Chicago Dermatological Society

March 2011
Monthly Educational Conference

Program Information
Continuing Medical Education Certification
and
Case Presentations

Wednesday, March 2, 2011
Stroger/Cook County Hospital
Sidney Barsky Lecture

Conference Host:
Division of Dermatology
Stroger Cook County Hospital
Chicago, Illinois

Program

Conference Locations

Stroger Cook County Hospital; 1900 W. Polk, Chicago
Main hospital – entrance corner of Ogden & Damen or through the CCH parking garage
Hektoen Institute – 627 S. Wood St.

Parking:
Cook County Hospital Garage: entrance on Polk St.
Alternate Parking: Rush Medical Center - Harrison just west of Ashland

Registration Table – beginning at 8:00 a.m.
Lobby area of the Hektoen Institute; 627 S. Wood
Protocol books will be distributed at patient viewing until 10:30 a.m. Registration will be located at the Hektoen Institute only.

Program Events

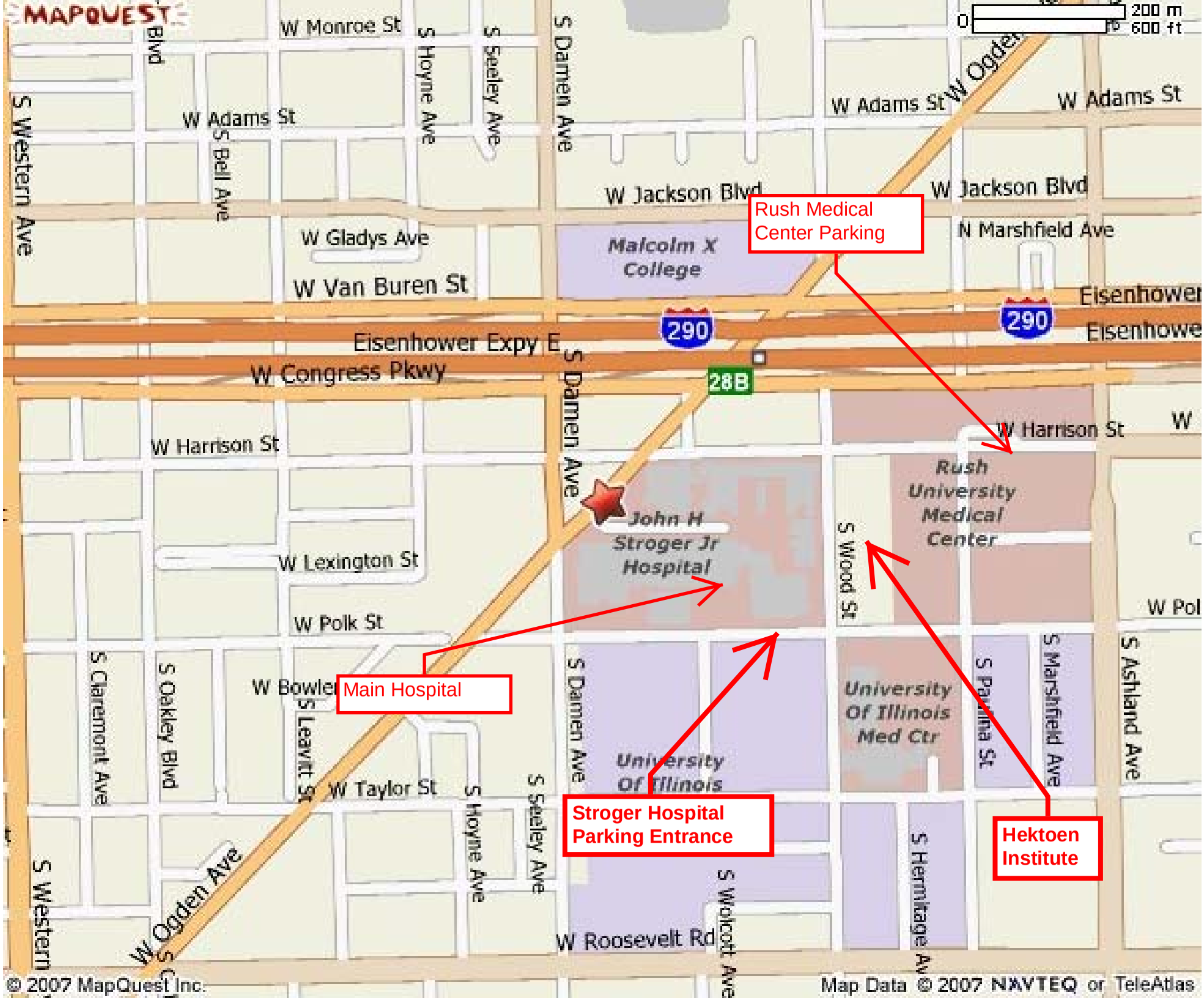
8:00 a.m.	Registration Opens for All Attendees *Hektoen Institute, 1st floor lobby*
9:00 a.m. - 10:00 a.m.	**Resident Lecture** – *Hektoen Auditorium* "I'm Itching to Tell You About Pruritus" *Timothy Berger, MD*
9:30 a.m. - 10:45 a.m.	**Clinical Rounds** Patient & Slide Viewing *Dermatology Clinic "G", 2nd floor, main hospital; use elevator #1*
11:00 a.m. - 12:15 p.m.	**General Session** - *Hektoen Auditorium* BARSKY LECTURE: "Dermatoimmunology for the Practicing Dermatologist" *Timothy Berger, MD*
12:15 p.m. - 12:45 p.m.	Box Lunches & visit with exhibitors *Hektoen Institute Lobby*
12:45 p.m. - 1:00 p.m.	**CDS Business meeting** – *Hektoen Auditorium*
1:00 p.m. - 2:30 p.m.	**Case Discussions** – *Hektoen Auditorium*
2:30 p.m.	**Meeting adjourns**

Mark the Date!

Next CDS monthly meeting – Wednesday, April 13, 2011 at the Stephens Convention Center in Rosemont

May Monthly Conference – Wednesday, May 11, 2011 at the Stephens Convention Center
Note new date and location!!! Hosted by Rush University with guest speaker Richard Edelson, MD

Watch for details on the CDS website: www.ChicagoDerm.org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Main Hospital
Stroger Hospital Parking Entrance
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Guest Speaker

TIMOTHY G. BERGER, MD
Professor of Clinical Dermatology
School of Medicine,
University of California - San Francisco

Delivering the Sidney Barsky Lecture

Dr. Berger specializes in complex dermatology and also treats patients with autoimmune bullous disease, viral skin disease, sexually transmitted disease of the skin, and tropical diseases, among others. He has lectured extensively nationally and internationally, and also has been deeply involved in implementing web-based teaching at UCSF.

Dr. Berger earned his medical degree at Southwestern Medical School, University of Texas Health Science Center in Dallas. He completed a residency in dermatology at Letterman Army Medical Center in San Francisco, as well as a fellowship in dermatopathology at the Armed Forces Institute of Pathology. As executive vice chair of the UCSF Department of Dermatology, Dr. Berger oversees all clinical activities in the UCSF dermatology clinics which have more than 53,000 annual patient visits.

CME Financial Disclosure: Dr. Berger has no significant financial relationships to disclose.

Continuing Education Credit

Chicago Dermatological Society

"Chicago Dermatological Society Monthly Conference"

March 2, 2011 *Chicago, IL*

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

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

Link address to evaluation form:
http://www.yourcesource.com/eval/?act=496!03022011

JOINT SPONSOR STATEMENT

This Continuing Educational activity is Joint-sponsored by the **Colorado Foundation for Medical Care, Office of Continuing Education** and the **Chicago Dermatological Society**. **CFMC is accredited by the ACCME to provide continuing medical education for physicians.**

GOAL / PURPOSE

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

SESSION OBJECTIVES

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

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

- Describe the primary autoimmune diseases likely to be encountered by a dermatologist.
- List the key factors leading to an accurate diagnoses with respect to autoimmune bullous disease.

- Discuss how a dermatologist can best incorporate complex diagnostic skills into his/her practice in order to better identify and treat patients with autoimmune conditions.

CREDIT STATEMENTS

CME CREDIT

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

Colorado Foundation for Medical Care designates this educational activity for a maximum of **4 *AMA PRA Category 1 Credits™*.** Physicians should only claim credit commensurate with the extent of their participation in the activity.

CFMC has no financial responsibility for this activity.

OTHER HEALTH CARE PROFESSIONALS

This educational activity has been planned and implemented following the administrative and educational design criteria required for certification of health care professions continuing education credits. Registrants attending this activity may submit their certificate along with a copy of the course content to their professional organizations or state licensing agencies for recognition for 4 hours.

DISCLOSURE STATEMENTS

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

**We extend our sincere thanks to
Dr. Darryl Bronson and Dr. Jesse Jiang
for their review of the histopathology
from these cases.**

CHICAGO DERMATOLOGIC SOCIETY

Key location(s): Right lower extremity **CASE 1**

Presented by Hal Weitzbuch, MS, MD; Anjeli K. Isaac, MD; and George Engel, MD

Unknown #1

61 year old Pakistani man with a mass on his right lower extremity for 1.5 years

Key location(s): Lips, medial canthi, conjunctivae, areolae, penis, buttocks **CASE 2**

Presented by August A. Natalie, MD; Joerg Albrecht, MD; and Warren Piette, MD

History of Present Illness

25 year old Hispanic male, who recently emigrated from Mexico to the United States three months prior, presented with complaints of painful oral erosions and a rash involving his areolae, penis, buttocks, perianal skin and anal mucosa. The skin changes had been present for 2.5 months. He was unable to eat or drink due to oral pain. He noted ocular discomfort, with frequent tearing and blinking. An abdominal CT scan revealed a large right lower quadrant mass measuring 5cm x 5cm x 9.7cm, and a bone scan was negative for metastases. A biopsy of a buttock lesion was taken, and he was started on oral steroids. His care was then transferred to our hospital.

Past Medical History

None

Medications/Allergies

None/NKDA

Social History

Carpenter; occasional tobacco use; drinks socially 2-3 drinks/week; no drug use

Physical Exam

Skin: Both lips with thick eschar crusting with erosions and fibrin deposition; mucopurulent discharge on medial canthi of eyes, pink conjunctivae, anicteric sclerae; tongue erosions; areolae and penis with hyperkeratotic grayish plaques; buttocks and perianal area with erosions, crusting, and fibrin deposition

Laboratory Data

The following labs were abnormal:

Phosphorus	5.0 mg/dL	[2.5 – 4.5 mg/dL]
Albumin	3.7 g/dL	[3.8 – 5.2 g/dL]
ALT	71 U/L	[5 – 35 U/L]
WBC	11.0 k/µL	[4.4 – 10.6 k/µL]
Neutrophil %	89.5 %	[45.3 – 74.5 %]
Lymphocytes %	5.5 %	[18.1 – 43.2 %]

The following labs were normal: Na, K, Cl, HCO3, BUN, Cr, Glucose, Mg, Uric acid, Total Protein, Total Bili, Direct Bili, Alk Phos, AST, LDH, Hgb, Hct, Plt, PT, PTT, HIV 1/2 Ab

Histopathology

1. SKIN

A. RIGHT BUTTOCK, PUNCH BIOPSY:

Hyperkeratosis, slight papillomatosis, focal hypergranulosis and irregular acanthosis. The underlying superficial dermis has a perivascular and lichenoid infiltrate of lymphocytes and melanophages. The infiltrate obscures the dermal epidermal junction in foci. Scattered dyskeratotic keratinocytes are seen at the dermal epidermal interface and at higher levels of the epidermis.

B. RIGHT BUTTOCK, PUNCH BIOPSY:

DIF positive for basement membrane zone IgG, C3, and fibrin. No intercellular staining seen.

2. RETROPERITONEAL MASS, BIOPSY:
Castleman's disease, unicentric, mixed variant.

Sections demonstrate a lymphoid mass with two adjacent small normal lymph nodes. The mass shows multiple widely separated lymphoid follicles with regressed germinal centers and thickened mantle zones. Some of the germinal centers have markedly dysplastic follicular dendritic cells. The paracortex is expanded and shows increased vasculature, numerous plasma cells, small lymphocytes, spindle cells, and dysplastic follicular dendritic cells. Stains for mycobacteria (AFB) and fungi (GMS) were negative.

Immunohistochemical stains (CD20, CD3, CD79a, CD21, CD10, clusterin, CD4, CD8, HHV8, CD23, SMA, EGFR, and kappa and lambda light chains) and EBER were performed at the NIH. CD20 and CD3 show normal distribution of B-cells and T-cells. Kappa and lambda light chains stains show polyclonal plasmacytosis in the interfollicular areas. HHV8 and EBER are negative. The dysplastic follicular dendritic cells in the germinal centers and the intrafollicular areas are highlighted by EGFR.

