Chicago Dermatological Society

June 2008
Monthly Educational Conference

Program Information
Continuing Medical Education Certification
and
Case Presentations

Wednesday, June 11, 2008

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

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Chicago Dermatological Society

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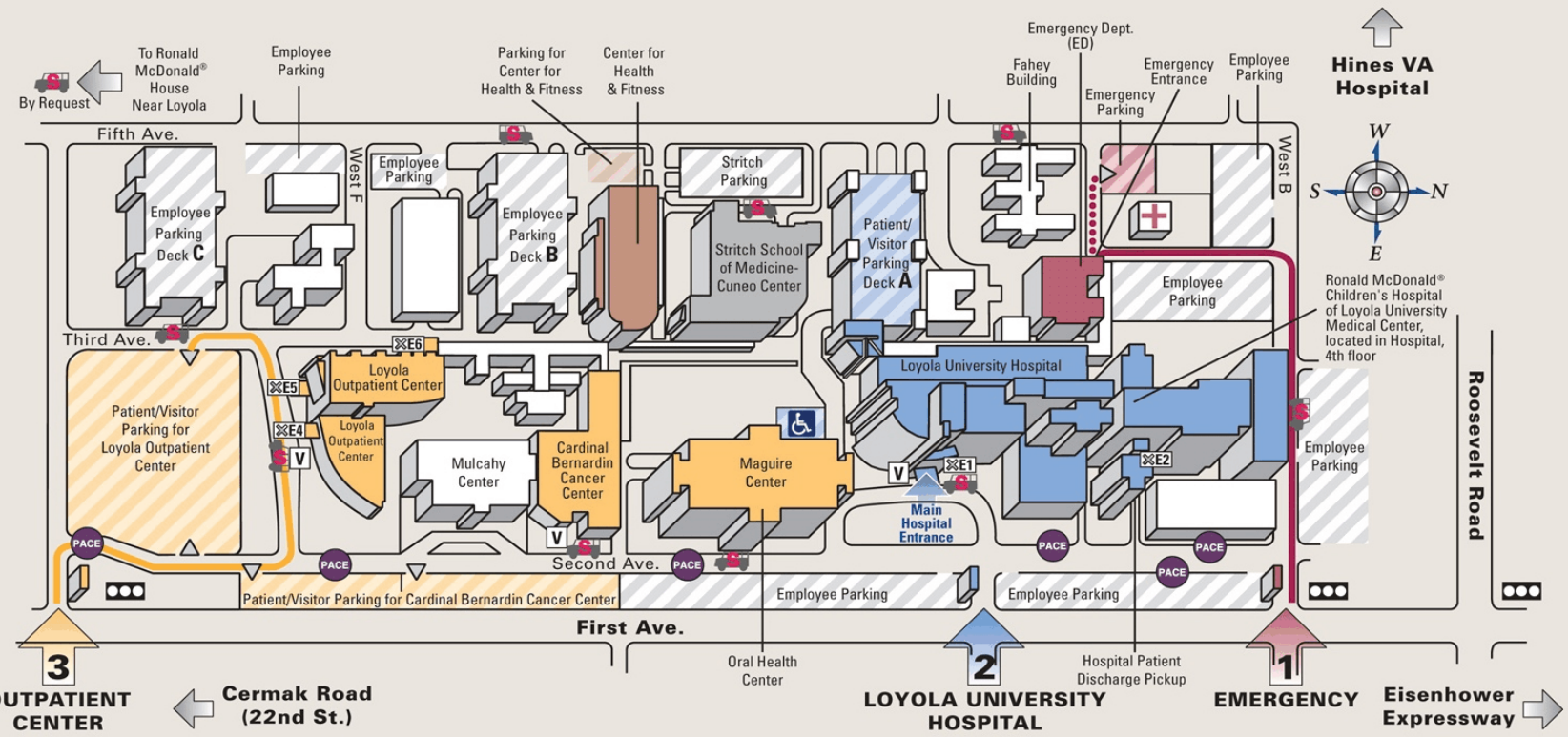
CDS Monthly Conference Program
June 2008 -- Loyola University Medical Center

June 11, 2008

8:30 a.m.	**REGISTRATION, EXHIBITORS & CONTINENTAL BREAKFAST** *Stritch School of Medicine - Main Lobby*
9:00 a.m. - 10:00 a.m.	**RESIDENT LECTURE** Overcoming the Apoptotic Resistance of Malignant Melanoma *BRIAN J. NICKOLOFF, MD, PHD* *Stritch School of Medicine - Lecture Hall*
9:30 a.m. - 11:00 a.m.	**CLINICAL ROUNDS** Patient Viewing *Loyola Outpatient Center, 3rd Floor - Dermatology Clinic* Slide Viewing *Loyola Outpatient Center, Room 3160*
11:00 a.m. - 12:00 p.m.	**GENERAL SESSION** *Stritch School of Medicine - Lecture Hall*
11:00 a.m.	CDS Business Meeting
11:15 a.m.	Cytokine Networking in Psoriasis: Validating the Cytokine Network Hypothesis *BRIAN J. NICKOLOFF, MD, PHD*
12:15 p.m. - 1:15 p.m.	**LUNCHEON** *Stritch School of Medicine - Main Lobby*
1:15 p.m. - 3:00 p.m.	**AFTERNOON GENERAL SESSION** *Stritch School of Medicine - Lecture Hall* Discussion of cases observed during morning clinical rounds *JOAN GUITART, MD, MODERATOR*



LUMC Buildings and Parking

Campus Entrance Key

Please note: Street entrances are indicated by large arrows. Parking lots are marked in stripes.

1 indicates the Emergency Entrance. Follow this sign to reach Emergency Department.

2 indicates the Hospital Entrance. Follow this sign to reach the hospital, Ronald McDonald® Children's Hospital of Loyola University Medical Center, the Ryan Center for Heart &Vascular Medicine and the Visitor Parking Deck.

3 indicates the Outpatient Entrance. Follow this sign to reach the Loyola Outpatient Center, the Cardinal Bernardin Cancer Center and Oral Health at the Maguire Center.

Building Entrance Key

Hospital

E1 Main Hospital Entrance

E2 McGaw Entrance - used for patient discharge

Loyola Outpatient Center

E4 Main Outpatient Entrance

E5 Ambulatory Surgery Entrance

E6 Radiation Oncology Entrance

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V Valet parking is available at the Main Hospital, Cardinal Bernardin Cancer Center and Loyola Outpatient Center entrances for the same small fee as public self-parking.

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CME Information

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

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

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

Guest Speaker

Brian J. Nickoloff, MD, PhD is a Professor and Vice Chairman of Research, Department of Pathology; Director of the Oncology Institute; Director of the Skin Disease Research Program and Deputy Director of the Cardinal Bernardin Cancer Center at Loyola University Medical Center. There are several different areas of scientific inquiry being pursued in Dr. Nickoloff's laboratory. They include focus on primarily three skin diseases: Kaposi's sarcoma, psoriasis, and basal cell carcinoma. The key questions addressed in their psoriasis-related work involve studies of the role of the immune system. Dr. Nickoloff received his MD and his PhD at Wayne State University. He completed residency training in pathology at University of California at San Diego Medical Center, and at Brigham and Women's Hospital. Fellowship training in pathology took place at Harvard University, and at Stanford University School of Medicine in dermatopathology.

Speaker CME Disclosure of Financial Interests

Dr. Nickoloff has no financial relationships to disclose.

CME Credit Documentation

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

Evaluation Forms

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

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CHICAGO DERMATOLOGICAL SOCIETY **CASE # 1**

Presented by Toral Patel, MD and Stacy McClure, MD
Division of Dermatology, Loyola University Medical Center

HISTORY OF PRESENT ILLNESS

This 65-year-old female with a history of right breast cancer, status post radiation in 1997, presented in August 2007 with a five-year history of a violaceous growth on the right breast. It had been slowly enlarging and had recently begun to bleed and become painful. A review of systems was negative.

PAST MEDICAL HISTORY

Infiltrating ductal breast carcinoma, biopsy proven in October 1997; status post radiation therapy, lumpectomy with lymph node dissection, and a five-year course of Tamoxifen
Atrial arrhythmia
Diabetes mellitus
Hypertension
Hyperlipidemia
Intracranial mass, thought to be meningioma

PAST SURGICAL HISTORY

Total knee arthroplasty
Total abdominal hysterectomy and bilateral salpingo-oophorectomy

MEDICATIONS

Atorvastatin
Glipizide
Metoprolol
Triamterene/hydrochlorothiazide
Aspirin

ALLERGIES

No known medication allergies

FAMILY HISTORY

Sister with liver cancer
Sister with breast cancer and lung cancer
Daughter with breast cancer at 37 years of age

SOCIAL HISTORY

The patient has no history of tobacco use or heavy alcohol use. She was a homemaker previously and currently works in security at a local high school.

REVIEW OF SYSTEMS

The patient denied any nausea, vomiting, fevers, chills, night sweats, chest pain, shortness of breath, diarrhea, constipation, abdominal pain, anorexia, melena, hematochezia, hematuria or vaginal bleeding.

PHYSICAL EXAM

The patient is a well developed African-American female in no acute distress. Skin exam reveals a 2cm x 2.5cm violaceous firm shiny plaque with satellite papules on the right medial breast.

HISTOPATHOLOGY
8/9/2007: Skin, right medial breast; shave biopsy: poorly differentiated spindle cell neoplasm with features suggestive of high grade angiosarcoma.
Sections of skin show a poorly differentiated spindle cell neoplasm infiltrating and replacing the dermis. Scattered extravasated red blood cells are noted and there are small spaces or lumina seen, reminiscent of poorly formed vascular structures. Immunostains reveal focal Factor VIII related antigen positivity, and limited CD31 positivity. No significant staining is seen with CD68, S-100, pan-cytokeratin, keratin 34BE12, or desmin.

LABORATORY DATA:
The following values were within normal limits:
Complete blood count
Complete metabolic panel
Thyroid stimulating hormone

DIAGNOSIS
Angiosarcoma of the breast, arising after radiation therapy

TREATMENT AND COURSE
The patient was referred to surgical oncology and underwent resection of the angiosarcoma and satellite lesions with simple mastectomy in September 2007. Surgical pathology revealed five lesions consistent with high-grade angiosarcoma. There was no evidence of lympohvascular invasion. The margins of resection were negative. The patient was staged as T1ANxMx.
The patient remained in relatively good health until February 2008, when she developed a new eruption on her right chest. A biopsy at that time was consistent with a recurrent high-grade angiosarcoma. An extensive malignancy workup revealed potential lymph node involvement in the right supraclavicular and left axillary regions (based on PET scan findings). She was started on a chemotherapy regimen of docetaxel and gemcitabine in March 2008; she completed one cycle, with some evidence of clinical response. The patient's treatment was subsequently interrupted due to an acute hospitalization for recurrent supraventricular tachycardia and an infection at her right chest port site. She started her second cycle of chemotherapy in April 2008 and is currently doing well.

DISCUSSION
Angiosarcomas are rare, comprising less than one percent of sarcomas overall. They are aggressive, tend to recur locally, spread widely, and have a high rate of lymph node and systemic metastases. These tumors display significant heterogeneity in terms of location, histology and clinical behavior. Breast sarcomas may arise de novo (primary lesions) or after treatment of breast carcinoma (secondary). The annual incidence of breast sarcoma has been estimated at 4.6 cases per million women.

Angiosarcoma of the breast has been strongly associated with prior treatment of breast cancer with radiation therapy, as in our patient. In a SEER program database of over 194,000 women treated for breast cancer, the relative risk of developing angiosarcoma in the group treated with radiotherapy was 15.9. The median duration between radiation exposure and the development of angiosarcoma has been reported to be seven years in several studies. Thorotrast, a colloid solution containing thorium dioxide that emits alpha and beta radiation, was used by radiologists in the 1930s-1950s and has been associated with the development of angiosarcomas decades out from exposure. Stewart-Treves syndrome refers to the post-mastectomy development of angiosarcoma in a lymphedematous extremity.

Histologically, angiosarcomas are clonal proliferations of malignant cells with endothelial differentiation. Pathology reveals an anastomosing network of ill-defined vascular spaces and endothelial cells demonstrating varying degrees of atypia. Most lesions display CD31 and CD34 positivity.

Standard treatment of angiosarcoma is wide local excision; mastectomies are often performed with lymph node dissection. Cytotoxic chemotherapy has been shown to be effective in the treatment of angiosarcoma (a 48% response rate was seen in one study); currently used regimens include gemcitabine-taxane (as in our patient) and anthracycline-ifosfamide.

In a recent study of 69 patients with angiosarcoma of the breast, overall survival time was 100 months, and recurrence-free survival was 37 months. Tumor size was the most important prognostic factor for survival in this study; survival was not favorably associated with neoadjuvant chemotherapy or radiation. Local-regional recurrences were most common, followed by liver, bone, and lung. Advanced stage at presentation and lack of adequate margins on excision are associated with higher recurrence, distant metastasis rates, and worsened survival.

Angiosarcoma of the breast is a rare but aggressive malignancy; the risk of development is significantly increased in patients with a history of breast cancer (both radiation and post-mastectomy, in the setting of lymphedema). The clinician should be aware of this relationship, and maintain a high index of suspicion for this diagnosis in breast cancer patients with an enlarging bruise-like area, blue-black nodules or non-healing ulcerations of the chest wall.

REFERENCES

1. Sher, T. et al. Primary angiosarcomas of the breast. *Cancer* 2007;110:173-8.
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3. Abraham, J. et al. Treatment and outcome of 82 patients with angiosarcoma. *Annals of Surg Onc* 2007;14(6):1953-67.
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CHICAGO DERMATOLOGICAL SOCIETY **CASE # 2**

Presented by Kathryn Barlow, MD and Stacy McClure, MD
Division of Dermatology, Loyola University Medical Center

HISTORY OF PRESENT ILLNESS

This 70 year-old female presented with a two-year history of a non-healing, draining sternal wound that began after coronary artery bypass grafting. Due to initial concerns for wound infection by outside services, multiple bacterial, fungal and mycobacterial cultures were obtained from the skin, muscle and bone, without significance. She also had surgical debridement on four separate occasions, most recently in September 2007. Her review of systems was negative. The wound persisted despite multiple courses of antibiotics, various wound dressings including the application of a vacuum-assisted closure device, and dermatology was consulted.

PAST MEDICAL HISTORY

Hypertension
Type II diabetes
Atrial fibrillation
Hyperlipidemia
Asthma

MEDICATIONS

Atorvastatin
Fluticasone/salmeterol inhaler
Metformin
Metoprolol
Warfarin
Multivitamin

ALLERGIES

Iron

FAMILY HISTORY

Noncontributory

SOCIAL HISTORY

Noncontributory

PHYSICAL EXAM

Overlying the central sternum is an approximately 20 centimeter linear sternal scar. Within the scar are multiple, scattered shallow ulcerations with an erythematous to violaceous border and slightly undermined edge. There is a small amount of associated serous drainage.

