Craig A. Elmets, MD

Dr. Sidney Barsky Lecture
John H. Stroger Jr. Hospital of Cook County

Dr Elmets' lecture is funded by the
Chicago Dermatological Society

TABLE OF CONTENTS

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

Key Locations: eyes, face, trunk, hands **Case # 1**

Presented by Victoria Negrete, MD and Warren Piette, MD

History of Present Illness:
This one day old neonate male was transferred to Stroger Hospital NICU after being delivered at an outside hospital to a 29 year old G2P1 mother at 38 weeks gestational age. The mother received prenatal care throughout her entire pregnancy, which was complicated by preeclampsia, gestational diabetes, and premature rupture of membranes. He was stable at the time of transfer.

Past Medical History:
None

Medications/Allergies:
Ampicillin, gentamycin, and acetaminophen. No known drug allergies.

Family History:
No family history of skin disorders. Parents are non-consanguineous.

Physical Exam:
General: neonate appropriate for gestational age, with reactive normal cry.
Skin: scalp and body with firm platelike skin interrupted by deep fissures.
HEENT: severe ectropion, severe eclabium, and hypoplastic malformed pinna with hyperkeratotic skin filling the external auditory canals.
GU: rudimentary penis and scrotum, epispadias, and undescended testicles.
Extremities: hypoplastic fingers and toes with mitten-like casing and distal cyanosis, hemorrhage, and erosion.

Laboratory Data:
The following were abnormal or positive:

Hemoglobin	7.9 g/dL	[13.5-22.0 g/dL]
MCV	160.1 fL	[88-120 fL]
Platelets	108 k/uL	[200-400 k/uL]
Calcium	7.1 mg/dL	[8.5-10.5 mg/dL]
Potassium	3.1 mEq/L	[3.5-5.0 mEq/dL]

The following were normal or negative:
Blood cultures, white blood cell count, BUN, and creatinine.

Diagnosis:
Harlequin ichthyosis

Treatment and Course:
The patient was placed in a high humidity chamber (90-95%) in reverse isolation. Petrolatum ointment was applied to his skin every two hours under loosely applied plastic wrap. He was closely followed for fluid and electrolyte imbalances by the primary NICU team. The prophylactic antibiotics were discontinued on day 5 of life. The ophthalmology service recommended lubricating ophthalmic drops and erythromycin ophthalmic ointment for management of his ectropion, but on day 10 of life he developed mucopurulent discharge with conjunctival injection. A conjunctival culture revealed multi-resistant *Staphylococcus epidermidis* and *Escherichia coli*. The erythromycin ointment was discontinued, and a triple antibiotic ointment and gatifloxicin drops were initiated with resolution of the discharge.

Case # 1 continued

By day 10 of life, much of the encasement on his trunk had sloughed and transitioned to diffuse erythema with clinical improvement in his ectropion and eclabium. The mitten like casing of his fingers and toes slowly sloughed with improvement in perfusion to the digits. He failed to gain weight, and his formula feeds were increased four-fold with supplemental nasogastric tube feeds. Given the natural sloughing of the plaques, systemic retinoids were not initiated. On day 29 of life, he developed few pustules on the right cheek, which were positive for hyphae and budding yeast on KOH examination. Nystatin cream was initiated with improvement of the lesions.

Discussion:

Harlequin ichthyosis (HI) is a rare, severe congenital ichthyosis presenting with ectropion, eclabium, flattened ears, and large plate-like scales with deep fissures affecting the entire body. The prognosis is very poor, with few neonates surviving beyond the first few weeks of life. HI is an autosomal recessive disease due to a deletion mutation in the ABCA12 gene, which encodes an ATP binding cassette protein that transports glucosylceramides from the Golgi apparatus into lamellar bodies. A missence mutation in the ABCA12 gene results in type 2 lamellar ichthyosis. Because few to no lipids are delivered to the stratum corneum, the epidermis compensates with an intense, hyperplastic response leading to thick plate-like encasement. This defect also results in a defective skin barrier, placing the neonates at increased risk of fluid loss, electrolyte imbalances, hypothermia, and sepsis. Of the few neonates who survive, they most commonly progress to a severe congenital ichthyosiform erythroderma.

The ATP binding cassettes (ABCs) are a large group of proteins that transport different substrates across cellular membranes and are divided into seven subfamilies, A-G. The ABCA transporters function as cellular lipid-transporting organelles. ABCA transporter gene mutations are associated with disorders of lipid metabolism, including Tangier disease (ABCA1) and Stargardt disease (ABCA4), as well as neonatal surfactant deficiency, which has been associated with ABCA3 deficiency.

Prior to 2001, only seven reported children with HI survived beyond one year of life. All had been on a systemic retinoid (isotretinoin in one, etretinate in five, and acitretin in one) for short or intermittent periods. Systemic retinoids have been shown to help slough the thick adherent plaques within weeks, as well as improve ectropion and eclabium. Anecdotal experience suggests that systemic retinoids may help prevent ischemia and autoamputation of the digits.

Peroxisome proliferators-activated receptors (PPARs) are a potential therapy on the horizon for HI. PPARs have been shown to stimulate corneocyte envelope formation, stimulate epidermal lipid synthesis, accelerate LB secretion, and improve epidermal permeability barrier homeostasis. Recently, it has been shown that PPAR-γ induces ABCA12 mRNA expression in normal cultured keratinocytes, and may improve epidermal permeability barrier homeostasis in HI patients with residual ABCA12 expression.

References:

1. Akiyama M. The pathogenesis of severe congenital ichthyosis of the neonate. J Derm Science 1999;21:96-104.
2. Elias PM, Williams ML, Holleran WM, et al. Pathogenesis of permeability barrier abnormalities in the ichthyoses: inherited disorders of lipid metabolism. J Lipid Res 2008;49:697-714.
3. Franco RC. Successful treatment of harlequin ichthyosis with acitretin. Int J Derm 2001;40:472-3.
4. Jiang YJ, Lu B, Kim P, et al. PPAR and LXR activators regulate ABCA12 expression in human keratinocytes. J Invest Derm 2008;128:104-109.

Key Locations: ears & extremities **Case #2**

Presented by Morayo Adisa, MD, Sidney Barsky, MD and Warren Piette, MD

History of present Illness:
A 23 year-old Mexican man with a 2-year history of borderline lepromatous leprosy presented to our clinic in 2004 with complaints of new recurrent cutaneous lesions despite treatment. He had completed 20 months of a two-year regimen of multidrug therapy including dapsone, rifampin and clofazamine prior to his visit. He denied any neurological symptoms. The new tender lesions were intermittent and were mainly on his legs, flanks and earlobes.

Past Medical History:
Borderline lepromatous leprosy

Medications/Allergies:
As above

Family History:
None

Review of Systems:
Intermittent fever, cough, and occasional wrist and ankle pain associated with the lesional flares

Physical Exam:
07/04 Calves, left earlobe and abdomen: erythematous nodules
Flanks: erythematous to violaceous reticulated patches
10/06 Trunk and extremities: slate-gray to brown patches
01/08 Earlobes: erythematous papules
Thighs and legs: erythematous plaques

Laboratory Data:
The following were normal or negative (throughout 4 years):
Complete blood count with differential, basic metabolic panel, liver enzymes

Histopathology:
04/05: Left ear: Diffuse lymphocytic and foamy histiocytic infiltrate within the dermis
10/06: Right thigh: foamy histiocytes within the dermis. Fite stain highlighting histiocytes but no intact organisms
01/08: Right leg: Suppurative lobular panniculitis with foamy histiocytes. Fite stain negative

Diagnoses:
Erythema nodosum leprosum

Treatment and Course:
The patient experienced similar intermittent episodes of tender red nodules on his ears and lower extremities during the next 3 years, and the triple-drug regimen continued through June 2007, with the exception of clofazamine, which was substituted with minocycline. He was later seen by an expert at an outside institution who recommended discontinuation of all therapy since he was clinically clear and a biopsy performed at that time was histologically clear. He was lost to follow-up on a number of occasions. In January 2008, he developed joint pains in association with his lesional flares, at which point dapsone, rifampin, prednisone and ibuprofen were started. A biopsy taken at this time demonstrated a suppurative lobular panniculitis with foamy histiocytes. Thalidomide was started at 50mg nightly, but 3

Case # 2 continued

weeks into his course he developed flu-like symptoms and a confluent dusky painful erythematous eruption on his trunk, which prompted discontinuation of the drug. He was again lost to follow-up.

Discussion:

Erythema nodosum leprosum (ENL) is an immune-mediated phenomenon that is a rare complication of lepromatous (LL) or borderline lepromatous (BL) leprosy. Patients generally present during the first year of treatment with multidrug therapy, complaining of recurrent crops of tender, erythematous nodules accompanied by fever and malaise, as well as symptoms of ocular, joint, lymph node and nerve inflammation. Virtually any organ or tissue infiltrated by mycobacteria can be affected in ENL. Other clinical manifestations may include orchitis, bone pain (tibia especially), dactylitis, edema of the extremities and mucosa, transient proteinuria and upper respiratory symptoms.

Prospective studies evaluating various facets of ENL are lacking. Small series and case reports have demonstrated an increased risk of developing ENL in patients with bacterial skin infiltration by *M. leprae*, HIV infection, pregnancy, lactation, vaccination and psychological stress. An estimated 30-40% of infected pregnant and lactating women are at risk for developing ENL. Geographic variation in clinical frequency of ENL is also seen. It is more common in Southeast Asian and Brazilian leprosy patients (25-49%), and as low as 5% in African patients.

Histologic changes seen in ENL include an early inflammatory neutrophilic infiltrate, followed by a lymphoplasmacytic infiltrate in lesions older than 3-4 days. Mast cells and histiocytes may be seen as well. In addition, a necrotizing vasculitis and/or panniculitis are frequently observed early, while late changes can show proliferative or obliterative vascular changes. Early ENL lesions may also show fragmented or granular acid fast bacilli on Fite staining, which represent dead *M. leprae* organisms. These fragmented organisms have been shown to potentially fix complement more effectively than intact bacilli.