The case shows features of stroma-rich variant of Castleman's disease of hyaline-vascular type with proliferation of follicular dendritic cells in the interfollicular areas. However, with the large numbers of plasma cells in the paracortex, we favor a mixed variant of Castleman's disease comprising features of both hyaline-vascular and plasma cell rich subtypes.

Cytogenetic studies were attempted on a portion of the mass at Rush Medical Center. Only six (6) mitotic cells were recovered from a single 24 hr unstimulated lymphocyte culture. These cells contained a 46,XY normal male karyotype. No consistent numerical or structural abnormality was observed, and there was no demonstrable clinically significant abnormality.

Diagnosis
Unicentric Castleman's disease complicated by paraneoplastic pemphigus

Treatment and Course
This unfortunate 25 year old Hispanic man was transferred to our hospital for diagnosis and management. He underwent an exploratory laparotomy with plans for excision of the abdominal mass. The surgery was complicated by extensive bleeding and a repair of the inferior vena cava was emergently performed. Excision of the mass was terminated and a biopsy was taken. The abdominal mass pathology was sent to the NIH for evaluation. He was ultimately diagnosed with the unicentric, mixed variant of Castleman's disease and paraneoplastic pemphigus (PnP). His hospital course was complicated by bilateral lower extremity DVTs, requiring lifelong treatment with subcutaneous low molecular weight heparin. Bone marrow biopsy revealed slightly hypocellular marrow with no atypical infiltrate. He was initially discharged on prednisone 60mg daily, pantoprazole, calcium and vitamin D, and triamcinolone cream. As an outpatient, he was treated with CHOP chemotherapy; however, it was stopped after 3 of 6 sessions due to sepsis. He received a total of five doses of rituximab. He received 3420 cGy to the abdomen in 19 fractions over a period of 31 calendar days and an abdominal boost of 1080 cGy in 6 fractions over a period of 8 calendar days. He has been admitted four times over the last year, all for respiratory distress, and intubated four times. During the last admission, he received a tracheostomy after failing to wean from the ventilator. His tumultuous course has been complicated by esophageal candidiasis, pneumococcal and MSSA pneumonia, VRE colonization, necrotizing cavitary Aspergillus pneumonia, and a culture negative febrile pneumonia only responsive to antituberculous therapy. Outpatient PFTs showed severe obstructive disease and multiple CT scans have shown bronchiectasis and tracheo-bronchomalacia with no evidence to date, clinically or radiologically, of cryptogenic organizing pneumonia. His lung disease worsened with steroid tapering, and this directly led to his second hospitalization and intubation. His skin involvement cleared early after prednisone initiation and

healed with post-inflammatory hyperpigmentation. The oral mucosa was less responsive, always waxing and waning in severity. He used topical oral clobetasol, a stomatitis cocktail, and oral opiates in order to tolerate eating. After his last hospitalization, he was transferred to a nearby long term acute care (LTAC) hospital due to his continuous ventilator requirement. He was never able to wean from the ventilator. After two months in the LTAC and 13 months from his initial diagnosis, he died of respiratory failure and sepsis.

Discussion

The most characteristic clinical feature of PnP is intractable, painful stomatitis affecting the entire oral cavity and the lips. It is usually the first symptom and quite treatment resistant. Conjunctival involvement is present in approximately two thirds of patients. Anogenital involvement and esophageal erosions can also be present. Skin lesions are polymorphic. Descriptions have varied from erythematous macules, lichenoid lesions, erythema multiforme-like lesions, erosions, and flaccid bullae.

Histologically, an interface dermatitis that resembles erythema multiforme or lichen planus is present with basal layer keratinocyte apoptosis and suprabasal acantholysis. Acantholysis may be focal, or not present, as in our case. Direct IF usually reveals intercellular IgG and C3 and basement membrane zone IgG and C3, occasionally IgM. Indirect IF is almost invariably positive for intercellular IgG. 25% of cases may have a negative direct or indirect IF study. Negative direct IF leads to delay in diagnosis. Multiple combinations of IF and immunoprecipitation results have been reported. Antigens identified include plectin, desmoplakin 1 and 2, BP antigen 1, envoplakin, periplakin, desmoglein 1 and 3, and an unknown 170-kDa protein. Of note, it has yet to be determined whether the best site for DIF testing is lesional or perilesional skin.

Mortality has approached 90 percent in many studies. The major complications of PnP include direct involvement of the tracheobronchial tree, which can lead to obstructive respiratory failure and death. Patients with PnP secondary to Castleman's disease have a particular association with developing cryptogenic organizing pneumonia. Therefore, all respiratory complaints should be aggressively pursued in this population. In a 2003 retrospective study of Castleman's disease and PnP, only two of 28 patients had no apparent pulmonary symptoms throughout their illness, 22 died of respiratory failure, and four were still alive but with severe pulmonary disease and an uncertain prognosis. In PnP due to other tumors, causes of death have included respiratory failure, sepsis, gastrointestinal bleeding and multiorgan failure.

Seventy five percent of patients are known to have cancer at the time of diagnosis. The most common associations are with non-Hodgkin's lymphoma, chronic lymphocytic leukemia, Castleman's disease and less commonly thymoma and retroperitoneal sarcomas. In patients younger than 20 years of age, Castleman's disease is essentially the only disorder associated with PnP. Treatment of the cancer is not always associated with skin improvement. Rituximab has showed some promise in treating these patients.

References

1. Ahmed AR, Avram MM, Duncan LM. Case 23-2003 - A 79-Year-Old Woman with Gastric Lymphoma and Erosive Mucosal and Cutaneous Lesions. N Engl J Med 2003;349:382-91.
2. Barnadas MA, Curell R, Alomar A, Gelpi C. Paraneoplastic pemphigus with negative direct immunofluorescence in epidermis or mucosa but positive findings in adnexal structures. J Cutan Pathol 2009; 36:34-8.
3. Nikolskaia OV, Nousari CH, Anhalt GJ. Paraneoplastic pemphigus in association with Castleman's disease. Br J Dermatol 2003; 149:1143-51.

Key location(s): Left upper extremity **CASE 3**

Presented by Jordan Carqueville, MD and Jerry Feldman, MD

History of Present Illness
58 year old Hispanic man presented with a large, tender and malodorous mass on his dorsal left arm that had been growing for 1.5 years. He stated that the lesion grew quickly, and often bled with minor trauma. The patient denied any prior trauma or chronic inflammation to the region. The patient lives in Chicago and had no recent travel.

Past Medical History
Tobacco abuse (twenty pack year smoking history, currently smokes 1 pack per week)

Medications/Allergies
None/NKDA

Review of Systems
Denied fevers, chills, cough, night sweats, weight loss, shortness of breath

Physical Exam
Lymph: No axillary lymphadenopathy
Skin: Left dorsal distal arm with 5cm x 6cm x 3cm cauliflower-like, exophytic mass with overlying yellow-brown crust; malodorous and macerated scale present within the crypts of the mass

Laboratory Data
The following were normal: CBC with differential, BMP

Histopathology
LEFT DORSAL FOREARM, PUNCH BIOPSY:
Verrucous epidermal hyperplasia with areas of atypia extending into the subcutaneous tissue. There were large keratinocytes with eosinophilic cytoplasm, nuclear enlargement, and scattered mitotic figures present at the base. No perineural or lymph-vascular invasion was present. Special stains for fungi were negative.

Microbiology
LEFT DORSAL FOREARM, TISSUE CULTURE:
Candida albicans 1+

Radiology
Chest radiograph: No active lung disease

Diagnosis
Verrucous carcinoma

Treatment and Course
The patient was treated with wide local excision to the affected area on the left forearm with a full thickness skin graft from the left shoulder. There was no residual tumor remaining histologically. The patient tolerated the procedure well and has had no further complications or recurrence of the carcinoma.

Discussion
In the late 19th century, Buschke and Lowenstein first described this entity in the anogenital region as a "carcinoma-like condyloma acuminata." In 1948, Lauren Ackerman originated the

clinicopathologic term, verrucous carcinoma, demonstrating similar lesions in the oral cavity of 31 patients. Aird et al. later described it occurring on non-mucosal skin in 1952 as epithelioma cuniculatum. 'Cuniculatum' is the Latin word for 'rabbit warren' and was used to describe the keratin-filled crypts and foul smelling, debris-filled sinuses akin to rabbit burrows. Four types have been distinguished based upon anatomical location: (a) verrucous carcinoma of the oral cavity, also known as Ackerman carcinoma or oral florid papillomatosis; (b) verrucous carcinoma of the anogenital region, also known as giant condyloma of Buschke and Lowenstein; (c) verrucous carcinoma occurring on the soles, also known as epithelioma cuniculatum; and (d) verrucous carcinoma occurring in other sites, as it may potentially arise on any area of the skin. Compared to oral, anogenital, and palmoplantar verrucous carcinomas, cutaneous verrucous carcinomas occurring elsewhere on the skin is especially rare. We describe verrucous carcinoma of the skin occurring on the dorsal forearm.

Verrucous carcinoma is characterized by slow, locally invasive growth with a low incidence of metastases. It typically manifests as a persistently enlarging, exophytic mass rather than as an endophytic tumor. It is usually well-circumscribed, and when found on non-mucosal skin, is often on the lower extremity. The etiology of verrucous carcinoma of the skin is unclear. It may be associated with areas of chronic inflammation, such as ulcers or in areas of previous injuries, such as scars. Most squamous cell carcinomas that develop within scars, i.e., Marjolin's ulcer, are not verrucous carcinoma and have a high metastatic potential. Tobacco is a risk factor for oral florid papillomatosis. Human papilloma virus likely plays a role in verrucous carcinoma, and has been found consistently in oral and anogenital verrucous carcinoma. In cutaneous verrucous carcinoma, various strains of HPV DNA have been identified in case reports, but this is not consistent among all studies.

The clinical differential diagnosis includes reactive epidermal hyperplasia (including deep fungal infections), giant verruca vulgaris, pyoderma vegetans, giant keratoacanthoma, and verrucous squamous carcinoma. The histologic differential includes typical squamous cell carcinoma, verruca vulgaris, keratoacanthoma and pseudoepitheliomatous hyperplasia. Small, superficial punch biopsies are often misleading, and tissue sections including the basal layer are needed for proper diagnosis.

Treatment of choice for verrucous carcinoma is complete surgical excision. Mohs micrographic surgery may be indicated when tissue sparing is of primary importance. If surgery is not possible because of the patient's age or condition, imiquimod with or without laser ablation may be considered. Retinoids may be of value for some patients. Radiation therapy is not recommended given risk for anaplastic transformation, although this is controversial. Sentinel lymph node biopsy may be indicated if there is a history of radiation and clinically unsuspicious regional lymph nodes. If there is clinical or sonographic suspicion of lymph node metastases, regional dissection of the nodes is recommended. Furthermore, this well-differentiated squamous cell carcinoma does have potential to invade neighboring structures. If there is suspicion of bone invasion, X-rays or CT scans should be obtained, as amputation may be necessary. Morbidity is mostly secondary to local skin and soft tissue destruction and rarely from perineural, muscle or bone invasion.

References

1. Assaf C, Steinhoff M, Petrov I. Verrucous carcinoma of the axilla: case report and review. J Cutan Pathol 2004; 31:199-204.
2. Ackerman LV. Verrucous carcinoma of the oral cavity. Surgery 1948; 23:670-8.
3. Koch H, Kowatsch E, Hödl S, Smola MG, Radl R, Hofmann T, Scharnagl E. Verrucous carcinoma of the skin: long-term follow-up results following surgical therapy. Dermatol Surg.2004; 30(8):1124-30.
4. Schwartz RA. Verrucous carcinoma of the skin and mucosa. J Am Acad Dermatol 1995; 32: 1.

Key location(s): Forehead, left hand **CASE 4**

Presented by Julia M. Kasprzak, MD and Warren Piette, MD

Unknown #2

35 year old male with HIV/AIDS and a one month history of intermittent fevers, right throat mass odynophagia, neck pain and a rash

Key location(s): Chest, upper extremities **CASE 5**

Presented by Michelle Chevalier, MD and Warren Piette, MD

History of Present Illness

45 year-old Caucasian male who presented with a three year history of a recurrent, pruritic rash of his arms, chest, and back following any sun exposure. He noted almost immediate (within 5 minutes) diffuse redness of sun-exposed areas, sparing his face. He admitted to associated pruritus/burning, throat tightness, and minor respiratory difficulty during these episodes. All systemic symptoms resolved within five minutes of withdrawal to the shade, with rash resolution within one hour. Although the patient has lived in Chicago for more than twenty years, he had grown up in California and had spent much of his life in the sun.