HISTOPATHOLOGY

Excisional biopsy at time of debridement, sternum: The overlying epidermis demonstrates an area of ulceration. In the mid-dermis, there is an interstitial dermal neutrophilic infiltrate without any evidence of vasculitis.

LABORATORY DATA

The following tests were either normal or within normal limits: complete blood count, comprehensive metabolic panel, urinalysis, fecal occult blood, antinuclear antibody, extractable nuclear antigens, anti-native DNA, anticardiolipin antibodies, antiphospholipid antibodies, antineutrophil cytoplasmic antibodies, RPR, lupus mixing study, serum and urine protein electrophoresis. A colonoscopy was also normal.

Serum beta-2 microglobulin was markedly elevated: 108 (0-20)

DIAGNOSIS
Pyoderma gangrenosum occurring at site of sternotomy

TREATMENT AND COURSE
The patient was initially started on topical metronidazole gel and tacrolimus ointment once daily. After six weeks, there was mild improvement in the number and depth of several of the ulcerations. Consultation with hematology/oncology has been sought for possible bone marrow biopsy and the patient was started on minocycline.

DISCUSSION
Pyoderma gangrenosum (PG) is an uncommon disorder, characterized by painful, progressive ulcerations. The exact etiology is unclear, but alterations in immune function have been implicated. In approximately one-half of all patients there is an underlying systemic condition. Inflammatory bowel disease, rheumatoid arthritis, and hematological malignancies are some of the more common associations, but reports of chronic active hepatitis, systemic lupus erythematosus, AIDS, sarcoidosis, and several other entities have also been reported.

Lesions of pyoderma gangrenosum tend to occur following trauma, a phenomenon known as pathergy. Despite this, reports of PG complicating post-surgical wounds are rare. As of 2001, there were only four reported cases of PG occurring after coronary artery bypass grafting in the literature. PG has also been reported to complicate numerous other surgical procedures including aortic valve replacement, cesarean section, and breast augmentation and reduction mammoplasty.

The diagnosis is often one of exclusion, having ruled out other causes of cutaneous ulceration, including infection, malignancy, vasculitis, or vascular insufficiency. The second obstacle is ascertaining whether or not there is an underlying associated disorder. The histopathology may be non-specific, but dense neutrophilic infiltrates with leukocytoclasia are characteristic of the ulcers advancing edge. Tissue necrosis, neutrophilic vascular reaction with variable vascular involvement, and mononuclear or mixed inflammatory cell infiltrates may be associated histologic features.

There are many ways to treat PG, however, no uniformly successful treatment exists. Superpotent topical or intralesional steroids or calcineurin inhibitors may be utilized. Systemically, prednisone, cyclosporine, tacrolimus, mycophenolate mofetil, azathioprine and the anti-tumor necrosis factor alpha inhibitors have all been reported with varying success rates. Surgical modalities including skin grafting, application of bioengineered skin equivalents like Apligraf, and hyperbaric oxygen are other reported alternatives.

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4. Rand RP, et al. Pyoderma gangrenosum after coronary artery bypass grafting. *Ann Thorac Surg* 1993; 55: 1016-8.
5. Koss-Harnes D, et al. Pyoderma gangrenosum as a complication of coronary artery bypass grafting. *Eur J Cardio-thorac Surg* 1995; 9: 163-5.

CHICAGO DERMATOLOGICAL SOCIETY **CASE # 3**

Presented by Brian Bonish, MD, PhD and Eva R. Parker, MD
Division of Dermatology, Loyola University Medical Center

HISTORY OF PRESENT ILLNESS

This 51-year-old female presented to the emergency department with increasing pain and drainage from chronic wounds on her trunk. She has known metastatic inflammatory breast carcinoma which had progressed over the past 2 years despite aggressive treatment. As a result of disease progression, she developed extensive ulcerations on her trunk. At the time of her admission, she was no longer on systemic chemotherapy. Her wound care regimen consisted solely of alginate dressings. She reported significant pain with dressing changes and exposure to air, requiring premedication with narcotics. Her review of systems was positive for worsening shortness of breath. She denied fevers and chills.

PAST MEDICAL HISTORY

Chronic lymphocytic leukemia diagnosed in 1997, in remission status-post chemotherapy.
Inflammatory breast carcinoma diagnosed in 2006, status-post bilateral mastectomy, radiation, and multiple chemotherapy regimens.
Left upper extremity deep vein thrombosis
Hypothyroidism
Tubal ligation
Tonsillectomy

MEDICATIONS

Enoxaparin
Fentanyl
Filgrastim
Gabapentin
Hydrocodone
Acetaminophen
Hydromorphone
Levothyroxine
Prochlorperazine

ALLERGIES

Penicillin, sulfa drugs, tape adhesives

FAMILY HISTORY

Father – gastric carcinoma

SOCIAL HISTORY

Married
No tobacco, alcohol, or illicit drug use

PHYSICAL EXAM

Extensive, malodorous, erythematous, eroded plaques with purulent drainage are noted on the chest, abdomen, and back. The ulcers are very painful on exposure to air and with palpation. There is pitting edema of the upper extremities bilaterally.

HISTOPATHOLOGY

Skin, punch biopsy, left chest: Within the dermis the lymphatics are filled with markedly atypical carcinoma cells with hyperchromatic nuclei. Atypical mitotic figures are seen. There is a surrounding chronic lymphocytic infiltrate.

LABORATORY RESULTS

The following were positive or abnormal:
Hemoglobin 10.7 (normal 12-16)
Albumin 1.6 (normal 3.6-5.0)
Total protein 4.4 (normal 6.5-8.3)
Alkaline phosphatase 120 (normal 30-110)
Wound culture - methicillin-resistant *Staphylococcus aureus* (MRSA) and *Achromobacter xylosoxidans*

The following tests were negative or normal:
White blood cell count
Blood cultures

RADIOLOGY

CT chest and abdomen: Infiltration of the soft tissue of the chest, increased pleural effusions with pleural thickening, and increased retroperitoneal lymphadenopathy.

DIAGNOSIS

Extensive metastatic inflammatory carcinoma of the breast with secondary wound infection.

TREATMENT AND COURSE

The patient was started on intravenous imipenem-cilastatin and oral linezolid to treat the secondary infection. Her wound care regimen was changed to mupirocin ointment and Acticoat dressings (non-adherent alginate dressing impregnated with silver particles) applied once to twice weekly. Dressings were soaked with normal saline prior to removal and pain medication timed to minimize discomfort. The secondary MRSA infection resolved with the aforementioned antibiotic regimen with significant improvement in her comfort level. On clinical follow-up, the ulcerations were smaller and less exudative. Unfortunately, her metastatic disease has continued to progress and she is now in hospice care.

DISCUSSION

Inflammatory breast carcinoma (IBC) is an uncommon neoplasm, accounting for only 1-6% of all malignancies of the breast. It represents a very aggressive form of breast cancer with a median survival time of only less than four years compared to nine years with other breast malignancies. Cutaneous involvement results from lymphatic spread and typically presents as a well-defined, painful, erythematous plaque, often with peau d'orange changes. Due to its appearance, inflammatory breast carcinoma is frequently misdiagnosed as cellulitis, and hence is also known as carcinoma erysipeloides.

Treatment of IBC is complicated by the small cohort of patients affected by this disease and a lack of defined treatment criteria. Recent research has focused more closely on molecular phenotyping in an attempt to develop more appropriate, targeted therapeutic regimens. In general, IBC is estrogen receptor negative and HER-1 and HER-2 positive, with activation of NF-kB and overexpression of p53. However, these characteristics may vary greatly from patient to patient, thus necessitating individually tailored chemotherapeutic regimens.

Although the skin generally remains intact with IBC, ulceration can occur and results in significant morbidity for patients and presents a therapeutic challenge for clinicians. In Europe, small areas of affected skin have been treated with topical miltefosine 6% solution with reported efficacy. Miltefosine is an alkylphosphocholine and a cytostatic chemotherapeutic agent. While readily absorbed through the skin, it has only minor cutaneous side effects, but this agent may cause profound gastrointestinal toxicity when administered systemically. Due

to the large surface area involved and lack of intact barrier function in our patient, miltefosine was not applied due to concern for transepidermal absorption with resultant systemic toxicity. However, this medication has shown promise as an effective therapy for more localized cutaneous metastases of IBC.

We present this case for clinical interest to illustrate the potentially aggressive nature of metastatic inflammatory breast carcinoma.

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2. Dirix LY, Van Dam P, Prové A, et al. Inflammatory breast cancer: current understanding. Curr Opin Oncol. 2006;18:563-71.
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CHICAGO DERMATOLOGICAL SOCIETY **CASE # 4**

Presented by Jessica Kappelman, MD and James Swan, MD
Division of Dermatology, Loyola University Medical Center

HISTORY OF PRESENT ILLNESS

This 51-year-old African-American female patient presented with a two year history of hair loss and pruritic folliculocentric papules beginning on the trunk and spreading to the extremities, including the hands and feet. She also reported hair loss in the axillae and groin. The patient noted widespread pruritus with worsening in the summer months. She denied any oral lesions. Biopsy at the University of Chicago two years prior to presentation at Loyola University Medical Center revealed extensive lichen planopilaris. Despite prior trials of topical steroids and multiple oral medications, including prednisone, cyclosporine, and acitretin, the condition continued to progress.

PAST MEDICAL HISTORY

Hypothyroidism
Hypertension

MEDICATIONS

Atenolol
Cetirizine
Diphenhydramine
Levothyroxine
Vitamin B complex

ALLERGIES

No known medication allergies.

FAMILY HISTORY

No family history of alopecia or inflammatory skin conditions.

SOCIAL HISTORY

The patient denied the use of tobacco, alcohol, or illicit drugs.

PHYSICAL EXAM

The patient has alopecia of the entire scalp with scattered spiny follicular papules on the occipital scalp and few normal tufts of hair at the posterior occipital hairline. Her trunk, arms, legs, hands, and feet show extensive 1-2 mm hyperpigmented, follicular-based hyperkeratotic papules. Flexures are spared. Scattered inflammatory papules and nodules are noted on her breasts and groin. The oral mucosa is clear.

LABS

The following laboratory studies were within normal limits or negative:
Hepatitis B antibodies, hepatitis C antibodies, comprehensive metabolic panel, white blood cell count, platelets, hemoglobin, iron studies (ferritin, iron, transferrin, total iron binding capacity)

HISTOPATHOLOGY

Skin, punch biopsy, scalp (University of Chicago, 2005): There is a dense lichenoid infiltrate diffusely throughout the dermis as well as around adnexal structures. There is extensive fibroplasia with decreased number of hair follicles. Parakeratotic spines are present within

follicular infundibula. The elastic stain shows normal elastic fibers throughout the dermis except in areas of scarring. The PAS shows a normal appearing basement membrane along the dermal-epidermal junction.

DIAGNOSIS
Graham-Little-Piccardi-Lasseur Syndrome

TREATMENT AND COURSE
Initial treatment included a two-week course of metronidazole 500 mg twice daily, but was unsuccessful. Per recommendations from the Mayo Clinic, the patient then completed a four-week course of topical wet wraps with triamcinolone 0.1% ointment. After no improvement, a two-month trial of hydroxychloroquine sulfate 200 mg twice daily was initiated, with subsequent addition of methotrexate 7.5 mg weekly. The methotrexate was gradually increased to 15 mg weekly with only mild improvement. After no further improvement in the disease state after two months of therapy, the patient discontinued both medications. Finally, cyclosporine 3 mg/kg/day was initiated, but after four months of therapy, failed to improve the cutaneous lesions or halt progression of the disease. The patient is currently on no systemic or topical medications.

DISCUSSION
Graham-Little-Piccardi-Lasseur syndrome (GLPLS) is considered to be a rare variant of lichen planopilaris (LPP). It is characterized by the triad of multifocal scalp cicatricial alopecia, nonscarring alopecia of the axillae and/or groin, and keratotic follicular papules of the trunk and the extremities. Nonscarring alopecia of the eyebrows and follicular papules involving the face has also been reported in this syndrome. In contrast to lichen planopilaris, it rarely occurs in association with cutaneous and/or mucosal lichen planus and typically has a poor response to topical or systemic steroids. Only 40 cases of Graham-Little-Piccardi-Lasseur syndrome have been identified in the literature.

Both GLPLS and LPP affect females more frequently than males. Most patients are middle aged and there is no racial predilection. The course of the disease is variable, but often follows a slowly progressive and chronic course. The earliest lesions appear on the scalp, with violaceous papules, erythema and desquamation, followed by follicular hyperkeratosis and replacement of follicular units with atrophic scars. In active phases of the disease, the follicular papules are present near the margin of the lesion. Common areas of scalp involvement include the frontal-central scalp and crown.

The etiology of GLPLS is unknown, but several hypotheses exist. The strongest evidence supports an autoimmune pathogenesis. This is thought to be mediated by T lymphocytes that are activated by Langerhans cells in the dermis and epidermis. The inflammatory cells attack and destroy keratinocytes expressing viral, pharmacologic, or self antigens. A case report by Viglizzo et al in 2004 demonstrated a genetic origin of the disease when he described a familial case of GLPLS in mother and daughter, both HLA-DR1 positive. Both GLPLS and LPP have been reported following hepatitis B virus vaccination and the latter has been associated with hepatitis C virus. In a study conducted by The Cleveland Clinic Foundation, 31% (9/29) of patients with lichen planopilaris exhibited nutritional deficiencies, defined by low levels of zinc and ferritin. Finally, a hormonal theory has been proposed, but not studied.

In early scalp lesions, histopathology shows a lichenoid lymphocytic inflammatory infiltrate localized to the bulge region of the hair follicle, sparing the epidermis. Infundibular dilatation and follicular plugging are usually present. Chronic scalp lesions may show perifollicular fibrosis, with reduction or absence of sebaceous glands and arrector pili muscles. In late-

stage lesions, inflammation can be minimal or slight with loss of distinctive lichenoid changes. Many late-stage biopsies are not diagnostic and can only be categorized as primary scarring alopecia. Histopathology of the follicular papules reveals a lichenoid lymphocytic infiltrate in the upper dermis, hyperkeratosis and hypergranulosis, acanthosis with occasional saw-toothed rete ridges, and Civatte bodies. Direct immunofluorescence typically shows granular IgG deposits along the epidermal and follicular basement membrane zone and IgA and IgM within colloid bodies.