The immunopathology of ENL involves both antibody and cell-mediated immune responses. Immune complex deposition including IgG, IgM, C3, C1q and C3d both intra- and extracellularly can be detected in ~60% of patients, and 70% demonstrate detectable lesional *M. leprae* antigens. Both findings are best observed in lesions less than 24 hours old. Serum immune complex levels are normal, which parallels the pathogenesis of rheumatoid arthritis in which immune complexes are localized to synovial tissues alone. In addition, a reversed ratio of CD4:CD8 (2:1) T-cells is seen, with a reduction in suppressor T-cells. There has been little research on the role of B-cells in this process. Both a Th1 and a Th2 -type reaction have been reported in ENL. While evidence of a polymorphism in toll-like receptor 2 has been shown to influence susceptibility to developing reversal reactions in leprosy, the same has not been seen with ENL.

Thalidomide is the treatment of choice for ENL with response rates greater than 90%. Thalidomide can reduce serum TNF-α level by over 90%, and response is generally within 7 days of therapy. Systemic corticosteroids, clofazamine and infliximab are additional options.

References:

1. Kahawita IP, Lockwood DNJ. Towards understanding the pathology of erythema nodosum leprosum. Trans R Soc Trop Med Hyg 2008;102:329-37.
2. Teo SK, Resztak KE, Scheffler MA, et al. Thalidomide in the treatment of leprosy. Microbes Infect 2002;4:1193-1202.
3. Bochud-P, Hawn TR, Siddiqui MR, et al. Toll-like receptor 2 (TLR2) polymorphisms are associated with reversal reaction in leprosy. J Invest Dermatol 2008;197:253-61.
4. Feuth M, Brandsma JW, Faber WR, et al. Erythema nodosum leprosum in Nepal: a retrospective study of clinical features and response to treatment with prednisolone or thalidomide. Lepr Rev 2008;79:254-69.

Key Locations: trunk, palms, and soles **Case# 3**

Presented by Giacomo Maggiolino, MD and Warren Piette, MD

History of Present Illness:
A full term, 3700 gram baby boy was born with a generalized eruption encompassing the baby's trunk and extremities. The baby was born by vaginal delivery without any complications to a 26 year old healthy G2P1 mother. The mother was group B streptococcus (GBS) positive and received ampicillin at 6 hours and 2 hours before delivery. There was no known maternal history of herpes simplex infection, candidal vaginitis, intrauterine device usage, cervical cerclage, or amniocentesis.

Past Medical History:
None; uncomplicated pregnancy

Medications/ Allergies:
None/ no known drug allergies

Physical Exam:
Vitals: afebrile; slight tachypnea
Oral mucosa: clear, without lesions
Trunk and extremities: generalized erythematous vesiculopustular eruption extending to palms and soles
Nails: unaffected

Laboratory Data:
The following were normal or negative:
Complete blood count, basic metabolic panel, viral and bacterial cultures of cutaneous lesions, cerebral spinal fluid culture, blood culture, urine culture, and RPR

Radiology:
09/08 Chest X-ray: clear

Hospital Course:
At birth, the baby was immediately started on gentamicin, ampicillin, and acyclovir. Dermatology was then consulted for evaluation of the eruption. Skin scrapings were taken for Wright stain which showed no evidence of eosinophils. The next day, the baby's lesions started to dry up. Repeat skin scrapings were done for potassium hydroxide (KOH) preparation.

Histopathology:
9/08 Wright Stain on skin scraping: no eosinophils seen
9/08 KOH of skin scraping: positive for pseudohyphae and budding yeasts

Diagnosis:
Congenital cutaneous candidiasis

Treatment and Course:
By the third day of life, the majority of the eruption had begun to resolve without any treatment. The baby's vital signs were always stable and laboratory data showed no signs of infection.

Case # 3 continued

Discussion:

Congenital cutaneous candidiasis (CCC) is a rare condition, with only about 100 cases reported, that results from infection from *Candida spp.* acquired in utero. The infection is characterized by a generalized eruption of various morphologies, representing different stages of evolution, and includes erythematous macules, papules, vesicles, and pustules. The back, extensor surfaces of extremities, and skin folds are usually most involved. Pustules are usually seen on the palms and soles. Nail dystrophy has also been documented. Thrush on the oral mucosa is not commonly seen. The eruption usually presents within the first 6 days of life, although most present at birth.

Risk factors for CCC include a history of maternal candidal vulvovaginitis, intrauterine foreign body (such as an IUD or cervical cerclage), diagnostic amniocentesis, infant prematurity (less then 27 weeks gestational age), and low birth weight. There have been no reported associations between either systemic antibiotic or corticosteroid administration and the development of CCC. The exact pathogenic mechanism of infection is unknown. The infection is thought to be acquired in utero by the ascension of organisms from an infected vagina into the uterine cavity. The preterm infant's immature and compromised mucocutaneous barrier as well as systemic host defenses are thought to be predisposing factors.

The differential diagnosis of CCC includes neonatal candidiasis, which differs from CCC by appearing after the first week of life and manifesting as thrush or a diaper dermatitis. Some other conditions that may resemble CCC include erythema toxicum neonatorum, transient neonatal pustular melanosis, miliaria, group B streptococcal infection, and herpes simplex/varicella infection.

In almost all full-term infants, the disease tends to follow a self-limited, benign course. Skin lesions typically resolve within 1-2 weeks with desquamation. Neonates less than 27 weeks and less than 1,000 grams at birth are at greatest risk for systemic infection and death (67% and 40%, respectively, of infants weighing less than 1,000 grams in one study). These neonates are more likely to present with a widespread desquamating and/or erosive dermatitis. They may present with respiratory distress, elevated white blood cell count, persistent hyperglycemia and/or glycosuria. Chorioamnionitis and funisitis (inflammation of the umbilical cord) have also been reported. Neonates with burn-like lesions are at particular risk for systemic infection and death, with death occurring in 55% of such neonates weighing less than 1,000 grams in one study.

Treatment in full-term healthy infants has not been shown to have any benefit. Topical and/or systemic therapy has been recommended by some authors based on anecdotal experience. Infants with respiratory distress or signs of systemic infection (including positive blood, urine, or cerebrospinal fluid cultures) should be treated with systemic anti-fungal therapy. Amphotericin B has been documented to be first line of therapy. Prompt initiation of systemic anti-fungal therapy should be given in any infant with burn-like lesions.

References:

1. Darmstadt GL, Dinulos JG, Miller Z. Congenital Cutaneous Candidiasis: Clinical Presentation, Pathogenesis, and Management Guidelines. Pediatrics 2000: 105; 438-444.
2. Rowen JL, Tate J, Judy M. Management of neonatal candidiasis. The pediatric infectious disease journal, volume 17 (11) Nov 1998, 1007-1011.
3. Cosgrove BF, Reeves K, Mullins D, Ford MJ, Ramos-Caro FA. Congenital cutaneous candidiasis with respiratory distress and elevation of liver function tests: A case report and review of the literature. Journal of American Academy of Dermatology, 37 (5); Nov 1997; 817-823.

Key Location: Right shoulder **Case #4**

Presented by Joerg Albrecht, MD, PhD, Marc Boddicker, MD and Lissette Ortiz-Ferrer, MD

History of Illness:
This is a 63 year old male who presented in January 2009 with a one-month history of an asymptomatic red bump on the right shoulder. The patient denied any suppuration or bleeding. He has a history of metastatic prostate carcinoma, diagnosed in February 2008 that has been unresponsive to hormonal therapy.

Past Medical History:
Adenocarcinoma of the prostate, stage D3, cT2bNxM1, Gleason score 5+5, atrial fibrillation with left ventricular mobile thrombus, and normocytic anemia secondary to marrow infiltration from bony metastasis

Medications/Allergies:
Metoprolol, pantoprazole, warfarin, morphine sulfate controlled release, morphine sulfate immediate release, zoledronic acid, docetaxel/prednisone (first cycle 1/15/09)/ no known drug allergies

Review of Systems:
Non-contributory

Physical Examination:
Right anterior shoulder: there is a non-tender, firm, erythematous nodule measuring 1cm by 1.5cm. There is no ulceration or discharge.

Laboratory Data:
The following were abnormal or positive as per history:

08	PSA	201.3 ng/ml	[< 4ng/ml]
1/08	PSA	1136 ng/ml	[< 4ng/ml]
1/09	PSA	3017 ng/ml	[< 4ng/ml]

Histopathology:
01/09 Right shoulder: There is a diffuse dermal infiltrate reaching to the fat layer. It consists of pleomorphic, sometimes hyperchromatic cells arranged in cords without significant gland formation between collagen bundles. The tumor cells are positive for keratin, PSA (prostate specific Antigen) and PSAP (prostate specific acid phosphatase).

Radiology:
12/08 Total body bone scan: mild generalized increased uptake throughout the bony skeleton with increase uptake bilaterally in the shoulders, mandible, right posterior 10^{th} rib and bilateral clavicals as well as in the long bones.
08/08 CT chest, abdomen, pelvis: prostatic enlargement with diffuse bone metastasis throughout all bones as well as numerous enlarged lymph nodes.
11/08 CT head: no abnormality

Diagnosis:
Prostatic adenocarcinoma with metastasis to the skin

Case #4 continued

Treatment and Course:

The patient was started on a palliative chemotherapy regimen with docetaxel and prednisone. He was seen about 2 weeks after the first course of treatment and the cutaneous nodule was significantly smaller and softened. He continues to undergo chemotherapy.

Discussion:

Prostate cancer has an extremely high prevalence. In the US in 2004, 189,075 men were diagnosed with the disease and 29,002 men died from it. In spite of this high prevalence cutaneous metastasis due to carcinomas of the prostate are very rare. The estimated rates ranges from 0.3 to 0.6%. However, some large series reported no cases, thus it is likely that the cumulative rate may well be lower.