Past Medical History

Hyperthyroidism (diagnosed 3 months prior to initial evaluation)
Gastritis

Medication/Allergies

Methimazole (started ~ 2 months prior to initial presentation)
NKDA

Social History

Patient has worked in a paper factory x 20 years; father with eczema

Review of Systems

The patient admitted to frequent postprandial abdominal pain. He also had symptoms associated with the skin eruption as noted above.

Physical Exam

Vitals: Normal

Skin: On initial evaluation, the patient had no cutaneous findings; the patient then insisted on standing in front of the window, at which point he developed a diffuse erythema of his arms and chest in a V-neck T-shirt pattern (distal arms, V-neck area of chest, and face were completely spared) within 4 minutes of sun exposure; at a subsequent visit, similar cutaneous findings were elicited with associated symptoms of pruritus (at 2.5 minutes post initial sun exposure) and burning (3.5 minutes); shortly thereafter, the patient reported profound skin sensitivity, light-headedness, and nausea; at this point the patient was quickly removed from the window, with gradual resolution of his symptoms over the next 30 minutes

Laboratory Data

The following were normal:
CMP, CBC, CRP, TFTs, ANA, RF, Centromere Ab, Microsomal Ab, Thyroglobulin Ab, RPR, HIV

Radiology

EGD (12/2009): antral gastritis
Colonoscopy (1/2010): normal
Chest radiograph (2/2010): normal
CT chest/abdomen/pelvis without contrast (5/2010): degenerative disc disease in thoracic spine; 1.7cm x 1.7cm soft tissue nodule in pancreaticoduodenal groove
EGD (6/2010): normal
CT scan of abdomen with contrast (6/2010): 1cm gastric polypoid lesion; normal pancreas

Diagnosis
Solar urticaria

Treatment and Course
The patient was initially started on hydroxyzine 25mg daily. He was advised on daily broad-spectrum sunscreen use as well as sun-protective clothing. After 3 weeks, he noted excessive drowsiness and no improvement of symptoms with sun exposure. He was subsequently switched to cetirizine 10mg twice daily. Fexofenadine 180mg daily was eventually added to his regimen. The efficacy of this regimen is largely unknown as the patient avoids sun exposure given a fear of severe symptoms. The patient continues to be symptomatic when off his medication regimen (as elicited in our clinic).

Discussion
Solar urticaria is a rare disease characterized by dramatic sensitivity to ultraviolet radiation or visible light, usually presenting in the fourth or fifth decade of life. Affected patients typically present with a report of erythema or urticarial lesions at sun-exposed sites which erupt almost immediately following any exposure. Common associated symptoms include pruritus or a burning sensation at the site of eruption. In rare cases, anaphylactoid reactions may occur, including light-headedness, nausea, angioedema, bronchospasm, and syncope. Characteristically, the skin lesions and associated symptoms resolve within twenty-four hours. The action spectrum varies for each patient, but usually falls between 300 and 500nm (visible: 380-700nm; UVA: 320-400nm; UVB: 280-320nm). Over time, the patient's disease may evolve and they may display sensitivity to different spectra. Patients may also experience reduced sensitivity at frequently exposed sites, a phenomenon known as "hardening". Atopic dermatitis is an associated disorder in 20-50% of cases.

The pathogenesis of solar urticaria has not been fully characterized; however, it is thought to be consistent with other forms of urticaria. IgE-mediated mast cell degranulation likely occurs in response to a photo-induced or other unknown allergen. Radiant energy may also be capable of direct mast cell degranulation.

The diagnosis of solar urticaria may be made in the clinic with exposure to natural sunlight, as in our patient. The patient's particular action spectrum and minimal erythema/urticarial dose may also be determined using artificial UVB, UVA, and visible light sources (slide projector or monochromator). Response to therapy may then be determined by subsequent provocation and minimal erythema dose measurement.

Important differential diagnoses include heat urticaria, erythropoietic protoporphyria, and polymorphous light eruption (PMLE). Heat urticaria can be ruled out with use of a water filter in front of a visible light source. Erythropoietic protoporphyria will have an abnormal porphyrin profile and is characteristically painful with subsequent scar formation. PMLE often develops only after hours of sun exposure and usually persists for days. The diagnosis may also be complicated by the fact that up to one-quarter of solar urticaria patients also have PMLE or another photodermatosis.

Treatment of solar urticaria usually starts with a trial of second-generation H_1-receptor antagonists. The patient should also be advised on photoprotective strategies including broad-spectrum high-SPF sunscreen and sun-protective clothing. It is important to note that traditional sunscreen formulations usually do not protect against UVA and visible light, limiting their effectiveness in many patients. Faurschou and Wulf have reported that antihistamines and sunscreen act synergistically. Sunscreen was shown to increase the threshold for erythema, while antihistamines suppressed the urticarial reaction. Grundmann et al. report improved symptoms and reduced photoprovocation in four patients with aggressive high-dose combination anti-histamine treatment. Patients may also benefit from graduated exposure to

UVA or UVB which may be accomplished by natural sun exposure or by controlled light therapy. A "rush" hardening technique has also been described, allowing for desensitization in three days. Unfortunately, tolerance is typically lost if light treatments are not continued every few days. Other treatment modalities that may be tried in resistant cases include antimalarials, cyclosporine, plasmapheresis, and intravenous immunoglobulin (IVIg). Hughes et al. reported long-term remission (13 months, 4 years) of two patients treated with several courses of IVIg. Recently, there have been two reports of refractory disease resolution/partial improvement after treatment with omalizumab, a recombinant humanized monoclonal antibody against IgE. Although symptoms of solar urticaria may be improved with treatment, the disease is rarely cured. The natural history of this disease is one of persistence, with only 36% resolution noted at 15 years post-diagnosis.

References

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7. Waibel KH, Reese DA, Hamilton RG, et al. Partial improvement of solar urticaria after omalizumab. J Allergy Clin Immunol 2010;125(2):490-491.

Key Location(s): **Patient A – Trunk** **CASE 6**
Patient B – Trunk

Presented by Hal Weitzbuch, MS, MD and Anjeli K. Isaac, MD

Patient A

History of Present Illness

38 year old Hispanic man was diagnosed with psoriasis by an outside provider in 1996. Previous treatments included various topical corticosteroids. He had no history of phototherapy or systemic treatments. He denied joint pain. He first presented to the Cook County dermatology clinic in November of 2006, and was well-controlled with a topical regimen until April 2009. Since this flare, the patient's skin lesions have improved with a stronger topical regimen, but he developed abnormal pigment in areas of previous psoriatic lesions.

Past Medical History

None

Medications/Allergies

Different combinations of topical corticosteroids, salicylic acid, tazarotene, coal tar shampoo, calcipotriene, and tacrolimus
NKDA

Physical Exam

Skin: On the scalp, abdomen, back, arms and legs are scattered pink scaly plaques and papules, and large tan patches with dark brown macules in a speckled pattern within the lighter patches (areas of previously treated psoriasis)

Histopathology

BACK, PUNCH BIOPSY:
Hyperpigmentation at the basal layer consistent with a lentigo

Diagnosis

Lentigines arising in resolved psoriatic plaques

Patient B

History of Present Illness

52 year old Hispanic man with a 30-year history of psoriasis without joint pain presented to the Cook County dermatology clinic in February 2009. Previous treatments included various topical corticosteroids; he never received systemic medication or phototherapy. After restarting topical treatment, he soon noticed prompt resolution of all of his existing psoriatic lesions. However, in the areas of previous psoriasis he noted newly pigmented lesions. Also, for most of his life, the patient has had diffuse lentigines on sun-exposed skin.

Past Medical History

None

Medications/Allergies

Calcipotriene, topical corticosteroids, and salicylic acid/sulfur shampoo
NKDA

Social History

Unsure but believes his grandfather may have had psoriasis

Physical Exam

Skin: Few red, scaly, round, thin plaques on the back; on the abdomen, back, arms, and legs are scattered hypopigmented patches with dark brown macules in a speckled pattern within lighter patches (areas of previously treated psoriasis); the face is covered with many lentigines

Histopathology

BACK, PUNCH BIOPSY:
Mild superficial perivascular lymphocytic dermatitis and features suggestive of post-inflammatory pigment alteration

Diagnosis

Lentigines arising in resolved psoriatic plaques

Treatment and Course

Patients A and B: The patients were given reassurance of the likely benign nature of their lentigines, and they are being treated symptomatically for recurring plaque psoriasis along with observation of the lentigines for signs of evolution.

Discussion

The appearance of lentigines arising in lesions of resolved psoriasis, while rare, has been previously described, and although it is seen uncommonly, it is probably also underreported. Various reports in the literature discuss how individual therapy is a likely cause of the newly pigmented lesions. PUVA lentigines are a known consequence of UVA phototherapy used to treat psoriasis; our patients never had a history of phototherapy use. In the absence of phototherapy, other papers reported possible pathophysiological mechanisms pertaining to anti-TNF treatments in which the immunosuppressive effects of adalimumab were believed to cause an increase in melanocytic pigment. Our patients had never been on systemic agents. Coal tar has also been proposed in the literature as the culpable agent. The hypomelanocytic effects of topical corticosteroids are also well described, and are likely to play some part in the surrounding hypopigmentation. Calcipotriene may play a role in the activity of melanocytes as well.

On the other hand, while medications may play a role in this process, the psoriatic disease itself may be the main contributing factor to the development of lentigines. Inflammation from psoriasis may be the trigger, resulting in increased melanocytic activity with possible selective loss of melanocytes secondary to injury.

Additionally, it has been suggested that there is an association between vitiligo and chronic plaque psoriasis, which could explain hypo- or depigmented patches that are observed. Previous literature maintains that the lentigines could simply be follicular repigmentation or post-inflammatory hyperpigmentation in patches of vitiligo-like lesions. Supporting the possibility of post-inflammatory hyperpigmentation are the reports of large patches of previous lentigines actually clearing in areas of resolved plaque psoriasis.

It is important to distinguish benign lentigines from multiple benign eruptive melanocytic nevi caused by biological agents, and lentigines arising secondary to phototherapy, as atypical cells might be observed in the setting of prior PUVA. As lentigines associated with topical therapy have typically been benign in nature, treatment is likely observation and reassurance. Alternatively, patients may prefer to seek out cosmetic improvement by laser treatment; Mitra et al. have treated lentiginous hyperpigmentation with a Q-switched ruby laser. Hopefully, with long-term surveillance of these lesions, more can be learned in order to provide additional information and a more thorough prognosis for patients.

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Key Location(s): Fingers **CASE 7**

Presented by Morayo Adisa, MD and Warren Piette, MD

Unknown #3

58 year old woman with a restrictive cardiomyopathy and bulbous fingers

Key location(s): Upper and lower extremities **CASE 8**

Presented by Elizabeth Fahrenbach, MD; David Reid, MD; Anjeli Isaac, MD and Warren Piette, MD

History of Present Illness

22-year-old G1P1Hispanic female presented to the hospital with 4 days of new onset fever, rash, and joint pain. She initially developed a tender, nonpruritic, fixed eruption on the knees and elbows. Nearly simultaneously, she began to experience knee and ankle pain, which progressed to the point that she was unable to bear weight. She had no previous history of similar eruptions or joint discomfort in the past, and reported no recent sore throat, cough, shortness of breath, chest pain, nausea, vomiting, diarrhea, vaginal discharge, or dysuria. The patient denied taking any medications, except occasional ibuprofen for pain. She had no recent sexual activity and no history of sexually transmitted infections. There was no history of autoimmune or inflammatory disease, and she had no recent travel outside of the United States.

Past Medical History

Gestational diabetes (resolved after delivery of a healthy infant 10 months prior to presentation)
Herpes labialis

Medications/Allergies

Ibuprofen occasionally for pain
NKDA

Physical Exam

Vitals:	T 100.9°F, HR 110 bpm
General:	Alert and oriented, appearing uncomfortable
Cardiovascular:	2/6 systolic ejection murmur
Lymph:	No cervical, supraclavicular, axillary or inguinal lymphadenopathy
Musculoskeletal:	Moderate swelling, tenderness, and limited range of motion of knees/elbows
Skin:	Extensor forearms and knees with several symmetrically distributed erythematous, tender, indurated, 1cm subcutaneous nodules and erythematous blanching patches. The pretibial area was spared.