Early diagnosis leads to prompt initiation of treatment and better outcomes for patients. The mainstays of treatment for lichen planopilaris are topical high potency and intralesional corticosteroids. Systemic steroids are also effective and have not only been shown to decrease symptoms associated with the disease, but have a positive effect on hair regrowth in the active perimeter of the alopecic patch. More recently, oral tetracycline has proven to be effective in halting the progression of the disease. In contrast, no definite treatments have proven efficacious in the treatment of Graham-Little-Piccardi-Lasseur syndrome. In the literature, there have been a few documented treatment successes with cyclosporine A 3-5 mg/kg/day, thalidomide 50-100 mg/day, and oral metronidazole 500 mg twice daily for eight weeks. For patients displaying large areas of end-stage scarring alopecia, scalp reduction and hair transplant may be performed to improve cosmetic appearance.

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CHICAGO DERMATOLOGICAL SOCIETY **CASE # 5**

Presented by Tricia Hultgren, MD and James Swan, MD
Division of Dermatology, Loyola University Medical Center

HISTORY OF PRESENT ILLNESS

This 39 year-old male presented to our clinic for evaluation and treatment of previously diagnosed hidradenitis suppurativa. The patient reported onset of symptoms 15 years ago when he developed a large boil on the scalp. He was initially diagnosed with cellulitis but continued to develop draining nodules in the axillae and buttocks. He reports extreme pain in the right axilla that limits movement. He sought treatment after the condition spread to involve the face in November 2006. He was seen by a dermatologist and diagnosed with hidradenitis suppurativa. He was started on doxycycline 100mg twice daily. The patient noted some improvement with the medication but stopped after 6 months secondary to gastrointestinal distress. The condition then progressed with more facial involvement.

PAST MEDICAL HISTORY

Hidradenitis suppurativa
Iron-deficiency anemia

MEDICATIONS

Denies

ALLERGIES

No known drug allergies

FAMILY HISTORY

Denies family history of acne or hidradenitis suppurativa

SOCIAL HISTORY

The patient is unemployed and lives with his parents. He has smoked 1 pack per week for the past 20 years. He drinks alcohol occasionally and denies drug use.

REVIEW OF SYSTEMS

Negative for fevers, chills, weight loss, arthralgias, nausea, vomiting, diarrhea and constipation

PHYSICAL EXAM

The patient is a cachectic African-American male in no acute distress. Skin exam reveals:
Scattered boggy depressed scars with associated alopecia on the scalp.
Serpiginous dyspigmented fibrotic plaques with few draining nodules and crusts on the bilateral cheeks.
A sclerotic dyspigmented plague with central verrucous exophytic nodules and peripheral crust in the right axilla. Limited range of motion is noted.
A large hyperpigmented atrophic oval scar on the right tricep.
A dyspigmented plaque with few fibrotic sinus tracts in the left axilla.
Scattered hyperpigmented macules on the back.
Large dyspigmented indurated plaque studded with multiple punched out ulcers at various stages of healing on the buttocks. Many of the ulcers have ragged borders.
A hypopigmented sclerotic scar with contractures at the interphalangeal joints on the third digit of the left hand.

Hyperpigmented fibrotic plaques in the groin.

HISTOPATHOLOGY
Skin, punch biopsy, right inferior axilla: There is a suppurative folliculitis with surrounding edema and fibrosis. Acute and chronic inflammation is present, consistent with hidradenitis suppurativa.

LABORATORY DATA
The following were positive or abnormal:
White blood cell count 12.4 k/ul, hemoglobin 10.6 g/dl, mean corpuscular volume 65.8 fl, platelet count 675 k/ul, sodium 133 mm/l, glucose 111mg/dl, albumin 2.8 g/dl, total protein 9.5 g/dl, calcium 8.8 mg/dl.

The following were negative or normal:
Transaminases, HIV

Bacterial culture, buttocks ulcer: Many colonies of Streptococcus milleri and very few colonies of both coagulase negative Staphylococcus species and Streptococcus viridans.

DIAGNOSIS
Severe hidradenitis suppurativa. The diagnosis of atypical pyoderma gangrenosum was also considered.

TREATMENT AND COURSE
The patient was started on minocycline 100mg twice daily and chlorhexidine wash daily with some initial improvement. The patient also received a 14 day course of clindamycin for his scalp involvement. At follow-up he reported less pain in the axillae and denied any new areas of involvement. He is interested in more aggressive therapy including treatment with biologics.

DISCUSSION
Hidradenitis suppurativa (HS) is a chronic inflammatory disease manifested by recurrent abscesses, scarring and sinus tract formation. It favors but is not limited to skin rich in apocrine glands. The condition can be quite debilitating as patients often experience painful nodules and malodorous discharge requiring frequent dressing changes. Prevalence ranges from 0.4-3% and women are affected three times as often as men. Tobacco use appears to be a risk factor for HS, and a recent study by Kagan et al. reported tobacco use in 93% of men and 73% of women with surgically treated HS. Current theories suggest that cigarette smoke may contain comedogenic compounds, such as tar or dioxins, which may contribute to acne formation.

The pathogenesis of HS is thought to involve follicular occlusion with secondary involvement of apocrine glands. An occluding spongiform infundibulo-folliculitis causes dilatation and rupture of the follicle, with subsequent leakage of keratin and bacteria into the dermis. This stimulates an acute inflammatory response with chemotaxis of neutrophils, lymphocytes and histiocytes. In chronic HS lesions, granulomas with giant cells are variably present. Tumor necrosis factor alpha (TNF) induces pro-inflammatory cytokines, activates neutrophils and lymphocytes, and is involved in chemotaxis.

Treatment of HS remains a therapeutic challenge, and only three randomized control trials have been published. Current therapies include topical and oral antimicrobials, retinoids, systemic and intralesional steroids, and excisional and carbon dioxide laser surgery. Surgical

excision remains the most definitive treatment but has shown a variable recurrence rate, ranging from 3% to 50%, up to 72 months following surgery.

Derangement of monocyte function and antigen processing has recently been demonstrated in a group of HS patients. Giamarellos-Bourboulis et al. showed decreased CD4 lymphocytes and increased percentage of natural killer cells in HS patients compared to controls, inferring an autoimmune etiology. Consequently, anti-TNF therapies have recently been used to treat HS. Several recent case reports describe successful treatment of HS with infliximab. Mekkes et al. demonstrated prolonged reduction of symptoms in 10 HS patients treated with a single course of infliximab (5mg/kg infusion at 0, 2, and 6 weeks). Improvement was measured using the Sartorius severity score for acne and the Dermatology Quality of Life Score. Additionally, an open-label phase II study of 10 HS patients treated with etanercept 50mg subcutaneously once weekly showed greater than 50% improvement in 6 patients at week 12 and in seven patients at week 24. Improvement was graded using the Sartorius score and by self-assessment. Anti-TNF therapy appears to improve quality of life in HS patients and further studies will more fully delineate their role in therapy.

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CHICAGO DERMATOLOGICAL SOCIETY **CASE # 6**

Presented by Kathryn Barlow, MD and Eva R. Parker, MD
Division of Dermatology, Loyola University Medical Center

DIAGNOSIS
UNKNOWN

CHICAGO DERMATOLOGICAL SOCIETY **CASE # 7**

Presented by Brian Bonish, MD, PhD and Eva R. Parker, MD
Division of Dermatology, Loyola University Medical Center

HISTORY OF PRESENT ILLNESS

This 42-year-old male presented in July 2007 with a one-month history of progressively worsening painful fissures and thick scaling on his palms and soles. He also reported a history of recurrent crusting on his penis for the past nine months. Additionally, the patient stated he had been recently diagnosed with thrush which was resolving with clotrimazole. His current symptoms were accompanied by subjective fevers, chills, and joint pain in his feet with weight bearing. He denied recent illness, ocular complaints, dysuria, hematuria, urethral discharge, nausea, vomiting, diarrhea, bloody stool, and abdominal pain. He further denied a prior history of similar lesions, psoriasis, and sexually transmitted infections. He was prescribed cefadroxil and a five-day course of prednisone by an outside physician with limited benefit.

PAST MEDICAL HISTORY

Left knee arthroscopy

MEDICATIONS

Clotrimazole
Cefadroxil

ALLERGIES

No known drug allergies

FAMILY HISTORY

No psoriasis

SOCIAL HISTORY

Married October 2006 and honeymooned in Mexico; no children
Works as an electrician
22 pack-year tobacco history
Alcohol consumption of 3-4 drinks per day

PHYSICAL EXAM

Thick, hyperkeratotic papules and plaques with fissuring and foul odor are noted on the plantar feet bilaterally. Examination of the toes reveals a sausage-like appearance of several digits with prominent erythema, edema, and pain consistent with dactylitis. Hyperkeratotic plaques are also noted on the left palm. Multiple nails are thickened and dystrophic. Erythematous, scaling patches are observed on the distal shaft and glans of the penis. The knees bilaterally demonstrate 1-2cm well-demarcated, erythematous, mildly scaling, psoriasiform plaques. The conjunctivae and oral mucosae are unremarkable and the scalp is clear. No palpable lymphadenopathy is appreciated.

LABORATORY RESULTS

The following tests were negative or normal:
Complete blood count
Comprehensive metabolic panel
Urinalysis
Blood and urine cultures
HIV
Chlamydia antibody titer

The following tests were positive or abnormal:
Erythrocyte sedimentation rate – 46 (normal <15)
C-reactive protein – 1.3 (normal <0.8)
HLA B27 – positive

HISTOPATHOLOGY
Skin, punch biopsies, left palm and left foot: There is hyperkeratosis and psoriasiform epidermal hyperplasia with intracorneal neutrophils. Periodic acid Schiff and Giemsa stains are negative for microorganisms.

RADIOLOGY
Bilateral hand and foot x-rays: No significant bony, articular, or soft tissue abnormalities.

DIAGNOSIS
Reiter's syndrome

TREATMENT AND COURSE
Stool culture was recommended on multiple visits; however the patient failed to complete this test. Referrals to Rheumatology, Infectious Diseases, and Ophthalmology were made. No ocular abnormalities were found and no precipitating infectious trigger was identified. The patient was started on clobetasol 0.05% ointment twice daily to the hands and feet, hydrocortisone 2.5% ointment twice daily to the penis, acitretin 25mg daily, and ibuprofen 400mg three times daily. He developed a mild transaminitis after the first month of therapy with acitretin, which subsequently resolved with avoidance of alcohol consumption. The cutaneous lesions resolved within 2 months of treatment but he continues to have mild dactylitis and arthralgias of the feet. His current regimen consists of acitretin and ibuprofen. Smoking cessation has been repeatedly advised but the patient continues to abuse tobacco.

DISCUSSION
Reiter's syndrome, also known as reactive arthritis, is a seronegative spondyloarthropathy that classically consists of a clinical triad of urethritis, arthritis, and conjunctivitis, typically triggered by gastrointestinal or genitourinary infection. Reiter's syndrome has a male predominance with a peak incidence in the third decade. Urethritis and/or cervicitis is present in the majority of patients with this disorder but may be asymptomatic. Arthritis, often accompanied by enthesitis and dactylitis, is also a defining characteristic and most commonly affects the lower extremities. While conjunctivitis occurs in 30-60% of patients, uveitis and keratitis are features observed in a small minority of individuals but may be a source of considerable morbidity, specifically blindness. Despite the classic description, only one-third of patients with Reiter's syndrome actually present with the complete triad. Mucocutaneous manifestations of Reiter's syndrome are quite common and include keratoderma blennorrhagicum, balanitis circinata, ulcerative vulvitis, oral ulcerations, and psoriatic-type nail changes. Constitutional symptoms may also occur.

The most commonly associated infectious triggers include *Shigella, Salmonella, Yersinia, Chlamydia trachomatis, Streptococcus viridans, Mycoplasma pneumonia,* and *Cyclospora*. While the pathophysiology of Reiter's syndrome remains unclear, cross reactivity with bacterial antigens has been proposed as a possible pathogenic mechanism given the frequent association with infection. Additionally, Reiter's syndrome is strongly associated with HLA-B27, with up to 80% of patients carrying the allele. Concomitant HIV infection in the setting of HLA-B27 positivity triples the risk of developing this disorder.

Management of Reiter's syndrome consists of topical steroids and keratolytics for cutaneous lesions and NSAIDs and intra-articular steroid injections for joint complaints. Acitretin, sulfasalazine, and methotrexate may also be employed for more recalcitrant cases, particularly in the setting of HIV. More recently, case reports have demonstrated efficacy of anti-TNFα medications in the successful treatment of some patients. In most cases, the symptoms of Reiter's syndrome remit within six months, but recurrent or chronic arthritis may complicate the course in many patients.

Of historical note, the clinical triad of this syndrome was reported in 1916 by a German physician, Hans Reiter, who was later convicted of Nazi war crimes due to his belief in ethnic cleansing and his participation in enforced racial sterilization and euthanasia. As a result, many in the medical community have pushed for this entity to be referred to as "reactive arthritis" rather than Reiter's syndrome.

We present this case for clinical interest, and to illustrate the excellent response patients may demonstrate to treatment with a systemic retinoid.

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CHICAGO DERMATOLOGICAL SOCIETY **CASE # 8**

Presented by: Toral Patel, MD and Eva R. Parker, MD
Division of Dermatology, Loyola University Medical Center

HISTORY OF PRESENT ILLNESS

This 60-year-old female presented with a four-day history of a diffuse skin eruption, which began on the right arm and then quickly spread to her trunk and extremities. The rash was pruritic and tender, and was accompanied by arthralgias, non-productive cough, and low-grade fevers. The patient reported a ten-day history of a preceding upper respiratory illness, for which she was prescribed amoxicillin five days prior to her presentation.

PAST MEDICAL HISTORY

Endometrial carcinoma, status-post hysterectomy with bilateral salpingo-oophorectomy
Hypothyroidism
Hypertension
Gastrointestinal reflux
Seasonal allergies

MEDICATIONS

Levothyroxine
Rosuvastatin
Alendronate
Famotidine
Benzonatate
Loratadine
Ipratropium bromide nasal spray
Fluticasone nasal spray

ALLERGIES

No known medication allergies

FAMILY HISTORY

Mother – uterine cancer

SOCIAL HISTORY

15 pack-year tobacco history; quit 20 years ago
Denies alcohol use

PHYSICAL EXAM

Temperature 38.2ºC, respiratory rate 18, blood pressure 110/67, heart rate 84
Skin exam reveals multiple, infiltrative, erythematous to violaceous papules and plaques with dusky centers located on the extremities. Several lesions on the left proximal arm are noted to have pseudo-vesicular centers. Faint, patchy erythema of the bilateral peri-ocular skin is also noted. The mucosal surfaces, palms and soles are clear.
The right wrist and left ankle demonstrate small effusions, erythema, warmth, tenderness, and decreased range of motion secondary to pain.

