Topiramate
Travoprost
Trazodone

ALLERGIES

Lisinopril, atenolol, dipyridamole, felodipine

FAMILY HISTORY

Noncontributory.

SOCIAL HISTORY

The patient served almost four years of military service in Japan, Taiwan, and Hawaii. He had a history of exposure to photo-development chemicals. He consumed alcohol heavily in the past, but quit 30 years ago. He had a five-year history of pipe tobacco use.

PHYSICAL EXAM

Physical exam revealed scattered tender violaceous perifollicular papules and indurated plaques with areas of ulceration and hemorrhagic crust. There were scattered background hyperpigmented patches and a few atrophic scars on the crown and frontal scalp. No lymphadenopathy was noted on exam.

HISTOPATHOLOGY

Two punch biopsies of the scalp showed a nodular to diffuse atypical lymphoid infiltrate that exhibited areas of crush artifact. Immunohistochemical studies showed the cells of interest to

be positive for CD20, CD10, and bcl-6. Staining for bcl-2 was difficult to fully evaluate due to admixed T-lymphocytes and crush artifact. A CD3 stain highlighted the admixed T-cells. Rare cells expressed CD30 and the bcl-1 stain appeared negative. The changes were consistent with B-cell follicle center lymphoma, morphologic grade 3.

LABORATORY RESULTS
The following laboratory values were abnormal: CBC showed a normochromic, normocytic anemia.
The following laboratory values were normal or negative: CMP.

DIAGNOSTIC TESTS
Bone marrow biopsy showed a hypercellular bone marrow with multiple nodular lymphoid aggregates of small- to medium-sized lymphocytes, as well as focal paratrabecular lymphoid infiltrate consisting of small lymphocytes. Immunostains showed an equal mixture of CD3 and CD20 positive T- and B-lymphocytes. Flow cytometry failed to show monoclonal B-cell lymphocyte population. B-cell and bcl-2 gene rearrangement studies were negative.

RADIOLOGY
CT of the chest, abdomen, and pelvis showed no lymphadenopathy.

DIAGNOSIS
Primary cutaneous follicle center lymphoma

TREATMENT AND COURSE
Betamethasone 0.05% ointment was started, but the patient did not tolerate this medication due to a burning sensation when applied. Oral doxycycline was continued, and the patient was evaluated by oncology. As workup did not reveal systemic involvement, the patient was treated with radiotherapy to the scalp without chemotherapy. Although the scalp lesions showed improvement with radiotherapy, the patient developed new erythematous and violaceous plaques on the back. Biopsy of these lesions was consistent with B-cell lymphoma with a similar histologic appearance to the initial scalp lesions. These lesions are currently being treated with radiotherapy.

DISCUSSION
Primary cutaneous follicle center lymphoma (PCFCL) is a neoplastic proliferation of germinal center cells confined to the skin and represents a subtype of primary cutaneous B-cell lymphoma (PCBCL). Clinically it can manifest as single or grouped, pink to purple papules, plaques, or tumors surrounded by patches of erythema. Ulceration can occur, but is uncommon, and skin lesions are generally asymptomatic. Typical sites of involvement are the scalp, forehead, and the back. Back lesions have been called Crosti's lymphoma or reticulohistiocytoma of the dorsum. Serum lactate dehydrogenase (LDH) is within normal limits, in contrast to the elevations that can be seen with systemic lymphomas.

On histologic exam, nodular or diffuse infiltrates are seen within the entire dermis, often extending into the subcutaneous fat and sparing the epidermis. A percentage of cases show at least some follicular architecture with features of malignancy, such as a reduced or absent mantle zone, the lack of tingible body macrophages, and a monomorphic appearance. Large B-cell centrocytes and centroblasts predominate within the infiltrate, admixed with immunoblasts, small lymphocytes, histiocytes, and occasionally eosinophils and plasma cells. Up to 40% of PCFCLs are positive for t(14;18); however, presence of this translocation should raise suspicion for a primary systemic lymphoma with skin involvement. Virtually all cases of PCFCL are bcl-6 positive and bcl-2 negative. The cells are positive for CD20 and CD79a as well as either κ or λ

light chains and are negative for CD5 and CD43. A monoclonal gene rearrangement is found in 60-70% of cases. Morphologic variants of PCFCL exist which have a predominant spindle cell morphology or in which a few B-cell blasts are admixed with numerous T-lymphocytes.

In the World Health Organization and the European Organization for Research and Treatment of Cancer classification, PCFCL is a member of a group of cutaneous B-cell lymphomas with primary cutaneous manifestations, characterized by indolent clinical behavior. The disease has a favorable prognosis, although recurrences occur in up to 50% of patients, dissemination beyond the skin is rare. Despite the rarity of systemic involvement, the skin can be a site of secondary involvement, and complete staging of these patients must be performed, including: complete blood examination, flow cytometry of peripheral blood, and CT of the chest, abdomen, and pelvis. Bone marrow biopsy and flow cytometry of this tissue are optional.

Patients with solitary or few lesions can be treated with local radiotherapy, surgical excision with narrow margins, or excision followed by radiotherapy. For lesions on the back, radiotherapy with 10-20 cm margins is recommended, while 3-5 cm margins generally suffice for lesions in other locations. Systemic antibiotic therapy has been shown to achieve resolution in *Borrelia*-associated PCBCL, especially when initiated early in the disease course. Subcutaneous or intralesional interferon, preferred in patients with multiple lesions of different body sites, is associated with complete clearance in approximately 50% of patients. Rituximab, an anti-CD20 monoclonal antibody, has also been used in patients with indolent PCBCL. Patients with diffuse or disseminated disease can be treated with systemic chemotherapy (cyclophosphamide, doxorubicin, vincristine, prednisone) plus rituximab.

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CHICAGO DERMATOLOGICAL SOCIETY **CASE # 10**

Presented by Vanessa Lichon, MD, Sheetal Mehta, MD, and Madhu Dahiya, MD
Division of Dermatology, Loyola University Medical Center

HISTORY OF PRESENT ILLNESS

This 38-year-old Caucasian female was admitted to the hospital for vaginal bleeding and seen for evaluation of a tender nodule on her scalp. She reported rapid growth over the last two months with occasional drainage. She denied any pruritus or bleeding. Review of systems was positive for night sweats, fevers, chills, weight loss, dizziness, constipation, nausea, and pelvic pain.

PAST MEDICAL HISTORY

Cervical squamous cell carcinoma diagnosed one month prior
Depression

MEDICATIONS

Clozapine Sertraline

ALLERGIES

Penicillin

FAMILY HISTORY

Non-contributory

SOCIAL HISTORY

Patient has smoked cigarettes for 26 years, one pack per day. She denied use of alcohol. She worked as a cashier.

PHYSICAL EXAM

The left occipital scalp had a 3cm x 3cm firm, non-mobile exophytic erythematous tumor with central crater. She had no palpable preauricular, postauricular, occipital or cervical lymphadenopathy.

HISTOPATHOLOGY

Two 4mm punch biopsy were performed from the left occipital scalp, one for H&E and one for pan-culture. The mid-to-deep dermis was infiltrated by sheets and cords of poorly differentiated epithelial cells with markedly pleomorphic, enlarged nuclei, and eosinophilic polygonal cytoplasms. The cells strongly expressed pan-keratin. Given the patient's history of poorly differentiated cervical squamous cell carcinoma, these findings were consistent with metastasis.

LABORATORY RESULTS

The following lab results were abnormal:
-Tissue culture from scalp: moderate colonies of *Staphylococcus* species strain 1, moderate colonies of *Staphylococcus agalactiae,* Group B *Streptococci*, moderate colonies of *Staphylococcus* species strain 2, moderate colonies of *Corynebacterium* species, very few colonies of *Prevotella (Bacteroides) bivia*

The following lab results were normal:
-Tissue culture from scalp: No acid fast bacilli or fungal growth to date.

RADIOLOGY

CT chest/abdomen/pelvis: Notable findings include an abnormal cervix with probable disease extension to right obturator internus muscle, enlarged left common and right internal iliac lymph nodes, bilateral hilar lymphadenopathy, multiple lung lesions, endobronchial lesions, a liver lesion and a right subcapsular renal hematoma.

PET scan: Demonstrated a large area of increased metabolic activity in the cervix, consistent with the primary cancer. Multiple foci in the lungs, mediastinum, and liver as well as abdominal and pelvic lymph nodes, consistent with distant metastases. A superficial focus of intense uptake on the left occipital scalp.

DIAGNOSIS

Cervical squamous cell carcinoma with scalp metastasis

TREATMENT AND COURSE

Two 4mm punch biopsies were performed at initial consult, one for H&E and one for pan-culture. The patient was evaluated by gynecology-oncology and stable for discharge the following day. She recently started chemotherapy/radiation at an outside institution closer to her home.

DISCUSSION

Cutaneous metastases are reported in 0.7% to 9% of individuals with internal malignancies and account for 2% of all skin tumors. The most common internal malignancies to metastasize in women are breast and gastrointestinal and in men are lung and gastrointestinal. The pathogenesis of cutaneous metastasis includes lymphatic, hematogenous, extension, and rarely, direct implantation. Cutaneous metastases are classified as either loco-regional, in-transit, or distant, and can present as nodules, plaques, or inflammatory telangiectasias.

Cervical carcinoma metastasis to the skin is relatively uncommon and specifically to the scalp is rare. The most common sites of metastases for cervical carcinoma are the lung, bone, liver, and extrapelvic lymph nodes. Imachi *et al.* evaluated 1190 cervical cancer patients of which 1.3% (15) had cutaneous metastases most commonly occurring on the abdominal wall, vulva, and anterior chest wall, and none on the scalp. For these locations the most likely mode of metastasis has been described as lymphatic spread.

To the best of our knowledge only eleven cases have been reported in the literature of cervical carcinoma with scalp metastasis. Several authors have attributed scalp metastasis to hematogenous spread. Fay *et al*. suggested that due to the high degree of vascularity, immobility, and warmth, the scalp was an ideal location for metastases. As compared to the other eleven documented cases, our patient is the only case of cervical scalp metastasis presenting at the time of diagnosis and prior to previous therapy.

Cutaneous lesions can present as the initial sign of internal malignancy and Nashan *et al*. reports this in 20% of cases (in a review of 92 total) while Hu *et al*. documents this in 13.5% of cases (in a review of 141 total). Treatment options for patients with cutaneous metastatic cervical carcinoma can include excision, radiotherapy, chemotherapy, and palliative care. The prognosis for patients with cutaneous metastases from cervical cancer is extremely poor with a mean survival of three months and five-year survival of 17%.