Laboratory Data

The following labs were abnormal:

WBC	12.4 K/µL	[4.4 – 10.6 K/µL]
Hemoglobin	11.4 g/dL	[11.7 – 14.9 g/dL]
Neutrophil %	80.7 %	[45.3 – 74.5 %]
Lymphocyte %	12 %	[18.1 – 43.2 %]
Erythrocyte sedimentation rate	66 mm/hr	[0 – 17 mm/hr]
CRP	32.28 mg/dL	[0 – 0.5 mg/dL]

The following labs were normal: CMP, MCV, Platelet count, PT, PTT, INR, Ferritin, ANA, RF, Complement 3 & 4, rapid HIV screen, Parvovirus B19 IgM & IgG, Hepatitis A, B, & C panel, RPR; Blood, urine, joint fluid, throat, rectal, and cervical cultures; PPD negative with 0 mm of induration at 48 hours

Histopathology

LEFT EXTENSOR FOREARM, PUNCH BIOPSY:
Predominantly septal panniculitis. A dense neutrophilic infiltrate is present in the subcutaneous septae with extension into the underlying adipose tissue.

Radiology
Chest radiograph: no hilar lymphadenopathy
Echocardiogram: normal ejection fraction, no vegetations

Diagnosis
Subcutaneous Sweet's syndrome

Treatment and Course
The patient was admitted to the inpatient medicine service and initially treated with non-steroidal anti-inflammatory drugs. An echocardiogram, joint aspiration cultures, and blood cultures were obtained. During the first few days of hospitalization, the patient remained febrile, though her arthralgias and cutaneous eruption improved. After the echocardiogram revealed no evidence of endocarditis, she was treated with a three week taper of prednisone, with an initial dosage of 30mg daily. On hospital day 5, with her fevers resolved and continued symptomatic improvement, she was discharged home. At her outpatient follow-up appointment nine days after discharge she reported near complete resolution of skin lesions and joint pain.

Discussion
The subcutaneous variant of Sweet's syndrome differs clinically and histopathologically from classic acute febrile neutrophilic dermatosis. In contrast to classic Sweet's, which typically presents with papules and plaques, subcutaneous Sweet's often presents with tender, erythematous nodules. The eruption, which is acute, most frequently affects the lower extremities, although cases of upper extremity, trunk, and head involvement have been reported. Most lesions rapidly resolve with hyperpigmentation or atrophy. Similar to classic Sweet's syndrome, patients experience fever, malaise, and in many cases, a slight leukocytosis. Subcutaneous Sweet's syndrome can be difficult to distinguish clinically from erythema nodosum, and in rare cases, Sweet's syndrome and erythema nodosum may coincide.

Histopathologically, Sweet's syndrome affects subcutaneous tissue in two distinct patterns: a primarily septal, sometimes granulomatous infiltrate (erythema nodosum associated with Sweet's syndrome) and a neutrophilic infiltrate concentrated in adipose lobules (subcutaneous Sweet's syndrome). Although Sweet's syndrome is traditionally considered a neutrophil-predominant dermatosis without vasculitis, the presence of vasculitis may represent an epiphenomenon secondary to extensive neutrophilic dermal inflammation. Thus, the presence of vasculitis does not preclude a diagnosis of subcutaneous Sweet's syndrome.

As in classic Sweet's syndrome, there are several important disease associations with subcutaneous Sweet's syndrome. The most commonly reported associations are acute myelogenous leukemia, myelodysplastic syndromes, multiple myeloma, and breast carcinoma. Subcutaneous Sweet's syndrome, in particular, has a strong association with underlying hematologic malignancies. Other recognized associations are inflammatory or autoimmune disorders (e.g. inflammatory bowel disease), medications (especially in female patients), infections (including *Salmonella enteritidis*), and pregnancy.

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Key Location(s): Scalp **CASE 9**

Presented by Joerg Albrecht, MD and Anjeli K. Isaac, MD

History of Present Illness
56 year old man presented in October 2009 with an approximately 4-week history of an ulcer on his left occipital scalp. One week after noting the lesion, the patient went to the emergency room, where the lesion was diagnosed as a "boil" and drained. The patient reported similar lesions elsewhere on the body in the past, which healed well. Incision and drainage of the scalp lesion was repeated three times in the emergency room without success. The patient was prescribed antibiotics which he took intermittently. Due to the futility of the treatment attempts, the patient was sent from the emergency room to the dermatology clinic.

Past Medical History
Diabetes mellitus, hypertension

Medications/Allergies
Metformin, enalapril, aspirin
NKDA

Social History
Chronic alcoholism for more than 20 years, smoker, unemployed, lives with sister

Review of Systems
Intermittent fever and chills for about 2 weeks

Physical Exam
Skin: On the left temporoparietal extending to the occipital scalp was a round 7 centimeter boggy ulcerated plaque with significant suppurative discharge

Laboratory Data
The following were abnormal:

HbA1c	8.6 %	[4.40 – 6.70 %]

Histopathology
SCALP, PUNCH BIOPSY:
Suppurative inflammation with abscess formation and pseudoepitheliomatous hyperplasia. Gram stain positive with multiple cocci identified. Special stains for fungi (GMS, PAS) negative. On further review, organisms compatible with Blastomyces yeast forms were noted.

Microbiology

WOUND CULTURE:	3+ *Streptococcus agalactiae*
	1+ Corynebacterium species
TISSUE CULTURE:	3+ *Blastomyces dermatitidis*
	1+ Cryptococcus (non-neoformans) species
	Negative for acid-fast bacteria

Diagnosis
Cutaneous blastomycosis

Treatment and Course
On presentation to the dermatology clinic, the patient's clindamycin as prescribed by the emergency room was continued. He had been taking the medication for a couple of days with some success as per his observation. A biopsy was performed, and tissue cultures for acid-fast

bacilli, fungi, bacteria, as well as a bacterial swab of the wound were sent. The patient was to follow up in the dermatology clinic 4 days later, but he did not. At the end of November, approximately 6 weeks after his initial presentation, the patient returned to the emergency room again with weight loss, high intermittent fevers, and a non-productive cough. Chest radiograph demonstrated bilateral opacities. A CT scan of the brain demonstrated a large fluid collection under the ulcer reaching to the calvarium. He was admitted under the presumptive diagnosis of disseminated blastomycosis and started on intravenous amphotericin. One day after admission, he became tachypneic and oxygen-dependent and was transferred to the medical intensive care unit and intubated. Culture from bronchial lavage confirmed pulmonary blastomycosis. After 3 weeks of intensive treatment complicated by self-extubation, renal failure, and a stage IV sacral decubitus ulcer, he was transferred to Oak Forest Hospital to wean from the ventilator and for intensive physiotherapy. He was discharged one month later with the intent to finish a 6-12 month course of oral itraconazole. The patient was last seen in May in the infectious disease clinic with some smaller scalp lesions remaining, but since has not followed up at the infectious disease, dermatology, or internal medicine clinics.

Discussion

Blastomycosis is a fungal infection caused by the dimorphic fungus *Blastomyces dermatitidis*. It is endemic to the Chicago area. Cutaneous disease rather than widespread infection is more common in adults than in children, whereas children tend to develop symptomatic pulmonary disease. More often the disease affects men who have close contact with the soil that harbors the organism. Clinically cutaneous blastomycosis presents as a well-demarcated verrucous plaque. The plaque may be eroded, crusted, or have an eschar. Blastomycosis-like pyoderma, which is an exaggerated vegetative response to prolonged bacterial infections may be clinically identical and was one of the alternative diagnoses initially entertained. Other differential diagnoses include skin tumors, cutaneous metastases, or other infectious causes. Advanced ulcerated cases may clinically be confused with pyoderma gangrenosum.

However, blastomycosis is primarily a pulmonary disease, and the skin typically is secondarily affected with very rare exceptions. Pulmonary disease can range anywhere from asymptomatic to a high fever, productive cough, and shortness of breath. The central nervous system (CNS) may also be affected; clinical manifestations of CNS involvement can include headaches, confusion, and focal neurological deficits. The treatment guidelines by the American Society of Infectious Diseases differentiate the approach to therapy based on the clinical judgment of the practitioner, who assesses the disease severity. While virtually all patients with blastomycosis should be treated with 6-12 months of therapy, severity of disease determines whether intravenous amphotericin is necessary prior to oral treatment with itraconazole. Chest imaging, including a chest radiograph and CT scan, as well as bronchoscopy are important in determining the extent of pulmonary involvement. In the event of CNS symptoms, CNS imaging and/or lumbar puncture should be utilized, particularly in the immunosuppressed patient. All cases with systemic involvement should be treated with intravenous amphotericin. Our patient received a lumbar puncture in addition to imaging.

All cases of cutaneous blastomycosis are considered disseminated disease and require systemic treatment, even if the cutaneous lesion has been surgically removed. Duration of treatment by the dermatologist should be guided by skin findings and continue for a short time after the skin lesions have healed.

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Key Location(s): Left thigh **CASE 10**

Presented by Rachel Pritzker, MD and Warren Piette, MD

Unknown #4

55 year old woman with left thigh ulcers for 3 years

Key Location(s): Trunk **CASE 11**

Presented by Joerg Albrecht, MD and Warren Piette, MD

History of Present Illness

36 year old man presented with new onset of skin lesion on the right thigh for about 8 days that had not changed. A few days later he developed lesions on the other leg and the abdomen and back which did not change after their appearance. Prior to the eruption, the patient noted several days of severe chills and swelling in the left groin which had since resolved. The patient still felt hot during the night but was afebrile. He also complained of mild muscle pain, but no joint pain or swelling. He had traveled to Indiana three weeks prior and had vacationed in Wisconsin two weeks prior. He did not remember a tick bite or a circular lesion that may have preceded the current eruption and has otherwise been healthy.

Past Medical History

None

Medications/Allergies

Ibuprofen as needed/Ciprofloxacin

Physical Exam

Skin: On the left thigh, there were 2 to 6 cm round patches with an erythematous rim and violaceous center; multiple similar lesions on the right thigh and back were noted; a slightly larger circular patch with central clearing and no scale was on the right abdomen; no bite mark was seen

Laboratory Data

The following were abnormal:

WBC	11.7 k/µL	[4.4 – 10.6 k/µL]
IgG/IgM Elisa Borrelia	Positive	
Reflex Western Blot	Positive for IgM	

Diagnosis

Erythema chronicum migrans

Treatment and Course

Borrelia titers were ordered but the patient was not treated. At follow up in the dermatology clinic, the Borrelia titer Western Blot was found to be positive for IgM, doxycycline 100mg PO BID was begun, and pictures were taken again. At a further follow up visit 4 weeks later the skin lesions and arthralgias had completely resolved, and the doxycycline was stopped.

Discussion

Lyme disease is similar to syphilis in that it has a variety of manifestations in most organ systems. As in syphilis, the course of the disease can vary significantly between individuals depending on their immunoreactions. Both diseases begin with acute local symptoms, i.e. early limited disease, followed by early disseminated disease, and often years of latent or chronic disease which leads to tertiary symptoms. In addition to individual variations, Borrelia infections also vary between species of the pathogen. The primarily North American *Borrelia burgdorferi sensu stricto* is characterized by relatively frequent signs of systemic infections with erythema migrans and arthritis. In Europe, *Borrelia garinii* infection more frequently causes neurological symptoms, while *Borrelia afzelii* may induce acrodermatitis atrophicans and lymphoma cutis.

The bite of the tick is generally painless and leads to a local lesion that may be invisible or mimic a bite reaction in form of an urticarial papule only. Most patients do not remember the bite.

Erythema migrans usually develops after about 2 weeks, but may begin as early as 3 days or as late as 180 days. Often the serological tests are not yet positive at this point, and due to the characteristic clinical picture and the lack of specificity of the laboratory analysis, serological testing is not recommended by most guidelines. Thus the decision to treat is mostly based on clinical criteria. Classic locations of the lesions are the flexor surfaces of the large joints but they can be anywhere. On children, the head and neck are often affected. Erythema migrans may recur after insufficient antibiotic therapy or spontaneously. In some cases, Borrelia has been found in skin without visible change. Variants of erythema migrans are frequent and may hamper the diagnostic process: the erythema may not migrate, may be infiltrated, and may have some central vesicular changes or peripheral scaling. Particularly on the legs, the lesions may be deep red suggesting cellulitis, or even targetoid suggesting erythema multiforme. The size of the ring varies significantly but should be at least 5 cm. The usual size is about 10 to 16 cm, but the circles may be incomplete and can be as large as 80 cm in exceptional cases. Erythema migrans was called erythema chronicum migrans because while the symptoms may last only a day they can last several months with a median duration of 10 days. A third of the patients complain of itch, but more rarely also of burning pain or the feeling of localized warmth. Two thirds of the patients will complain of symptoms suggesting generalized infection with fatigue, slight arthralgias and myalgias as well as slight elevation of temperature. The American skin manifestations tend to be more inflammatory and faster growing.