Prostate carcinoma may metastasize via four mechanisms: extension from an underlying tumor, implantations within a surgical scar, lymphatic spread and hematogenous spread, often via the vertebral venous system. The route of cutaneous metastasis remains controversial.

The clinical presentation of cutaneous metastasis from prostate cancer varies. In 2008 Wang et al. analyzed all 78 cases that were available through pubmed search in the English and Japanese literature. They found multiple hard nodules were present in 56 cases (72%), a single nodule as in our case in 11 cases (14%), edema or lymphedema in 5 (7%) and unspecified rash in 5 cases (7%). Beyond this series a teleangiectatic cutaneous metastasis has been described. Wang et al. found that the metastasis were most frequently found in the inguinal area and the penis (28%), followed by the abdomen (23%), the head and neck (16%), the chest (14%), the extremities (10%) and the back (9%).

Cutaneous metastasis of a prostate carcinoma signals very poor prognosis. In spite of the dramatic response of the metastasis to the first round of chemotherapy the outlook of our patient remains grim. The mean survival time of the 78 patients mentioned above was 7 months.

References:

1. Mueller TJ, Wu H, Greenberg RE, Hudes G, Topham N, Lessin SR, Uzzo RG. Cutaneous Metastasis from genitourinary malignancies. Urology 2004; 63; 1021-1026.
2. Steinkraus V, Lange T, Abeck D, Mensing H, Ring J. Cutaneous metastasis from carcinoma of the prostate. JAAD 1994; 31; 665-666
3. Krathen RA, Orengo IF, Rosen T. Cutaneous Metastasis: A Meta-Analysis of Data. South Med J 2003; 96; 164-167
4. Wang SQ, Mecca PS, Myskowski PL, Slovin SF. Scrotal and penile papules and plaques as the initial manifestation of a cutaneous metastasis of adenocarcinoma of the prostate: case report and review of the literature. J Cutaneous Path 2008; 35; 681-684
5. Prostate cancer statistics www.cdc.gov accessed 02/03/09

Case #5

Presented by Carlos Rodriguez, MD and Warren Piette, MD

UNKNOWN #1

89 year old woman with a deep-seated, firm plaque on her lower back and buttocks present for 4 weeks

Key Locations: legs and arms **Case #6**

Presented by Erika Music, MD and Warren Piette, MD

Patient A

History of Present Illness:
This 26 year-old Hispanic male was admitted for a three week history of progressive rash, fever, and weakness. The rash began on his feet and legs and subsequently spread to his thighs and arms. He denied pruritus, but complained of tenderness on palpation. On further questioning, the patient reported a sore throat two to three weeks prior to onset of the rash. He complained of red eyes and a few sores in his mouth at the time. The patient was previously admitted at an outside hospital for ten days and did not improve on doxycycline. Multiple tests were performed during this admission, but no biopsy. He left AMA and presented to our ED a few days later. Here, he reported subjective fever, chills, muscle aches, fatigue, joint pain of wrists, knees, and ankles, nausea, vomiting, and diarrhea. He had difficulty walking secondary to joint pain and required crutches during admission.

Past Medical History:
Depression

Medications/Allergies:
Risperdol, sertraline; No known drug allergies.

Review of Systems:
Positive findings include fever, chills, muscle aches, fatigue, nausea, vomiting, diarrhea, and joint pain of wrists, knees, and ankles.
He denied headaches, chest pain, shortness of breath, hematuria, dysuria, and hematocheezia.

Physical Exam:
General: alert and oriented, NAD
Dorsal feet: partially-blanchable and completely blanchable purpuric macules
Thighs, legs, and forearms: erythematous , tender, completely blanchable subcutaneous nodules

Laboratory Data:
The following were abnormal or positive:

White blood count	15,000/mm^3	[nl: 4,000-10,000/mm^3]
Neutophils	88.2%	[nl: 45.4-75.1%]
Lymphocytes	5.1%	[nl: 16.5-43.4%]
Hemoglobin	9.0 g/dl	[nl: 12.0-16.0 g/dl]
Hematocrit	27.3%	[nl: 35-45%]
Platelets	466,000/µL	[nl: 185-395,000/µL]
Potassium	5.5 mEq/L	[nl: 3.6-5.1 mEq/L]
ESR	115 mm/hr	[nl: 0-26 mm/hr]
CRP	30.74 mg/dl	[nl:<0.5 mg/dl]
GGT	249 U/L	[nl: 3-60 U/L]
AST	112 U/L	[nl: 15-41 U/L]
ALT	231 U/L	[nl: 17-63 U/L]
LDH	275 U/L	[nl: 85-210 U/L]
PT	15.6 sec	[nl: 11.8-15.0 sec]
PTT	40.2 sec	[nl: 25.6-34.0 sec]

Case #6 continued

The following were normal or negative:

Sodium, chloride, bicarbonate, BUN, creatinine, urine analysis, Hepatitis B and C antibodies, p-ANCA, c-ANCA

Radiology:

05/08 Chest x-ray: within normal limits

Histopathology:

05/06/08 Right thigh: There is a lobular panniculitis with a sparse neutrophilic infiltrate and fat necrosis; suggestive, but not diagnostic of Sweet's syndrome.

05/30/08 Right great toe: There is a predominately neutrophilic infiltrate within the wall of a subcutaneous intermediate to large size blood vessel. The overlying dermis shows a small vessel vasculitis.

Diagnosis:

Benign cutaneous polyarteritis nodosa

Treatment and Course:

Based on the presentation of tender, subcutaneous nodules accompanied by fever and leukocytosis following a sore throat, in conjunction with the initial biopsy, a preliminary diagnosis of Sweet's syndrome, or acute febrile neutrophilic dermatosis, was made. The patient was started on 40 mg of prednisone daily, with prompt improvement of his skin lesions and systemic symptoms. The prednisone was tapered weekly, and once the patient was on 20 mg daily, new lesions on his palms and soles appeared, along with the recurrence of muscle pain and arthritis. A new biopsy was performed, and the diagnosis of cutaneous polyarteritis nodosa was made. The patient's prednisone was increased to 60 mg daily and upon tapering, dapsone 25 mg daily was initiated, based on the predominance of neutrophils in the biopsies. The patient again experienced prompt improvement. The prednisone was tapered within 3 months, and dapsone was slowly increased to 100 mg daily. The patient has had no new lesions for seven months and the dapsone has since been tapered.

Hematology was also following the patient for his anemia, the etiology of which was never determined. However, his hemoglobin returned to normal with therapy.

Patient B

History of Present Illness:

This 65 year-old male, visiting from Yemen, was admitted with a five day history of fever and a rash on both legs. The lesions were tender and non-pruritic. He also reported pain in his knees and ankles, fatigue, and muscle weakness. He denied any recent upper respiratory infection, but did report a two-month history of intermittent oral and genital ulcers.

Past Medical History:

Arthritis, low back pain

Medications/Allergies:

Naproxen, ibuprofen; No known drug allergies.

Review of Systems:

Positive findings include fever, chills, joint pain in knees and ankles, muscle weakness, and fatigue. He denies shortness of breath, chest pain, hematuria, dysuria, hematocheezia, nausea, vomiting, or abdominal pain.

Case #6 continued

Physical Exam:

General: alert and oriented, shivering

HEENT: Bilateral conjunctival erythema, lower buccal lip with shallow round ulceration with grayish base and surrounding erythema

Feet, anterior legs, thighs, and forearms: tender, erythematous subcutaneous nodules, and several erythematous, tender papules just below knees and scattered on forearms

Scrotum and base of penis: shallow, erythematous ulcerations

Laboratory Data:

The following were abnormal or positive:

ESR	58 mm/hr	[nl: 0-26 mm/hr]
CRP	18.21 mg/dl	[nl: <0.5 mg/dl]

The following were normal or negative:

Complete blood count, basic metabolic panel, liver function tests, p-ANCA, c-ANCA, Hepatitis B and C antibodies, G6PD enzyme activity, HSV culture

Histopathology:

07/08 Right leg and left forearm: There is a predominately neutrophilic infiltrate within the wall of medium to large size blood vessels in the subcutaneous tissue.

Diagnosis:

Benign cutaneous polyarteritis nodosa

Treatment and Course:

The patient was started on 40 mg daily of prednisone, with prompt resolution of skin lesions and systemic complaints. Dapsone therapy was initiated during tapering of the prednisone with continued improvement. The patient had no new lesions after initiation of therapy. He returned to Yemen six weeks after discharge.

Based on the patient's ethnicity and oral and genital ulcerations, Behcet's disease was considered in the differential. However, his ulcerations were superficial and relatively painless, compared to the deep, penetrating, painful, punched out ulcerations characterized by Behcet's. This patient's ulcers were more consistent with recurrent aphthous ulcerations. Furthermore, vasculitis of medium-sized vessels is not characteristic of Behcet's syndrome. Classic cutaneous lesions in Behcet's resemble erythema nodosum, both clinically and histologically.

Discussion:

The term polyarteritis nodosa (PAN) emcompasses three related, but distinct vasculitides: classical PAN, microscopic polyangiitis, and cutaneous PAN. These can be distinguished based on clinical symptoms, cutaneous lesions, laboratory data, and histopathology.

Classical PAN is considered to be a disease of predominately medium-sized, angiographically visible vessels accompanied by constitutional symptoms, such as fever, weight loss, arthralgias, and myalgias. However, the systemic vasculitis involves multiple organs and can result in renovascular hypertension, renal failure, myocardial infarction, congestive heart failure, orchitis, and cerebral hemorrhage or infarction. Untreated, classical PAN has a five year survival of 10-13%; prednisone therapy improves survival to 48-57%. Cutaneous involvement in classical PAN is rare and limited to palpable aneurysms and terminal digital infarcts. In classical PAN, c-ANCA is positive in only 10% of cases and p-ANCA in 20% of cases.