LABORATORY

The following laboratory tests were abnormal:
Complete blood count :
- Hemoglobin 11.4 (normal 12-16)
- Hematocrit 32.6 (normal 34-51)
- White blood cell count 9.6 (normal 4-10); lymphocytes 10% (normal 20-45), neutrophils 80% (normal 45-70)

C- reactive protein (CRP) – 10.4 (normal <0.8)
Erythrocyte sedimentation rate (ESR) – 95 (normal 0-30)

Bronchoalveolar lavage (BAL) fluid differential – 439 white blood cells composed of 43% neutrophils, 31% lymphocytes

The following laboratory tests were negative or within normal limits:
Comprehensive metabolic panel
Anti-nuclear antibody
Anti-neutrophilic cytoplasmic antibody
Rheumatoid factor
Angiotensin converting enzyme level
Anti-streptolysin-O titer
Parvovirus B19 antibody
Blastomyces antibody
Histoplasma antigen
Mycoplasma IgM and IgG antibodies
Quantiferon tuberculosis
Cold agglutinins
C3 and C4 complement levels
Serum protein electrophoresis

HISTOPATHOLOGY
Skin, punch biopsy, right thigh: Dermis and subcutis with neutrophilic infiltrate with giant cells. Gram, acid-fast bacilli, and Gomori's methanamine silver stains were negative for microorganisms.
Transbronchial biopsy, left lower lobe of lung: Fragments of alveolated lung tissue and bronchial tissue with focal minimal chronic inflammation.

MICROBIOLOGY
Skin biopsy for tissue culture: negative for growth of bacteria, fungus, and mycobacteria
BAL culture: negative for growth of virus, pathogenic bacteria, fungus, and mycobacteria
Blood cultures: negative

IMAGING
CT chest: Dense consolidation in the left lower lobe medially. Patchy airspace opacities are noted in the right middle lobe. There is a calcified granuloma in the right lobe. Scattered areas of air trapping are noted on expiratory imaging. There is no evidence of interstitial lung disease or bronchiectasis. Calcified mediastinal and right hilar lymph nodes are noted.

CT abdomen and pelvis: normal

DIAGNOSIS
Sweet's syndrome with pulmonary involvement

TREATMENT AND COURSE
After an extensive work-up to rule out infectious etiologies, underlying malignancy, and connective tissue disease, the diagnosis of Sweet's syndrome with pulmonary involvement secondary to recent upper respiratory infection was made. Due to worsening skin lesions, the patient was started on a four-week prednisone taper with a starting dose of 60mg daily. Her skin lesions dramatically improved within 24 hours and quickly resolved. The patient's ESR normalized, and her pulmonary symptoms continued to improve. A recent complete blood count and serum protein electrophoresis were normal, and the patient remains in good health, without recurrence of the cutaneous lesions or pulmonary symptoms.

DISCUSSION

Sweet's syndrome, or acute febrile neutrophilic dermatosis, was first described in 1964 with hundreds of cases reported. The major and minor diagnostic criteria for Sweet's syndrome are as follows:

Major:

1. Abrupt onset of painful erythematous plaques or nodules.
2. Histopathologic evidence of a dense neutrophilic infiltrate, without evidence of leukocytoclastic vasculitis.

Minor:

1. Fever > 38°C.
2. Association with an underlying hematologic or visceral malignancy, inflammatory disease, or pregnancy, or preceded by an upper respiratory or gastrointestinal infection or vaccination.
3. Excellent response to treatment with systemic corticosteroids or potassium iodide.
4. Abnormal laboratory values at presentation (three of four): ESR >20 mm/hr, elevated C-reactive protein, >8,000 leukocytes, >70% neutrophils.

Both major criteria and two of the four minor criteria must be met to establish a diagnosis of Sweet's syndrome. In the case of our patient, she met all 6 criteria. Specifically, she had painful, erythematous skin lesions demonstrating neutrophilic infiltrates on histology, accompanied by fever, markedly elevated ESR and CRP, and elevated neutrophil count at presentation. Her symptoms were preceded by upper respiratory infection and responded dramatically to systemic steroids.

While the majority of cases of Sweet's syndrome (approximately 75%) are classified as idiopathic, preceding infections, especially those of the upper respiratory and gastrointestinal tracts, may be the precipitating trigger in many patients. More concerning is the association of Sweet's syndrome with underlying malignancy, typically those of hematologic origin such as acute myelogenous leukemia. However, cases linked to solid tumors have also been reported. The first case of medication-induced Sweet's syndrome was reported with trimethoprim-sulfamethoxazole, but other commonly implicated drugs include granulocyte-colony stimulating factor and all-trans retinoic acid.

Extracutaneous involvement in Sweet's syndrome is rare, but when seen, the affected organs may include the lungs, eyes, kidneys, liver, and joints. Pulmonary involvement in Sweet's syndrome was first described in 1985. In a case series of 48 patients with Sweet's syndrome at the Mayo Clinic from 1980-1995, five patients had concomitant pulmonary infiltrates and responded to systemic steroids but not to antibiotics. The primary symptoms of pulmonary involvement include progressive dyspnea and dry cough. Unilateral or bilateral infiltrates are often seen on chest x-ray or CT scan. Lung histology or bronchoalveolar lavage (BAL) reveals a predominantly neutrophilic infiltrate, as in our patient. Additionally, three cases of bronchiolitis obliterans organizing pneumonia (BOOP) have been reported in association with Sweet's syndrome. While the pulmonary symptoms generally respond to treatment with systemic steroids, patient deaths secondary to lung involvement in this syndrome have been reported.

Sweet's syndrome is a relatively uncommon entity that is best known for its clinical characteristics of fever, acute onset of cutaneous lesions, and rapid response to systemic steroids. Extracutaneous involvement, while rare, may occur and involve various organ systems including the lungs. With the presence of neutrophilic inflammation on cutaneous histology and concomitant pulmonary infiltrates, an infectious etiology was of primary concern for this patient, emphasizing the importance of treating neutrophilic dermatoses, such as Sweet's syndrome, as a diagnosis of exclusion. In such cases, BAL can serve as a useful diagnostic tool as neutrophil

counts are generally markedly elevated but respiratory cultures are negative, as in our patient. Since prompt initiation of steroids is essential in the treatment of Sweet's syndrome, the clinician should maintain a high index of suspicion for this diagnosis in the setting of fever, skin lesions with neutrophilic infiltrates when no identifiable infectious etiology is found.

We present this case for clinical interest to highlight the rare association of pulmonary infiltrates with Sweet's syndrome.

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CHICAGO DERMATOLOGICAL SOCIETY **CASE # 9**

Presented by Jessica Kappelman, MD and Stacy McClure, MD
Division of Dermatology, Loyola University Medical Center

HISTORY OF PRESENT ILLNESS

This 87-year-old Caucasian male presented with a one year history of a left sided facial ulceration. The ulceration began with a nose bleed and rapidly progressed to involve the ipsilateral cheek, upper lip and lower eyelid, with complete destruction of the left nasal ala. The patient denied any pain, pruritus, or prior infection. He also denied manipulation of the area, but his son had recently noticed him picking and scratching at his face.
Prior treatment included silver sulfadiazine cream and oral clindamycin without any improvement. Biopsies done by plastic surgery approximately six months prior revealed chronic inflammation without evidence of malignancy.

PAST MEDICAL HISTORY

Acoustic neuroma (left) status post resection 20 years ago
Left sided deafness
Diabetes mellitus type II
Peripheral vascular disease status post stent (bilateral)
Status post cholecystectomy
Malaria

MEDICATIONS

Aspirin
Fluvastatin
Insulin
Silver sulfadiazine cream
Tamsulosin

ALLERGIES

None

FAMILY HISTORY

No family history of skin cancer.

SOCIAL HISTORY

The pateint is widowed and lives in a nursing home. He denied the use of tobacco, alcohol, or illicit drugs.

PHYSICAL EXAM

There is contiguous deep ulceration involving the left upper lip, left nasal sidewall, left medial cheek, and left lower eyelid with complete destruction of the left nasal ala. The ulcer base is clean and without exudate. There is mild surrounding inflammation and scarring.

HISTOPATHOLOGY

Skin, punch biopsy, left cheek: There is an impetiginized ulcer with acute and chronic inflammation and solar elastosis. There is no evidence of malignancy.
Skin, punch biopsy, left septum: Squamous mucosa with ulceration, crust formation, and granulation tissue. There is no evidence of malignancy.
Skin, punch biopsy, left ala: Fragments of hyperkeratotic and parakeratotic epidermis with underlying chronic inflammation. There is no evidence of malignancy.

LABS
The following labs were within normal limits or negative:
Liver function tests, calcium, BUN/creatinine, electrolytes, white blood cell count, AFB culture

The following labs were abnormal:

Glucose 200	[normal 70-100]
Albumin 2.6	[normal 3.6-5.0]
Platelets 527	[normal 150-400]
Hemoglobin 11.6	[normal 14-17]

RADIOLOGY
CT paranasal sinuses without contrast/ CT soft tissue neck with contrast were significant for soft tissue swelling and lymphadenopathy without a focal mass.

DIAGNOSIS
Trigeminal Trophic Syndrome

TREATMENT AND COURSE
The patient was instructed to cleanse the area twice daily, followed by application of petrolatum ointment and a hydrocolloid dressing. He was referred to psychiatry for behavior modification and/or pharmacological treatment, as well as plastic surgery for possible prosthesis.

DISCUSSION
Trigeminal trophic syndrome (TTS) is a rare condition characterized by the triad of trigeminal anesthesia, paresthesias, and ulceration. It occurs after damage to the sensory portion of the trigeminal nerve or its central connections. The most common location of ulceration is the nasal ala, although other areas have been reported, including the jaw, forehead, scalp and ear. In more severe cases, the ulceration can spread to the cheek and upper lip, resulting in scarring and fibrosis. The ulceration of trigeminal trophic syndrome is usually limited to the non-cartilaginous portion of the nose, but in severe cases, loss of the nasal ala may lead to necrosis of the cartilage framework. The tip of the nose is spared as a result of innervation by the ethmoidal branch of the ophthalmic division of the trigeminal nerve. The period of latency from trigeminal injury to ulceration varies from weeks to decades, with a mean of 1-2 years.

The ulceration is always self-induced, but patients are often unaware of their compulsive behaviors and deny wound manipulation. The differential diagnosis of trigeminal trophic syndrome is broad and relies on excluding other causes of nasal/facial ulceration, such as granulomatous disease, neoplasm, vasculitis, infection, and factitial dermatitis. The latter can be ruled out if neurological signs are present. An extensive laboratory work-up is negative. Biopsies will reveal minimal chronic inflammation without giant cells, granulomas, or vasculitic lesions. Secondary superinfection may occur.

An understanding of the predisposing factors of trigeminal trophic syndrome is important to ensure a timely diagnosis of this illness. A literature review of 63 cases performed by Weintraub et al revealed that 46% of cases occurred after trigeminal rhizotomy and 29% occurred after alcohol injection of the gasserian ganglion. Both procedures are used to treat trigeminal neuralgia that is refractory to pharmacologic therapy. Other predisposing disease states reported in the literature include vertebrobasilar insufficiency, acoustic neuroma, post-encephalitic parkinsonism, and syringobulbia. Less common associations include craniotomy, head trauma, herpes and varicella infection, neurologic injury after a complicated birth, and leprosy.

Treatment of trigeminal trophic syndrome is challenging and often unsuccessful. Educating the patient about the self-induced nature of the ulceration is most important. Psychological counseling for behavior modification may also be necessary, as well as pharmacologic management for control of paresthesias. Therapeutic success has been documented with pimozide, carbamazepine, chlorpromazine, amitriptyline, diazepam, vitamin B supplementation, gabapentin, and oxcarbazepine. A protective hydrocolloid dressing or a prosthetic device may be effective, but usually only for a brief time period. The latter will also improve cosmesis. Surgical repair has been documented in several cases, but outcomes are dependent on addressing underlying neurologic pathology prior to the reconstructive procedure. Flaps using tissue with functional innervation and its own blood supply are often required. Many other treatments have been documented with variable success, such as cervical sympathectomy, ionizing radiation, antibiotics, and transcutaneous electrical nerve stimulation.

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CHICAGO DERMATOLOGICAL SOCIETY **CASE # 10**

Presented by Brian Bonish, MD PhD, Linda Sheu, MD and Rama Vaitla, MD
Division of Dermatology, Loyola University Medical Center

HISTORY OF PRESENT ILLNESS

This 69 year old male presented to the dermatology clinic for treatment of a biopsy proven superficial basal cell carcinoma of the left shoulder. Upon further questioning, he reported having a birthmark extending from his left shoulder down to his elbow. As a young child, the birthmark was light brown in color. Sometime during his adolescence or teenage years, he noticed multiple pink papules along the lesion. In 1999, one of these papules was excised from the proximal segment of the birthmark at an outside institution. Histopathologic evaluation of this lesion was also consistent with a superficial basal cell carcinoma.

PAST MEDICAL HISTORY

Squamous cell carcinoma, left posterior auricular (3/9/2005)
Basal cell carcinoma, superficial type, left proximal shoulder (2/16/1999)
Thermal burn following an industrial accident involving his upper back, left posterior shoulder, and left posterior upper arm 20 years ago
Hypertension
Hyperlipidemia
Lyme disease
Rheumatic fever

MEDICATIONS

Captopril
Simvastatin

ALLERGIES

No known drug allergies

FAMILY HISTORY

No family history of congenital skin disease, skin cancer

SOCIAL HISTORY

Does not smoke, occasional alcohol

REVIEW OF SYSTEMS

The patient's review of systems was negative

PHYSICAL EXAM

Physical exam is remarkable for a linear, band like plaque with stria-like atrophy and overlying multiple, discrete, slightly shiny, pink papules extending from the left shoulder down to the elbow. At the distal most portion of the band, there are a few tan coalescent papules. Also notable on exam is a large hypopigmented scar involving the upper back, left posterior shoulder, and left posterior upper arm. No frontal bossing, milia, comedones, palmar pits or epidermal inclusion cysts are noted.

STUDIES

Chest radiographs: unremarkable
Panorex radiograph of the jaw: negative for odontogenic keratocysts

HISTOPATHOLOGY

1/2008: Left shoulder at acromion: Basal cell carcinoma, superficial type
3/2008: Left deltoid: Basal cell carcinoma, superficial type and focally nodular type
Left distal bicep: Basal cell carcinoma, superficial type and nodular type
4/2008: Left distal upper arm, 4.5 cm proximal to the antecubital fossa: small 'abortive' hair follicle with associated sebaceous glands, suggestive of hamartoma
Right posterior deltoid: Basal cell carcinoma, nodular type

DIAGNOSIS

Linear unilateral basal cell nevus

TREATMENT AND COURSE

The basal cell carcinoma on the left shoulder was treated with electrodesiccation and curettage. Treatment options for the remainder of the basal cell carcinomas were discussed with patient, including close follow up, imiquimod, and excision. He remains undecided, but is considering excision.