The diagnosis of erythema migrans is straightforward in cases of slowly migrating rings without scaling or itch. Often they are not annular when caught early. Of note, the Southern tick associated rash illness is similar to erythema migrans clinically, except for smaller rings. This disease has an unclear natural course or etiology but follows tick bites by the lone star tick (*Amblyomma americanum*), which can be found in southeastern, south-central states of the US as well as Maine. There is no specific treatment.

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Key Location(s): Arms, chest, abdomen, back, legs **CASE 12**

Presented by August A. Natalie, MD and Anjeli K. Isaac, MD

History of Present Illness

33 year-old female with a history of gastric bypass surgery for obesity in 2002 and alcohol abuse presents with complaints of a generalized rash for 3-4 weeks. The rash began on her feet and spread superiorly, sparing her face. She noted extensive pruritus, which worsened nocturnally. She received an oral prednisone taper for 10 days prior to evaluation, which provided no improvement. Topical triamcinolone was also ineffective. Review of systems revealed lower extremity tingling, burning, and numbness, lack of coordination and gait difficulty, blurry vision, amenorrhea, dull lower abdominal discomfort, and occasional diarrhea.

Past Medical History

Roux-en-Y gastric bypass for obesity in 2002 at bariatric center, lost 250 pounds post-surgery, surgery complicated by malnutrition and occasional diarrhea
Peripheral neuropathy NOS, diagnosed 1.5 years ago
Alcohol abuse

Medications/Allergies

Thiamine, folic acid/NKDA

Social History

Smokes two "small cigars" per day; drinks one bottle of wine per day; lives with mother

Physical Exam

Skin: Large reddish-brown symmetric geometrically-shaped plaques on arms, chest, abdomen, back, and legs with peripheral erythema and scale and central clearing; Face and body folds spared
Neuro: Broad based and unsteady gait

Laboratory Data

The following labs were abnormal:

BUN	3 mg/dL	[8 – 20 mg/dL]
Creatinine	0.5 mg/dL	[0.6 – 1.4 mg/dL]
Magnesium	1.5 mg/dL	[1.8 – 2.7 mg/dL]
Albumin	2.0 g/dL	[3.8 – 5.2 g/dL]
Total Protein	5.4 g/dL	[6.3 – 8.2 g/dL]
Total Bilirubin	1.7 mg/dL	[0.2 – 1.2 mg/dL]
Direct Bilirubin	1.3 mg/dL	[0.0 – 0.2 mg/dL]
Alkaline Phosphatase	246 U/L	[50 – 120 U/L]
AST	81 U/L	[0 – 40 U/L]
ALT	41 U/L	[5 – 35 U/L]
Hemoglobin	10.2 g/dL	[11.7 – 14.9 g/dL]
Hematocrit	30.3 %	[34.9 – 44.3 %]
MCV	104 fL	[81.8 – 96.9 fL]
25-Hydroxy Vitamin D	<4.0 ng/mL	[32.0 – 100.0 ng/mL]
Zinc, Plasma	54 µg/dL	[70 – 150 µg/dL]

The following labs were normal: Na, K, Cl, HCO3, Glucose, Phos, B12, Folate, PT, PTT, CPK, TFTs, CA-125, SPEP, RPR, Hep B/C

Histopathology

A. RIGHT BACK, PUNCH BIOPSY:
Psoriasiform dermatitis with hyperkeratosis, parakeratosis, focal diminished granular layer and basal vacuolar change, upper dermal mild lymphocytic and rare eosinophilic infiltrate.

B. LEFT FLANK, PUNCH BIOPSY:
Psoriasiform dermatitis with almost confluent hyperkeratosis, parakeratosis, diminished granular layer and minimal papillary dermal lymphocytic infiltrate.

Radiology

CT Abdomen/Pelvis with oral and IV contrast: severe diffuse hepatic steatosis; relative right lobe hepatomegaly; clear, normal, and diffusely atrophic pancreas; spleen, adrenals, and kidneys unremarkable; nonobstructing small gallstones

Diagnosis

Acquired zinc deficiency

Treatment and Course

This 33 year old female presented with a history of Roux-en-Y gastric bypass and alcohol abuse and an impressive papulosquamous rash. She was diagnosed with acquired zinc deficiency and started on zinc sulfate supplementation at 220 milligrams/day. Two months after our initial visit, her skin had begun to improve. However, she continued to drink alcohol. One week later, she was admitted to an outside hospital for jaundice, severe weakness, and diarrhea. Her hospital course was complicated by hepatic encephalopathy, seizures, and urosepsis. She remained encephalopathic, febrile, hypotensive, anemic, and thrombocytopenic at the outside hospital. Ultimately, her care was transferred to our hospital. She developed a left lower lobe pneumonia that grew methicillin-sensitive *Staphylococcus aureus* and *Pseudomonas aeruginosa* and required intubation. The patient went on to develop multisystem organ failure. Her family withdrew care after three weeks in the hospital.

Discussion

Acrodermatitis enteropathica is an autosomal recessive disorder due to mutations in the SLC39A4 gene that encodes the zinc transporter protein ZIP4, leading to clinical zinc deficiency. Alternatively, zinc deficiency may occur as a result of an acquired condition that involves the defective absorption of zinc, producing an acrodermatitis enteropathica–like syndrome. The classic presentation of acrodermatitis enteropathica is dermatitis, diarrhea, and alopecia. The dermatitis favors periorificial and acral areas. The lesions are variable in appearance and include eczematous or psoriasiform plaques, angular cheilitis, and paronychia, or less commonly, vesicles and bullae. The vast majority of patients with inherited zinc deficiency present during infancy. Signs and symptoms of acrodermatitis enteropathica develop in bottle-fed infants shortly after birth, whereas in breast-fed infants the signs occur days to weeks after weaning.

Acquired acrodermatitis can occur in association with malabsorption syndromes, extensive burns, Crohn's disease, sickle cell anemia, celiac disease, systemic cancers, pancreatic insufficiency, renal tubular dysfunction, a defect of mammary zinc secretion, short-bowel syndrome, diets high in phytates, total parenteral nutrition, HIV infection, and prematurity. Acquired zinc deficiency in alcoholism is the result of poor nutritional intake and increased urinary excretion. Roux-en-Y gastric bypass surgery is a well-known risk factor for multiple micronutrient deficiencies, including zinc deficiency.

Ackerman has stated that the histologic findings in acrodermatitis enteropathica, pellagra, and necrolytic migratory erythema may be indistinguishable from one another and the pallor of keratinocytes in the upper part of the epidermis is the major sign. Early lesions of acrodermatitis

enteropathica are characterized by loss of the granular layer, replacement of this layer by clear cells, and focal parakeratosis. As the condition progresses, the epidermis becomes increasingly psoriasiform, the parakeratosis becomes more confluent and the pallor of the upper part of the epidermis becomes more prominent. Later, the pallor disappears, but the psoriasiform hyperplasia persists. As the lesions involute, only parakeratosis remains. Dilation and tortuosity of the vessels in the papillary dermis, reminiscent of those in psoriasis, are present throughout most of the course of the process.

The diagnosis is suspected from the clinical features and the histologic findings. It is confirmed by low plasma zinc levels, such as this patient. A low serum alkaline phosphatase, a zinc-dependent enzyme, may be a valuable adjunctive test when the serum zinc level is normal or near normal. Our patient had alcoholic hepatitis and cirrhosis, making interpretation of her alkaline phosphatase in this context impossible.

Treatment is with oral zinc sulfate, 1-2 milligrams/kilogram/day in the acquired form and 3 milligrams/kilogram/day in acrodermatitis enteropathica. 10-50 milligrams of elemental zinc is routinely recommended for patients after Roux-en-Y gastric bypass for prevention.

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Key Location(s): Right retroauricular, lower lip, left calf **CASE 13**

Presented by Julia Kasprzak, MD and Anjeli K. Isaac, MD

History of Present Illness
11 year old girl presented for evaluation of a mass behind her right ear for the last one and a half years. During the three months prior to presentation, the mass had progressively enlarged. She had no pain or other symptoms associated with the mass. Approximately one month prior to presentation in our clinic, she noted a new lesion on her left calf which was similarly asymptomatic.

Past Medical History
History of atopic dermatitis (currently not active)

Medications/Allergies
None/NKDA

Social History
The patient is very active in middle school activities

Review of Systems
No fever, chills, nausea, vomiting, weakness, weight loss, night sweats or fatigue

Physical Exam
Lymph: No submandibular, cervical, or supraclavicular lymphadenopathy
Skin: Right retroauricular – 4 x 3 cm hard, immobile, nodule with a pebbled surface, scale and telangiectasias; Left superior calf – 2 x 1.5 cm hyperpigmented, slightly mobile, hard, smooth nodule with no surface changes

Histopathology
A. RIGHT RETROAURICULAR, PUNCH BIOPSY:
Pseudoepitheliomatous squamous hyperplasia and infiltration of the dermis with large cells with granular, dusty pink cytoplasm. These cells had a homogenous appearance and showed no nuclear pleomorphism or necrosis. S-100 stain was negative.

B. LEFT CALF, PUNCH BIOPSY:
Dermal infiltrate of large, homogenous cells with granular, dusty pink cytoplasm. S-100 and CD68 stains were positive.

Diagnosis
Multiple granular cell tumors

Treatment and Course
During the time the patient was being evaluated for the retroauricular and calf lesions at our clinic, she developed another nodule on her lower left lip. She was sent to an outside hospital for removal of all three lesions. Histopathology of the lip lesion was also consistent with a benign granular cell tumor. She is now monitored on a regular basis at that clinic for recurrence.

Discussion
Granular cell tumor (GCT) is a rare tumor of neural derivation, specifically of Schwann cell origin. They are most commonly found in the head and neck region, particularly in the mouth, but can appear anywhere on the skin and occasionally in the pulmonary or digestive tract. They are more common among black patients and have a slightly higher prevalence among females.

GCTs usually occur as solitary nodules in the dermis or subcutaneous tissues; however, multiple granular cell tumors (MGCTs) have been found in about 10-25% of patients. 36 cases of MGCTs have been reported in the pediatric literature; 14 of these cases were reported in association with somatic or genetic syndromes including Noonan syndrome and neurofibromatosis type I. The pathogenesis of multiple tumors is not understood.

The majority of GCTs are benign and are characterized by a proliferation of cells in the dermis or subcutis with PAS-positive and diastase-resistant granular cytoplasm due to the accumulation of lysosomes. The vast majority of tumors are S-100 positive since they neural in origin. In addition, CD68 is a marker that can be used to detect the presence of lysosomes. Although the majority of GCTs are benign, 1-2% of lesions are considered malignant and demonstrate aggressive clinical behavior including metastases to lymph nodes and lungs. Histopathologic examination of malignant GCTs reveals cytologically atypical cells, abundant granular cytoplasm, nuclear pleomorphism and necrosis. Approximately 2 out of 3 malignant GCTs are negative for S-100, which is thought to be secondary to altered differentiation processes in the malignant tumors. In this case, the patient's retroauricular tumor was found to be S-100 negative; however it did not demonstrate the cytologic atypia expected in malignancy.

Benign tumors are managed by local surgical excision and have a recurrence rate of 2-8% with clear margins and 21-50% when the margins are positive for tumor. Patients with multiple granular cell tumors should be monitored on a regular basis over several years for recurrence. With malignant lesions, recurrence rate and mortality are very high; metastases are usually detected within 2 years of discovering the primary tumor. Prognosis is poor for malignant lesions, with an estimated 60% mortality in the first 3 years after diagnosis. Management of malignant tumors includes wide en bloc surgical excision and lymph node dissection.

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Key location(s): Flanks **CASE 14**

Presented by Morayo Adisa, MD and Warren Piette, MD

History of Present Illness

70 year old African American man was referred for evaluation of multiple bullous eruptions on his flanks of two days duration. The patient was admitted a month earlier for a complete proctectomy but his hospital course was complicated by the development of pulmonary embolism and acute tubular necrosis. The rash consists of bullae and vesicles with underlying erythema. Associated symptoms could not be elicited from the patient as he was sedated and intubated. He was on vancomycin, which was started two days prior to the onset of the eruption, and imipenem-cilastatin, which was started 11 days prior to the onset of the eruption, for the treatment of *Staphylococcus epidermidis* bacteremia.