Microscopic polyangiitis is a systemic vasculitis involving small vessels, as well as cutaneous arterioles and capillaries. The vasculitis leads to alveolar capillaritis and most commonly, glomerulonephritis. Skin manifestations affect 25-60% of patients, presenting as palpable purpura, ulcerations, and subcutaneous nodules. Nearly 90% of patients with microscopic polyangiitis have a

Case #6 continued

positive ANCA; 45% exhibiting c-ANCA positivity, and 45% with positive p-ANCA. Histopathology demonstrates a leukocytoclastic vasculitis of the small vessels in the papillary dermis.

In 1931, Lindberg first described a form of panarteritis nodosa which predominately affected vessels in the cutaneous tissue, with patients experiencing a more favorable prognosis. In contrast to classical PAN, cutaneous PAN is distinguished by involvement of medium to large sized vessels of the lower dermis and superficial fat. Subcutaneous nodules are the most common skin lesion in the cutaneous PAN. Over half of patients with cutaneous PAN experience some extracutaneous symptoms such as fever, arthralgias, myalgias, and even neuropathy. However, these symptoms are limited to the areas of the body affected with skin lesions. Overwhelmingly, the lower extremities are the most common site of involvement in cutaneous PAN. Patients may experience spontaneous remission or continue with a chronic, relapsing course, but an overall good prognosis. ANCA is negative and biopsy demonstrates a necrotizing arteritis involving vessels in the lower dermis and subcutaneous fat.

The etiology of cutaneous PAN is unknown. An association with Hepatitis B infection, or other viral or bacterial infections such as streptococcus or tuberculosis has been proposed. There are also associations with other inflammatory diseases such as Crohn's disease and ulcerative colitis. Some authors have proposed an immune-complex mediated mechanism as the etiology, despite a negative direct immunofluorescence in most cases.

Treatment for benign cutaneous PAN consists initially of dapsone and/or prednisone if severe, followed by a slow taper of prednisone and the addition of a long-term immunosuppressant, if required. Methotrexate, cyclophosphamide, and azithioprine have all been reportedly effective. Because classical PAN can have skin involvement, and the distinction is often difficult, close follow-up of any patient with cutaneous PAN is recommended.

A 2009 review by Nakamura and colleagues followed 22 patients with the cutaneous form of PAN and found none of them to progress to systemic PAN, despite 64% having systemic symptoms, which were limited to same areas as the skin lesions. The confusing and controversial distinction between cutaneous PAN with systemic symptoms and classical PAN prompted them to propose new diagnostic criteria. According to the existing criteria created by the American College of Rheumatology, a patient with cutaneous disease and one systemic symptom can be diagnosed with classical PAN. However, these patients have very different clinical courses and outcomes. Their new diagnostic criteria for cutaneous PAN is based on classical skin findings, histopathology, and ten exclusion criteria that would favor systemic PAN.

In a 2008 article in the *Archives of Dermatology*, Lee and colleagues describe a series of five women with lower extremity patchy reticular hyperpigmentation and palpable subcutaneous induration and nodules. On biopsy, lesions demonstrate a lympho-histiocytic vasculitis with a hyalinized fibrin ring within the vessel lumen. These vessels are at the dermal-subcutaneous junction. The authors propose a new disease, "Lymphocytic Thrombophilic Arteritis", based on the inability to classify this entity in either the American College of Rheumatology or Chapel Hill Consensus Conference criteria. Also, they cite the absence of purpura and ulcerations as exclusion critera for PAN. However, the clinical description, histologic features, benign course, and laboratory data all indicate this new entity may be the often misunderstood cutaneous variant of polyarteritis nodosa.

References:

1. Bauzá A, et al. Cutaneous polyarteritis nodosa. Br J Dermatol 2002;146:694-9.
2. Fiorentino D. Cutaneous vasculitis. J Am Acad Dermatol 2003;48:311-40.
3. Lee J, et al. Lymphocytic Thrombophilic Arteritis. Arch Dermatol 2008;144:1175-1182.
4. Nakamura T, et al. Cutaneous polyarteritis nodosa: revisiting its definition and diagnostic criteria. Arch Dermatol Res 2009;301:117-121.
5. Piette W. (2004). Primary Systemic Vasculitis. In R. Sontheimer & T. Provost (Eds.), *Cutaneous Manifestations of Rheumatic Diseases* (159-196). Philadelphia: Lippincott, Williams and Wilkins.
6. Rogalski C, et al. Panarteritis cutanea benigna—an entity limited to the skin or cutaneous presentation of a systemic necrotizing vascultlis? Report of seven cases and review of the literature. Int J Dermatol 2007;46:817-821.

Key Locations: face, upper trunk and extremities **Case #7**

Presented by Robert Lieberman, MD, and Jerry Feldman, MD

History of Present Illness:
The patient is a 26 year old woman who presented with a four-month history of itchy papules and plaques on her face, neck, chest, back, and upper and lower extremities.

Past Medical History:
None

Medications/Allergies:
None

Review of Systems:
The patient reports a one month history of joint pains, decreased appetite, and a 15-pound weight loss over the past four months. She denies fever, chills, chest pain, dyspnea, hematuria, headaches, photosensitivity, or acral sensitivity to cold.

Physical Exam:
Extensor arms and face: violaceous, hyperpigmented scaly papules coalescing into plaques.
Back, chest, neck, and legs: multiple retiform plaques - some characterized by erythematous rims and hyperpigmented, atrophic centers and others with hyperpigmented rims and hypopigmented, atrophic centers.
Occipital scalp: erythematous patches of alopecia characterized by loss of follicular ostia.
Nails: no periungual telangiectasias.

Laboratory Data:
The following were abnormal or positive:

White blood cell count	2.5K/μL	[4.2-10.0K/μL]
Platelets	143K	[185-395 k/μL]
Urine protein	20	[neg]
Urine RBC	17	[neg]
Antinuclear antibody (ANA)	>1:160, speckled	[neg]
anti-Ro antibody	1.17	[<0.9]
C4	15	[16-47]

The following were normal or negative:
Comprehensive metabolic panel, hemoglobin, liver function tests, anti-dsDNA antibody, anti-Smith antibody, anti-RNP/Smith antibody, anti-La antibody, anti-centromere antibody, CH50, C3 level, and high sensitivity C-reactive protein

Histopathology:
10/08 A) left arm and B) back: Interface dermatitis, vacuolar type, with occasional dyskeratosis, melanophages in the papillary dermis, dermal mucin, and a superficial and deep perivascular and periadnexal lymphocytic infiltrate, consistent with discoid lupus erythematosus.

Diagnosis
Disseminated discoid lupus erythematosus (DLE)

Case # 7 continued

Treatment and Course:

At the time of diagnosis, treatment was initiated with hydroxychloroquine 200 mg orally twice daily and triamcinolone 0.1% ointment. Additionally, the patient was referred to nephrology for evaluation of possible kidney involvement. Unfortunately, this patient was lost to follow-up.

Discussion:

Discoid lupus erythematosus is a form of chronic cutaneous lupus erythematosus characterized by atrophic indurated erythematous plaques found most often on the face, scalp, and ears, though they may be present in a widespread distribution (above and below the neck). Adnexal inflammation is often prominent, manifested clinically as scarring alopecia and follicular plugging. In longstanding lesions, classic central hypopigmentation and surrounding hyperpigmentation may develop. Discoid lesions are most common in women ages 20 to 40, with a male-to-female ratio of three to one. While eighty percent of cases of discoid lupus are localized to the face and scalp, twenty percent of cases involve the upper trunk and upper extremities, though it is highly unusual to identify only discoid lesions below the neck.

Our patient is unique due to the widespread nature of her discoid lesions. Only five to ten percent of patients with chronic discoid lupus erythematosus eventually develop systemic lupus erythematosus (SLE), and this transition may take more than five years. However, widespread discoid lesions are recognized as a warning sign for the presence or development of SLE; in a retrospective review by Callen of 17 patients who developed SLE either before, concurrent with, or after the diagnosis of DLE, 15 of the patients exhibited widespread disease at initial evaluation, and the two patients with initially localized disease eventually developed widespread disease. In 14 of the 17 patients, the SLE was diagnosed concurrent with or years after the diagnosis of DLE.

Several studies have attempted to identify other markers indicating systemic involvement in patients with cutaneous lupus. In a prospective study of 246 patients with DLE or subacute cutaneous lupus (SCLE) and 51 patients with SLE, Tebbe et al. utilized seven clinical and laboratory criteria to identify the most significant variables distinguishing between cutaneous disease and SLE. On multivariate analysis, signs of nephropathy, the presence of arthralgias, and an ANA titer $\geq$ 1:320 were most significant. Photosensitivity and elevation of the erythrocyte sedimentation rate (ESR) were less statistically relevant, and the presence of recurrent headaches and anti-dsDNA antibodies, though a predictor of renal disease in systemic lupus, were not useful in distinguishing between cutaneous and systemic disease.

The underlying problem in evaluating for SLE in patients with cutaneous lupus, however, is that the main criteria utilized are those which were developed by the American Rheumatism Association (ARA). The criteria poorly define cutaneous disease, excluding completely lesions of SCLE. In fact, 20-30 percent of all patients with DLE exhibit greater than 4 positive ARA criteria (usually including LE-specific skin lesions, photosensitivity, and serological findings) and could therefore be classified as SLE, although many clinicians recognize that this group of patients has a much different prognosis than those SLE patients with nephritis and arthritis. Therefore, a need exists to develop better criteria suitable for patients with cutaneous disease.

References:

1. Callen J, et al. Systemic lupus erythematosus in patients with chronic cutaneous (discoid) lupus erythematosus. *J Am Acad Dermatol* 1985; 12:278-88.
2. Parodi A, et al. ARA and EADV criteria for classification of systemic lupus erythematosus in patients with cutaneous lupus erythematosus. *Dermatology* 1997; 194:217-20.
3. Tebbe B, et al. Clinical course and prognosis of cutaneous lupus erythematosus. *Clin Dermatol* 2004; 22:121-24.
4. Tebbe B, et al. Markers in cutaneous lupus erythematosus indicating systemic involvement: a multicenter study on 296 patients. *Acta Derm Venereol* 1997; 77:305-8.