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CHICAGO DERMATOLOGICAL SOCIETY **CASE # 11**

Presented by Linda Sheu, MD, Elaine Kung, MD, and Madhu Dahiya, MD
Division of Dermatology, Loyola University Medical Center

HISTORY OF PRESENT ILLNESS

This 42-year-old female with a history of myelofibrosis treated with bone marrow transplantation. The bone marrow transplant was complicated by chronic graft-versus-host disease of the skin, gastrointestinal tract, and liver. A family member reported that the patient had developed small, tense, hemorrhagic blisters that resulted in non-healing wounds during the month prior to admission resulting in black eschars of the arms and legs.

PAST MEDICAL HISTORY

Myelofibrosis diagnosed June 2008
Bone marrow transplantation with matched unrelated donor stem cells July 2008

MEDICATIONS

Cyclosporine eyedrops
Pantoprazole
Fluconazole
Prochlorperazine
Levothyroxine
Tacrolimus
Methylprenisolone
Sulfamethoxazole with trimethoprim
Mycophenolate mofetil
Valacyclovir

ALLERGIES

None

FAMILY HISTORY

No hematologic abnormalities

SOCIAL HISTORY

Non-contributory

PHYSICAL EXAM

The patient was ill-appearing. She had scleral icterus and hemorrhagic crusting of the mucocutaneous lip. She had multiple ulcers ranging from one to six centimeters on the upper and lower extremities. These ulcers had a purple-black base and had borders that were slightly undermined with adjacent purpura.

HISTOPATHOLOGY

Left deltoid skin specimen revealed focal tissue necrosis, acute inflammation and ribbon-like hyphae with no diagnostic septations. These findings were suggestive of zygomycete. Immunoflourescence of peri-lesional skin was negative for IgG, IgA, IgM and C3 staining. Fibrin and kappa/lambda staining showed a non-specific pattern.

LABORATORY RESULTS

Tissue culture of skin specimen revealed few colonies of *Mucor* species. Sequencing demonstrated *Mucor ramosissimus*.

The following were abnormal:
Hgb 9.1, Hct 26.4, MCV 97.3, platelet 48, segmented neutrophils 88, lymphocytes 3
BUN 39, Cr 0.38, glucose 120

Albumin 1.4, alkaline phosphatase 2113, ALT 84, AST 159, bilirubin 6.9

RADIOLOGY
CT of the sinus, chest and abdomen showed no evidence of invasive fungal disease.

DIAGNOSIS
Cutaneous zygomycosis caused by *Mucor ramosissimus*

TREATMENT AND COURSE
The patient was treated with intravenous amphotericin. Given that patient was not a candidate for surgical debridement, she was treated with topical nystatin powder and acticoat dressing. Her clinical lesions were stable and she had no systemic involvement of the fungal infection. However, the patient expired shortly thereafter secondary to bacterial sepsis.

DISCUSSION
The zygomycoses are a group of cutaneous diseases caused by fungi in the phylum Zygomycota. They are often referred to as mucormycosis, as most fungi pathogenic to humans are found in the order *Mucorales*. Within the order *Mucorales*, the genera responsible for zygomycoses include *Rhizopus, Mucor* and *Absidia*.

The classic presentation is a diabetic patient with ketoacidosis who develops a rapidly progressive necrotizing infection of the nasal sinuses. Additional risk factors for development of rhinocerebral zygomycosis include immunosuppression, neutropenia, trauma, protein-calorie malnutrition, and iron overload. Regardless of the predisposing condition, the infection often follows an aggressive course characterized by vascular invasion, occlusion, and infarction. Early in the course of the disease, patients may report a history of fever, unilateral facial pain, nasal congestion or headache. As the infection progresses, purulent, necrotic and gangrenous ulcers and abscesses may form. Mortality can be as high as eighty percent. Treatment includes surgical debridement and systemic therapy with amphotericin B.

While rhinocerebral zygomycosis is the most common form, pulmonary, cutaneous, gastrointestinal, central nervous system, and disseminated disease may also occur. Primary cutaneous zygomycosis is rare and observed almost exclusively in immunosuppressed individuals. It can be locally invasive but can also be angio-invasive resulting in embolization and necrosis of surrounding tissue. The most frequent etiologic agent is *Rhizopus oryzae*. Species of *Mucor* are rarely agents of primary cutaneous zygomycosis.

The first reported case of *Mucor ramosisissimus* zygomycosis occurred in 1993 in an immunosuppressed patient with aplastic anemia. A second case involved a 39-year-old alcoholic, diabetic male who presented with rhinocerebral disease. Both patients responded well to amphotericin B. In recent years, the incidence of zygomycosis has increased, particularly in the immunodeficient population. Our case reaffirms the necessity of considering zygomycosis when an immunosuppressed patient presents with necrotic ulcers.

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Presented by Anita Satyaprakash, MD, James Swan, MD, Anthony Peterson, MD, Madhu Dahiya, MD, Jonathan Curry, MD, and Brian Nickoloff, MD
Division of Dermatology, Loyola University Medical Center

PATIENT A

HISTORY OF PRESENT ILLNESS

This 66-year-old male presented with a 50-year history of an eruption on the left abdomen, flank, and back. He had occasional pruritus, but denied any pain or burning. Prior to presentation, he had used various over-the-counter emollients, as well as a 10-day course of acyclovir prescribed by his primary care physician. Despite these treatments, the lesions persisted without change in size, quantity, or quality. Initial biopsy done by an outside doctor was consistent with Grover's disease.

PAST MEDICAL HISTORY

Hypertension
Diabetes mellitus type 2
Depression
Benign prostatic hyperplasia
Erectile dysfunction
Non-melanoma skin cancer

MEDICATIONS

Dutasteride
Ezetimibe-simvastatin
Glipizide
Insulin detemir
Valsartan-hydrochlorothiazide
Venlafaxine
Vitamin D
Metformin
Pioglitazone
Sildenafil
Tamsulosin
Ibuprofen

ALLERGIES

No known drug allergies

FAMILY HISTORY

Non-contributory

SOCIAL HISTORY

The patient has a 30-pack-year smoking history but quit several years prior to presentation. He denied use of alcohol or illicit drugs.

PHYSICAL EXAM

Physical exam revealed multiple pink to erythematous papules with slight crust in a band-like distribution following lines of Blaschko on the left abdomen, flank and back. The nails were clear.

HISTOPATHOLOGY

A 4 mm punch biopsy of the left flank demonstrated foci of acantholysis, some of which were suprabasal, while others were intraepidermal. Keratinocytes resembling corps ronds and grains were noted, along with a superficial perivascular lymphohistiocytic infiltrate.

LABORATORY RESULTS
The following laboratory values were abnormal: CMP demonstrated an elevated glucose of 135 mm/L, fasting lipid panel demonstrated elevated triglycerides of 161 mg/dL, urinalysis showed microalbuminuria of 49.7 mg/L, and hemoglobin A1C was elevated to 7.2%.
The following laboratory values were normal or negative: CBC

DIAGNOSIS
Linear Darier's disease following lines of Blaschko

TREATMENT AND COURSE
The patient was initially treated with amcinonide 0.1% cream daily for 2 weeks. The patient did not return for follow up until 10 months later; at that time, as he showed no improvement, ketoconazole 2% cream BID was added in addition to amcinonide 0.1% cream daily. At follow-up, the patient declined further treatment, as he had minimal symptoms from the eruption.

PATIENT B

HISTORY OF PRESENT ILLNESS
A 66-year-old male presented with a ten-year history of an eruption on the right arm, shoulder, chest, abdomen, groin, and thigh. He had sharp pain in the area, but denied pruritus. The eruption worsened when he was under stress and improved with exposure to sunlight or tanning beds. Prior to presentation, he had used triamcinolone 0.1% ointment once to twice daily without improvement.

PAST MEDICAL HISTORY
Hyperlipidemia
Benign prostatic hyperplasia
Anxiety associated with depression
Lower back pain secondary to trauma

MEDICATIONS
Alprazolam
Finasteride
Lisinopril
Ibuprofen
Tamsulosin
Acetaminophen
Varenicline
Multivitamin

ALLERGIES
Niacin

FAMILY HISTORY
Non-contributory

SOCIAL HISTORY
The patient smoked one pack of cigarettes daily. He drank one to two glasses of wine daily. He denied use of illicit drugs.

PHYSICAL EXAM
Physical exam revealed multiple 1-2 mm pink to erythematous discrete and confluent papules with scale and occasional vesicles, following lines of Blaschko, on the right upper arm, shoulder, chest, mid-back, inguinal fold, and thigh. The nails were clear.

HISTOPATHOLOGY

Three punch biopsies of the right shoulder, right chest, and right thigh showed acantholytic dermatosis exhibiting foci of intraepidermal acantholysis with accompanying hyperkeratosis and corps ronds. Eosinophilic spongiosis was not seen. Periodic-acid Schiff stain was negative for fungal organisms and special stains for herpes simplex with analyte specific reagent were negative.

LABORATORY RESULTS

The following laboratory values were normal or negative: CBC, CMP.

DIAGNOSIS

Linear Darier's disease following lines of Blaschko

TREATMENT AND COURSE

The patient has had treatment with various mid- and high-potency topical steroids with only minimal improvement. He used tazarotene gel for a short time, but discontinued treatment due to irritation. He lived too far from our clinic to initiate phototherapy three times weekly. Acitretin was considered, but the patient declined due to the potential side effects. Currently, the lesions are symptomatically controlled, but not cleared, with use of clobetasol ointment to the body and triamcinolone ointment alternating with tacrolimus ointment to the inguinal fold. The patient has recently undergone treatment of limited areas with pulsed dye laser in conjunction with topical steroids, with some improvement.

DISCUSSION

Darier's disease (DD) is an autosomal dominant genodermatosis, the prevalence of which has been estimated between 1:30,000-100,000. Typical onset of disease is in the first two decades of life, but later presentation may be seen. Characteristically, there are hyperkeratotic, verrucous, yellow or brown papules and plaques distributed symmetrically in a seborrheic pattern (central trunk, scalp, forehead, flexures, groin, natal cleft). Characteristic nail changes may also be seen, such as red and white longitudinal bands and a V-shaped nick at the free margin of the nail. Ultraviolet exposure, occlusion, sweat, heat, or stress can exacerbate lesions.

DD is caused by a mutation in the region of chromosome 12 that encodes *ATP2A2*, the gene for the sarco/endoplasmic reticulum Ca^{2+}-ATPase type 2 isoform (SERCA2) pump. Abnormalities in SERCA2 function lead to inadequate Ca^{2+} stores in the endoplasmic reticulum, which is thought to impair cellular processing of proteins necessary for cell-cell adhesion, leading to acantholysis.