DISCUSSION

Linear unilateral basal cell nevus (LBCN) was originally described by Carney in 1952 in a 69-year-old white man. The patient had hyperpigmented linear bands composed of comedones and smooth globular papules presenting at birth and involving the left scalp, face, arm, and leg. Histopathologic examination of the papules was consistent with basal cell carcinomas (BCCs). Since Carney's initial publication, LBCN has remained a rare entity, with few cases having been reported. Classically, lesions appear at birth, but there have been reported cases occurring in early adulthood. Nevi may appear on the face, trunk or extremities, distributed linearly or follow the lines of Blashko. Although Carney's initial report of LBCN had associated comedones, lesions lacking this finding do not exclude the diagnosis. Subsequent case reports have noted associated epidermoid cysts, hypopigmentation, and stria-like atrophy. The smooth globular papules of LBCN are histologically consistent with superficial and nodular subtypes of basal cell carcinomas.

Some authors believe linear basaloid follicular hamartoma (BFH) and LBCN to be one and the same. Linear BFH is composed of islands of basaloid proliferations arranged in branching cords and strands in the papillary dermis. Superficial and nodular basal cell carcinomas have been noted to arise within these basaloid islands. However, others maintain linear unilateral basal cell nevus to be a distinct entity, since not all lesions have demonstrated histologic evidence of basaloid follicular hamartomas.

There have also been a few reports of LBCN presenting with associated anomalies such as scoliosis, osteoma cutis, anodontia, and other bony abnormalities as in epidermal nevus syndrome. This raises the possibility that LBCN may be a variant of epidermal nevus, however with such few cases reported and a lack of unifying associated signs, this has yet to be established.

LBCN must be distinguished from nevoid basal cell carcinoma syndrome (NBCCS). NBCCS is an autosomal dominant disorder arising from mutations in the PTCH gene. It is associated with multiple aggressive BCCs, jaw keratocysts, calcified falx cerebri, bifid ribs, and palmar/plantar pits. NBCCS has not been associated with stria-like atrophy or comedones, features found in LBCN. Post zygotic somatic mutations in the PTCH gene giving rise to unilateral or segmental NBCCS with variable expression of associated anomalies has been reported. In contrast, molecular studies of LBCN revealed no mutations in the PTCH or SMO genes.

Linear basal cell carcinoma is another entity that should be included in the differential diagnosis of LBCN. Linear BCC usually develops in older individuals on photo-damaged skin along relaxed skin tension lines. Unlike LBCN, linear BCCs tend to be composed of more aggressive histologic subtypes and are more likely to have a higher rate of subclinical spread. In contrast,

invasive behavior of LBCN has not been reported. LBCN is felt to behave in an indolent manner. Most authors advocate only close monitoring, while others have opted to treat with surgical excision.

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CHICAGO DERMATOLOGICAL SOCIETY **CASE # 11**

Presented by Tricia Hultgren MD and Eva R. Parker MD
Division of Dermatology, Loyola University Medical Center

HISTORY OF PRESENT ILLNESS

This 56-year-old female was transferred from an outside hospital for evaluation of large, painful lesions on the lower extremities that appeared one week prior to admission and subsequently spread to involve the bilateral breasts. The patient denied a history of trauma, clotting disorders, anticoagulant use, connective tissue disease, and miscarriage. She felt well and denied recent illness, headaches, fever, chills, abdominal pain, and arthralgias.

PAST MEDICAL HISTORY

Grave's disease
Hypertension
Asthma
Depression
Cholecystectomy

MEDICATIONS

Propranolol
Propylthiouracil
Escitalopram

ALLERGIES

No known drug allergies

FAMILY HISTORY

Non-contributory

SOCIAL HISTORY

Married with four children
72 pack-year smoking history; quit 2006
Occasional alcohol consumption

PHYSICAL EXAM

The patient is a well-appearing, non-toxic female with extensive, large, geographic purpura with necrosis and bullae formation on the lower extremities and breasts, bilaterally.

HISTOPATHOLOGY

Skin, punch biopsy, right medial shin: There is full thickness epidermal necrosis with upper dermal vascular thrombi and minimal inflammation. Gram, acid-fast bacilli, and Gomori's methanamine silver stains are negative for microorganisms.

LABORATORY:

The following tests were negative or normal:

Comprehensive metabolic panel
White blood count and platelets
Urinalysis
Prothrombin and partial thromboplastin times
Fibrinogen and fibrin split products
Protein C and S levels and activity
Activated protein C resistance
Factor 8 inhibitor
Heparin-induced platelet antibodies
C3, C4 complement levels
Anti-nuclear antibody
Extractable nuclear antibody
Anti-phosphoserine IgA, IgG, IgM antibodies
ß2 glycoprotein IgA antibody
Anti-cardiolipin IgA antibody
T3 and T4 thyroid hormone levels
HIV titer and viral hepatitis panel
Blood and urine cultures
Cutaneous biopsy for pan tissue cultures

The following tests were positive or abnormal:
Hematocrit – 28.6 (normal 34-51)
Hemoglobin – 9.4 (normal 12-16)
D-dimer – 2380 (normal <1100 ng/mL)
Factor VIII – >170 (normal 50-150)
ß2 glycoprotein IgG and IgM antibodies – positive
Anti-cardiolipin IgG antibody – inconclusive
Anti-cardiolipin IgM antibody – moderately positive
Lupus anticoagulant – positive
Rheumatoid factor – 20 (normal <20)
Perinuclear anti-neutrophilic cytoplasmic antibody – 1:20
Anti-myeloperoxidase antibody – positive
Anti-proteinase 3 antibody – positive
Thyroid stimulating hormone – <0.03 (normal 0.4-4.4)
Anti-thyroid peroxidase antibodies – 626.1 (normal <9)

RADIOLOGY
CT scan of chest, abdomen, pelvis: Complete occlusion of the distal abdominal aorta and proximal common iliac arteries.

DIAGNOSIS
Purpura fulminans secondary to antiphospholipid antibody syndrome

TREATMENT AND COURSE
The patient was anticoagulated with warfarin and bridged with enoxaparin, and her pain was managed with narcotics and gabapentin. Her course has been complicated by poor wound healing and secondary infection with methicillin-resistant *Staphylococcus aureus* and *Pseudomonas aeruginosa*, requiring prolonged systemic antibiotic therapy and repeated wound debridement. In April 2008, she underwent successful split-thickness skin grafting to the lower extremities. She will remain on life-long anticoagulation.

DISCUSSION
Purpura fulminans is a term used to describe the sudden onset of wide-spread retiform purpura with necrosis. This condition classically occurs in the setting of sepsis-induced disseminated intravascular coagulation but has been linked to malignancy, connective tissue disease including antiphospholipid antibody syndrome (APS), and initiation of anticoagulant medications. Purpura fulminans due to infection is most commonly associated with *Meningococcus*, but *Staphylococcus aureus, Streptococcus, Haemophilus influenzae,* and, more recently, *Capnocytophaga canimorsus* have been implicated as causative agents as well. Additionally, post-infectious purpura fulminans has been reported following varicella infection, particularly in children. Warfarin-induced purpura fulminans appears within the first 10 days following initiation of warfarin therapy. In both anticoagulation- and infection-associated presentations, plasma levels of protein C and/or S are believed to fall, resulting in a hypercoagulable state with the propensity to develop thrombotic occlusions of the cutaneous microvasculature.

APS is an acquired hypercoagulable state characterized clinically by multiple thrombotic events and pregnancy complications including fetal loss. A diagnosis of APS may be established by following the Sapporo criteria if at least one clinical and one laboratory criteria are met. Clinical criteria include one or more episodes of venous, arterial, or small vessel thrombosis confirmed by imaging or histology; loss of a normal fetus after 10 weeks gestation; one or more premature births prior to 34 weeks gestation secondary to eclampsia,

preeclampsia, or placental insufficiency; or three or more unexplained losses of an embryo prior to 10 weeks gestation. Laboratory criteria include the presence of antiphospholipid antibodies on two or more occasions at least 12 weeks apart as defined by anticardiolipin IgG and/or IgM antibodies in moderate or high titer, anti-ß2-glycoprotein-I (ß2-GPI) IgG and/or IgM antibodies at a titer >99th percentile for the testing laboratory, or detection of lupus anticoagulant.

The pathogenesis of APS is not definitively understood but likely involves multiple mechanisms including endothelial cell damage and activation, release of prostacyclins, platelet activation, and modulation of protein C and S activity. In recent years, the role of ß2-GPI in preventing coagulation and platelet aggregation and the importance of neutralizing antibodies predisposing to thrombosis in APS has begun to be elucidated, shedding further light on the pathogenesis of this disorder.

In addition to thrombotic events and pregnancy complications, cutaneous manifestations of APS are common but often non-specific. The most frequent findings include livedo reticularis, atrophie blanche, livedoid vasculitis, malignant atrophic papulosis, and anetoderma. The least common but most specific cutaneous lesions of APS are retiform purpura, including the rare presentation of purpura fulminans.

The prognosis of APS can vary widely depending on the organ systems involved and the underlying etiology. However, the risk of secondary infection and extensive scarring in purpura fulminans contributes to significant morbidity and potential mortality in this disorder. The mainstay of treatment in APL is anticoagulant therapy, while treatment options for purpura fulminans are aimed at both the underlying cause as well as reversal of disease progression and range widely to include heparin, protein C, antithrombin III, recombinant tissue plasminogen activator, epoprostenol, dextran, epsilon aminocaproic acid, ketanserin, hirudin, topical nitroglycerine, hyperbaric oxygen, and plasmapheresis. Additionally, adequate pain control, surgical debridement of necrotic tissue, and treatment of secondary infection are also critical aspects in the management of purpura fulminans.

Interestingly, our patient has a history of Grave's disease managed with propylthiouracil. Although exceedingly rare, treatment of Grave's disease with PTU has been associated with transient antiphospholipid antibody formation and the development of purpura fulminans. Whether this was a contributing factor in our patient's presentation is unclear; however the presence of antiphospholipid antibodies in patients with Grave's disease is well documented and inquiry into a history of thyroid disease should be pursued in patients presenting with purpura fulminans due to APS.

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CHICAGO DERMATOLOGICAL SOCIETY **CASE # 12**

Presented by Kathryn Barlow, MD, Eva R. Parker, MD, and Rama Vaitla, MD
Division of Dermatology, Loyola University Medical Center

HISTORY OF PRESENT ILLNESS

This 21-year-old female with a history of renal transplant was admitted with a five-day-history of headache, low-grade fever, photophobia and tender subcutaneous skin nodules. The patient had noted the skin lesions two days after the onset of headache.

PAST MEDICAL HISTORY

End stage renal disease secondary to focal segmental glomerulosclerosis, status-post kidney transplant
Hypertension
Avascular necrosis of bilateral hips, status-post right hip replacement
Anemia

MEDICATIONS

Prednisone
Mycophenolate mofetil
Tacrolimus
Metolazone
Atorvastatin
Ferrous sulfate
Furosemide
Valganciclovir
Sulfamethoxazole/trimethoprim
Metoprolol
Calcitriol

ALLERGIES

Allopurinol
Iodine
Acetaminiophen

FAMILY HISTORY

Noncontributory

SOCIAL HISTORY

Two pack-year smoking history
Occasional alcohol consumption

PHYSICAL EXAM

A firm, tender, 3cm subcutaneous nodule with mild overlying erythema is noted on the left lower abdomen. Similar, 1cm erythematous nodules are located on the right ventral forearm and left dorsal hand.

LABORATORY RESULTS

The following were negative or within normal limits:
Cebrebrospinal fluid (CSF) analysis – cell counts, glucose, protein
CSF culture – negative for growth of bacteria, fungus, and herpes virus.

The following were abnormal:
Creatinine – 3.49 (normal 0.7-1.5)
Blood urea nitrogen – 32 (normal 7-22)
Complete blood count – hemoglobin 8.2 (normal 12-16), hematocrit 24.2 (normal 34-51), white blood cell count 3.4 (normal 4-10)
CSF analysis – cryptococcal titer 1:2
Serum cryptococcal titer – 1:1024
Skin biopsy for tissue culture – few colonies of *Cryptococcus neoformans*

HISTOPATHOLOGY
Skin, punch biopsies, right ventral forearm and left lower abdomen:There is marked acute and chronic inflammation in the deep dermis and subcutis. Within the infiltrate, multiple yeast forms with a surrounding mucoid capsule are noted. Periodic acid-Schiff, Fontana-Masson silver, and mucicarmine stains all demonstrate the organism and its capsule.

DIAGNOSIS
Disseminated cryptococcosis with cutaneous and CNS involvement

TREATMENT AND COURSE
Treatment with oral fluconazole 400mg daily was initiated. Serum cryptococcal titers were followed weekly for the first month of therapy. Titers decreased from 1:1024 to 1:4 during her initial month of treatment and were noted to be negative following a six-month course of treatment. The patient remains in her usual state of health, without recurrence of infection.

DISCUSSION
Cryptococcus neoformans is an encapsulated yeast that is ubiquitous in soil and bird droppings. Humans usually acquire the infection via inhalation with subsequent hematogenous spread, although traumatic direct inoculation has been reported. Skin is the third most common site of dissemination after the central nervous system and respiratory tract. Less frequently, *Cryptococcus* may disseminate to the prostate, eye, bone, and urinary tract.

Immunosuppressed patients are at increased risk, and cryptococcosis has been reported in 2.8% to 5.3% of solid organ transplant recipients. Cryptococcosis is the third most common invasive fungal infection in solid organ transplant recipients after candidiasis and aspergillosis. Clinically, cutaneous cryptococcosis may present with a variety of morphologies. While molluscum-like lesions have been described in HIV-infected patients, other presentations include acneiform papules, purpura, vesicles, abscesses, pustules, ulcers, plaques, draining sinuses, and cellulitis.

Given the vast array of clinical presentations, the definitive diagnosis of cutaneous cryptococcosis can only be established by biopsy for tissue culture and histopathologic examination. Special staining techniques with periodic acid-Schiff, alcian blue, and methenamine silver stains can be helpful in highlighting the organism within the biopsy specimen. Mucicarmine positivity will more precisely differentiate cryptococcosis from other deep fungal infections with similar morphology, namely blastomycosis and histoplasmosis, which are mucicarmine negative. Further supporting the diagnosis are examination and culture of CSF fluid and serum positivity for cryptococcal antigen, which is reportedly positive in 91% of organ transplant recipients with cutaneous disease.

Recommended treatment for patients with limited pulmonary disease, without HIV infection, is a three to six-month course of oral fluconazole. Treatment options for patients with severe pulmonary symptoms and/or disseminated disease with cryptococcal meningitis include amphotericin B with or without 5-flucytosine administered for at least 6 weeks. Despite the presence of disseminated disease, oral fluconazole was chosen over amphotericin B to treat our patient due to concern over exacerbating her declining renal function and pancytopenia.