Key Locations: lower extremities **Case #8**

Presented by Lauren Fine MD and Warren Piette MD

History of Present Illness:
This is a 75 year old woman admitted for a colonoscopy to investigate the etiology of her chronic anemia. 5 days prior she had received 3 units of packed red blood cells for a hemoglobin of 4.7. One day after transfusion she developed pruritic, mildly painful and burning red lesions on her legs, arms, and abdomen. Some were initially up to 10 cm in diameter. 4 days later they were asymptomatic and much smaller, but still present. She had similar lesions with a previous blood transfusion.

Past Medical History:
Iron deficiency anemia, uterine cancer s/p radiation & hysterectomy (1988), radiation proctitis, atrial fibrillation, hypertension, congestive heart failure, hypothyroidism

Medications/ Allergies:
valsartan, metoprolol, synthroid, hydochlorathiazide, pantoprozole, calcium, FeSO4, acetaminophen/ NKDA

Review of Symptoms:
Positive findings include fatigue, a 20 pound weight loss over a 4 month period, and black stools.

Physical Exam:
BP 112/92 HR 92 RR 16 Temperature 99˚C
The patient is a pleasant woman in NAD.
Lower extremities: scattered well-demarcated round (5mm–2cm) and linear circumferential palpable non-blanching red papules and plaques
Left forearm and flanks: clustered non-blanching red macules and papules ranging in size from 2mm-5 mm

Laboratory Data:
The following were abnormal or positive:

Hemoglobin	9.1 g/dL	[11.5-16.5 g/dL]
Hematocrit	28.3 %	[40-52%]
BUN	31 mg/dL	[8-20 mg/dL]

The following were normal or negative:
Sodium, potassium, calcium, white blood cell count and differential, platelets, TSH, liver enzymes, CK-MB and troponin

Radiology:
11/4 Colonoscopy: There are few small localized angioectasias in the cecum and rectum. No active bleed or stigmata of a recent bleed is present.
11/4 CT abdomen: normal

Histopathology:
1/12/09 Left arm: Superficial dermis with leukocytoclastic vasculitis and focal few erythrocytes, suggestive of urticarial vasculitis.

Diagnosis: Post-transfusion urticarial vasculitis secondary to serum sickness

Case #8 continued

Treatment and Course:

When we first saw this patient, her skin lesions were markedly improved from their onset, and no treatment was initiated. At two-week follow up, the patient was doing well and all skin lesions had resolved, except for residual post-inflammatory hyperpigmentation. Her medical team continues to follow her for anemia, and no specific cause has been found.

Discussion:

Transfusion-induced reactions involving immune complex formation or serum sickness are rarely reported. Foreign proteins present in the plasma of the transfused red blood cells which are not routinely screened for serve as an antigen to which the patient's preformed antibodies react. Serum sickness is a Type III hypersensitivity reaction occurring when a person is sensitized with a foreign protein and is later re-exposed. The antigen-antibody complexes deposit in small vessel walls, activate the complement cascade, and recruit inflammatory cells, which can ultimately result in tissue damage and necrosis. Immune complex deposition within vessel walls leads to a characteristic leukocytoclastic vasculitis, as was seen in our patient. The vasculitis can affect organs other than the skin, such as the kidneys, joints, nerves, and the heart, and lead to hypocomplementemia secondary to the consumption of complement. Furthermore, a wide range of physical findings such as fever, malaise, myalgias, nausea, abdominal pain, and lymphadenopathy are commonly associated with a serum sickness reaction. Interestingly, our patient did not have significant constitutional symptoms or any sign of internal organ involvement. Unfortunately, complement levels were not drawn.

Serum sickness should be distinguished from serum sickness-like reactions, which do not exhibit circulating immune complexes. They present with fever, pruritus, urticaria, and arthralgias 1 to 3 weeks after drug exposure. The pathologic finding of leukocytoclastic vasculitis in our patients strongly suggests an immune complex etiology.

The purpuric lesions as well as the clinical findings of tenderness and burning are also consistent with an urticarial vasculitis (UV). UV can be associated with autoimmune connective tissue disease such as SLE, viral infections, drugs, and less commonly with the hypocomplementemic urticarial vasculitis syndrome (HUVS). An acute event like serum sickness is a rare but well documented cause of UV. Palpable purpura is a frequent finding in UV secondary to a serum sickness reaction, as was present on our patient. The unique linear circumferential distribution of lesions suggests the Koebner phenomenon. The location and shape of these lesions on the lower extremities can be explained by pressure from a tight sock or stocking. The Koebner phenomenon is commonly seen in urticarial vasculitis as well as other chronic urticarias.

Serum sickness is almost always a self-limiting disorder. The immune complexes are cleared by the reticuloendothelial system. For patients with multisystem involvement, a short course of systemic corticosteroids usually results in the resolution of symptoms after 10 days. To prevent this uncommon complication from occurring in the future, patients should only be transfused with plasma-free washed RBCs and washed platelet preparations. This results in the removal of the plasma proteins or immunoglobulins to which the patient's antibodies are directed, thereby preventing immune complex formation.

References:

1. Proctor L, Renzulli B, Warren S, Brecher M. Monoclonal antibody-stimulated serum sickness. *Transfusion Medicine Illustrated*. 2004; 44:955.
2. Saegman V, Wynendaele W, Kerre S, Dedeurwaerdere F, Van der Driessche M, Moerman J. Transfusion-induced serum sickness. *Transfusion*. 2008;
3. Wisnieski J. Urticarial vasculitis. *Current opinion in Rheumatology*. 2000; 12:24-31.

Key Location: generalized **Case # 9**

Presented by Jordan Carqueville, MD, Warren Piette, MD, and Lissette Ortiz-Ferrer, MD

History of Present Illness:
The patient is a 56 year old Pakistani male who presented with an asymptomatic, generalized eruption located on his arms, chest, upper back, face and legs for 11-12 months. He complained of limited range of motion of his hands and increased sensitivity of his fingertips. He was unhappy with his physical appearance, and stopped attending church because acquaintances asked what was wrong with his face.

Past Medical History:
None

Medications/Allergies:
None/ no known drug allergies

Social History:
10 years ago the patient moved to the United States from Pakistan.

Review of Symptoms:
He reported shortness of breath for 3 months, and was unable to jog one-block. He denied cough, hemoptysis, chest pain, fever, weight loss, numbness or tingling sensation in his extremities.

Physical Exam:
Face: coarsening of facial features and increased thickness of skin folds
Ears: enlarged and erythematous with folds in the lobe
Trunk, abdomen, arms, legs: generalized, indurated, erythematous and blanching retiform plaques without scale or ulceration

Laboratory Data:
The following were normal or negative:
Complete blood count and differential, basic metabolic panel, liver function tests, thyroid function tests, hepatitis B and C, HIV antibody, RPR , anti-nuclear antibody, rheumatoid factor

Diagnostic Procedures and Tests:
8/08 AFB smear: 3+ acid fast bacilli colonies
8/08 PCR-restriction fragment length polymorphism analysis: positive for hsp65 gene
8/08 Chest X-ray: no active pulmonary disease
8/08 Electrocardiogram: normal sinus rhythm with possible left atrial enlargement

Histopathology:
8/08 Arm: The dermis contains non-caseating granulomas. The fite stain is positive for acid-fast mycobacteria.

Diagnosis:
Borderline lepromatous leprosy

Treatment and Course:
The patient was started on rifampicin 600 mg once monthly, dapsone 100 mg daily, and minocycline 100 mg twice daily for treatment duration of 1-year. At one month follow-up, the erythematous plaques were less red and indurated. After specific questioning, the patient reported a

Case # 9 continued

history of leprosy 30 years ago while living in Pakistan. Both he and his brother were treated for leprosy, most likely with a 3-year course of dapsone.

Discussion:

The World Health Organization (WHO) classification divides leprosy into 3 types to determine multi-drug treatment protocol: paucibacillary single lesion, paucibacillary (2-5 lesions), and multibacillary (more than 5 lesions). The Ridley-Jopling classification system is a 5-category spectrum based on clinical, bacteriologic, histologic, and pathologic criteria, where paucibacillary disease is equivalent to TT (tuberculoid), and BT (borderline tuberculoid) disease, and multibacillary is equivalent to BB (borderline), BL (borderline lepromatous) and LL (lepromatous) disease. Our patient was classified as multibacillary, borderline lepromatous disease, as he had greater than 5 symmetrical, erythematous plaques, 3+ bacterial index on split-skin AFB smear, and moderately defined granulomas with many bacilli on histology. Our patient did not have palpable ulnar or peroneal nerves or anesthesia.

Leprosy is a chronic mycobacterial infection that affects genetically predisposed individuals to mount a widely variable immune response. Although multi-drug treatment has decreased the prevalence of disease, the reported number of new cases remains the same. *Mycobacterium leprae* is not cultivable, and to date, there are no practical early detection methods for clinically unapparent disease, emphasizing the need for further investigation of new mycobacterial antigens.

Our patient was the first confirmed *M. leprae* diagnosis in the Cook County Public Health System using the PCR-restriction fragment length polymorphism analysis (PRA) of the hsp65 gene. This gene, present in all mycobacteria, produces a heat shock protein that elicits a T cell response in the host. PRA requires biopsy of infected tissue, amplification of the 439-bp portion of the hsp65 gene, two distinct digestions of the PCR product, and identification with electrophoresis. Previously, heat shock protein antibody levels were useful in diagnosis of LL and BL patients with >2+ bacillary index. Heat shock proteins correlate with bacterial load, being higher in lepromatous than tuberculoid cases. The major limitation of the heat shock protein antibody assay is low sensitivity for BB, BT and TT disease. Thus these methods cannot be used to diagnose, but rather to confirm LL and BL disease and to monitor chemotherapy success. PCR analysis of the hsp65 gene allows a more sensitive and specific method of identification of M. leprae in its full spectrum of disease.