"Mosaicism" is used to describe individuals composed of cells of different genotypes; this condition can be due to normal lyonization of the X chromosome in females, somatic mutation, half-chromatid mutation, chromosomal non-disjunction, and chimerism. Mosaicism in cutaneous disorders may result in lesions following Blaschko's lines, which are thought to be determined by migration of cells originating from epidermal keratinocytes during embryogenesis. Several inherited and spontaneous cutaneous conditions have been shown to occur along Blaschko's lines. Patients with mosaic mutations for DD, whose lesions are localized and present along Blaschko's lines, often lack both a family history of DD and the characteristic nail changes of the disease. Over 100 different mutations have been identified in DD. These mutations have been demonstrated in the affected skin of patients with mosaic DD, while the unaffected skin of these patients is genotypically normal. There are currently no reports of patients with linear DD transmitting generalized DD to their offspring, but patients should be counseled of the possibility of transmission, as there may be mosaic involvement of

gonadal tissue. The entity “acantholytic dyskeratotic epidermal nevus” has been shown through genetic analysis to be a form of localized DD.

Oral retinoids appear to be the most effective treatment in generalized DD and can also be utilized in localized DD; however, topical or localized treatments are generally preferred for localized forms of DD. Topical treatments include salicylic or lactic acids, steroids, retinoids, 5-fluorouracil, and vitamin D3 analogs. Localized treatment includes photodynamic therapy, dermabrasion, carbon dioxide laser, cryosurgery, surgical excision, and pulsed dye laser.

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CHICAGO DERMATOLOGICAL SOCIETY **CASE #13**

Presented by L Julia Kamalpour, MD, Rama Vaitla, MD, and Darryl Oble, Md
Division of Dermatology, Loyola University Medical Center

HISTORY OF PRESENT ILLNESS
This 12-year-old African American male presented with a three-year history of uneven pigmentation over both feet. More recently, he had noted similar loss of pigment over the fingers. The patient denied ever having had associated redness, pain, itching, scale or burning. The lesions were asymptomatic and had not been previously treated.

PAST MEDICAL HISTORY
Adenoidectomy at age 8
Seasonal allergies

MEDICATIONS
None

ALLERGIES
No known drug allergies

FAMILY HISTORY
Patient denied having a family history of skin cancer or vitiligo. Patient reported that no family members had similar disorders of pigmentation.

SOCIAL HISTORY
Non-contributory

PHYSICAL EXAM
Focused exam of the bilateral feet and hands showed numerous hypopigmented macules over the bilateral dorsal feet and sides of toes with a confetti-like pattern. Subtle hypopigmented macules were also seen over distal digits and bilateral dorsal hands and sides of digits. Wood's lamp exam was negative. Examination revealed no palmar punctiform pits or breaks in the epidermal rete ridge patterns.

HISTOPATHOLOGY
Punch biopsy of the right dorsal foot revealed increased basilar hyperpigmentation as well as multifocal hyperpigmentation of the upper stratum malpighii, with a gradual tapering towards the epidermal surface. A sparse perivascular lymphocytic inflammatory infiltrate was noted. By immunohistochemical analysis, a normal to slight increase in the number of melanocytes was appreciated on Mart-1 staining. There was no epidermal atrophy.

DIAGNOSIS
Reticulate acropigmentation of Dohi

TREATMENT AND COURSE
Reassurance was provided. After consultation with the patient and his mother regarding the nature of the condition, the decision was made not to pursue treatment at this time. The patient was advised to return to clinic should progression of the pigmentary disorder occur.

DISCUSSION

Reticulate acropigmentation (RA) comprises dyschromic disorders occurring predominantly among Japanese individuals, with only a few cases having been reported from Europe and some parts of Asia. Two main types of RA have been described, namely reticulate acropigmentation of Dohi (RAD) and reticulate acropigmentation of Kitamura (RAK). This case represents the third reported case of RAD in an individual of African descent.

RAD (also known as “dyschromatosis symmetrica hereditaria”) is an autosomal dominant skin disorder characterized by the presence of hyperpigmented and hypopigmented macules, mainly on the dorsal aspects of the extremities. The macules commonly stop spreading before adolescence, and last for life. The skin lesions are otherwise asymptomatic and are not associated with other manifestations. Disease onset occurs most often during infancy or childhood, with 73% of patients developing skin lesions before age six.

On histopathologic exam of RAD, epidermal atrophy is seen with an increased number of melanocytes. Molecular studies have uncovered mutations in double-stranded RNA-specific adenosine-deaminase (DSRAD or ADAR) on chromosome 1q21-2 in patients with RAD. The mechanism by which these mutations cause RAD remains unknown.

RAD differs significantly from RAK in its clinical and histopathologic manifestations. RAK is most commonly an autosomal dominant disease in which sharply demarcated brown macules develop on the extensor surfaces of the hands and feet. These macules may progress and darken with time. In patients with RAK, the palms often contain punctiform pits and breaks in the epidermal rete ridge pattern. No leuokodermic macules are seen. Histologically, the abnormality is characterized by epidermal atrophy with an increased number of basal melanocytes.

Our patient’s clinical presentation, in correlation with histopathologic findings, suggests a diagnosis of reticulate acropigmentation of Dohi. This case of a unique genodermatosis is presented for clinical interest.

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CHICAGO DERMATOLOGICAL SOCIETY **CASE # 14**

Presented by Tricia Hultgren, MD, Steven Goulder, MD, and Brian Nickoloff, MD
Division of Dermatology, Loyola University Medical Center

HISTORY OF PRESENT ILLNESS

This 85-year old male reported history of Merkel cell carcinoma of the right nasolabial fold diagnosed in May 2006. He began seeing dermatology in 2008 for the management of his severe actinic damage and for the diagnosis and treatment of lesions concerning for melanoma and non-melanoma skin cancer. In February 2010, he presented to dermatology clinic for follow-up for his non-melanoma skin cancers. He reported a two-month history of numerous non-tender lesions on the bilateral lower legs.

PAST MEDICAL HISTORY

Merkel cell carcinoma:
-Diagnosed by punch biopsy 5/2006 followed by wide local excision 6/06.
-Preoperative imaging with CT and PET scan of the chest, abdomen and pelvis revealed possible metastasis to anterior mediastinal nodes
-Patient elected not to undergo radiation to the primary site and repeat CT imaging 10/06 was negative for metastasis
-Right submandibular nodule appeared 7/08, and CT and PET scans showed an enlarged lymph node with increased uptake. Subsequent lymphadenectomy revealed 1/40 lymph nodes positive for metastatic Merkel cell carcinoma
-Adjuvant radiation therapy was performed, with a total dose of 60 Gy in 30 fractions to the right cheek and preauricular node. Treatment was completed 12/08.

Lentigo Maligna melanoma left lower cheek (non-ulcerated 0.11 mm, s/p square procedure 8/09)
Melanoma left forearm (0.22 mm, nonulcerated, s/p WLE 11/09)
Multiple non-melanoma skin cancers
Mitral valve regurgitation
Aortic valve replacement
Atrial fibrillation
Hypertension
Diabetes mellitus
Benign prostatic hyperplasia

MEDICATIONS

Warfarin
Glipizide
Valsartan
Diltiazem
Tamsulosin
Finasteride
Omeprazole
Vitamin B6

ALLERGIES

None

FAMILY HISTORY

No family history of skin cancer

SOCIAL HISTORY
Non-contributory

PHYSICAL EXAM
Numerous firm, non-tender, discreet infiltrated nodules ranging in size from 0.5 to 1.5 cm were present on the bilateral anterior legs. A well-healed scar without nodularity or evidence of recurrence was present on the right cheek at site of primary Merkel cell carcinoma. Lymph node examination of the bilateral preauricular, cervical, submental, and parotid lymph node basins were unremarkable.

HISTOPATHOLOGY
Shave biopsy of three lesions on the right distal anterior leg, right proximal anterior leg and the left anterior leg revealed an expansile collection of undifferentiated tumor cells consistent with Merkel cell carcinoma. Tumor cells immunostained positive for dot-like perinuclear CK20 and neurofilament expression. Tumor cells were negative for CD20, CD30, TTF-1, and MART-1.

LABORATORY RESULTS
The following tests were negative or normal:
Complete blood count
Liver function tests

The following tests were positive or abnormal:
Sodium 128 (136-144) MM/L

DIAGNOSIS
Metastatic merkel cell carcinoma

TREATMENT AND COURSE
The patient is currently undergoing palliative excisions of the metastatic cutaneous lesions. With our concern for minimal benefit and poor tolerance as well as in accordance with the patient's wishes, we have not initiated treatment with chemotherapy. Further work-up including CT imaging of the chest, abdomen and pelvis was negative for metastatic disease. At our recommendation he pursued a second opinion at the University of Michigan multi-disciplinary Merkel cell carcinoma clinic, and they concurred with the decision to manage his disease with palliative excisions and to avoid chemotherapy.

DISCUSSION
Merkel cell carcinoma (MCC) is a rare, clinically aggressive cutaneous malignancy of neuroendocrine origin. First described by Toker in 1972 as "trabecular carcinoma of the skin", the finding of neurosecretory granules by electron microscopy and immunohistochemistry suggested its derivation from merkel cells. MCC primarily affects the elderly, with the average age at diagnosis 69 years. Although rare, the incidence of MCC in the United States has tripled in the past two decades, with up to 1500 cases reported per year. The tumor is more common in people of European ancestry and is slightly more prevalent in men.

Ultraviolet light, immunosuppression and infection with a novel polyomavirus have all been suggested to play a role in the pathogenesis of MCC. Sun-exposed areas of involvement, older age at onset, and increasing incidence with decreasing latitude all point towards ultraviolet radiation as a contributing factor. History of PUVA treatment for psoriasis has been associated with a 100-fold increased incidence of MCC, and patients with MCC have higher rates of non-melanoma skin cancer. Immunocompromised states seem to increase the risk of developing MCC. For example, HIV and organ transplant patients have an 11-fold and 5-fold

increase in incidence of MCC, respectively. Recently, prevalence of second malignancy (hematologic, breast, ovarian, and squamous cell carcinoma) occurring before, with or after MCC has been reported as high as 25-28%.