Prognosis for cryptococcal infections varies depending on the site of involvement. Husain *et al* reported an overall mortality rate of 42% in transplant recipients with *C. neoformans* infection. Specifically, the mortality rate ranged from 21-22% in patients with pulmonary, cutaneous, soft

tissue, and osteoarticular involvement to 49% in those with CNS disease, highlighting the importance of early diagnosis and treatment in organ transplant patients.

We present this case for clinical interest.

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CHICAGO DERMATOLOGICAL SOCIETY **CASE # 13**

Presented by Brian Bonish, MD., Ph.D. and Anthony Peterson, MD
Division of Dermatology, Loyola University Medical Center

HISTORY OF PRESENT ILLNESS

This 35-year-old woman presented with a several year history of slowly growing papules on her face and nodules on her scalp. These lesions interfered with grooming and were occasionally pruritic.

PAST MEDICAL HISTORY

Asthma
Obesity

MEDICATIONS

Albuterol inhaler

ALLERGIES

Fish (Anaphylaxis)
Penicillin (Urticaria)
Morphine (Nausea)

FAMILY HISTORY

Mother with end stage renal disease
Gastric cancer
Obesity, diabetes mellitus, hypertension, depression

SOCIAL HISTORY

The patient denied the use of tobacco, alcohol or illicit drugs.
She is a student and lives with her mother.

PHYSICAL EXAM

The patient exhibits scattered 2-3mm dome-shaped, firm, flesh colored papules on her nose, malar cheeks and upper cutaneous lip as well as multiple, firm, flesh colored 2-8mm papules on her right temple and scalp.

HISTOPATHOLOGY

Skin, punch biopsy, right frontal scalp (2008): There are numerous dermal polygonal tumor nests arranged in a jigsaw pattern surrounded by a thickened hyaline membrane are seen. These nests are composed of two cell types: palisading peripheral cells and central larger, paler staining cells. An adjacent dermal proliferation of “tad pole” shaped nests with central lumen and clear cytoplasm is also seen.

Skin, punch biopsy, anterior scalp, and shave biopsy, left nostril (2006): Multiple nodules are seen in the upper dermis, composed of uniform basaloid cells. The nodules show peripheral palisading and are connected to the epidermis in a fibrous stroma. No clefting is seen.

DIAGNOSIS

Brooke-Spiegler syndrome

TREATMENT AND COURSE

The patient continues to develop new cylindromas and trichoepitheliomas on her cheeks, nose, and scalp. The cylindromas have been treated, when symptomatic, with excision.

DISCUSSION

Brooke-Spiegler syndrome is an uncommon autosomal dominant disorder, in which patients are prone to develop benign appendigeal tumors such as cylindromas, trichoepitheliomas, spiradenomas, trichoblastomas, basal cell carcinomas, follicular cysts, and organoid nevi. Rarely, malignant transformation of the pre-existing tumors has been known to occur. Most commonly, individuals develop cylindromas, trichoepitheliomas, and spiradenomas on the head and neck. Trichoepitheliomas tend to occur on the central face, whereas cylindromas, often found on the scalp, may eventually grow to encompass the entire scalp as a so called "turban" tumor. Cylindromas may also rarely transform into cylindrocarcinomas. In addition, these patients are prone to developing basal cell adenomas and adenocarcinomas of the salivary glands.

Brooke-Spiegler syndrome is caused by mutations in the CYLD gene. The CYLD gene is also associated with familial cylindromatosis and multiple familial trichoepithelioma syndrome. Variation in the location of the mutation in the CYLD gene results in the varied phenotype of Brooke-Spiegler syndrome. CYLD normally functions as a deubiquitinase, removing ubiquitin chains from specific proteins. Following TNF-α stimulation and Toll receptor activation, CYLD removes ubiquitin from signaling proteins in the NF-κB pathway. This results in inhibition of stimulation and decreased activity of NF-κB. Loss of this inhibition in Brooke-Spiegler syndrome leads to decreased cell death and loss of tumor suppression. This pathway is also inhibited by salicylates and prostaglandin A1. Targeted therapy for cylindromas using sodium salicylate and prostaglandin A1 have been tried in the hope of inhibiting NF-κB and restoring normal growth patterns. Unfortunately, this form of treatment neither decreases new tumors nor suppresses tumor growth. Treatment options for the tumors of Brook-Spiegler syndrome include dermabrasion, electrodesiccation, cryotherapy and excision.

We present this patient for clinical interest.

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CHICAGO DERMATOLOGICAL SOCIETY **CASE # 14**

Presented by Kathryn Barlow, MD and Eva R. Parker, MD
Division of Dermatology, Loyola University Medical Center

HISTORY OF PRESENT ILLNESS

This 58-year-old man presented with a two-month history of a worsening eruption on his chest, which subsequently spread to his back. The lesions were associated with pruritus, a burning sensation, and pain. Previous treatment included triamcinolone 0.1% cream without improvement. His review of systems was positive only for fatigue.

PAST MEDICAL HISTORY

Malaria in 1969
Splenic marginal zone B-cell lymphoma with bone marrow involvement diagnosed in 1997, status-post splenectomy followed by fludarabine/mitoxantrone chemotherapy.
Progression of non-Hodgkins B-cell lymphoma with follicular phenotype diagnosed in 2005 status post chemotherapy.
Recurrent, stage 4A follicular lymphoma diagnosed in 2006, treated with two salvage chemotherapy regimens, followed by radiation and autologous stem cell transplant in January 2007.
Laryngeal squamous cell carcinoma in 2008.

MEDICATIONS

Rabeprazole
Folic acid
Multivitamin

ALLERGIES

Rituximab

FAMILY HISTORY

Noncontributory

SOCIAL HISTORY

No alcohol
Previous history of smoking, quit in 1998

PHYSICAL EXAM

Numerous, infiltrative, erythematous nodules, coalescing into plaques are noted extensively over the chest and upper back. Several nodules have a pseudovesicular appearance. There is palpable cervical, supraclavicular, and inguinal lymphadenopathy.

HISTOPATHOLOGY

Skin, punch biopsy, right upper back: There is a dense dermal infiltrate consisting of small lymphocytes. Immunohistochemistry demonstrates positivity for CD-10, CD-20, and bcl-2. Bcl-6 is also positive in a subset of cells.

LABORATORY

The following were negative or within normal limits:
White blood cell count
Platelets
Comprehensive metabolic panel
Lactate dehydrogenase
Cutaneous tissue culture for bacteria, fungus, mycobacteria

The following were abnormal:
Hemoglobin 12.9(normal 14-17)
Hematocrit 38.2 (normal 40-54)

DIAGNOSIS
Stage 4a B-cell follicular lymphoma with secondary lymphoma cutis

TREATMENT AND COURSE
The patient received two cycles of clofarabine followed by 3 cycles of liposomal doxorubicin. A cord-blood allogenic bone marrow transplant was then performed in February 2008. The patient is doing well and remains in clinical remission.

DISCUSSION
The World Health Organization recognizes three main subtypes of lymphoma including Hodgkins, B-cell, and T-cell/natural killer cell types, the latter two falling under the classification of non-Hodgkins lymphoma (NHL). NHL comprises a mixed group of lymphoproliferative neoplasms, of which approximately 80-90% are B-cell lymphomas. Prognostically, NHL can be divided into indolent or aggressive forms. While indolent lymphomas have a better overall prognosis, with median survival of approximately 10 years, cure rates are quite low in advanced stages. On the other hand, aggressive lymphomas have a shorter median survival of 2-5 years but are more responsive to chemotherapy and have higher rates of cure.

Of the approximately 56,000 cases of NHL diagnosed in 2005, 15-20% were follicular lymphoma. The most common presentation is slowly enlarging, painless lymphadenopathy. Several etiologic factors have been implicated, including immune suppression, exposure to chemicals such as pesticides, and acquired chromosomal translocations, particularly t(14;18)(q32;q21), which was present in our patient. This translocation juxtaposes the bcl-2 apoptotic inhibitor oncogene with the immunoglobulin heavy-chain gene, resulting in increased bcl-2 expression and thus conferring a survival benefit to malignant cells by inhibiting apoptosis.

NHL is two to three times more common in Caucasians, with men and women equally affected. Typically, NHL occurs in the seventh decade. In the last forty years, the incidence of NHL has increased dramatically at a rate of 3% per year with an 80% increase since 1973 alone. Many factors are thought to contribute to this rise including improved imaging and biopsy techniques, the use of gene rearrangement and molecular studies to establish clonality in patients who may have otherwise been diagnosed with atypical lymphoid hyperplasia, the aging population, increased use of immunosuppressant drugs, and the HIV/AIDS epidemic.

The occurrence of cutaneous lymphoma without evidence of extracutaneous disease at the time of diagnosis is referred to as ‘primary’ cutaneous lymphoma. In contrast, secondary cutaneous infiltration by NHL, or lymphoma cutis, is a rare phenomenon. Therefore, it is critical to distinguish primary cutaneous follicular cell lymphoma from a secondary cutaneous lymphoma, where a nodal follicular lymphoma has spread to involve the skin. While history and imaging play the primary role in distinguishing the two, immunohistochemistry and cytogenetics of the cutaneous biopsy can serve as a useful tool in separating these entities as primary cutaneous follicular cell lymphoma usually lacks expression of the bcl-2 protein and the t(14;18) translocation, which if present suggests a systemic follicular lymphoma, as demonstrated by our patient.

We present this case for clinical interest.

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CHICAGO DERMATOLOGICAL SOCIETY **CASE # 15**

Presented by Linda Sheu, MD and David Eilers, MD
Division of Dermatology, Loyola University Medical Center

HISTORY OF PRESENT ILLNESS

This 57-year-old man presented with a 10-year history of malodorous, verrucous brownish gray plaques involving the inguinal folds and buttocks. In addition, he reported a forty-year history of scaling and crusting of the scalp, with intermittent flares that increased in frequency during the summer months. At the time of presentation, he had not yet received any treatment.

PAST MEDICAL HISTORY

Coronary artery disease
Arthritis

MEDICATIONS

Metoprolol
Aspirin
Acitretin 25mg daily
Chlorhexidine wash daily
Clobetasol 0.05% ointment twice daily

ALLERGIES

No known drug allergies

FAMILY HISTORY

Patient with two brothers and two sisters. Neither they nor their parents have similar skin findings.

SOCIAL HISTORY

Lives in the extended care facility of Hines VA
Retired truck driver

PHYSICAL EXAM

The buttocks are most markedly affected with malodorous, verrucous gray-brown plaques. On the inferior and superior buccal mucosa are a few scattered flesh colored papules and areas of cobblestoning. The lateral buccal mucosa has lacy white patches. On the temporal and parietal scalp are scattered erythematous, exudative, crusted papules. There are several nails with faint longitudinal erythronychia and mild distal onycholysis. The palms have a few, pink, pinpoint, hyperkeratotic papules. The inguinal folds have erythematous, slightly eroded coalescing papules.

HISTOPATHOLOGY

Right groin, punch biopsy: there is focal acanthosis with focal acantholysis. A superficial mild dermatitis is also present with occasional melanophages. Direct immunoflourescence of IgG, IgM, IgA, C3 and fibrinogen are negative.

DIAGNOSIS

Darier’s disease

TREATMENT AND COURSE

The patient was initially treated with topical chlorhexidine wash and topical clobetasol propionate ointment applied twice daily for two-week periods for many months. Most recently, in mid February 2008, he was started on acitretin 25mg daily. Improvement thus far has been marginal.

DISCUSSION

In 1889, Professor James C. White of Harvard University and French dermatologist Jean Darier independently described a novel skin disease characterized by malodorous, follicular based, brown, crusted papules in seborrheic distribution. Based on histologic abnormalities in the malpighian layer, Darier believed it represented an abnormality in keratinization. Observing the disease in a father and daughter, James C. White reported the hereditary nature of Darier's disease. This disease has come to be known as keratosis follicularis, Darier disease or Darier-White disease.

Classic physical findings in Darier's disease include brown keratotic, often coalescing brown papules in a seborrheic distribution which may progress to malodorous, papillomatous, vegetating growths. Pebbling of the oral mucosa, specifically on the gingiva and palate, may be present. Punctate keratoses involve the palms and soles. Nail involvement may include longitudinal red and white bands, subungual hyperkeratosis, and triangular nicking of the distal nail. Psychosocial consequences from the appearance and odor of the lesions can lead to major morbidity for severely affected patients.

Darier's is an autosomal-dominantly inherited disease with complete penetrance and variable expressivity. Clinical severity varies greatly, even among family members harboring the same mutation. Changes can be subtle and remain unnoticed, or may be severe. Recently, multiple cases of segmental Darier's following Blashko lines have been reported.

The genetic basis for Darier's lies in the mutation of ATP2A2, also known as SERCA2, which normally transports calcium from the cytosol of the cell to the endoplasmic reticulum. This results results in inadequate calcium stores in the endoplasmic reticulum, and disruption of normal calcium regulation. As cell adhesion molecules, including the desmosomal plaque protein desmogleins, desmoplakin I and II, and plakoglobin are regulated by calcium, impairment of cell-to-cell adhesion results in acantholysis. Depletion of calcium in the endoplasmic reticulum is also associated with apoptosis leading to the histologic findings of acantholysis and dyskeratosis that characterize Darier's disease.

Treatment includes topical antimicrobial agents or oral antibiotics, as a potentially serious complication is increased susceptibility to cutaneous bacterial and viral infections, particularly herpes simplex virus and poxvirus infections. Topical keratolytics may also be beneficial. During acute flares, short-term topical corticosteroids or cyclosporine may be used. Acute flares may be prevented in some patient with light, loose fitting clothing and use of topical sunscreens. For localized disease, topical retinoids may be effective. The mainstay of treatment for severe disease is oral retinoids, with improvement in up to 90% of patients.

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CHICAGO DERMATOLOGICAL SOCIETY **CASE # 16**

Presented by Tricia Hultgren, MD and Eva R. Parker, MD
Division of Dermatology, Loyola University Medical Center

HISTORY OF PRESENT ILLNESS

This 55-year-old female with multiple medical problems and an extensive, complicated medical history, including heart transplant with organ rejection, presented for evaluation of a painful plaque on the right forearm that she believes began after the placement of several peripheral intravenous catheters during a hospitalization 2 months prior. Three weeks before presenting to our clinic, attempted aspiration of the lesion yielded minimal fluid that demonstrated no growth on culture. She was treated for presumed cellulitis with levofloxacin and clindamycin followed by vancomycin without improvement, prompting the referral to dermatology in July 2007. She denied fevers and chills but did report several new lesions that had recently appeared on her abdomen.