Past Medical History

Ulcerative colitis
History of invasive colon adenocarcinoma s/p total colectomy
Pulmonary embolism
Staphylococcus epidermidis bacteremia

Medications/Allergies

Albuterol, acetylcysteine, ascorbic acid, bacitracin, famotidine, ipratropium, multivitamin, metoprolol, vancomycin, imipenem-cilastatin, haloperidol as needed/NKDA

Physical Exam

General: Sedated
Skin: No oral or genital mucosal involvement; Flanks, anterior lower abdomen, and left lower back with multiple flaccid 3-4cm bullae with very mild underlying erythema; Proximal medial thighs with well demarcated erythematous patches and few scattered overlying bullae

Laboratory Data

The following labs were abnormal:

Creatinine	2.0 mg/dL	[0.6 – 1.4 mg/dL]
WBC	24.4 k/µL	[4.4 – 10.6 k/µL]
Blood cultures	*Staphylococcus epidermidis* (1 of 4 bottles)	

The following labs were normal: remainder of BMP, remainder of CBC including eosinophil count

Histopathology

A. LEFT FLANK, PUNCH BIOPSY:
Subepidermal vesicular dermatitis with neutrophil-predominant inflammatory infiltrate.

B. LEFT FLANK, PERILESIONAL PUNCH BIOPSY:
Direct immunofluorescence staining in a linear pattern at the dermal epidermal junction with IgA.

Diagnosis

Vancomycin induced linear IgA disease

Treatment and Course

Vancomycin was discontinued and the patient's eruption gradually improved and cleared with no scarring. The improvement was noted days after the discontinuation of vancomycin.

Discussion

Linear IgA bullous dermatosis (LABD) is an autoimmune blistering disease characterized clinically by the presence of tense vesicles or bullae and immunologically by linear IgA staining at the dermal-epidermal junction with a neutrophilic collection in the dermal papillae. Multiple antigens have been incriminated in this process and some of these include proteins with a molecular weight of 285-kDa; as well as 97-kDa and 120-kDa antigens, which are fragments of the extracellular domain of bullous pemphigoid antigen BP 180 (type XVII collagen); BP 230 antigen located in the lamina lucida of the basal membrane; 250-kDa corresponding to collagen VII, which is a component of anchoring fibrils; as well as some still unidentified antigens. The occurrence is typically idiopathic but there have been reported cases of its association with systemic illnesses (e.g. SLE), underlying malignancy and drug administration. A similar disease occurring in children less than 5 years of age is termed chronic bullous disease of childhood. The drug-induced form has been reported with many medications such as vancomycin, phenytoin, captopril, penicillin, lithium, ampicillin, interleukin-2, amiodarone, iodine contrast agents, trimethoprim/sulfamethoxazole, glyburide, somatostatin, and diclofenac. Of all the reported associated medications, vancomycin is by far the most common.

Vancomycin-induced LABD (VILABD) occurs within 7-21 days after initiation of the offending drug and resolves spontaneously within 3 weeks of discontinuation. It often presents clinically with tense bullae but other varied clinical presentations have been reported in the literature. These include target lesions as seen in erythema multiforme, morbilliform eruptions, urticarial plaques, and toxic epidermal necrolysis-like eruptions. Because of the spontaneous resolution of the skin lesions in this entity, therapeutic intervention with dapsone, systemic corticosteroids or other immuno-modulators is not necessary. The time frame of occurrence with rechallenge is shorter than with the initial clinical manifestation and development of skin lesion as early as 24 hours after administration has been reported. The development of the condition does not appear to be dose or drug manufacturer dependent as it has been reported with vancomycin troughs of various levels and various manufacturers. The histopathological findings seen in VILABD are the same as that seen in the idiopathic variant; however, according to Neughebauer et al., the immune deposits in the skin in VILABD disappear after the spontaneous resolution of the lesions, whereas in the idiopathic variant, the immune deposits in the skin tend to persist even after clinical resolution of skin lesions.

The underlying pathogenesis of the drug-induced LABD has not been characterized. Clinically, this differs from the idiopathic variant in that the vancomycin variant does not have frequent oral involvement.

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Key Location(s): Penis, scrotum **CASE 15**

Presented by Hal Weitzbuch, MS, MD; Anjeli K. Isaac, MD; and Warren Piette, MD

History of Present Illness
61 year old Caucasian man presented with a slowly enlarging, asymptomatic lesion in his genital region that he first noticed about one year prior. He denied pruritus, pain, or discharge. Review of systems was negative for fevers, chills, nausea, vomiting, diarrhea, constipation, hematuria, bright red blood per rectum, melena, weakness, weight change, or fatigue.

Past Medical History
Depression, insomnia, hypertension, hypercholesterolemia, fibromyalgia

Medications/Allergies
Lisinopril, simvastatin, levothyroxine, citalopram, trazodone, clonazepam, zolpidem, lorazepam, hydrocodone, dextroamphetamine, doxepin, gabapentin, bupropion
NKDA

Physical Exam
Lymph: No lymphadenopathy
Skin: Left lateral penoscrotal junction with a 1cm x 1cm hypopigmented pinkish plaque with a sharply demarcated border

Laboratory Data
The following studies were normal: Complete blood count, complete metabolic profile including liver enzymes, prostate specific antigen (PSA), and carcinoembryonic antigen (CEA)

Histopathology
SCROTUM, PUNCH BIOPSY:
Skin with epidermal infiltration of pale staining cells which are mucin, CK7, and CEA positive; S100, Melan A, and HMB45 immunostains were negative.

Radiology
Chest radiograph: normal
CT Abdomen/Pelvis with and without IV contrast: no pathologically enlarged lymph nodes or evidence of metastasis

Diagnosis
Extramammary Paget's disease

Treatment and Course
He was referred to urology and a digital rectal exam performed, which was normal. After ruling out malignancy, the urological team performed a wide local excision, and the patient has fully recovered.

Discussion
Extramammary Paget's disease (EMPD) of the penis and scrotum is a rare form of an already uncommon neoplasm. In the United States, EMPD is found much more often in women, and the age at diagnosis ranges from 37 to 87 years old. There is much controversy surrounding this disease, particularly with respect to multiple etiologies and to the most effective treatment.

EMPD may be either a primary lesion, or secondary from direct extension of a neoplasm or metastasis. Although the pathogenesis is unknown, proposed mechanisms include intraepidermal adenocarcinoma, dermal sweat gland origin, and primary adenocarcinoma of

sweat ducts. It has also been theorized that there is a signal, which stimulates the epithelial and internal neoplasms simultaneously. However, one of the greatest concerns when relating to the diagnosis of EMPD is the risk of associated malignancy. It has been reported that 5% of patients with EMPD have an adnexal neoplasm, and 10-20% of patients have an underlying internal malignancy. Associations with malignancy can be used to divide EMPD into three types: those with an associated visceral malignancy, those with underlying cutaneous adenocarcinoma, and those without any associated malignancy. The first type of EMPD is most often associated with adenocarcinoma of the rectum or anal canal, but the malignancy may be secondary to carcinoma of the cervix, bladder, apocrine glands, or sebaceous glands.

Clinically, EMPD presents most often as a pruritic, erythematous, scaly plaque that is slowly growing. It is because of this non-diagnostic presentation that EMPD is often treated as an inflammatory dermatologic condition for some time prior to biopsy, but it does not respond to therapy. Common incorrect diagnoses may be eczematous dermatitis, lichen sclerosus, Bowen's disease, or a fungal infection. When men have lesions, it may involve the perianal region, scrotum, or penis, while vulvar lesions are most common in women.

Histopathology shows a similar picture to that of mammary Paget's disease. Pale, round, enlarged cells, otherwise known as Paget cells, are scattered throughout the epidermis, but are usually grouped near the basal layer. Usually, these cells stain positively for mucin, and occasionally can form glandular structures. Keratohyaline granules may be seen within the atypical cells in the granular layer. Based on these findings, malignant melanoma in situ is high on the differential diagnosis, and immunohistochemistry can help discern these diseases. Cytokeratin-7 is usually positive in EMPD.

Once a diagnosis of EMPD has been made, the next step is searching for an underlying malignancy. CT scan of the abdomen and pelvis, chest x-ray, pelvic, prostate and breast exams, colonoscopy, cystoscopy, and tests for oncogenic markers have all been recommended. While there is significant and warranted impetus to search for a neoplasm, the practitioner should be mindful that most patients will not have more extensive disease.

Multiple treatment options can be offered, but, in general, there are two groups of patients: those with underlying invasive malignancy, and those without. If an associated neoplasm is found, therapy will be aimed at treating the primary mass.

However, for the majority of patients, the goal of therapy is to attain the lowest rate of recurrence possible with excision. In most studies, it seems that Mohs micrographic surgery (MMS) leads to a lower recurrence rate, but wide local excision may achieve similar rates. MMS is limited by irregular margins, "skip lesions", and multicentricity, but is superior to wide excision because of frequent clinically occult disease. Recurrence rates vary by case series and are difficult to compare since lesions in different locations carry different rates. Fluorescein visualization for tumor mapping has helped improve treatment, but regardless, recurrence is common. Alternatively, radiotherapy may be beneficial. 5-Fluoruracil is mainly ineffective in the treatment of EMPD, although imiquimod has been shown to clear disease. Regardless of the therapy used, close long-term monitoring is essential in catching recurrent disease.

Diagnosing a patient with extramammary Paget's disease may properly trigger an extensive workup for associated or underlying disease, but with the multidisciplinary team working together with the patient, there is ample opportunity for success.

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Key Location(s): Popliteal fossae **CASE 16**

Presented by Rachel Pritzker, MD and Anjeli K. Isaac, MD

History of Present Illness
64 year old man presented to our dermatology clinic with a 12-year history of multiple nodules on both legs. Originally, the nodules grew slowly, but growth subsequently halted several years ago. These are asymptomatic. Initially, the lesions were originally flesh-colored, but after using "wart remover" to the area the surrounding skin became hyperpigmented. The patient also mentioned a dark patch on his left chest present for unknown duration. Upon further questioning, the patient reported no learning difficulties in childhood.

Past Medical History
Hypertension, hypercholesterolemia, asthma

Medications/Allergies
Aspirin, albuterol, simvastatin, hydrochlorothiazide, enalapril
NKDA

Family History
No family members with similar skin findings or neurological disease

Physical Exam
Skin: Popliteal fossae and medial upper leg with few clusters of 1cm x 1cm skin-colored to hyperpigmented rubbery nodules superimposed on tan hyperpigmented patches in a linear distribution; lateral malleoli with few skin-colored rubbery nodules; right inferior chest with 2cm x 2cm tan patch

Histopathology
LEFT POSTERIOR KNEE, PUNCH BIOPSY:
Well-demarcated dermal spindle-cell proliferation with pale stroma and occasional mast cells, consistent with a neurofibroma

Diagnosis
Bilateral segmental neurofibromatosis (NF5)

Treatment and Course
The existing lesions were not changing, and no new lesions appeared since the first appointment. The patient was referred to ophthalmology, and he had a normal exam. He desired excision of these lesions, and one lesion on each leg was excised in October 2010. The pathology was again consistent with neurofibromas.

Discussion
Segmental neurofibromatosis is defined as neurofibromas only or both neurofibromas and café-au-lait macules limited to an area of the body. It has been described as limited to only one dermatome, but several reports have demonstrated the lesions covering up to three dermatomes or following a Blaschkoid distribution. Most reports of segmental neurofibromatosis are located unilaterally, but approximately 20 cases of a bilateral distribution can be found, as is the case in our patient.

Segmental neurofibromatosis was initially described in 1931. Subsequently, in the early 1980s, Vincent Riccardi classified neurofibromatosis (NF) into the well-known 8 categories, which include segmental neurofibromatosis as NF5. The other classifications designated were NF1 (von Recklinghausen), NF2 (acoustic schwannoma), NF3 (mixed), NF4 (variant), NF6 (café-au-lait

macules only), NF7 (late-onset), and NF8 (not otherwise specified). He described segmental neurofibromatosis as involving only the skin and not having a hereditary component. However, after more cases of segmental neurofibromatosis had been reported, Roth et al. reclassified segmental neurofibromatosis into 4 subtypes. These were true segmental (NF5 according to Riccardi), localized cases with deep involvement (non familial), hereditary segmental (no deep involvement, familial), and bilateral segmental (no deep involvement, non familial). Our patient appears to fall into the bilateral segmental phenotype.