The association of MCC with immunosuppression led researchers to investigate infectious agents as possible etiological factors in MCC. Recently, a novel double-stranded DNA polyomavirus termed Merkel cell polyomavirus was identified in MCC tissue, suggesting its possible role in the pathogenesis. A clonal pattern of viral integration exists, implying that infection occurs prior to clonal expansion. In several recent studies, Merkel cell polyomavirus was detected in 24-89% of MCCs. A study by Sihto et al. analyzed 114 MCCs and found Merkel cell polyomavirus in 80% of cases. Infection with the virus was associated with less frequent regional nodal metastasis and better overall survival than those tumors without Merkel cell polyomavirus (5-year survival 45.0% vs 13.0%). More studies are needed to further define the role of Merkel cell polyomavirus in MCC tumorigenesis.

MCC lacks specific features and most often presents as a rapidly enlarging, asymptomatic, dome-shaped red to violaceous nodule. Lesions most commonly involve sun-exposed areas of the head and neck, with the median size at diagnosis ranging from 1-4 cm. Histologically, MCC appears as a dermal nodule comprised of sheets of small round basophilic cells. Cells exhibit large nuclei, scant cytoplasm and granular cytoplasm. Numerous mitotic figures are present, and MCC cells stain positively for cytokeratin 20 (CK20) in a characteristic peri-nuclear dot-like pattern. Using immunohistochemical stains, MCC can be differentiated from other “small blue cell” dermal tumors such as small cell lung cancer and other neuroendocrine tumors, lymphoma, squamous cell carcinoma, melanoma and Ewing’s sarcoma. In addition to CK20, MCC stains positive for chromogranin and synaptophysin and negative for thyroid transcription factor-1 and cytokeratin 7 (positive in small cell lung cancer). Additionally, MCC stains negative for S100 (positive in melanoma) and LCA (positive in lymphoma). Electron microscopy may also aid in diagnosis, demonstrating intracytoplasmic neurosecretory granules.

MCC has a much higher rate of lymph node involvement compared to melanoma (30% vs 5%), necessitating routine sentinel lymph node biopsy (SNLB). In a study of 122 patients with MCC, Gupta et al. demonstrated 32% of patients with clinically nonpalpable lymph nodes had a positive SLNB. Prognosis depends on the size of the tumor and on nodal involvement, with 3-year survival of 90% with localized disease <2 cm. Survival decreases to 70% with localized disease >2.0 cm, and drops to 60% and <20% with nodal disease and distant metastasis, respectively. Most (90%) recurrences occur within 24 months of diagnosis.

Given its rarity, optimal treatment guidelines for MCC have yet to be established. The majority of MCC studies have been retrospective with small sample sizes, making it difficult to devise treatment recommendations. Width of surgical margins, treatment of surgically negative regional lymph nodes and use of adjuvant radiation therapy continue to be debated. Surgical excision in the form of wide local excision or Mohs surgery is the standard of care for primary MCC. Local recurrence rates with Mohs surgery range from 4-8% and may be considered preferable to wide local excision, where local recurrence ranges from 20 to 60%. Surgical margins of 2.0 to 3.0 cm are commonly advocated, with a trend towards decreased local recurrence with wider margins seen in the literature. A study by Boyer et al. using Mohs micrographic surgery (with 1cm safety margins) revealed that 25% and 12% of tumors would have been transected if 2.0 cm and 3.0 cm margins were obtained, respectively. Radiation therapy to the primary site is advocated, as several studies have demonstrated decreased local recurrence and regional node metastasis with radiation treatment. In a study by Gupta et al, nodal radiation appeared to improve relapse-free survival only when the SLNB was

positive. In the setting of positive SLNB, complete lymph node dissection with adjuvant nodal radiation therapy is recommended with imaging to rule out distant metastasis. Chemotherapy serves only a palliative role in cases with distant metastasis as it has not been shown to increase survival.

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CHICAGO DERMATOLOGICAL SOCIETY **CASE # 15**

Presented by Krisanne Sisto, MD, and David Eilers, MD
Department of Dermatology, Hines Veteran's Administration Hospital

HISTORY OF PRESENT ILLNESS

This is a 58-year-old man who presented with an 8-year history of slowly enlarging lesions on his left arm. There was no associated itching, pain, bleeding or crusting. The lesions were biopsied several years and thought to be consistent with granuloma annulare. The patient had been treated with topical steroids, tacrolimus ointment and terbinafine cream with minimal response.

PAST MEDICAL HISTORY

Coronary Artery Disease
Diabetes Mellitus
Depression
Hypertension

MEDICATIONS

Clopidogrel
Losartan
Metformin
Metoprolol
Niacin
Paroxetine
Simvastatin

ALLERGIES

No known drug allergies

FAMILY HISTORY

Non-contributory

SOCIAL HISTORY

Non-contributory

PHYSICAL EXAM

On physical examination there were two large annular erythematous plaques with hypopigmented centers on the left forearm. The largest of the two plaques measured 6 cm x 8 cm.

HISTOPATHOLOGY

Punch biopsy of the left forearm revealed an interstitial infiltrate of histiocytes palisaded around small necrobiotic foci. There were many multinucleated giant cells and prominent elastophagocytosis was noted.

LABORATORY RESULTS

The following laboratory results were normal or negative:
CBC
CMP

RADIOLOGY

Not applicable

DIAGNOSIS

Actinic granuloma

TREATMENT AND COURSE

The patient was treated with clobetasol 0.05% ointment twice daily for two weeks alternating with tacrolimus 0.1% ointment twice daily for two weeks. He noted some improvement in the lesions. He is receptive to starting a systemic agent if the plaques do not clear with topical medications.

DISCUSSION

Actinic granuloma as described by O'Brien is a rare granulomatous dermatitis that affects middle-aged and older adults. The typical lesion is a large annular plaque with a raised erythematous border and hypopigmented atrophic center. Lesions usually occur on sun-exposed areas of skin but have, less commonly, been reported to occur on non-sun exposed sites. The plaques may be pruritic or asymptomatic.

The pathogenesis of actinic granuloma is not well understood. Actinic damage of elastic fibers in the dermis appears to play a role. Lesions may result from an inflammatory and reparative response to damaged elastic fibers or from a cell mediated immune response incited by actinically damaged elastic fibers that function as weak antigenic determinants. This latter theory is supported by the fact that helper T-cells are the predominant lymphocyte cell found in biopsy specimens.

Histologically there is a granulomatous infiltrate of histiocytes, lymphocytes and multinucleated giant cells in the mid to upper dermis. Elastic fibers are present near the infiltrate and the finding of elastic fibers within multinucleated giant cells, an entity termed elastophagocytosis, is a characteristic finding of actinic granuloma.

Annular elastolytic giant cell granuloma (AEGCG) shares the same histological findings as actinic granuloma. Some authors consider AEGCG and actinic granuloma to be the same entity, however others believe that the two can be distinguished by their clinical presentation. AEGCG as described by Meischer has two distinct clinical presentations. It may present as a thin yellow atrophic plaque on the forehead or as erythematous plaques with central clearing on the trunk. The latter presentation usually occurs in young women and favors sun exposed sites.

Aside from AEGCG, the differential diagnosis of actinic granuloma includes granuloma annulare and erythema annulare centrifugum. Treatment is challenging. Systemic, topical and intralesional corticosteroids have varying degrees of effectiveness and even responsive lesions may relapse when treatment is stopped. PUVA and antimalarials may be utilized. There are several case reports of successful treatment with cyclosporine or methotrexate.

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Acknowledgement: This patient has previously been presented at a Chicago dermatological meeting.

CHICAGO DERMATOLOGICAL SOCIETY **CASE # 16**

Presented by Vanessa Lichon, MD, David Eilers, MD, and Scott Wickless, DO
Division of Dermatology, Hines Veterans Administration Hospital

HISTORY OF PRESENT ILLNESS

This 58-year-old African American male with past medical history significant for intravenous (IV) drug use was admitted to general medicine and seen for evaluation of lesions on his legs and right arm. The patient reported that he first developed skin lesions on his legs about eight years ago after IV drug use led to skin abscesses. Six months ago he developed similar lesions on his arms after "skin popping" heroin. He stated his legs had drained pus in the past and he had been treated with multiple courses of oral and IV antibiotics at various outside hospitals. On the day of evaluation he had pain in his right arm greater than his legs. He stated he was HIV negative at an outside hospital approximately three months prior. He had no other cutaneous concerns.

PAST MEDICAL HISTORY

Hypertension, polysubstance drug abuse, post-traumatic stress disorder, depression

MEDICATIONS

Aspirin
Clonidine
Furosemide
Methadone
Potassium
Sertraline
Zolpidem
Bisacodyl
Ergocalciferol (Vitamin D)
Lisinopril
Omeprazole
Risperidone
Trazodone

ALLERGIES

No known drug allergies

FAMILY HISTORY

Non-contributory

SOCIAL HISTORY

The patient denied history of smoking or alcohol use. He did admit to IV drug use as described above. He is married with no children.

PHYSICAL EXAM

On examination the right forearm was notably edematous with mottled dyspigmented scars and the right distal volar forearm had an 8 cm x 5 cm vegetative plaque with multiple punched out ulcers draining purulent material. The bilateral lower extremities from below the knees to the toes were edematous with mottled dyspigmented, firm verrucous nodules with overlying scale.

HISTOPATHOLOGY

An excisional biopsy of the right distal volar forearm demonstrated effacement of the rete ridges with irregular acanthosis. Within the dermis was dense fibroplasia extending into the deep dermis with fragments of refractile foreign body material surrounded by foreign body giant cells, histiocytes, and lymphocytes. These findings may represent exogenous material including talc, metal, or other substances. Telangiectasia and a perivascular mononuclear cell

infiltrate were also noted. Atypia was not identified. Scattered fragments of polarizable material were identified in the stratum corneum, papillary dermis, and reticular dermis. A gram stain demonstrated scattered gram-positive cocci within the superficial portion of the stratum corneum. A DPAS stain revealed scattered yeast forms within the superficial portion of the stratum corneum while GMS and AFB stains were negative for microorganisms.

LABORATORY RESULTS

The following lab results were abnormal:
An admission urine drug screen was positive for cocaine, methadone, and opiates.
Tissue culture of the right distal volar forearm was positive for heavy growth *Staphylococcus aureus*, light growth *Proteus mirabilis,* and heavy growth aerobic diphtheroids.

The following lab results were normal:
AFB and fungal culture were negative.

DIAGNOSIS

Talc granulomas and cellulitis secondary to injected drug use

TREATMENT AND COURSE

At admission patient was started on intravenous vancomycin and ciprofloxacin for suspected cellulitis. After excisional biopsy was performed and tissue culture susceptibilities were reviewed, the patient was then switched to a ten-day course of vancomycin, aztreonam, and metronidazole. Of note, he was also treated concomitantly with ciprofloxacin and linezolid for left hip osteomyelitis/septic arthritis. He was seen four weeks after his initial visit and had much improvement with decreased edema of the right forearm and resolution of the ulcer.