PAST MEDICAL HISTORY

Coronary artery disease
Congestive heart failure
Heart transplant
Hypertension
Hyperlipidemia
Diabetes mellitus type II
Gastrointestinal reflux
Hypothyroidism
Depression

MEDICATIONS

Cyclosporine
Mycophenolate mofetil
Prednisone
Clonidine
Amlodipine
Bumetanide
Levothyroxine
Valganciclovir
Hydralazine
Gemfibrozil
Atorvastatin
Lansoprazole
Rosiglitazone
Glyburide
Insulin

ALLERGIES

No known drug allergies

FAMILY HISTORY

Non-contributory

SOCIAL HISTORY

Married
Denies tobacco, alcohol, and illicit drug use
No recent travel, pets, or fish tanks

PHYSICAL EXAM

At initial presentation, a 10cm erythematous to violaceous non-scaly, indurated plaque is noted on the right proximal volar forearm. Scattered erythematous, indurated papulonodules are present on the central abdomen.

HISTOPATHOLOGY
Skin, punch biopsy, right proximal volar forearm: There is suppurative and granulomatous dermal inflammation. Periodic acid Schiff and acid fast bacilli stains show elongate bacillary organisms.

LABORATORY DATA
The following were negative or within normal limits:
Bacterial and fungal cultures.

The following were abnormal:
Skin biopsy for tissue culture - positive for growth of *Mycobacterium chelonae*
Blood cultures – negative

DIAGNOSIS
Refractory cutaneous *Mycobacterium chelonae* infection

TREATMENT AND COURSE
The patient's antimicrobial regimen was managed by the Infectious Disease service. She was treated empirically with clarithromycin, linezolid and moxifloxacin until susceptibilities were obtained. She was unable to tolerate clarithromycin secondary to nausea and was discharged on azithromycin, vancomycin and tobramycin. She developed acute renal failure and tobramycin was discontinued. Her symptoms resolved until November 2007 when she developed recurrent painful, draining, erythematous nodules on the right forearm and abdomen. Skin biopsy and tissue cultures again revealed *Mycobacterium chelonae* infection. The therapeutic regimen was then changed to vancomycin, clarithromycin, and ciprofloxacin. Due to failure to improve, treatment with tigecycline and tobramycin was initiated in December 2007. Despite this treatment regimen, she continued to develop new lesions on the arm and abdomen, prompting a third skin biopsy for tissue culture in January 2008. The sample was then sent to National Jewish Hospital in Denver, Colorado for determination of sensitivities, which demonstrated multi-drug resistant *M. chelonae* sensitive only to aminoglycosides and vancomycin. Therapy with vancomycin, tigecycline, and tobramycin was continued with anticipation of long-term treatment. However, her course has been complicated by ongoing cardiac rejection, transplant vasculopathy, renal failure requiring hemodialysis, liver failure, sepsis, cardiogenic shock, respiratory failure secondary to pulmonary infection with stenotrophomonas and aspergillus, and bowel perforation requiring emergent laparotomy with bowel resection. Post-operatively, she was noted to have deteriorating mental status and a CT scan of the head demonstrated a subarachnoid hemorrhage. The choice was made by her family to withdraw care and the patient died on May 20, 2008.

DISCUSSION
Mycobacterium chelonae is a non-tuberculous mycobacterium that is a facultative human pathogen resulting in a variety of infections including cutaneous, soft tissue, bone, ocular, and pulmonary disease. Non-tuberculous mycobacteria are acid-fast, weakly gram positive, nonsporulating, nonmotile rods that are divided into four groups based on pigment production and growth rate, a taxonomic system known as the Runyon Classification. *M. chelonae,* along with *M. abscessus* and *M. fortuitum*, belongs to Runyon group IV and is a non-pigment producing rapid grower widely distributed in soil, dust, and water. Water sources, including tap water, serve as important reservoirs for *M. chelonae* infection. Inoculation occurs via trauma or invasive medical procedures and has been reported following acupuncture, liposuction, augmentation mammoplasty, cardiothoracic surgery, intravenous catheter placement, and dermatologic surgery. Additionally, pedicures have been implicated in recent years as a new source of inoculation in a number of mycobacterial infections.

Soft tissue infection appears several weeks after inoculation and typically presents as an erythematous, infiltrated nodule or plaque with abscess formation and ulceration. Disseminated cutaneous disease may occur in immunocompromised patients. Diagnosis of cutaneous mycobacterial infections is often delayed as swabs from wounds submitted for culture are frequently negative. A recent retrospective chart review by Uslan *et al* reported a median duration of symptoms of 86 days prior to diagnosis of the rapidly growing mycobacterial infection in a cohort of 63 patients. This study highlights the importance of pursing infectious etiologies of cutaneous ulcers and abscesses with tissue culture from either punch or excisional wedge biopsies, since other means of detection may fail to isolate these organisms.

While therapy often consists of a three- to six-month course of systemic antibiotics, treatment guidelines are not clearly established, and no prospective studies have been conducted to compare antimicrobial regimens. Atypical mycobacteria are generally susceptible to macrolides, fluoroquinolones, aminoglycosides, cephalosporins and tetracyclines; however, current guidelines recommend susceptibility testing of all isolates. Clarithromycin has been shown to be effective as monotherapy, but inducible resistance, attributed to a point mutation in the gene coding for 23S rRNA, has been reported and often necessitates the use of multidrug regimens. Despite prolonged courses of antibiotics, surgical excision of the lesions may ultimately be required for effective treatment in some patients.

We present this case today for clinical interest, and to illustrate that patients with resistant mycobacterial infections are often immunocompromised and may present with disseminated cutaneous infection.

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CHICAGO DERMATOLOGICAL SOCIETY **CASE # 17**

Presented by Linda Sheu, MD and Anthony D. Peterson, MD
Division of Dermatology, Loyola University Medical Center

HISTORY OF PRESENT ILLNESS

This 43-year-old HIV-positive male presented to our clinic as a consultation from rheumatology for several, rapidly growing, painful bumps on his arm, penis and thumb. Diagnosed with HIV in 1994, the patient had been on highly active anti-retroviral therapy, and was closely followed by his infectious disease physician. The painful bumps were present for 1 month, had not drained, and besides pain, were asymptomatic. He denied any antecedent trauma as well as any fevers or chills.

In January of 2008 the patient had a toe amputation due to intractable pain from a similar rapidly growing bump, which began in October the previous year. Prior to the amputation an extensive medical evaluation was performed by the Infectious Disease, Podiatry and Vascular Surgery services, which included blood and tissue cultures, plain films, magnetic resonance imaging as well as oral and IV antibiotics (doxycycline, trimethoprim-sulfamethoxazole, vancomycin) for presumed cellulitis/osteomyelitis. Histological evaluation of the amputated digit was notable for chronic inflammation with eosinophils and exuberant granulation tissue. Tissue cultures were notable for few coagulase-negative Staphylococcus aureus species.

PAST MEDICAL HISTORY

HIV / AIDS
Pneumocystis carinii pneumonia
Methicillin-Resistant Staphylococcus Aureus
Molluscum contagiosum
Herpes simplex virus
Hyperlipidemia
Depressive disorder

MEDICATIONS

Abacavir, atazanavir, lamivudine, trimethoprim-sulfamethoxazole

ALLERGIES

Clindamycin

FAMILY HISTORY

Non-contributory

SOCIAL HISTORY

Tobacco (1.5 packs per day for 5 years), marijuana

REVIEW OF SYSTEMS

No nausea, vomiting, fevers, chills, diarrhea, joint pain, weight loss, fatigue, cough, dizziness, weakness, depression, headaches, blood in stool or urine, visual disturbances, decreased appetite.

PHYSICAL EXAM

The patient exhibits two slightly tender, 0.6 cm violaceous papules on the right lateral thumb as well as on the glans penis. A painful, violaceous, 1.6 cm oval plaque is noted on the left volar forearm. A well-healing surgical amputation wound is notable on the left foot at the second metatarsal phalangeal joint.

LABORATORY DATA:

CD4 count: ..... 7.....[415-1852 CMM]
CD4/CD8:..... 0.....[0.7-3.5]
HIV viral load:..... .....337,194 copies/mL

Complete blood count was normal except for the following:
Wbc..... 2.6.....[4.0-10.0]
Hgb ..... 11.2.....[14.0-17.0]
Hct ..... 32.9.....[40.0-54.0]
Lymp ..... 16% .....[20-45%]
Eos..... 25% .....[0-7%]

Complete Metabolic Profile was normal except for the following:
AST ..... 59.....[5-40]
ALT ..... 52.....[10-40]

Imaging:
10/2007 Magnetic Resonance Imaging, left foot:
Subcutaneous edema involving the second toe with focal region of cortical disruption involving the medial cortex of the middle phalanx. No involvement of the proximal interphalangeal joints or distal interphalangeal joints. Impression: Cellulitis with osteomyelitis.

11/2007 X-ray, left foot:
Ill-defined cortical and bony resorption of the middle phalanx of the second toe consistent with osteomyelitis

HISTOPATHOLOGY

Left second toe amputation (1/2008): Digit with marked chronic inflammation including eosinophils and exuberant granulaton tissue. Bone and skin resection margins are viable.

Skin, punch biopsy, left volar forearm (2/2008): An irregular vascular proliferation is seen throughout the dermis. In addition, red blood cells, hemosiderophages and plasma cells are present. The vascular channels are lined by CD34 immunoreactive cells.

DIAGNOSIS

Kaposi's Sarcoma

TREATMENT AND COURSE

The diagnosis of Kaposi's sarcoma on skin biopsy prompted a re-evaluation of the second left toe amputation histology, which also returned consistent with Kaposi's sarcoma. The patient returned two weeks later for suture removal and it was noted that he had developed approximately 20 additional violaceous papules on this face, trunk and extremities. Due to the presence of disseminated cutaneous disease, Oncology was consulted. The patient was started on systemic chemotherapy with liposomal doxorubicin 20mg every three weeks for a total of four cycles. Physical examination four weeks later was notable for significant reduction in the size and tenderness of his lesions. He continues to improve.

DISCUSSION

Kaposi's sarcoma (KS), first described by Moritz Kaposi in 1872, was understood for over a century to be a rare disorder of older men of Eastern European, Mediterranean and Jewish

origin. In 1981, however, the appearance of this tumor became much more commonplace, being seen in young homosexual men as one of the first signs of the AIDS epidemic.

As KS was more commonly observed in gay and bisexual patients with AIDS than in the hemophiliac, heterosexual or pediatric AIDS population, it was initially suspected that KS had an infectious etiology that was sexually transmitted. Early studies of KS tissue found viral DNA sequences homologous, but not identical to, other human herpes viruses. These studies led to the discovery of KS-associated herpesvirus-like (KSHV) which defined a new human herpesvirus now known as HHV-8. HHV-8 is a member of the gammaherpesvirus, along with EBV, which are known to cause lymphoproliferative disorders in humans and animals. KS is caused by an abnormal proliferation of vascular endothelial cells and HHV-8 is detected in greater than 95 percent of lesional tissue irrespective of clinical type (classic, endemic, epidemic/AIDS-associated, immunosuppression-associated). HHV-8 positivity in the blood of HIV+ males predicts development of KS within 2-4 years. The virus encodes proteins homologous to human oncoproteins, as well as a Bcl-2-like protein. These two proteins inhibit the retinoblastoma protein as well as prevent apoptosis in humans. HHV-8 also encodes IL-6 and several chemokines which affect replication, activate angiogenesis, and inhibit the type I helper T-cells responses. Transmission of this virus is considered to be sexual or fecal-oral, with virus found in blood, semen and saliva.

AIDS associated KS appear as slow growing, erythematous to violaceous papules, nodules and plaques with a predilection for the head, neck, trunk and mucous membranes. Up to twenty-five percent of patients have cutaneous involvement alone; however, if untreated, progressive systemic involvement is expected with visceral involvement occurring in more than 70% of patients. Lymphoreticular malignancy risk is 20 times greater and includes malignant lymphoma, leukemia and myeloma. AIDS-related KS is progressive but rarely fatal, with most patients succumbing to AIDS-related opportunistic infections. Improvement of immune status correlates to improvement of KS.

Four clinical subtypes of Kaposi’s, including AIDS-associated KS, are recognized. Classic KS, occurring in Eastern European, Mediterranean and Jewish elderly males, presents as indolent blue-red macules on the lower legs that progress to a multifocal, disseminated pattern. Initial lesions may regress while new ones evolve, resulting in lesions of differing stages. Mouth and gastrointestinal tract involvement may occur and are usually asymptomatic.

Endemic KS, found mainly in Africa, has a variable presentation that can be classified into four subgroups: nodular, florid, infiltrative and lymphadenopathic. While the nodular variant is most similar to classic KS in clinical appearance and course, florid and infiltrative KS are biologically aggressive. The lymphadenopathic variant affects children; primary lesions involve lymph nodes and this variant is often fatal.

Immunosuppresive iatrogenic KS (transplant-associated KS) is clinically similar to classic KS and may resolve completely with withdrawal of immunosuppressive therapy. With prolonged high-dose immunosuppression, KS may become aggressive and result in death due to internal involvement.

Histologic presentation is dependent on the stage of the lesion. Early lesions of patch stage KS demonstrate slit-like vascular spaces formed by a superficial dermal proliferation of vessels often described as jagged or angulated. Protrusion of newly formed vessels into vascular lumen is known as the *promontory sign*. There are scattered lymphocytes and plasma cells. Mature lesions of plaque and nodular stage KS show proliferation of spindle cells with cytologic aytpia and a variable degree of erythrocyte extravasation.

Highly active anti-retroviral therapy (HAART) has decreased the prevalence of AIDS-related KS and patients undergoing therapy present with less aggressive disease and decreased morbidity and mortality. Meanwhile, treatment of KS is limited by high recurrence rates. Topical therapy for local disease includes cryotherapy and laser therapy for thin lesions, excision of solitary lesions and radiation for localized, multifocal KS. The FDA has recently approved alitretinoin (9-cis-retinoic acid) (Panretin), a naturally occurring retinoid, as topical therapy for KS.

Systemic therapy is indicated for the following: development of more than ten new lesions in one month, symptomatic visceral involvement, pulmonary involvement or lymphedema. Anthracycline and paclitaxel are FDA first- and second-line approved monotherapies for advanced KS. Vincristine, doxorubicin and bleomycin are common single agents, but have been also used in combination. The most widely used intralesional therapy is vinblastine. On the horizon are targeted therapies such as aniogiogenesis (VEGF) inhibitors, matrix metalloproteinase (MMP) inhibitors, and tyrosine kinase inhibitors such as platelet derived growth factor (PDGF) inhibitors.