The gold standard for diagnosis continues to be a full-thickness skin biopsy sample obtained from an advancing margin of an active lesion with hematoxylin-and-eosin staining and identification of acid fast bacilli using Fite-Faraco modification of the carbol fuschin stain.

Treatment for *M. leprae* is determined by the WHO classification system. Our patient had multibacillary, borderline lepromatous disease, which warranted a multi-drug treatment including rifampicin, dapsone, and clofazamine for one year. We used minocycline in place of clofazamine, as clofazamine is not available in the United States.

References:

1. Anderson H, Stryjewska B, Boyanton BL, et al. Hansen disease in the United States in the 21st century. Arch Pathol Lab Med 2007; 131: 982-986.
2. Moshella SL. An update on the diagnosis and treatment of leprosy. J Am Acad Dermatol 2004; 51:417-26.3.
3. Rojas RE, Segal-Eiras A. Immunoglobulin G response against 10-kDa and 65-kDa heat-shock proteins in leprosy patients and their household contacts. Immunology and Medical Microbiology 1996; 15: 189-198.
4. Rastogi N, Seng Goh K, Berchel M. Species-specific Identification of mycobacterium leprae by PCR-restriction fragment length polymorphism analysis of the hsp65 gene. Journal of Clinical Microbiology 1999; 37: 2016-2019.
5. Scollard DM, Adams LB, Gillis TP, et al. The continuing challenges of leprosy. Clinical Microbiology 2006; 19: 338-381.

Case #10

Presented by Warren Piette, MD

UNKNOWN #2

23 year old woman with rash, oral ulcers, gastrointestinal complaints, joint pain and bronchitis

Case #11

Presented by Pedro Dammert, MD and Warren Piette, MD

UNKNOWN #3

Man with pulsating chest mass

(Video to be presented)

Key Location: face **Case #12**

Presented by Erika Music, MD and Lissette Ortiz-Ferrer, MD

History of Present Illness:
This 58 year old African American female presented to our clinic complaining of progressive facial skin darkening over the past three years. She initially had dark areas limited to her upper cheeks, for which she began using multiple over the counter bleaching creams. Over time, the darkness worsened and spread to involve most of her face. She continued to use multiple over the counter bleaching creams for the progressive hyperpigmentation. The most recent cream the patient was using was an over the counter bleaching agent, Ultra Glow, containing 2% hydroquinone.

Past Medical History:
Hypertension

Medications/Allergies:
Lisinopril and hydrochlorthiazide/ no known drug allergies

Review of Systems:
She denied fever, chills, headaches, vision changes, joint pains, heart palpitations, chest pain, dark urine

Physical Exam:
On the forehead, temples, malar cheeks, nose, and lower cheeks, there was a confluent, bluish grey to dark brown plaque studded with small uniform papules.

Histopathology:
9/08 Forehead: There are multiple yellow-brown banana-shaped deposits in the upper to mid dermis.

Diagnosis:
Exogenous ochronosis

Treatment and Course:
The patient has stopped all bleaching creams. She has undergone three localized treatments with the 1064 nm Nd:Yag laser with slight improvement.

Discussion:
Ochronosis is characterized by a blue-grey hyperpigmentation of skin and connective tissues and presents in two forms: endogenous and exogenous.

Endogenous ochronosis, or alkaptonuria, is an autosomal recessive disorder due to a lack of the enzyme homogentisic acid oxidase (HGAO). This enzyme deficiency allows homogentisic acid (HGA) to accumulate in the blood and bind to collagen in various tissues leading to hyperpigmentation of the skin, as well as systemic involvement of joints and other organs. The hyperpigmentation is most commonly found on the cartilaginous portions of the ears and nasal tip, as well as sclera. Systemic involvement manifests as dark urine upon standing, arthritis (due to calcification of cartilage), prostate gland calcification, and calcification and stenosis of the cardiac valves.

Exogenous ochronosis has no systemic involvement, and is most commonly due to topical use of bleaching agents containing hydroquinone. However, ochronosis has also been reported with the use of products containing resorcinol, phenol, mercury, picric acid, and anti-malarials. The hyperpigmentation usually appears after six months of continued use. Although it was initially believed that only high concentrations of hydroquinone led to ochronosis, there have been many reports after use of only 2% hydroquinone, and many over the counter products. The FDA currently recommends that over the counter bleaching agents contain less than 2% hydroquinone.

Case #12 continued

South African black patients have the highest reported incidence of exogenous ochronosis, likely due to high hydroquinone and resorcinol content available in non-prescription bleaching agents. In the US, exogenous ochronosis is relatively rare, with only 28 reported cases from 1983-2001.

There are three stages of exogenous ochronosis described: stage 1 involves erythema with mild hyperpigmentation. Stage 2 demonstrates progression of the hyperpigmentation with "caviar-like" papules. Hyperpigmented papulo-nodules with or without inflammation characterize stage 3.

The exact etiology of the hyperpigmentation remains controversial. Hydroquinonone is a phenolic compound structurally similar to HGA. In a study on goldfish skin, lower concentrations of hydroquinone inhibited tyrosinase, whereas higher concentrations had an activating effect. Another theory proposes that hydroquinone inhibits the local HGAO activity which polymerizes to form the ochronotic pigment.

Treatment of ochronosis is disappointing. Withdrawal of the bleaching agents is mandatory and may result in very slow improvement. Topical retinoids have reportedly been effective in some patients, but cause worsening hyperpigmentation in others. The Q-switched ruby laser has been effective in some reports, as well as dermabrasion and CO_2 laser treatments.

References:

1. Huerta Brogeras M, et al. Exogenous ochronosis. J Drugs Dermatol 2006;5:80-1.
2. Kramer K, et al. Exogenous ochronosis. J Am Acad Dermatol 2000;42:869-71.
3. Levin C, et al. Exogenous ochronosis: an update on clinical features, causative agents, and treatment options. Am J Clin Dermatol 2001;2:213-217.

Key Location: face **Case #13**

Presented by Joerg Albrecht, MD, PhD and Lissette Ortiz-Ferrer, MD

History of Illness:
This is a 40 year old male who presented in July 2009 with a 3 months history of red small, slowly growing papules below the right naris and in the jaw line. These lesions regularly shed scabs. There was no history of discharge, bleeding or irritation.

Past Medical History:
HIV diagnosed 1996, (CD4 455 2/08 per history on presentation), rosacea, borderline hypertension.

Medications/Allergies:
None/ no known drug allergies

Physical Examination:
Below the right naris there were two confluent, firm, red-colored papules 1 mm and 2 mm in diameter. A 1 mm eroded papule was seen on the jawline.

Laboratory Data:
The following were abnormal or positive as:

6/08	CD 4 count	375/µl	[359-1519/µl]

Histopathology:
07/08 Left naris and right jawline: There is a dermal nodule composed of spindle cells arranged in fasicles and sheets. There are some slit-like vascular spaces with extravasated red blood cells and dilated dermal vessels.

Radiology
12/08 CT chest/abdomen/pelvis: No abnormality detected

Diagnosis:
Kaposi sarcoma

Treatment and Course:
The patient was classified as having AIDS and was started on highly active antiretroviral therapy (HAART). Over the next 4 months, he developed new lesions on face, oral mucosa and trunk. Some of the lesions were treated with liquid nitrogen. After 6 months of HAART the patient noted no new lesions and some improvement of the existing ones.

Discussion:
Kaposi sarcoma (KS) is a well known complication of HIV and is an AIDS defining illness, according to the 1993 revised CDC classification for HIV. The diagnosis of Kaposi sarcoma mandates the initiation of HAART.

Kaposis sarcoma is a viral disease caused by Kaposi Sarcoma-Associated Herpesvirus (KSAH, Human Herpesvirus 8). This is also the cause of primary effusion lymphoma and is a stimulant for multicentric Castleman disease. The seropositivity rate for the virus varies between 1-3% of blood donors in the US and more than 70% in areas where the virus is endemic. Saliva and parental transmission have been suggested. Infection with KSAH is a necessary but not sufficient prerequisite for development of a Kaposi sarcoma. There is evidence that HIV and KSAH enhance the replication of one another.

Clinical presentation of KS is variable and it is currently more commonly seen in the later stages of AIDS rather than as a presenting symptom of HIV infection. The skin lesions of KS can occur

Case #13 continued

anywhere but concentrate on the lower extremities, face and genitalia. The lesions may be elliptic along the skin tension lines. Early lesions, as in our patient, may be difficult to recognize, if AIDS or even HIV infection is not suspected based on other symptoms. These lesions may appear as faint, innocent-looking pink, red-violet, or brown macules. Differential diagnosis may be purpura, hematomas, pyogenic granuloma, angiomas, dermatofibromas, verrucae vulgaris or nevi. Most commonly, KS lesions are more characteristic millimeter to centimeter large papules of varying colors such as pink, red, purple to brown. Typically, older lesions are dark violaceous-brown, often with yellow perilesional halos. Particularly on the soles and the thighs, KS lesions may rarely be plaque-like; other tumors are exophytic and fungating leading to breakdown of overlying skin. Lymphedema, particularly in the face, genitalia, and lower extremities, may be out of proportion to the extent of the cutaneous disease and is possibly related to cytokines involved in the pathogenesis of KS.

The mainstay of the treatment of Kaposi sarcoma is HAART. Additional antivirals have not been shown to be effective. For smaller tumors and limited disease destructive therapy can be used; alternatively intralesional chemotherapy with most commonly vinblastine and topical treatments such as with alitretinoin gel can be attempted. For more extensive involvement a variety of chemotherapy regimens are available.