DISCUSSION

Talc is a soft mineral which chemically is defined as hydrous magnesium silicate ($Mg_3Si_4O_{10}(OH)_2$). It is frequently used as a dilutant in heroin or can be used as a filler to hold tablets together which are then crushed and injected intravenously or subcutaneously. If talc is extravasated into soft tissues, it acts as an irritant thereby activating neutrophils, lymphocytes, and mononuclear cells which eventually leads to granuloma formation. Histologically, talc appears as strongly birefringent, plate-like crystals seen using a polarizing filter on light microscopy. In addition to cutaneous foreign body granulomas, injection drug users are also at increased risk for other systemic complications including pulmonary talc granulomatosis which may cause pulmonary fibrosis and retinal arterial occlusive disease.

Cellulitis is a common complication among injection drug users and many studies list soft tissue infections (abscesses and cellulitis) as the leading cause of emergency department visits for injection drug users. For this particular patient population, *Staphylococcus aureus* is the most common pathogen.

Risk factors cited in the literature for infections in injection drug users include subcutaneous or intramuscular injection of drugs (“skin popping”), injection of a mixture of heroin and cocaine (“speedball”), use of non-sterile/dirty needle, increased frequency of injection, drawing blood into the syringe before injecting intravenously (“booting”), and lack of adequate skin cleaning prior to injection.

The prevalence of soft tissue infections in cutaneous injection drug users ranges in the literature, most commonly cited between 10-30%. One recent paper by Lloyd-Smith *et al*., discussed the discrepancy by stating the differences may be attributed to variations in measuring occurrence (i.e., current infection vs. ever-having an infection), the definition of

infection (injection-related vs. any drug-related), and the lack of a gold standard for reporting these types of infections. In their study of 1096 patients in a supervised injection facility, they found a 6-10% prevalence of soft tissue infection and they noted associated risk factors as female users, living in unstable housing, borrowing used syringes, requiring help injecting, and injecting cocaine daily. Interestingly, other studies have also reported an increase occurrence of infection in females. A study by Phillips and Stein amongst injection drug users in Denver, Colorado, demonstrated a self-reported bacterial skin infection in 55% of participants (28/51) at some point in their lifetime. They found that intramuscular injection of drugs and increased number of heroin injections in the month prior to the study were independently associated with skin infection for participants in the past year.

Treatment of drug use and abuse is the most effective means of preventing infections among this patient population. Many resources have focused on harm reduction through education including needle exchange programs and supervised injection facilities.

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CHICAGO DERMATOLOGICAL SOCIETY **CASE # 17**

Presented by Joshua Mandrell, MD, Omar Habeeb, MD*, Darryl Oble, MD*, and Anthony Peterson, MD
Division of Dermatology and Department of Pathology*, Loyola University Medical Center

PATIENT A

HISTORY OF PRESENT ILLNESS

This 77-year-old Caucasian male patient with a previous diagnosis of psoriasis was referred to our clinic for management of a flare of his disease. He had been managed by his primary care physician for three years with betamethasone and triamcinolone cream. The patient noted only occasional pruritus, increasing in severity, and occasional chills.

PAST MEDICAL HISTORY

Inguinal hernia
Essential benign hypertension
Hyperlipidemia
Colon polyps
Benign prostatic hyperplasia
Psoriasis
Beta thalassemia trait
Urothelial carcinoma (later diagnosed)

MEDICATIONS

Amlodipine
Benazepril-hydrochlorothiazide
Docusate sodium
Hydrocodone-acetaminophen prn
Omega-3 fatty acid
Once-a-day multivitamin
Betamethasone cream
Triamcinolone acetonide cream

ALLERGIES

Gabapentin

FAMILY HISTORY

Psoriasis

SOCIAL HISTORY

The patient had a smoking history of 0.5 packs/day for 60 years with no history of alcohol or illicit drug use.

PHYSICAL EXAM

On the trunk, extremities, and hands, the patient exhibited extensive arcuate and fungiform erythematous scaly plaques with hyperkeratosis. Several of the truncal plaques were indurated, however, no cervical, axillary, or inguinal lymphadenopathy was noted.

HISTOPATHOLOGY

Two punch biopsies from left abdomen revealed an epidermotropic CD30+ atypical lymphoproliferative disorder with immunophenotypic studies displaying a prominence of CD30+ cells with lack of expression of CD3, CD4, CD8, CD20, CD5, ALK-1, and pankeratin, but positive for LCA.

Molecular studies for gene rearrangement to establish clonality were negative for both T-cell and B-cell gene rearrangements.

Flow cytometry on a skin specimen revealed a population of cells with high side-scatter characteristics expressing bright CD30 and bright HLA-DR. This population was negative for

surface CD2, CD3, CD5, CD7, CD4, CD8, and cytoplasmic CD3. There was no evidence of a significant increase in the blast population. CD30+ cells: 93%.

A TCR-beta stained section did demonstrate that the intraepidermal tumor cells were negative for the expression of the antigen, while the dermal lymphocytes showed strong expression of TCR beta. By further immunohistochemical analysis, the tumor cells were positive for CD43 but negative for EMA, fascin, and CD56.

Two additional punch biopsies from the left infraaxillary vault and left flank exhibited a pleomorphic population of cells isolated to the epidermis and a smaller population of reactive lymphocytes was seen in the upper dermis. A CD30 immunostained section confirmed tumor cells confined to epidermis with no involvement of the dermis or the subcutaneous fat.

Flow cytometry evaluation of a separate shave specimen revealed a large population of cells exhibiting the following aberrant immunophenotype: CD45+ bright, CD30+, CD1a-, CD2-, CD3-, CD4-, CD5-, CD7-, CD8-, TCR alpha beta-, and TCR gamma delta-. CD30+ cells: 68%.

LABORATORY RESULTS

The following results were normal or within normal limits: platelets, sodium, potassium, chloride, CO2, BUN, glucose, total protein, albumin, bilirubin, ALT, AST, alkaline phosphatase, iron, transferrin, iron binding capacity, TSH, and vitamin B12 levels.

The following results were abnormal: WBC 11.1, hemoglobin 10.0, MCV 67.2, and creatinine 1.65.

RADIOLOGY

CT of pelvis: proximal and mid left ureteral masses (later leading to a diagnosis of urothelial carcinoma) resulting in left hydronephrosis, diffuse bladder wall thickening, enlarged prostate, bilateral inguinal lymphadenopathy, gallstones, bilateral inguinal hernias, and few hepatic cysts.
CXR: no significant abnormalities

DIAGNOSIS

Primary cutaneous anaplastic large cell lymphoma

TREATMENT AND COURSE

After the diagnosis of a CD30+ lymphoproliferative disorder, the patient started narrow-band UVB treatment three times weekly in October 2009 and continued topical steroids while further diagnostic work-up ensued. Treatment with systemic chemotherapy was held pending workup of his ureteral masses seen on CT.

The patient underwent a left ureteroscopy and biopsy of two tumors in the left ureter which revealed urothelial carcinoma. Laparoscopic left nephroureterectomy with open excision bladder cuff revealed a multifocal high-grade papillary urothelial carcinoma arising from the left ureter and found in the upper pole of the left kidney. Margins were free of involved tumor, and the patient was staged pT1 Nx Mx.

When further biopsies confirmed primary cutaneous anaplastic large cell lymphoma, treatment options were discussed with the patient by oncology. The patient deferred biopsy of borderline palpable right axillary lymphadenopathy (confirmed by CT). Due to relatively extensive multicentric disease, the patient was started on etoposide 50mg daily every other day for 6

weeks. The patient showed considerable improvement with this therapy but developed a 6.0 cm x 5.5 cm firm, ulcerated, non-tender tumor on his left abdomen. A punch biopsy from this nodule exhibited an atypical epidermotropic CD30+ lymphoproliferative disease consistent with the prior diagnosis. Immunostains confirmed widespread CD30 expression and only focal staining for CD3, CD4, CD8, and rare CD20+ cells. Etoposide was stopped, and the patient began radiotherapy for this nodule.

PATIENT B

HISTORY OF PRESENT ILLNESS

This 51-year-old Caucasian male with a history of hepatitis C, cirrhosis, and pulmonary infiltrates and effusions presented to our facility in July 2009 with a four to five month history of occasionally tender nodules on his legs. He stated that they were increasing in number and size. He also thought one of the nodules was “lanced open” at an outside hospital, and he was treated for an infection. Otherwise, the patient denied previous treatment and had no other cutaneous complaints.

PAST MEDICAL HISTORY

Alcoholism
Anemia
Hepatitis C
Pneumonia
Pleural effusions
Liver cirrhosis with esophageal varices and portal gastropathy

MEDICATIONS

Folic acid
Zinc sulfate
Vitamin B-1 (thiamine)
Multivitamin
Zolpidem

ALLERGIES

Furosemide caused a rash.

FAMILY HISTORY

Non-contributory

SOCIAL HISTORY

The patient denied current use of alcohol, tobacco, or illicit drug use.

PHYSICAL EXAM

The patient exhibited multiple erythematous nodules and plaques ranging from one to five cm in size, few with ulceration, present on his bilateral lower extremities, right upper back, lower abdomen, and right upper arm. On the left posterior thigh, the patient had an indurated, warm, erythematous tender plaque.

HISTOPATHOLOGY

Punch biopsy of the leg showed pseudoepitheliomatous hyperplasia and overlaid a dermis containing a diffuse infiltrate of monotonous, medium-sized mononuclear cells exhibiting variable nuclear irregularity. The infiltrate effaced the reticular dermis and subcutaneous tissues with relative sparing of the papillary dermis. Scattered larger cells, some with multinucleation and nuclei arranged in a horseshoe configuration (hallmark cells), were appreciated. Frequent mitotic figures, apoptotic debris, and scattered tingible body macrophages imparting a starry-sky appearance were also appreciated. By immunohistochemical analysis, the neoplastic cells were negative for pan-cytokeratin, TTF-1,

and CK20. The neoplastic cells were strongly positive for CD45, CD4, CD30, EMA, and ALK-1 (cytoplasmic but not nuclear staining). The lymphoma cells were negative for CD3, CD5, CD8, and TdT. The proliferation index, as assayed by Ki-67 immunostaining, was greater than 90%. A CD20 immunostained section highlighted exceedingly rare admixed B-cells but did not highlight the neoplastic population.