Segmental neurofibromatosis is thought to be inherited as a postzygotic somatic mutation in the NF-1 gene encoding the protein neurofibromin. This mutation has been shown to cause a somatic mosaicism, where the individual has cells with different genotypes. Therefore, only small areas of the body are clinically involved, usually in a linear pattern for fibroblasts and a segmental pattern for nerve cells. Furthermore, when the mutation occurs late in embryonic development, a localized form of the disease is seen, whereas an earlier mutation results in more widespread bilateral disease often mistaken for NF1. Most patients with segmental neurofibromatosis do not have systemic involvement or malignant transformation, but visceral neurofibromas, Lisch nodules, optic pathway tumors, and learning difficulties have been reported. Although most cases have no family history of neurofibromatosis, there a few reports where patients with segmental neurofibromatosis have children with generalized neurofibromatosis type 1. It has been hypothesized that in these parents the mutation occurred early enough in a pluripotent stem cell and resulted in both a somatic cell and a gonadal cell mosaicism with the ability to be transmitted.

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Key Location(s): Patient A – Arms, legs, upper back, abdomen **CASE 17**
Patient B – Dorsal hands/fee, wrists/ankles

Presented by Michelle Chevalier, MD; Hal Weitzbuch, MS, MD; and Anjeli K. Isaac, MD

CASE A

History of Present Illness

24 year old African-American female presented with a twelve-year history of progressive, asymptomatic "skin discoloration". At the age of twelve, she noted lightening of her right upper arm. This gradually progressed to more diffuse involvement, which spared her face. The patient had "light therapy" (unknown type) in the past. She noted some improvement but was unable to continue treatment because of insurance-related complications. She does not recall ever being given a definitive diagnosis.

Past Medical History

None

Medications/Allergies

None/NKDA

Review of Systems

The patient denied any fevers, chills, night sweats, or weight loss.

Physical Exam

Abdominal:	No hepatosplenomegaly
Lymph:	No cervical, supraclavicular, axillary, or inguinal lymphadenopathy
Skin:	Legs, arms, upper back, and abdomen with several large, poorly circumscribed hypopigmented patches without scale; Wood's light examination of all lesions was negative

Histopathology

RIGHT UPPER LEG, PUNCH BIOPSY:
In the epidermis, there is exocytosis of lymphocytes displaying large convoluted nuclei. The dermis demonstrates a patchy lymphocytic lichenoid infiltrate.

Diagnosis

Hypopigmented mycosis fungoides

Treatment and Course

PUVA treatment was initially recommended. However, given the patient's concerns related to prolonged treatment, broad-band UVB therapy was initiated instead.

CASE B

History of Present Illness

45 year old African-American male presented with a five-year history of asymptomatic skin discoloration of his hands and feet. The patient had no prior treatment or work-up of this condition.

Past Medical History

None

Medications/Allergies
None/NKDA

Social History
The patient was incarcerated at the time of evaluation.

Review of Systems
The patient denied any fevers, chills, night sweats, or weight loss.

Physical exam
Abdominal: No hepatosplenomegaly
Lymph: No cervical, supraclavicular, axillary, or inguinal lymphadenopathy
Skin: Dorsal hands/feet, wrists/ankles with several erythematous, depigmented, non-scaly patches with several central flesh-colored macules

Histopathology
LEFT LATERAL FOOT, PUNCH BIOPSY:
In the epidermis, there is exocytosis of lymphocytes with cells lining up at the basal layer. The dermis demonstrates a lymphocytic lichenoid infiltrate and papillary dermal fibrosis.

Diagnosis
Hypopigmented mycosis fungoides

Treatment and Course
The patient was started on clobetasol 0.05% ointment twice daily to the affected areas on his hands and feet. He was subsequently lost to follow-up after being released from prison.

Discussion
Hypopigmented mycosis fungoides (MF) is a rare variant of early-stage cutaneous T-cell lymphoma. Most cases represent TNM stage I disease. An equal male to female ratio has been reported, differing from the male preponderance seen in classic MF. The frequency is largely unknown; however, over one-hundred patients have been reported in the literature. This variant usually presents between 30-40 years of age, though there appears to be a much higher proportion of children affected with this than with classic MF. Ardigo et al. report that 17.7% of hypopigmented MF cases in the literature were children compared to 0.5-2.3% in classic MF. In addition, the diagnosis of hypopigmented MF is made more often in individuals with darker skin although several cases of Caucasian patients have also been reported. Affected patients may either present solely with hypopigmented patches or with lesions in association with erythematous patches, plaques, or tumors. Typically, the hypopigmented lesions are nonatrophic, nonscaling, asymptomatic, and have normal sensation. Diagnosis is often delayed several years given the often subtle presentation, and the propensity not to make a diagnosis of cancer in children.

The histopathological evaluation of characteristic lesions shows identical findings to that of classic MF. There is epidermotropism of atypical lymphocytes, sometimes grouped in Pautrier microabscesses. Electron microscopy may demonstrate decreased melanosomes within epidermal keratinocytes, with preservation of normal melanosomes within melanocytes. The total melanocyte number may be normal or decreased. It has been proposed that defective melanosome transfer may be the etiology of the hypopigmented phenotype. Immunohistochemical analysis may show a predominantly CD8-positive, CD4-positive, or mixed epidermal infiltrate. This varies from classic MF, in which a mostly CD4+ infiltrate is usually seen. In many reports, especially those featuring children, a higher percentage of cases have been reported with a CD8+ predominant phenotype (up to 70% of cases). It has been suggested that CD8+ suppressor T-cells may cause direct cytotoxic destruction of melanocytes, leading to

hypopigmentation. T-cell receptor-gene rearrangement studies often reveal monoclonal T-lymphocyte proliferation; however, this finding is not synonymous with malignancy. Benign dermatoses, including inflammatory vitiligo, may also reveal a monoclonal T-cell infiltrate. The clinical differential diagnosis for hypopigmented patches includes vitiligo, lichen sclerosus et atrophicus, atopic dermatitis, pityriasis alba, pityriasis lichenoides chronica, post-inflammatory hypopigmentation, sarcoid, tinea versicolor, onchocerciasis, syphilis, and Hansen's disease. Differentiation between vitiligo and hypopigmented mycosis fungoides may be especially challenging, given often similar histopathological features. Both disorders may display epidermotropic lymphocytes with a predominance of CD8+ cells. El-Darouti et al. have suggested a series of diagnostic histopathological criteria for differentiating MF and vitiligo. Features in favor of MF include partial (vs. total) melanocyte and pigment loss, hydropic degeneration, papillary dermal lymphocytes, high density (vs. low density) dermal infiltrate, and wiry dermal fibrosis. The finding of basement membrane thickening is more common in vitiligo. They did not find monoclonality or immunohistochemistry to be helpful in differentiating these two disorders.

As patients with hypopigmented MF typically present with early-stage disease (T1a/T2a), prognosis is favorable. Survival rates have not been found to be different from same-stage classic MF, with life expectancy similar to control populations. Agar et al. found an overall survival of 98% in a 20-year follow-up of fifty-one hypopigmented MF patients. The treatment of choice for hypopigmented MF includes psoralen plus ultraviolet light (PUVA). Concerns regarding side effects (nausea, vomiting, liver damage, cataracts, skin cancers) may limit its use. There have been reports of therapeutic success with narrowband UVB. As in classic early-stage MF, topical therapies including corticosteroids, mechlorethamine (nitrogen mustard), carmustine (BCNU) and bexarotene may be tried. Radiotherapy is also an option. The natural history of this disease is remission with therapy, but most patients relapse with similar stage disease (75% at 10-year follow-up).

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Key Location(s): Right lateral neck **CASE 18**

Presented by Jordan Carqueville, MD and Anjeli K. Isaac, MD

History of Present Illness
50 year old Hispanic woman presented with a lesion on the right lateral neck that had been present since age 2. She had no prior history of trauma to the area and no developmental defects as a child. She had occasional pruritus and frequently experienced white keratinous discharge from the lesion. She had been treated with oral antibiotics for recurrent episodes of cellulitis by her primary care physician, but she had no symptoms of inflammation or irritation at the time of presentation.

Past Medical History
None

Medications/Allergies
None/NKDA

Physical Exam
Skin: Right lateral neck with groups of dilated open and closed comedones filled with dark brown keratinous material arranged in a linear to Blaschkoid distribution

Diagnosis
Nevus comedonicus

Treatment and Course
The patient had the lesion for nearly fifty years and declined surgical or medical intervention. Since establishing medical care in our clinic, she has not developed any inflammatory papules or cysts requiring oral antibiotics.

Discussion
Nevus comedonicus, initially described by Kofmann in 1895, is a rare hamartomatous proliferation of the pilosebaceous unit that is often present at birth or develops before age 10 years. First described in the U.S. as nevus follicularis keratosis, the condition has also been called comedone nevus, nevus acneiformis unilateralis, and nevus zoniforme. It is characterized by a linear array of grouped comedones, often in a Blaschkoid distribution, but may also be dermatomal or segmental. It is typically unilateral and found on the neck, face, chest or upper arm. Involvement of the palms, soles and the glans penis has been reported. Over time, these comedones become engorged with keratinous material and are mostly a cosmetic nuisance. The plaques usually are stable and asymptomatic, but inflammatory or cystic acne lesions have been frequently reported. Nevus comedonicus is separated into two types: type one is predominantly bland and comedonal, and in type two, the comedones become inflammatory, often with late sequelae including scars, keloids, and fistulae. Our patient has had multiple episodes of inflammatory papules and cysts requiring systemic antibiotics.

Reports of rare developmental defects of the central nervous system, skeletal system, eyes and skin are referred to as nevus comedonicus syndrome. Central nervous system involvement includes mental retardation, seizures, and transverse myelitis. Skeletal system abnormalities include scoliosis, hemi vertebrae, spina bifida occulta, absence of fingers, syndactyly, and supernumerary digits. Ocular abnormalities include congenital cataracts. Skin findings include perforating elastomas, ichthyosis, trichilemmal cysts, leukoderma and hemangiomas.

The etiology of nevus comedonicus is unclear, but thought to occur from a somatic mutation during embryogenesis. There is no gender or racial predilection.

A minority of cases develop at or near puberty, reflecting a role of androgens. Adult onset of nevus comedonicus is infrequent and often associated with chronic trauma or irritation. Histologic examination demonstrates dilated infundibula filled with keratin plugs and no hair shafts. These orifices represent rudimentary follicles that do not produce terminal hair follicles or functioning sebaceous glands, but can produce keratin.

Treatment is mostly for cosmetic purposes, and is often challenging and unsatisfactory. Medical modalities include topical or oral retinoids, ammonium lactate lotion or other keratolytics, and systemic antibiotics for infection or cystic inflammation. Intralesional triamcinolone may also be used for inflamed cysts. Surgical options that have been reported include excision, dermabrasion, manual keratin extraction, CO2 laser resurfacing, and diode and erbium:YAG lasers. Intervention is generally indicated for patients with cosmetic concerns and for treatment of inflammation and/or superinfection. No spontaneous regression of nevus comedonicus has been reported.

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Key Location(s): **Patient A – Face, upper extremities** **CASE 19**
Patient B – Nares, neck

Presented by Elizabeth Fahrenbach, MD; David Reid, MD; and Warren Piette, MD

CASE A

History of Present Illness

29-year-old African American male presented with a two-month history of red papules on his back, upper extremities, and face. He noted that the lesions primarily arose within or near tattooed areas. The tattoos had been present for 2 years before the development of the papules. The patient also reported a 6 to 8 month history of nontender lymph node enlargement in his neck. He denied weight loss, night sweats, fevers, chills, dizziness, vision changes, cough, chest pain, palpitations, nausea, vomiting, abdominal pain or arthralgias.