In our patient the diagnosis of Kaposi sarcoma was unexpected because the lesions were clinically uncharacteristic, suggesting more benign conditions such as pyogenic granuloma or verrucae vulgaris. Other HIV related diseases were unlikely given the patient's CD 4 count of 455 five months prior with stable HIV disease of 12 years. Bacillary angiomatosis can present with a similar picture but is uncommon in patient's with CD4 counts lower than 200 cells/ul.

References:

1. Sullivan RJ, Pantanowitz L, Casper C, Stebbing J, Dezube BJ. HIV/AIDS: epidemiology pathophysiology, and treatment of Kaposi sarcoma-associated herpesvirus disease: Kaposi sarcoma, primary effusion lymphoma, and multicentric Castleman disease. Clin Infect Dis 2008; 47; 1209-1215.
2. Dezube BJ. Clinical presentation and natural history of AIDS--related Kaposi's sarcoma. Hematol Oncol Clin North Am 1996; 10; 1023-1029.
3. Castro K.G., Ward J.W, Slutzker L., Buehler J.W., Jaffe H.W., Berkelman R.L. et al. 1993 Revised Classification System for HIV Infection and Expanded Surveillance Case Definition for AIDS Among Adolescents and Adults, http://www.cdc.gov accessed 1-11-2009.
4. Guidelines for the Use of Antiretroviral Agents in HIV-1-Infected Adults and Adolescents (11/08), http://www.aidsinfo.nih.gov/Guidelines accessed 1-11-2009.

Key Locations: eyes, nasal creases, lip, tongue **Case # 14**

Presented by Victoria Negrete, MD and Warren Piette, MD

History of Present Illness:
A 31 year old African American man without significant past medical history was admitted for anemia, dyspnea, fatigue, and hypotension. The dermatology service was consulted for asymptomatic periorbital lesions of eleven months duration, as well as perioral, nasal, and oral cavity lesions that developed three months prior to admission.

Past Medical History:
DeQuervain's tenosynovitis

Medications/Allergies:
Pantoprazole. No known drug allergies.

Review of Systems:
Positive for macroglossia, numbness consistent with carpal tunnel syndrome, progressive anorexia, weight loss (15-20 pounds), and blood tinged emesis. Negative for chest pain, fever, chills, cough, dysphagia, visual disturbance, jaundice, diarrhea, nausea, and headache.

Physical Exam:
Face: periorbital hyperpigmented waxy papules coalescing into plaques with punctuate hemorrhage. Nasal creases, upper cutaneous lip, and mucosal lip with flesh colored clustered waxy papules with punctate hemorrhage.
Oropharynx: macroglossia with dentate impressions bilaterally.

Laboratory Data:
The following were abnormal or positive:

Total protein	5.0 g/dL	[6.4-8.3 g/dL]
Albumin	3.4 g/dL	[3.8-5.2 g/dL]
Hemoglobin	9.8 g/dL	[13.0-16.8 g/dL]
Urine protein	30 U	[Normal: no detectable protein]
Immunoglobulin G	248 mg/dL	[694-1618 mg/dL]
Immunoglobulin A	27 mg/dL	[68-378 mg/dL]
Immunoglobulin M	5 mg/dL	[77-220 mg/dL]
Serum immunofixation	Monoclonal lambda light chains	
Urine immunofixation	Monoclonal lambda light chains	

The following were normal or negative:
Liver enzymes, BUN, creatinine, and white blood cell count.

Radiology/Procedures:
7/08 CT - chest, abdomen, pelvis: diffuse low density infiltration, pronounced in mesentery.
7/08 CT - neck: prominent parotid glands and submandibular glands.
7/08 ECHO: all four valves thickened, increased ventricular filling pressure, consistent with diastolic dysfunction.
7/08 EGD: Class B esophagitis, thickened mucosa of the antrum and gastric folds.

Case #14 continued

Histopathology:

7/08 Nasolabial fold: Amorphous eosinophilic deposits in the dermis and subcutis. Congo red revealed green birefringent deposits in polarized light.

7/08 Antrum: Chronic gastritis with amorphous eosinophilic deposits. Congo red revealed small foci of eosinophilic material with green birefringence in polarized light.

7/08 Bone marrow: 70-80% cellularity, with diffusely increased plasma cells throughout. In situ hybridization studies for immunoglobulin light chain mRNA show mostly lambda positive plasma cells. Congo red stain negative.

Diagnosis:

Primary systemic (AL type) amyloidosis

Treatment and Course:

The patient was started on thalidomide 100 mg daily, dexamethasone 40 mg weekly, and bortezomib 1.3 mg/mm^2 weekly for treatment of amyloidosis. He is currently awaiting approval for stem cell transplantation.

Discussion:

Amyloidosis is characterized by the deposition of extracellular fibrils, which are the result of protein misfolding from its normal α-helical configuration into a β-pleated sheet. The structure of the β-pleated sheet allows the binding of Congo red stain, which emits a characteristic apple-green birefringence under polarized light. To date 24 different proteins have been discovered to be amyloidogenic in humans. Immunoglobulin light chain amyloidosis (AL type) is the most common form of systemic amyloidosis, with an estimated incidence of 0.8 per 100,000 person years. The protein in AL amyloidosis is produced by a clonal population of plasma cells in the bone marrow, which are often atypical. Although symptomatic multiple myeloma occurs in only 10-15% of cases, it is likely that this is because patients die from progressive amyloidosis before they develop lytic bone lesions or over 1 gram of protein in the serum that would meet criteria for multiple myeloma.

In a retrospective study of 705 patients with AL amyloidosis, kidney disease was reported as the most frequent manifestation (74%), usually presenting as nephrotic syndrome. Sixty percent of patients had cardiac involvement, resulting in rapidly progressive heart failure from restrictive cardiomyopathy. The median survival of patients with heart involvement is significantly shorter when compared to those without – 21 months versus 76 months. Other organs commonly involved include liver (hepatomegaly), peripheral and autonomic nervous systems (carpal tunnel syndrome, orthostatic hypotension, delayed gastric emptying, erectile dysfunction), and soft tissue (macroglossia, submandibular gland enlargement, hoarseness).

Although skin lesions are not uniformly found in patients with AL amyloidosis, a study of 223 patients presenting to the Amyloid Treatment and Research Center in Boston revealed that 28% had at least one dermatological manifestation. These skin findings include: purpura, petechiae, and ecchymoses in the skin from amyloid infiltration of vessel walls; subcutaneous nodules, papules, and plaques due to direct dermal infiltration of amyloid; alopecia; nail dystrophy; and rarely, bullae.

The diagnosis of AL amyloidosis requires demonstration of amyloid in tissue and a plasma cell dyscrasia. In the absence of cutaneous lesions, fine-needle aspiration of abdominal fat reveals amyloid deposits in 70-95% of patients with AL amyloidosis. Once tissue diagnosis is made, a plasma cell dyscrasia must be confirmed. In the study by Obici et al., 97% of patients with AL amyloidosis had detectable monoclonal components in serum and/or urine on immunofixation, and a monoclonal plasma cell population could be detected in 84% of patients on bone marrow aspirate.

The aim of therapy in AL amyloidosis is to rapidly reduce the supply of amyloidogenic monoclonal light chain by suppressing the underlying plasma cell dyscrasia with chemotherapy. The most effective treatment for AL amyloidosis is a course of the alkylating agent melphalan followed by autologous stem cell transplantation (ASCT), which has a 50-60% response rate. However, ASCT is

associated with high treatment related mortality, especially in patients with heart failure and multi-organ involvement. Low-dose oral melphalan plus prednisone is currently offered to poor risk patients. The combination of melphalan and dexamethasone results in a rapid response in patients with advanced disease who do not qualify for ASCT. Thalidomide is effective in AL amyloidosis due to the medication's immunomodulatory and anti-angiogenic effects. Although poorly tolerated, when combined with dexamethasone, thalidomide can produce rapid responses.

References:

1. Obici L, Perfetti V, Palladini G, et al. Clinical aspects of systemic amyloid diseases. Biochem et Biophys Acta 2005; 1753:11-22.
2. Rajkumar SV, Gertz MA. Advances in treatment of amyloidosis. N Eng J Med 2007; 356: 2413-5.
3. Sanchorawala V. Light-chain (AL) amyloidosis: diagnosis and treatment. Clin J Am Soc Nephrol 2006; 1: 1331-41.
4. Silverstein SR. Primary systemic amyloidosis and the dermatologist: where classic skin lesions may provide the clue for early diagnosis. Derm Online J 2005; 11(1): 5.

Case #15

Presented by Victoria Negrete, MD, Sidney Barsky, MD, and Warren Piette, MD

Patient A

Key Locations: Face, neck, trunk, extremities

History of Present Illness:
This 54 year old man was admitted in September 2008 and underwent a left radical nephrectomy and tumor thrombectomy for treatment of renal cell carcinoma. His post operative course was complicated by respiratory failure s/p tracheostomy placement, hemicolectomy, cholecystectomy with biliary T tube placement, atrial fibrillation, and sacral decubitus ulcer with osteomyelitis. He was discharged to an outside hospital for long term ventilatory support, but returned to Stroger Hospital four days later because of hemorrhage from his T tube. On admission the patient had a new asymptomatic generalized eruption which had been present for less than 24 hours.

Past Medical History:
Metastatic renal cell carcinoma, diabetes mellitus, and primary varicella as child.

Medications/Allergies:
Piperacillin/tazobactam, pantoprazole, morphine, vitamin K, insulin, acetylcysteine. NKDA.

Review of Systems:
Negative for dyspnea, cough, abdominal pain, nausea, vomiting, diarrhea, weakness, fevers, chills, night sweats, or weight loss.

Physical Exam:
Vitals: temperature 100.0
Face and neck: multiple diffuse 3-6 mm intact tense vesicles with clear to yellow fluid on a minimally to non-inflammatory base, more prominent on right side. (-) Nikolsky sign.
Trunk, upper extremities, lower extremities: scattered tense vesicles on a minimally to non-inflammatory base.