Bone marrow biopsy: Normocellular bone marrow with variable cellularity (overall 30-40%) and preserved trilineage hematopoiesis with moderate eosinophils (5%), plasma cells (7%), blasts (5%), and lymphocytes (5%). The lymphocytes appeared small and reactive and did not exhibit hyperchromasia or marked nuclear contour irregularities. Immunohistochemical staining for ALK-1 on the bone marrow core biopsy was negative, while a CD30 immunostained section highlighted exceedingly rare bone marrow cells.

LABORATORY RESULTS

The following results were normal or within normal limits: potassium, chloride, CO2, BUN, ALT, alkaline phosphatase, and HIV 1 and 2 antibodies.

The following results were abnormal: WBC 15.4, hemoglobin 8.3, platelets 143, sodium 124, glucose 58, albumin 1.2, total protein 5.3, calcium 7.6, AST 104, and bilirubin 1.9, PT 18.2, APTT 81.3, and INR 1.7, LDH 283, and Hepatitis C antibody 4.7.

RADIOLOGY

Lung CT and cervical-thoracic spine MRI: collapsed T5 vertebrae with a posterior mediastinal soft tissue mass extending into spinal canal at T5/6, right lower lobe consolidation and small pleural effusion, cirrhosis, and gynecomastia.
CT of chest and thorax with PE protocol: left upper and lower lobe pulmonary embolus
CT of head: within normal limits
TEE: within normal limits
CT of pelvis: colonic pneumatosis, ascites, splenomegaly, cirrhosis, portal venous hypertension
CXR: bibasilar atelectasis
Liver U/S: right hepatic cyst, right pleural effusion, small amount of ascites

DIAGNOSIS

Small-cell Systemic ALK+ Anaplastic Large Cell Lymphoma

TREATMENT AND COURSE

Oncology initiated CHOP (cyclophosphamide, doxorubicin, vincristine, and prednisone) chemotherapy as an inpatient with a plan for a complete PET scan upon discharge. During hospitalization, the patient developed an episode of respiratory arrest followed by cardiac arrest with pulseless electrical activity. Unfortunately, he subsequently expired.

DISCUSSION

Cutaneous lymphomas are best classified by their cell of origin. T-cell lymphomas are the most common type of primary cutaneous lymphoma, most notably, mycosis fungoides. Once T-cell markers have determined the T-cell as the cell of origin, and mycosis fungoides and its variants have been excluded, the CD30-staining pattern (Ki-1) is used to further classify the lymphoma. CD30 is the marker found on activated, but not resting, T- and B-cells, as well as a marker for the Reed-Sternberg cells of Hodgkin's disease. A cutaneous lymphoma is considered to be CD30+ if there are large clusters of CD30+ cells, or more than 75% of the anaplastic cells are CD30+. In general, primary cutaneous T-cell lymphomas (CD30 positive) are considered to be biologically low-grade but histologically high-grade malignancies.

Histologically, cutaneous CD30+ T-cell lymphomas show a dense dermal nonepidermotropic infiltrate with atypical tumor cells. Large nuclei and one or several prominent nucleoli, along with abundant cytoplasm are generally seen. In addition to CD30 positivity, most possess CD4 positivity as more evidence of T-cell lineage.

CD30+ anaplastic large cell lymphomas are further classified into primary and systemic cutaneous categories depending on involvement of either nodal or extranodal sites. Primary cutaneous ALCL appears to have a different pathogenesis than systemic ALCL, lacking the classic chromosomal translocation, occurring more often in adults, and having a better prognosis. Systemic ALCL often presents in advanced clinical stages with B symptoms. Unlike lymphomatoid papulosis which has similar immunostaining, and considered by most to be a clinically benign type of primary cutaneous ALCL, lesions in primary or systemic ALCL usually do not regress spontaneously.

Staining, as well as staging, also can help determine the patient's prognosis. CD30+ T-cell lymphomas should be stained with ALK (anaplastic lymphoma kinase), which is a phosphorylated tyrosine kinase, activated by chromosomal translocation, resulting in unregulated growth of affected T lymphocytes. Primary cutaneous large T-cell lymphomas that are CD30+ are typically ALK-1 negative and have a better prognosis than the systemic type. However, patients with extensive limb disease appear to have a more aggressive course, a differential gene expression profile, and may require more aggressive treatments. If present, ALK-1 expression favors a systemic ALCL with primary nodal involvement. In fact, many use ALK-1 expression to differentiate between extranodal involvement of a systemic (nodal) ALCL and primary extranodal ALCL. It seems that ALK-1 negative ALCL has a different site of origin with poor survival in most patients. In general, systemic CD30+ lymphomas with cutaneous involvement have a poor prognosis, while those that express ALK-1 (anaplastic lymphoma kinase) have a better prognosis and better response to chemotherapy. Furthermore, in patients with primary systemic anaplastic large cell lymphomas, elevated LDH levels are correlated with an unfavorable prognosis. Other than ALK-1 staining, the immunophenotype of primary cutaneous and systemic ALCLs are similar.

In patient A, the diagnosis of primary cutaneous anaplastic large cell lymphoma was determined, but his case was not typical in that he lacked classic T-cell markers. Some cases of ALCL lack all detectable T-cell markers and have been called null cell ALCL. In this patient, the absence of TCR beta expression was suggestive of a primary cutaneous gamma-delta T-cell lymphoma, a subset of which assume a pattern similar to disseminated (Ketron-Goodman type) pagetoid reticulosis. However, there was no demonstration of gamma-delta TCR expression on flow cytometry, and gamma-delta T-cell lymphoma usually lacks CD30 expression. Negativity for EMA, ALK-1, and fascin argued against a diagnosis of systemic ALK-negative anaplastic large cell lymphoma. The presence of CD30+ expression with extensive pan T-cell antigen loss, negative T-cell gene rearrangement studies, and negative staging work-up (including bone-marrow biopsy) supported the diagnosis of an unusual pattern (pagetoid reticulosis-like) of primary cutaneous anaplastic large cell lymphoma.

Primary cutaneous anaplastic large cell lymphoma has an excellent prognosis with a 5-year survival of 90%, and regional lymph node involvement does not usually suggest a poorer prognosis. Treatment typically includes excision for individual lesions, radiotherapy, and low-dose methotrexate. However, in patients with multicentric (as in our patient) or extracutaneous disease, other treatment options may be considered, including chemotherapy with CHOP and etoposide. Due to toxicity, attempts to avoid chemotherapy in most cases should be made in this entity with a usually benign course.

Most cases of simultaneous skin and lymph node involvement (systemic) cannot be absolutely classified as primary because the origin of the lymphoma cannot be determined. In patients with extracutaneous disease preceding or seen near the time of skin disease, the prognosis is poor. In patient B, systemic ALK+ anaplastic large cell lymphoma was determined. However, the cytoplasmic, but not nuclear, ALK immunoreactivity suggested the presence of a variant translocation involving the ALK gene on chromosome 2 rather than the classical t(2;5) associated with this entity. About 15-85% of systemic (nodal) ALCLs contain the t(2;5)(p23;q35) translocation, which fuses the ALK gene on chromosome 2 with the nucleophosmin (NPM) gene on chromosome 5, resulting in a fusion protein NPM-ALK. In about 15% of cases, including our patient, genetic aberrations other than the t(2;5) translocation occur resulting in a different fusion protein. There is no difference in prognosis, as of yet, between ALCL with the classic translocation and those with variant translocations. As earlier mentioned, the prognosis of cases of ALK-1 positive ALCL is better than ALK-1 negative ALCL. The overall 5-year survival of ALK-1 positive ALCL is 70-80%, while ALK-1 negative cases is around 50%. The 5-year disease free survival of ALK-1 positive ALCL is 60% and ALK-1 negative ALCL is 40%.

In systemic ALCL, the pathology is distinctive with primary infiltration of the sinuses and paracortical T-cell-rich regions of the lymph nodes often sparing B-cell follicles. In the common variant, tumor cells are usually large, have prominent eosinophilic nuclei, multinucleated cells, and Reed-Sternberg-like cells. “Hallmark cells” (cells with reniform indented nuclei) and “doughnut cells” (cells with convoluted ring-shaped nuclei) are also classically seen. In the small cell variant, the neoplastic cells are smaller with irregular nuclei. Although patient B had a few scattered “hallmark cells” and “doughnut cells,” his pathology predominantly displayed these smaller tumor cells, and he was given the diagnosis of the small-cell variant of systemic ALK+ ALCL. Small-cell ALCL has a worse prognosis over conventional ALCL. Other histologic variants include lymphohistiocytic, Hodgkin-like, sarcomatoid, and neutrophil-rich. Treatment of systemic ALCL usually includes chemotherapy with CHOP chemotherapy being the most common regimen employed. Antibody inhibitors to CD30 and ALK-1 are being developed as other treatment options. Bone marrow transplant is indicated for refractory cases.

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CHICAGO DERMATOLOGICAL SOCIETY **CASE # 18**

Presented by Vanessa Lichon, MD, David Eilers, MD, Scott Wickless, MD, Sheetal Mehta, MD, Brian Nickoloff, MD, Madhu Dahiya, MD, and Anthony Peterson, MD
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Division of Dermatology, Loyola University Medical Center

PATIENT A:

HISTORY OF PRESENT ILLNESS
This 83-year-old Caucasian male presented to our clinic for evaluation of a lesion on his right temple. He had no other cutaneous concerns and denied any other new, changing, or symptomatic lesions.

PAST MEDICAL HISTORY
Hypertension, diabetes mellitus type II, glaucoma, benign prostate hyperplasia, hypothyroidism, cataracts

MEDICATION
Amlodipine
Atenolol
Cyanocobalamin injections
Finasteride
Levothyroxine
Metformin
Terazosin
Aspirin
Calcium/vitamin D
Ferrous sulfate
Glyburide
Lisinopril
Simvastatin

ALLERGIES
Hydrochlorothiazide

FAMILY HISTORY
Patient's daughter and son have a history of non-melanoma skin cancer.

SOCIAL HISTORY
Non-contributory

PHYSICAL EXAM
On total body skin exam the patient was noted to have a solitary well-demarcated 1.1 cm x 2.2 cm thin pink plaque on the mid-lower back, consisting of focal brown pigmentation at the inferior border, dark brown pigment scattered throughout the lateral border, and a red papule at the superior border. Dermatoscopic evaluation revealed an absent central pigment network, heavily pigmented inferior border, and flecks of brown-grey globules at the lateral border.

He was also noted to have a 0.4 cm x 0.9 cm tan to pink patch with brown hyperpigmentation at the superomedial border on the right lower back and a 0.6 cm x 0.7 cm tan patch with dark brown speckles throughout on his left posterior arm.