Past Medical History

Childhood heart surgery for a murmur

Medications/Allergies

None/NKDA

Social/Family History

No tobacco, ethanol, or illicit drug use; the patient participates in a work release program, prior to which he was incarcerated for 13 months; No family history of chronic skin disease

Physical Exam

Cardiovascular:	Bradycardic (58 bpm), regular rhythm, normal S1 and S2
Lymph:	Marked bilateral, nontender lymphadenopathy of the anterior and posterior cervical chains
Skin:	Medial canthi, right nostril, and lips with clusters of skin-colored and pink shiny papules; Dorsal hands, forearms and upper back with pink and erythematous shiny papules arising primarily within tattooed skin

Laboratory Data

The following labs were normal: CMP, CBC, HIV 1&2 antibody, RPR

Histopathology

MID UPPER BACK, PUNCH BIOPSY:
Non-caseating granulomas throughout the dermis. GMS, PAS, and AFB negative

Radiology

Chest radiograph: Bilateral hilar lymphadenopathy

Electrocardiogram

October 2010 (initial visit):
Sinus bradycardia (56 bpm) with marked sinus arrhythmia and 1st degree AV block (PR interval 216 ms); Right bundle branch block (QRS complex 154 ms) and left anterior fascicular block (bifascicular block); Left ventricular hypertrophy
January 2011:
Normal sinus rhythm (65 bpm); PR interval 206ms; Right bundle branch block (QRS complex 170 ms) and left anterior fascicular block (bifascicular block); Left ventricular hypertrophy

Diagnosis

Cutaneous sarcoidosis with profound cervical lymphadenopathy, lung, and cardiac involvement

Treatment and Course

The patient was diagnosed with cutaneous sarcoidosis based on clinical appearance. A punch biopsy of the skin was obtained for confirmation of diagnosis. Electrocardiogram performed in the dermatology clinic revealed evidence of left ventricular hypertrophy as well as asymptomatic conduction abnormalities. The patient was started on prednisone 20mg PO daily and hydroxychloroquine 200mg PO daily. At a follow-up visit 11 days after the patient's initial visit, there was marked improvement in the degree of cervical lymphadenopathy. Pulmonary function tests were normal. Ophthalmology evaluation showed no ocular involvement. A follow up electrocardiogram performed approximately three months after the initiation of oral prednisone and hydroxychloroquine showed little change from the initial EKG. The patient was referred for cardiology evaluation; the consulting team favored a diagnosis of cardiac sarcoidosis given the degree of conduction abnormalities, which could not be attributed solely to post-operative change. Further workup, including transesophageal echocardiogram and a cardiac MRI, are pending.

CASE B

History of Present Illness

30-year old male presented to the emergency room with subacute pain and diffuse thickening of the third finger of his left hand. He reported injuring his hand several weeks before in a basketball game, and had been informed by an outside provider that the left third finger was fractured. He incidentally reported a two-month history of nodules on the neck and nose. He denied fever, chills, chest pain, shortness of breath, or ocular changes.

Past Medical History

Gunshot wound 6 years ago, with subsequent hand surgery for removal of debris

Medications/Allergies

None/NKDA

Social History

Tobacco 1 pack per day, no ethanol use, 2-3 marijuana cigarettes per day; History of incarceration from 1998 to 1999; Grew up in the Chicago area; Recent travel to Alabama

Physical Exam

Skin: Anterior neck and nares with yellow superficial nodules, some grouped into large plaques along the neck; One similar lesion on the nape of the neck

Laboratory Data

The following labs were abnormal:

WBC	3.2 k/µL	[4.4 – 10.6 k/µL]
Hemoglobin	11.9 g/dL	[12.9 – 16.8 g/dL]
Platelets	146 k/µL	[161 – 369 K/µL)

The following tests were normal: CMP, HIV 1&2 antibody, RPR

Histopathology

LEFT NECK, PUNCH BIOPSY:

Granulomatous dermatitis. GMS, PAS, and AFB negative. Polarizable foreign material not identified.

Microbiology
LEFT NECK, TISSUE CULTURE:
Fungal, AFB, and bacterial tissue cultures: no growth

Radiology
Hand radiographs: mottled lucencies and fracture of left third phalanx; 1st, 2nd and 3rd right fingers with irregular lytic lesions
Chest radiograph (PA/lateral): lung fields show mild increase in interstitial markings; suggestion of a soft tissue density posterior to the trachea in the lateral view; heart size is within normal limits
CT chest with contrast: upper lobe-predominant interstitial opacities with axillary adenopathy; multiple vertebral body sclerotic lesions, and mottled sternum

Electrocardiogram
Normal sinus rhythm; minimal voltage criteria for left ventricular hypertrophy

Pulmonary Function Tests
No restrictive or obstructive pathology

Diagnosis
Cutaneous sarcoidosis with pulmonary, osseous and probable bone marrow involvement

Treatment and Course
The clinical diagnosis of sarcoidosis was confirmed by the findings of a 4mm punch biopsy. Special stains ruled out deep fungal or acid-fast bacilli infection. The patient began a course of hydroxychloroquine 200mg PO twice daily, prednisone 40mg PO every other day, and triamcinolone 0.1% ointment to the affected areas. Pulmonary, ophthalmologic, orthopedic and physical medicine and rehabilitation evaluations were obtained. At a follow-up dermatology visit, the patient had 90% resolution of skin lesions. He was continued on hydroxychloroquine 200mg PO twice daily as well as a slow prednisone taper prescribed by the pulmonology service. Topical steroids were discontinued. In light of the patient's pancytopenia and the mottled appearance of the sternum on chest radiograph, multiple myeloma was suspected. However, SPEP was negative and calcium level was within normal limits. Repeat CBC several months after presentation demonstrated persistent leukopenia-lymphopenia.

Discussion
Due to the frequent cutaneous involvement of sarcoidosis, the dermatologist often has the opportunity to make the initial diagnosis and evaluate the patient for systemic disease. After pulmonary and lymphoid disease, cardiac involvement is the next most common site of involvement, and is an often-unrecognized process in patients with sarcoidosis. Osseous and bone marrow involvement is often detected in later stages of sarcoidosis.

While cardiac sarcoidosis is clinically evident in 5% of patients with known sarcoidosis, 25% of patients with sarcoidosis are found to have cardiac involvement on autopsy. Clinical signs of cardiac sarcoidosis include cardiomyopathy with loss of muscle function, tachyarrhythmias, and bradyarrhythmias. In rare cases, sudden death may be the first sign of cardiac disease. Electrocardiogram is a useful initial screening test for newly diagnosed individuals. Additional suggested modalities include Holter monitoring, echocardiogram, cardiac MRI with gadolinium enhancement, and PET scanning. Due to the risk for sudden death, an evaluation by a cardiologist is imperative for individuals with abnormalities on initial screening tests or pertinent positives in review of systems. An electrocardiogram should be considered in the initial work-up of every patient with suspected sarcoidosis to screen for cardiac involvement.

There are few studies reporting the incidence of bone marrow involvement in sarcoidosis. In one series, 17% of sarcoidosis patients had bone marrow granulomas at autopsy. Bone marrow

involvement in sarcoidosis is associated with higher incidences of extrapulmonary involvement, as well as anemia and leukopenia-lymphopenia. In one large study, lymphopenia was a predictor of bone marrow involvement.

Bone involvement is present in 3 to 13% of sarcoidosis cases. The classic radiographic sign of osseous sarcoidosis is a "honeycomb" pattern representing a lytic process resulting in punched-out cortical and medullary defects, classically of the phalanges of the hands. While corticosteroid treatment is usually effective in treating the granulomas of sarcoidosis, osseous sarcoidosis responds poorly to steroids. Cases of osseous sarcoidosis highlight the importance of nonsteroidal anti-inflammatory drugs, hydroxychloroquine, and chloroquine, for both pain relief and attenuation of granuloma formation. In cases of osseous sarcoidosis where prolonged courses of steroids were used, salmon calcitonin and alendronate have been useful in preventing the risk of osteoporosis.

While some clinicians consider deviation from normal levels of angiotensin converting enzyme (ACE) to be useful in confirming or excluding the diagnosis of sarcoidosis, the utility of the ACE level is controversial. Only 60% of sarcoidosis patients displaying elevated ACE levels, and the test has relatively poor sensitivity and specificity. In one study, the reported positive and negative predictive values were only 84% and 74%, respectively. Thus, ACE levels are not recommended to confirm or exclude a diagnosis or to be used as a marker for response to therapy. Likewise, response to systemic steroids is commonly used as a pertinent positive in the diagnosis of sarcoidosis. However, other non-sarcoidal causes of cutaneous granulomas (such as cutaneous mycobacterial infection) may also initially improve after administration of steroids. Current diagnostic and therapeutic guidelines maintain that response to steroids should not be used to confirm or exclude a diagnosis of sarcoidosis.

These two cases highlight that, in addition to the typical concern for pulmonary and ocular involvement, the clinician must also suspect involvement of other organ systems when performing the initial work-up for sarcoidosis. Cardiac sarcoidosis can be screened for in the dermatology clinic with a detailed review of systems and electrocardiogram. Patients with suspected cardiac involvement should be referred for further testing directed by a cardiologist. When bone marrow or osseous involvement is detected on laboratory or radiologic tests, the patient is at higher risk for extrapulmonary disease, and later stage sarcoidosis may be suspected.

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Key Location(s): Left buttock **CASE 20**

Presented by August A. Natalie, MD and Warren Piette, MD

History of Present Illness

73 year old Hispanic man with no known past medical history presented to the emergency department with 2 weeks of increasing left buttock pain and induration. Three weeks prior to evaluation, while in Mexico, he received an injection of "vitamins" in the left buttock. One week prior to our evaluation, he was seen in the emergency department with the same lesion. A handheld ultrasound at the time revealed a multilayered collection of fluid; however, needle aspiration was negative. An incision and drainage of the lesion was attempted at that time, but no abscess was identified. He was treated with IV clindamycin and then sent home on a 7 day course of oral clindamycin. He returned to the emergency department one week later, three weeks after the injection, and was not improving. Dermatology was consulted to evaluate. During the interview, he noted burning and pinprick sensation in the affected area. The burning sensation radiated from the buttock around the left hip and down along the left inguinal crease.

Past Medical History

Intermittent symptomatic hypotension

Medications/Allergies

Clindamycin 300mg PO TID, on day 6 of 7
NKDA

Physical Exam

Vitals: 98.3, 79, 120/76, 18, 98% RA
Skin: Left buttock with 4 cm ovoid erosion with central early eschar and crust; superior retiform/dendritic edge; surrounding tense induration 1cm off the margin; tender to palpation

Laboratory Data

The following labs were abnormal:

Platelet	154 k/µL	[161 – 369 k/µL]

The following labs were normal: remainder of CBC; BMP

Histopathology

LEFT BUTTOCK, PUNCH BIOPSY:
Acanthotic epidermis with neutrophils and scale crust. Dermis with perivascular and interstitial mixed lymphocytic and neutrophilic infiltrate, hemorrhage, and fibrosis. No evidence of leukocytoclastic vasculitis, granulomatous change, or foreign material identified.

Microbiology

LEFT BUTTOCK, TISSUE CULTURE:
No bacterial or fungal growth. No AFB growth after 6 weeks.

Radiology

Sacrum/Coccyx radiograph: no radiopaque foreign body

Diagnosis

Nicolau Syndrome (a.ka. livedo-like dermatitis or embolia cutis medicamentosa)

Treatment and Course

Symptomatic treatment was given in the emergency department. Patient missed follow up appointment and has not returned to the Cook County health care system since.

Discussion

Nicolau syndrome (NS) is a rare complication of intramuscular injection of various drugs. It was first described by Freudenthal in 1924, then again by Nicolau in 1925. The first reports occurred after injecting bismuth salts for the treatment of syphilis.

NS typically manifests as severe pain immediately after the injection with rapid development of cyanotic patches in a retiform or livedoid pattern. This can lead to aseptic necrosis of dermis, fat, and even muscle, at the injection site. The lesion usually fully demarcates in 1-2 weeks, the eschar sloughs, and the underlying ulcer heals over months leaving an atrophic scar devoid of adnexal structures. The evolution is unpredictable and NS has been associated with serious complications, such as: myositis, myonecrosis, and muscle atrophy; transitory or permanent ischemia of the ipsilateral limb; abscess formation; and various nerve palsies.

The syndrome has been associated many medications: phenylbutazone, local anesthetics, antihistamines, corticosteroids, vitamin B complexes, sulfonamides, benzathine penicillin, procaine penicillin G, pyrazolone, chlorpromazine, camphor-quinine combinations, phenobarbitone, recombinant interferon α, interferon β, iodine sclerosing substances, vaccines (varicella and DTP), and etanercept. NS has also been reported after sclerotherapy of varicose veins. Reinjection with the same implicated medication in the same patient does not lead to recurrence.

Histologic examination reveals necrosis of eccrine glands with thrombosis of medium- and small-sized vessels of the reticular dermis without vasculitis. Our biopsy was taken from the peripheral viable tissue, which likely explains the lack of pathological correlation.

The etiology is unclear and at least four theories exist. Injection may produce intense pain with sympathetic vasospasm leading to ischemia and subsequent overlying necrosis. Another theory suggests intraarterial injection may cause embolic occlusion of small skin arteries. This is supported by the histologic finding of intra-vessel bismuth in Nicolau's original cases. Injection may cause progressive inflammation leading to necrosis of the intima and destruction of the whole arterial wall. Lastly, an injection that perforates the arterial wall may lead to thrombosis and ischemia.

The only treatment is prevention. Intramuscular injections should be performed in the upper outer quadrant of the gluteal region, which has fewer large blood vessels, and should only be performed after having aspirated the syringe in order to ensure an extra-vascular location. Other treatments have included plexus blocks, anticoagulant therapy, arteriotomy with extraction of the clot, and local wound care.

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