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CHICAGO DERMATOLOGICAL SOCIETY **CASE # 18**

Presented by Brian Bonish, MD, Ph.D., James Swan, MD, and Rama Vaitla, MD
Division of Dermatology, Loyola University Medical Center

HISTORY OF PRESENT ILLNESS

This 14-year-old girl presented with a history of a hypopigmented patch on her right posterior thigh. Her mother stated that this hypopigmentation had been present since age 1. She had been treated in the past with topical steroids, with reported transient improvement in hypopigmentation. The area had never been hyperpigmented or blistered, and the size of the lesion had been stable for the past year in our clinic.

PAST MEDICAL HISTORY

Normal spontaneous vaginal delivery
No developmental abnormalities

MEDICATIONS

None

ALLERGIES

Ibuprofen (angiodema)
Kiwi (pruritus)
Pineapple (pruritus)

FAMILY HISTORY

No family history of pigmentation disorders.

SOCIAL HISTORY

She is a student and lives with her parents.

REVIEW OF SYSTEMS

The patient's review of systems was negative.

PHYSICAL EXAM

The patient is a well developed caucasian female. She exhibits a 1-2 cm wide, linear, hypopigmented, patch on her right posterior leg, thigh and extends to her buttock. There is no significant scale and Wood's lamp reveals a uniform off white accentuation. No bright white accentuation of vitiligo is appreciated.

LABORATORY DATA

Free T4 1.1 ng/ml (normal 0.8-1.7)
Thyroid stimulating hormone (TSH) 2.27 U/ml (normal 0.4-4.4)

HISTOPATHOLOGY

Skin, punch biopsy, right posterior thigh: Intact unremarkable epidermis with normal melanocyte distribution is seen. Normal melanocyte distribution is confirmed by Melan-A, S-100 and CD117 (c-kit receptor) immunostaining. The dermis demonstrates a mild perivascular lymphocytic infiltrate with rare pigment laden macrophages.

DIAGNOSIS

Segmental nevus depigmentosus

DISCUSSION

Nevus depigmentosus is a stable, circumscribed hypomelanosis usually present from birth. The hypomelanosis may take a localized form as a patch with geographic borders, a segmental unilateral linear Blaschko distribution, or rarely a systematized form with whorls and streaks. There is no known pattern of inheritance and the etiology is unknown, but it has been hypothesized to be a local defect in melanosome transfer. In the past there have been reports of associated mental retardation and defects, especially with more generalized lesions. These reports were mainly from the neurology literature and may suffer from referral bias; in the dermatology literature the risk of associated systemic defects is low. A case series from Di Lernia et al. showed only 2 of 20 patients with segmental disease had systemic defects and a series of 67 patients from Lee et al. did not describe any systemic defects.

Kim et al. reported in a study of 60 patients that 30% presented at birth and that an additional 31% presented within the first 3 years of life. Unlike vitiligo and hypomelanosis of Ito, nevus depigmentosus is stable and does not change over time. Patients usually have only a single area affected (45%), although there may be multiple areas. Histology of nevus depigmentosus shows only a slight decrease in melanocytes compared to unaffected skin, as opposed to mature vitiligo which has absent melanocytes. Surface markers for melanocytes are normal.

Reports of treatment of nevus depigmentosus are limited to small case reports. Treatment with 308nm excimer laser has been reported to be effective as have skin grafts. However, there is a report of recurrence of hypopigmentation on the face of a child following skin grafting to treat his nevus depigmentosus.

We present this case for clinical interest.

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CHICAGO DERMATOLOGICAL SOCIETY **CASE # 19**

Presented by Jessica Kappelman, MD and James Swan, MD
Division of Dermatology, Loyola University Medical Center

HISTORY OF PRESENT ILLNESS

This 45-year-old Caucasian male presented with a four month history of a skin lesion in the left axilla. The lesion started as a small, tender papule in the posterior axillary line and gradually increased in size. Initial treatment by a primary care physician included incision and drainage plus a ten-day course of amoxicillin-clavulanate. Bacterial tissue culture was negative at that time. At subsequent visits to an outside dermatologist, the patient was treated with intralesional triamcinolone, topical triamcinolone cream, and fluconazole 100 mg twice weekly for eight weeks. These treatments were not effective and the lesion continued to increase in size. The patient did note significant improvement with his father's oral terbinafine pills, which he took for a total of six days. Review of systems was positive for fatigue, decreased energy, and shortness of breath. He denied any weight loss, fevers, chills, night sweats, chest pain, cough, or abdominal pain.

PAST MEDICAL HISTORY

Basal cell carcinoma, right cheek and left scapula
Squamous cell carcinoma, right preauricular
Hypothyroidism
Testicular cancer status post orchiectomy and chemotherapy

MEDICATIONS

Levothyroxine

ALLERGIES

None

FAMILY HISTORY

Noncontributory

SOCIAL HISTORY

The patient is a resident of Arizona, but had been living in Chicago for the past two months. He is a non-working pharmacist and also worked as a fireman many years ago. Hobbies include scuba diving. He is divorced and has no children. He denies having any pets at home. He denies tobacco or alcohol use.

PHYSICAL EXAM

At the superior posterior axillary line and extending onto the mid back is an erythematous, shiny linear plaque with satellite papules and few small overlying pustules. On adjacent skin is an erythematous eczematous plaque with scale and lichenification.

HISTOPATHOLOGY

Skin, punch biopsy, left axilla: Granulomatous dermal changes with acute and chronic inflammation, including multinucleated giant cells and fungal elements, are seen. PAS-D spores are identified. Fite and AFB stains are negative.

LABS

The following labs were negative or within normal limits:
Liver function panel, fungal smear, complete blood count, comprehensive metabolic panel, human immunodeficiency virus, angiotensin converting enzyme level, qualitative cocci IgM by EIA, lumbar puncture (including coccidioides antibody)

The following labs were abnormal:
Fungal culture (1/07)- *Coccidioides immitus*
Qualitative cocci IgG by EIA (2/07)- positive
Cocci antibody by complement fixation (2/07)- 1:16
Cocci antibody by complement fixation (6/07)- 1:8

RADIOLOGY
Chest X-ray (outside hospital, 11/06)- normal
Chest X-ray (re-read at Loyola, 1/07)- There is a questionable small right mid lung nodule projecting over the anterior right fourth rib.
Chest X-ray (Mayo-Scottsdale, 2/07)- An ill-defined 2.5 cm opacity is present in the right suprahilar region. There is mild prominence of the mediastinum and hilar region bilaterally. There are scattered nodular densities in both lungs.
Whole body bone scan (2/07)- negative
CT scan thorax with IV contrast (Mayo-Scottsdale, 2/07)- There is mild to moderate adenopathy in both hila, the right paratracheal region, the aortic pulmonic window, the subcarinal region, and the posterior mediastinum adjacent to the lower esophagus. There are innumerable small nodules up to 2 mm in size throughout both lungs, more marked in the upper lungs then the lower lungs. The nodules are along the lymphatic spaces. Numerous nonenhancing nodules up to 1.4 cm are seen throughout the spleen.

DIAGNOSIS
Disseminated Coccidioidomycosis

TREATMENT AND COURSE
After a positive culture for *Coccidioides immitus*, the patient was started on itraconazole 200 mg twice daily for one month without any improvement. Due to the patient's subjective improvement with oral terbinafine, a trial of this medication was initiated at 250 mg daily for two weeks before being switched to fluconazole 400 mg daily by the dermatology department at Mayo-Scottsdale. The patient noted resolution of skin lesions approximately one month after initiation of fluconazole. One year later, he continues to take oral fluconazole daily and follows up every 3-4 months with Mayo's valley fever clinic. He has not yet had a follow-up CT scan.

DISCUSSION
Coccidioidomycosis, also known as valley fever, results from inhaling the spores of *Coccidioides* species, most commonly *Coccidioides immitis,* a dimorphic fungus endemic to the southwestern United States, Mexico, and Central and South America. The fungus lives in the soil, and is acquired as a result of soil disturbances, such as earthquakes, dust storms, or heavy rains. There is an estimated 150,000 new cases annually. Of these infections, one-half to two-thirds are subclinical and virtually all are protected from second primary infections. Most cases are limited to the lungs, but symptomatic extrapulmonary disease develops in 1 of 200 people infected with *C. immitis.* The most common sites of extrapulmonary involvement are the meninges, bones, joints, and skin. Widespread miliary dissemination is extremely rare. Risk factors for dissemination include male sex, pregnancy, immunocompromised states, and African or Filipino ancestry.

The most common clinical presentation of coccidioidomycosis is a self-limited acute or subacute community-acquired pneumonia, which becomes evident 1-3 weeks after infection. It is often accompanied by systemic symptoms, such as fever, chills, night sweats, anorexia, weakness, fatigue, cough, sputum production, and chest pain. Disease outside the lung

usually develops within a year after the initial infection. Progressive disease is suggested to be the result of ineffective helper T cells, evidenced by depressed cellular immunity and elevated levels of antibody and IgE in these patients. With disseminated infection, skin involvement may take a variety of forms, although verrucous nodules are the most common. Erythema multiforme, urticaria, morbilliform eruptions, and erythema nodosum have also been reported. Histopathology of early lesions reveals a dense infiltrate of lymphocytes, neutrophils, and plasma cells and numerous spherules. Later lesions are characterized by granulomatous and epithelioid inflammation with giant cells, lymphocytes, and fewer organisms.

Primary cutaneous coccidioidomycosis is extremely rare, and represents approximately 1% of all cases and the least common type of *Coccidioides* infection. Only twenty cases have been reported in the literature. Most cases have been acquired by trauma in endemic areas or laboratory or autopsy inoculation. Cutaneous lesions are characterized by papules, nonhealing ulcers, and verrucous nodules. In 1993, Wilson et al. defined the diagnostic criteria for primary cutaneous coccidioidomycosis, which includes (1) lack of pulmonary symptoms, (2) evidence of traumatic inoculation, (3) incubation period of 2-3 weeks, (4) painless, indurated nodule or plaque with central ulceration, (5) positive coccidioidan skin test, (6) negative complement-fixation test initially with low titers after several weeks, (7) spontaneous healing of the lesions, and (8) regional lymphadenopathy.
Primary cutaneous disease has an excellent prognosis with resolution in 3-10 weeks.

The mainstays of diagnosis are culture and serologic testing. Specific DNA probes applied to culture material are diagnostic. Serologic testing is best performed using experienced laboratories. Use of the mycelial-phase antigen, coccidioidin, is a reliable method for detection of antibody and differentiation of primary disease from disseminated disease. Generally, primary disease is associated with the presence of IgM coccidioidal antibodies early in the course of the disease and undetectable or low titers of IgG later in the disease course. In contrast, disseminated coccidioidomycosis is characterized by the absence of IgM antibodies and the presence of IgG antibodies in high concentrations. Changes in the serum antibody titer reflect the course of the disease and, therefore, predict prognosis. Skin tests to coccidioidal antigens are also available, but less reliable than serologic tests. Anergy is common in progressive disease and a positive test indicates a prior infection of unknown duration.

Management of coccidioidomycosis depends on the extent and location of the infection. As mentioned above, primary cutaneous infection is usually self-limited. Pulmonary disease requires treatment with azole antifungals, such as fluconazole, itraconazole, or ketoconazole. These agents are not currently FDA approved for the treatment of coccidioidomycosis, but provide a safer alternative than amphotericin B and the response rates appear to be similar. Treatment duration should be continued for six or more months after the disease has become inactive. Disseminated disease can also be treated effectively with azole antifungals, but treatment duration is often greater than one year and may sometimes be life long, particularly in immunocompromised patients. Amphotericin B can also be used in addition to azole antifungals, most commonly in patients with respiratory failure secondary to Coccidioidomycosis, rapidly progressive Coccidioidal infections, patients with meningeal disease, and pregnant women. Management should routinely include repeat patient encounters every 3-6 months for two years, as well as radiologic documentation of disease resolution. It is important to note that the cost of antifungal medication can be as high as $20,000 per year. Current studies are examining the use of purified antigens as vaccines that will be well tolerated and effective.

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CHICAGO DERMATOLOGICAL SOCIETY **CASE # 20**

Presented by Toral Patel, MD and Stacy McClure, MD
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HISTORY OF PRESENT ILLNESS

This 32-year-old female presented in October 2007 with a six year history of a brown patch on the left palm. The lesion had not grown in size, and was not painful or pruritic. The patient first noticed the lesion while she was traveling in Thailand. She had not had any treatment for the lesion at the time of presentation.

PAST MEDICAL HISTORY

Migraine headaches
Endometriosis

MEDICATIONS

Ketorolac
Promethazine
Rizatriptan
Multi-vitamin

ALLERGIES

Sulfa, meperidine, danazol

FAMILY HISTORY

Paternal grandfather- melanoma
Maternal grandfather- basal cell carcinoma

SOCIAL HISTORY

The patient is married and works as a massage therapist. She has a previous history of tobacco use. She denies use of alcohol or illicit drugs.

PHYSICAL EXAM

The patient is a well developed well nourished Caucasian female who is alert and oriented and in no acute distress.
There is a 3 centimeter square-shaped discrete uniform tan patch on the left palm without visible scaling.

KOH

Positive for hyphal forms

DIAGNOSIS

Tinea nigra

TREATMENT AND COURSE

The patient was started on ciclopirox gel twice daily. Initial improvement of the lesion was noted in two weeks, and complete clearance was seen in six weeks. She is currently in good health.

DISCUSSION

Tinea nigra is an uncommon superficial mycosis, most commonly caused by Hortaea werneckii (formerly known as Exophiala werneckii). Other fungi (such as Stenella araguata)

may also be associated with tinea nigra, although much more rarely. The disease is seen most frequently in warm, humid climates, such as Central and South America, Asia, Africa, and the Caribbean. It has also been reported in the United States, primarily in Florida, Texas, and North Carolina. The condition occurs mainly in children and young adults, and females are affected more often than males.

Tinea nigra presents as an asymptomatic brown or black nonscaly patch, usually on the palms, and less commonly on the feet. The lesions slowly enlarge and darken in color over weeks to months.

Hortaea werneckii is a dematiaceous fungus that is ubiquitous; it is found in soil, sewage, on wood and even on clinically normal appearing skin. Inoculation due to minor trauma is thought to be the inciting event in most cases. Hyperhidrosis may be a risk factor in the development of tinea nigra.

The lesions of tinea nigra are often mistaken for junctional nevi or even melanoma; a potassium hydroxide scraping is a fast and easy method of establishing the diagnosis. Culture on Sabouraud's agar produces moist, shiny black colonies. The pigmentary changes seen on the skin are due to the accumulation of a melanin-like substance in the fungus.

Topical antifungals remain the mainstay of treatment for tinea nigra; agents from the imidazole family (ketoconazole, econazole, etc.) are considered to be the most effective. weeks. Topical keratolytics have also been used with success. Complete resolution is generally seen within two to three weeks of treatment.

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