HISTOPATHOLOGY
An excisional biopsy of the lesion in the lower mid-back demonstrated an epidermis with focal lobules of basaloid cells with scant cytoplasm, hyperchromatic nuclei infiltrating into the superficial dermis with peripheral palisading, and focal stromal retraction with a

lymphohistiocytic infiltrate. There was an interspersed melanocytic proliferation, consisting predominantly of atypical epithelioid shaped single melanocytes and nests along the dermal-epidermal junction with marked pagetoid changes. In one section, there were ecstatic lymphatic channels with attenuated endothelial cells. Immunohistochemistry with Melan-A, HMB-45, and S-100 immunostains revealed atypical appearing melanocytes and nests within the epidermal compartment.

A 10mm punch biopsy was taken of the lesion on the right lower back and an 8mm punch biopsy of the lesion on the left posterior arm. Each demonstrated a proliferation of atypical melanocytes involving the epidermal compartment and with focal involvement of the papillary dermis. There were nests and fascicles of atypical melanocytes with pleomorphic nuclear detail and hyperchromasia along the dermal-epidermal junction with pagetoid spread of melanocytes into the upper epidermis. Nests of atypical melanocytes were also seen invading the papillary dermis. The Breslow depth of the lesion on the right lower back was measured at 0.5mm and the Breslow depth of the lesion on the left posterior arm was 0.32 mm. Immunohistochemistry of each specimen with Melan-A, HMB45, and S100, revealed atypical appearing melanocytes and nests within the epidermal compartment and focally within the papillary dermis.

DIAGNOSIS

Melanoma-in-situ (MIS), superficial spreading type, with concomitant basal cell carcinoma (BCC), superficial type, and lymphangioma, mid-lower back

Malignant melanoma, superficial spreading type x 2, left posterior arm (Breslow depth 0.32 mm), and right lower back (Breslow depth 0.5 mm)

TREATMENT AND COURSE

Our patient was referred to general surgery for further excision of his three malignancies all of which were excised with no residual tumor seen on pathology. He is followed closely by our clinic with skin exams every four months and has had no additional skin cancers to date.

PATIENT B

HISTORY OF PRESENT ILLNESS

This 83-year-old Caucasian male presented to our clinic with complaint of a growth on the left ear. He was unsure of the duration of the lesion. He reported previous treatment of a BCC of his left ear with radiation treatment about twenty years ago at an outside hospital. In 2004, he underwent Mohs surgery for an infiltrative BCC that resulted in loss of the left superior and mid helical rim.

PAST MEDICAL HISTORY

Coronary artery disease, hyperlipidemia

MEDICATION

Aspirin
Calcium/magnesium
Atorvastatin
Multivitamin

ALLERGIES

No known drug allergies

FAMILY HISTORY
Unknown skin cancer history

SOCIAL HISTORY
Non-contributory

PHYSICAL EXAM
On the left inferior helical rim there was a firm exophytic red nodule with a dark brown to black rim of pigment along the inferior border. The superior and mid helix had a well-healed surgical defect.

HISTOPATHOLOGY
An excisional biopsy of the lesion demonstrated extensively ulcerated and deeply invasive malignant melanoma (Breslow thickness at least 3.25mm) with "polyclonism" of the invasive component, consisting of discrete epithelioid and spindle cell areas, melaninized and non-melanized cells, and zones of antigenic heterogeneity. These findings are focally intimately associated with an infiltrating basal cell carcinoma. Epithelioid appearing tumor cells were positive for S100, HMB45, and MART-1 while the spindle cell component was negative for these markers but positive for vimentin.

RADIOLOGY
CT neck, soft tissue: There was no dominant mass, no significant lymphadenopathy, and no evidence of metastasis.
CT chest/abdomen/pelvis: No evidence of metastatic disease.
CT head with and without contrast: No evidence of intracranial mass, hemorrhage, or significant recent infarction.

DIAGNOSIS
Invasive malignant melanoma with concomitant basal cell carcinoma

TREATMENT AND COURSE
This patient was referred to surgical oncology/plastic surgery for further treatment of his malignant melanoma/BCC with plans for complete removal of his ear, sentinel lymph node biopsy, and plastics reconstruction with either a skin graft/flap. Despite numerous phone calls and social work involvement, the patient refused further treatment.

DISCUSSION
Cutaneous collision neoplasms are a well-documented and relatively uncommon occurrence, the most common of these being BCC and nevus, BCC and seborrheic keratosis (SK), as well as nevus and SK. Reports of cases with co-existing malignant melanoma (MM) and BCC are exceedingly rare. One study discovered 11 cases of MM contiguous with BCC after examining 78,000 excisions of primary skin cancers while a more recent review accounts for 36 documented cases of BCC associated with MM. These lesions occur more frequently in older males and are most commonly found on the head/neck and then the trunk. Distinguishing these concomitant proliferations may pose clinical-pathologic pitfalls, as some lesions may present as melanoma, others as BCC, and some with overlapping features, thus, emphasizing the importance of careful histological examination. To date, there is no set consensus for the nomenclature of these lesions. The four most agreed upon categories are termed: collision tumor, colonization, combined tumor, and biphenotypic tumor. Two variants

of combined tumor have also been proposed: those with a clear demarcation between two cell types (collision) and those with both cell types growing closely together (intermingled).

Indeed, several case reports highlight the unpredictable behavior of these lesions including one tumor originally documented as melanoma in-situ (MIS) colonizing BCC which was re-excised, thereafter demonstrating residual BCC and invasive lentigo maligna melanoma extending beyond the depth of the BCC. Another so-called basomelanocytic BCC later recurred as metastatic melanoma resulting in the death of the patient. Whether the melanoma arose de novo at the same location or was present in the original lesion but not in the biopsy specimen is unclear. Therefore, clinical pathologic correlation and maintaining effective communication between the clinician and pathologist is essential in providing optimal patient care.

These two cases emphasize the importance of an excisional biopsy in lesions that clinically exhibit features suspicious for collision or concomitant tumors. Excisional biopsy aids in preventing sampling error and ensures an accurate histopathologic diagnosis.

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CHICAGO DERMATOLOGICAL SOCIETY **CASE #19**

Presented by Krisanne Sisto, MD, and Anthony Peterson, MD
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HISTORY OF PRESENT ILLNESS

This 62-year-old female with a history of non small cell lung cancer undergoing chemotherapy presented for evaluation thickened and scaly skin on her palms and soles for past six months. She also noted enlargement of her fingertips for an unknown duration. There was no associated pain or pruritus. Her skin changes began three months prior to the diagnosis of lung cancer.

PAST MEDICAL HISTORY

Poorly-differentiated non-small cell lung cancer, favoring adenocarcinoma
Cerebral vascular accident
Hypertension

MEDICATIONS

Aspirin
Atorvastatin
Cisplatin
Etoposide
Ferrous sulfate
Metoprolol
Pantoprazole

ALLERGIES

No known drug allergies

FAMILY HISTORY

Non-contributory

SOCIAL HISTORY

The patient had a 40 pack-year history of tobacco (quit seven years ago). She denied illicit drug or alcohol use.

PHYSICAL EXAM

On physical exam the bilateral palms and soles were notable for hyperkeratosis with accentuation and prominence of the papillary ridges. Clubbing of all ten fingers was noted on her hands.

HISTOPATHOLOGY

Punch biopsy of the left hypothenar prominence showed hyperkeratosis, acanthosis and papillomatosis.

LABORATORY RESULTS

Non-contributory

RADIOLOGY

CT chest, abdomen and pelvis revealed a 7.7 x 6.4 cm mass in the right lower lobe.

DIAGNOSIS

Tripe palms

TREATMENT AND COURSE

The patient was started on urea 40% cream to the palms and soles twice daily with a decrease in hyperkeratosis and roughness of the skin. Despite treatment, her lung cancer continued to progress and she died less than one year after being diagnosed.

DISCUSSION

Paraneoplastic dermatoses are a diverse group of cutaneous disorders associated with internal malignancy. Cutaneous findings and symptoms of internal malignancy often present simultaneously and follow a parallel course, although it is not uncommon for the onset of skin findings to precede a cancer diagnosis.

The pathogenesis of paraneoplastic dermatoses is not well understood. Skin findings are most likely the result of a cutaneous inflammatory reaction. This inflammatory reaction may be induced by tumor secreted cytokines or may represent a host immune response to the tumor.

The term tripe palms was formally introduced into the medical literature by Clarke in 1977. The term is used to describe palmar and sometimes plantar changes that resemble tripe, a food prepared from the rugose appearing bovine foregut. Tripe palms has numerous synonyms including, acanthosis nigricans of the palms, acanthosis palmaris, pachydermatoglyphy, palmar hyperkeratosis and palmar keratoderma.

Clinically patients present with hyperkeratosis and accentuation of skin ridges on the palmar surface of the hands and sometimes the feet. Like its name sake, the skin has a rugose, velvety appearance. Changes are exaggerated over pressure points, such as the fingertips, thenar and hypothenar eminences. Tripe palms is frequently seen in conjunction with other paraneoplastic dermatoses. Seventy-two percent of patients have acanthosis nigricans. Ten percent have the sign of Leser-Trelat.

Histologically tripe palms shows hyperkeratosis, acanthosis and papillomatosis.

Tripe palms is highly associated with malignancy. Over ninety percent of patients have an internal malignancy. Lung carcinoma is the most commonly associated malignancy, followed by gastric carcinoma. As in our patient, the skin findings of tripe palms present prior to the identification of internal malignancy in about half of reported cases and at the same time as cancer diagnosis in another twenty percent of cases. There is no gender or race predication.

Recognition of tripe palms and the other paraneoplastic dermatoses is essential and should trigger a malignancy work-up in patients who do not already carry a cancer diagnosis.

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CHICAGO DERMATOLOGICAL SOCIETY **CASE # 20**

Presented by Aaron Pace, MD, Rama Vaitla, MD, and Madu Dahiya, MD
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HISTORY OF PRESENT ILLNESS

This 60-year-old male reported pruritic red bumps in his scalp since 2004. He has noticed a slight progressive hair loss over this time, which he attributes to the scalp eruption. He is particularly bothered by the redness and hair loss. At the onset of the eruption the patient had lesions on the face and neck as well as the scalp, but these have since resolved.

PAST MEDICAL HISTORY

Hypercholesterolemia and spinal stenosis

MEDICATIONS

Aspirin
Multivitamin
Enalapril
Fentanyl patch
Hydrocodone
Acetaminophen
Niacin
Vitamin E

ALLERGIES

Minocycline causes headaches.

FAMILY HISTORY

Non-contributory

SOCIAL HISTORY

Non-smoker

PHYSICAL EXAM

Throughout the scalp, but most prominent over the posterior scalp, there are several 3-4 mm erythematous scars with loss of follicular ostia, scattered pink papules with overlying crust, and rare pustules. In addition, he has decreased hair density over the crown, vertex and temporal scalp.

HISTOPATHOLOGY

Punch biopsy of the scalp from October of 2006 revealed multiple granulomata, mild edema, perivascular lymphocytic infiltrate, and chronic folliculitis.

Repeat biopsy of the scalp in November of 2008 revealed acute folliculitis. It showed a hair follicle with perifollicular neutrophils and lymphocytes as well as intrafollicular neutrophils. Few areas of follicular epithelial necrosis were seen.

LABORATORY RESULTS

Aerobic culture of scalp pustules in December 2006 and November 2008 grew coagulase negative *Staphylococcus* species
Tissue culture and smear in November 2008 was negative for fungal growth
Aerobic culture of the nares November 2008 grew coagulase negative *Staphylococcus* species and *Corynebacterium* species

DIAGNOSIS
Acne necrotica miliaris with underlying androgenic alopecia

TREATMENT AND COURSE
The patient has had a relapsing remitting course. He initially began treatment with a 2-month course of cephalexin and ketoconazole shampoo. He had minimal improvement. He then presented to dermatology, and was started on oral doxycycline with topical betamethasone valerate foam. The patient continued to develop new pustules. He was switched to minocycline but had to stop due to headaches. At this point he restarted doxycycline and initiated treatment with clindamycin foam. However, doxycycline resulted in stomach upset so he discontinued the drug; tetracycline was begun in addition to fluocinonide solution and tazarotene 0.1% gel. Due to joint pains and minimal response with persistent low-grade folliculitis, the patient's treatment was again changed to amoxicillin, adapalene 0.3% gel, and salicylic acid and sulfur shampoo. The patient was maintained on this regimen with good control, but still continued to get new lesions, although less frequent. The decision was made to attempt a ten-day course of clindamycin of which the last three days he also took rifampin however this was not felt to be superior to amoxicillin and resulted in diarrhea. Currently the patient is using amoxicillin 500mg po daily, which he increases to twice a day for flares. He also continues to use salicylic acid and sulfur shampoo. The patient was offered treatment with isotretinoin and dapsone but declined due to their side effect profiles. The patient has been maintained on amoxicillin and attempts to wean him have resulted in flares. He is satisfied with his current response to amoxicillin and the salicylic acid and sulfur shampoo.

DISCUSSION
It is appropriate to begin the discussion of acne necrotica with the words of Plewig and Kligman, "Awareness of this bizarre disease is a prerequisite for an accurate diagnosis." Acne necrotica is generally classified into a more superficial variant termed acne necrotica miliaris and a deeper, scarring variant called acne necrotica varioliformis (also called necrotizing lymphocytic folliculitis). This patient falls more into the miliaris type; however, both types will be covered in the following review, with distinctions made where necessary.

Both acne necrotica miliaris and varioliformis are thought to result from an abnormal immune response to *Staphylococcus* aureus or *Proprionibacterium* acnes. The degree of the response determines the subtype. Both forms are typically seen in middle-aged adults and may be slightly more common in men. This condition is chronic and typically only a small number of lesions appear with each outbreak. In miliaris, the most commonly affected area is the scalp sparing other sites. In varioliformis, disease is more commonly seen in a seborrheic distribution. The non-scarring lesions of acne necrotica miliaris are often intensely pruritic compared to the less pruritic varioliformis type.

The differential diagnosis includes lichen planopilaris, gram-negative folliculitis, erosive pustular dermatosis of the scalp, folliculitis decalvans, perifolliculitis capitis abscedens et suffodiens, discoid lupus erythematosus, tuberculid, lupus miliaris disseminatus, and tertiary syphilis. Many of these can be eliminated with a thorough history, appropriate testing, and biopsy.

Histopathologic examination typically reveals a dense perivascular and perifollicular lymphocytic infiltrate with dermal edema. In early lesions of varioliformis, there are rare necrotic keratinocytes, but later there is often confluent necrosis of the central follicle and scarring. Neutrophils can be seen in the superficial dermis along with fragmented pieces of hair.

Treatment is often frustrating because there are frequent relapses and the disease typically persists for decades. First-line therapy consists of antibiotics either empirically or directed against cultured organisms when identified. There is a component of manipulation involved in a subset of these patients and doxepin has been useful in this setting. Second-line treatment consists of oral retinoids, intralesional triamcinolone, or staphylococcal toxoid injections. Doses of isotretinoin are similar to those used in cystic acne vulgaris.

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CHICAGO DERMATOLOGICAL SOCIETY **CASE #21**

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HISTORY OF PRESENT ILLNESS
This 69-year-old male presented with a biopsy confirmed basal cell carcinoma on the nasal tip and was scheduled to undergo Mohs micrographic surgery (MMS). Two weeks prior, the patient underwent Mohs micrographic surgery for a basal cell carcinoma on the left medial canthus that was repaired with a "lazy s" complex closure. He also recently had another basal cell carcinoma on the right medial cheek treated by Mohs micrographic surgery and repaired with a crescentic complex closure.

PAST MEDICAL HISTORY
Non-contributory

MEDICATIONS
Non-contributory

ALLERGIES
Penicillin

FAMILY HISTORY
Non-contributory

SOCIAL HISTORY
Non-smoker

PHYSICAL EXAM
On the nasal tip there was a 0.9 cm x 0.9 cm pearly pink telangiectatic papule. Preoperatively he had bilateral constricted internal and distal nasal valves leading to audible inspiration.

HISTOPATHOLOGY
Histopathologic examination of the lesion on the nasal tip revealed an infiltrating basal cell carcinoma.

DIAGNOSIS
Basal cell carcinoma, infiltrative growth pattern

TREATMENT AND COURSE
The patient underwent MMS for definitive tumor extirpation due to the tumor location, aggressive growth pattern, need for tissue conservation, and clinically ill-defined borders. There was extensive subclinical disease and the patient was cleared in 5 stages of Mohs surgery. The final defect was 3.6 cm x 3.2 cm and involved the nasal supratip, tip, infratip and medial crus. After a lengthy discussion with the patient, the decision was made to proceed with a paramedian forehead interpolation flap to minimize disruption of the anatomic free margins of the alae and to restore proper anatomic functional relationships. As this patient had restricted tissue reservoirs from which to recruit for the repair of his resultant defect due to his recent MMS to the left medial canthus and right medial cheek, his forehead skin provided the best available tissue with no clinical signs of significant actinic damage. This tissue also provided a good color, textural, sebaceous and pore-sized match for his nasal tip. A delayed

skin graft or healing by secondary intention was avoided due to the exposed cartilage and concern for contraction and notching of the alae. Furthermore, with this defect, a skin graft would provide suboptimal tissue match and poor cosmesis. Post-operatively the patient was placed on prophylactic antibiotics, acetaminophen with hydrocodone for pain and ondansetron for possible post-operative nausea. The patient was seen every other day for the first week for dressing changes and then weekly until the division and inset of the flap three weeks post-operatively.

DISCUSSION

The purpose of this presentation is two-fold: to briefly discuss the role of Mohs micrographic surgery (MMS) in the treatment of cutaneous malignancies and to demonstrate the use of two-staged reconstructive interpolation flaps and the excellent cosmetic and functional results that can be obtained. Given the correct setting, MMS serves an invaluable and necessary role in cutaneous oncology, and two-staged interpolation flaps add to the armamentaria in the repair of challenging defects.

Mohs micrographic surgery is indicated for the treatment of primary tumors greater than 1cm on the scalp, face (especially periocular, nose, temples, ears and perioral skin), neck, hands, feet and genitalia and for treatment of tumors located elsewhere that are greater than 2 cm. Clinically ill-defined tumors, those occurring on hair-bearing skin or radiated fields and those that are recurrent also have an indication for Mohs micrographic surgery. Tumors with an aggressive histologic growth pattern or perineural or angiolymphatic invasion regardless of location benefit with the margin control obtained via MMS. In addition, MMS is indicated for tumors occurring in solid organ transplant recipients and in patients who are immune suppressed or have a skin cancer gene defect. Other tumor types that can be effectively treated with MMS include dermatofibroma sarcoma protuberans, atypical fibroxanthoma, microcystic adnexal carcinoma, lentigo maligna, malignant fibrous histiocytoma, sebaceous carcinoma, merkel cell carcinoma, extramammary Paget's disease, adenoid cystic carcinoma and leiomyosarcoma.

Interpolation flaps used in the repair of surgical defects following MMS can frequently provide superior cosmetic results while restoring normal anatomic and functional relationships. These are two-staged flaps that use an attached vascular pedicle which is subsequently divided and inset approximately 2-3 weeks postoperatively, thereby permitting time for a new vascular bed to develop in the primary defect. These flaps have a rich history. The cheek interpolation flap was used in 600 BC in India, as was the forehead flap. The forehead flap was first reported in the medical literature in 1793 and the postauricular helical flap was first described in 1950.

The interpolated forehead flap is typically used to repair extensive defects of the distal nose and is often based on the ipsilateral supratrochlear artery when done with the axial paramedian technique. The melolabial interpolation flap can be used to repair small defects on the ala and nasal tip and is based on the angular artery or the random blood supply of the medial cheek. The postauricular interpolation flap is used to repair medium and large defects on the helix and antihelix and is a random pattern flap. Technical description of these flaps and how to perform them is beyond the scope of this discussion.

The decision to choose an interpolation flap must be made after a thorough discussion with the patient. Patient education is crucial for those who undergo two-staged reconstruction. Interpolation flaps require a significant commitment from both the patient and the surgeon. Postoperative discomfort and the risk for postoperative bleeding may be temporarily increased for interpolation flaps. In the setting of the paramedian forehead flap postoperative headaches for one to two days may occur. Most importantly, patients must be prepared for the temporary

cosmetic change they will experience for two to three weeks while the flap is in place. Fortunately, in our experience most patients become somewhat accustomed to the appearance of the interpolated flap prior to division and inset. Until the division and inset patients may have difficulty properly wearing eyeglasses due to poor fit and the risk of compressing the vascular supply of a paramedian forehead flap. Due to the temporary unusual appearance of these flaps, patients often require more guidance during the postoperative period and may benefit with repeated office visits for wound checks and suture removal. Finally, beginning one of these flaps commits the patient to another procedure approximately 3 weeks postoperatively.

In conclusion, MMS has an important role for the treatment of clinically indicated tumors where 100% margin evaluation is preferred versus approximately 1% with standard excisions. This is especially important prior to performing a complicated repair such as the two-staged interpolation flaps, which can provide patients with superior functional and aesthetic results.

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