Laboratory Data:
The following were abnormal or positive:

Creatinine	69 mg/dL	[8-20 mg/dL]
BUN	2.0 mg/dL	[0.6-1.4 mg/dL]
Alkaline phosphatase	263 U/L	[50-120 U/L]
GGT	146 U/L	[3-60 U/L]
WBC	11.9 k/uL	[4.0-10.8 k/uL]
Hemoglobin	8.3 g/dL	[12.8-17.0 g/dL]
Viral culture	Positive for varicella zoster virus (VZV)	

The following were normal or negative:
Basic metabolic profile, blood culture, sputum culture, and urine culture.

Histopathology:
12/08 Right neck: intraepidermal vesicle with numerous multinucleated giant cells, ballooning degeneration, and intranuclear inclusion bodies, consistent with varicella or herpes simplex virus.

Case #15 continued

Diagnosis:
Atypical generalized herpes zoster without primary dermatomal involvement

Treatment and Course:
The patient was placed in contact isolation, and was started on intravenous acyclovir. He continued to hemorrhage from his T tube, and an angiogram revealed a large round 2.3 cm pseudoaneurysm arising from the proper hepatic and gastroduodenal artery bifurcation, which was deemed surgically and angiographically unfixable. Ventilatory support was withdrawn. VZV IgG and IgM levels were not obtained prior to withdrawal of support.

Patient B

Key Location: Abdomen

History of Present Illness:
This 37 year old man was admitted in July 2008 for lymphadenopathy, weakness, and an eruption on his chest and back. A biopsy in June 2008 of an enlarged lymph node was highly suspicious but not diagnostic of a B-cell lymphoproliferative disorder. A bone marrow biopsy in July 2008 revealed nodular and diffuse interstitial marrow involvement by Burkitt lymphoma. The patient noticed the onset of lesions on his trunk and back two weeks prior to admission, which subsequently spread to his face and neck. The lesions were occasionally painful and pruritic.

Past Medical History:
Idiopathic thrombocytopenic purpura s/p splenectomy in 1993, Burkitt lymphoma.

Medications/Allergies:
Prednisone, discontinued two weeks prior to admission. No known drug allergies.

Review of Systems:
Positive for right eyelid ptosis, fevers, night sweats, unquantifiable weight loss, and fatigue. Negative for dyspnea, cough, nausea, vomiting, diarrhea, or urinary symptoms.

Physical Exam:
Vitals: temperature 98.8
Lymph nodes: multiple enlarged 2-3 cm firm lymph nodes under right mandible, axillae, groin.
Neck: multiple intact umbilicated vesicles on an erythematous base.
Abdomen: scattered vesicles on an erythematous base, few with central umbilication, few with dusky centers.

Laboratory Data:
The following were abnormal or positive:

BUN	48 mg/dL	[8-20 mg/dL]
Creatinine	2.0 mg/dL	[0.6-1.4 mg/dL]
Alkaline phosphatase	168 U/L	[50-120 U/L]
Aspartate aminotransferase	111 U/L	[0-40 U/L]
Lactate dehydrogenase	4023 U/L	[85-210 U/L]
White blood cell	39.0 k/μL	[4.2-10.0 k/μL]
Hemoglobin	11.0 g/dL	[13.0-16.8 g/dL]
Tzanck smear	Positive for multinucleated giant cells	
Viral culture	Positive for varicella zoster virus	

The following were normal or negative:
Blood cultures x2, urine culture, and platelets.

Histopathology:
07/08 Abdomen: suprabasal vesicular dermatitis with multinucleated giant cells, ballooning degeneration, and intranuclear inclusion bodies, consistent with herpes or varicella zoster virus.

Diagnosis:
Atypical generalized zoster without primary dermatomal involvement

Treatment and Course:
The patient was placed in contact isolation and was started on intravenous acyclovir. His hospital course was complicated by tumor lysis syndrome with acute renal failure and pancytopenia. Blood cultures grew *Escherichia coli* and *Klebsiella pneumoniae* and he was started on vancomycin and imipenem. He developed respiratory failure and was intubated. Despite many efforts to maintain his blood pressure, the patient became non-responsive and ventilatory support was withdrawn.

Discussion:
Herpes zoster disseminates in as many as 40-50% of immunosuppressed individuals, especially those with a history of lymphoproliferative malignancies (particularly Hodgkin's lymphoma) and organ transplantation. Disseminated VZV infections result in a fatal outcome in 28-80% of adult immunocompromised patients. The most frequent causes of death in these patients are pneumonia, encephalitis, hepatitis, and disseminated intravascular coagulopathy.

Four distinct subtypes of VZV reactivation have been described in immunocompromised individuals. These include local (classic) zoster, dermatomal zoster with dissemination, atypical generalized zoster with or without visceral involvement, and visceral involvement without skin lesions. Other unusual manifestations of herpes zoster include multidermatomal zoster, verrucous nodules, and postherpetic hyperhydrosis.

Visceral involvement is rare and occurs in 3-15% of immunosuppressed patients with herpes zoster. It manifests in 10% of those with cutaneous dissemination and almost always follows the cutaneous eruption. The organs most commonly affected include lungs, liver, and brain. Visceral zoster is classically defined as organ involvement with histologic, culture, or other laboratory evidence of varicella zoster virus. Visceral involvement indicates a particularly poor prognosis, with a 55% mortality rate.

Very few reports of atypical generalized zoster have been reported in the dermatological literature. As a result, many dermatologists may overlook this variant when evaluating a patient with generalized vesicles. Establishing the diagnosis is essential in order to provide timely and adequate treatment. However, conventional methods such as Tzanck smears and viral cultures frequently fail to confirm the diagnosis of VZV in immunocompromised individuals. Thus, it is recommended in these cases to obtain PCR, which has high specificity for VZV.

References:
1. Chopra KF, Evans T, Severeson J, et al. Acute varicella zoster with postherpetic hyperhidrosis as the initial presentation of HIV infection. JAAD 1999;41:119-21.
2. Oh KH, Ahn C, Kim YS, et al. Atypical generalized zoster with suspicious esophageal involvement and early relapse in an adult renal transplant recipient. Trans Proc 2002;34:1174-7.
3. Stratman E. Visceral zoster as the presenting feature of disseminated herpes zoster. JAAD 2002; 46:771-4.

Key Locations: Face, trunk and extremities **Case #16**

Presented by Morayo Adisa, MD and Jerry Feldman, MD

History of Present Illness:
This is a 24 year old male that presented for evaluation of a two-month history of a pruritic, erythematous, scaly annular rash on his face, trunk, and extremities. The rash developed after a two week prodromal illness consisting of headaches, prostration, weight loss and subjective "high" fevers. The eruption began on his trunk and then progressed to his face and extremities. He was initially seen in the ED and treated for a non-specific eruption with prednisone.

Past Medical History:
Anemia and asthma

Medications/Allergies:
None/ no known drug allergies

Social History:
Homosexual relations

Review of Systems:
Malaise, subjective fevers, recent non-quantified unintended weight-loss

Physical Exam:
Face, trunk and extremities: annular plaques with central hyperpigmentation
Palms and soles: hyper pigmented macules with collarette of scale

Laboratory Data:
The following were abnormal or positive:

White blood cell count	3.1	[4.0-10.5 K/uL]
Hemoglobin	11.0	[12.5-17.0g/dL]
Hematocrit	32.4	[36.0-50.0%]
Rapid plasmin regain (RPR)	reactive	[non reactive]
LDH	225U/L	[85-210U/L]
RPR quantitative titer	1: 128	
Confirmatory *T pallidum*		
Particle agglutination	positive	
HIV 1 Antibody	positive	

The following were normal or negative:
Platelet count, liver enzymes, chemistry profile, hepatitis A, B & C tests

Histopathology:
10/08 Right forearm: lichenoid lymphohistiocytic dermatitis with occasional plasma cells consistent with secondary syphilis

Diagnosis:
Secondary syphilis with HIV co-infection

Case #16 continued

Treatment and Course:

He was treated with one dose of intramuscular penicillin G 2.4 million as recommended by Infectious Disease and referred to the Cook County HIV specialty clinic. Post therapy, the patient experienced mild transient 'flu-like' symptoms consistent with Jarisch-Herxheimer reaction, which was responsive to ibuprofen. Two weeks post-therapy, there was gradual clearing of skin lesions as well as decreased adenopathy. The repeat RPR titer performed one month later was 1:64. He has not followed up for subsequent appointments.

Discussion:

Syphilis is a systemic, sexually or congenitally transmitted infection caused by the spirochete *Treponema pallidum.* The organism, identified in 1905 by Schaudinn and Hoffman, is a spiral shaped flagellated, obligate intracellular bacteria. The CDC, which has been documenting cases of syphilis since 1941, reports a continued increase in the number of reported cases since a nadir in the late 1990s; a 9.5% increase was documented in 2005. The male to female ratio has also steadily increased, suggesting a rise in incidence among heterosexuals. There remains a high rate of disease incidence among men who have sex with men (60% of new infections) in addition to a high rate of HIV co infection in this population.

The risk of HIV infectivity is increased because of the disruption of the mucosal barrier and the increased number of CD4+ T-cells and other inflammatory cells present at the ulcerated sites of syphilitic chancres. HIV co-infection with syphilis alters the clinical manifestation of syphilis and hence the presentation, diagnosis, disease progression and response to therapy. These patients often present with atypical disease, a higher propensity for asymptomatic primary disease and a rapid progression from primary syphilis to secondary and tertiary syphilis. The presence of opportunistic infections may also further confuse the clinical picture. In these cases, a skin biopsy may elucidate the diagnosis. Due to the high incidence of asymptomatic syphilis in HIV infected homosexual men, regular screening for syphilis is recommended in this population.

The diagnosis of syphilis can be achieved by direct visualization of treponemes through dark field microscopy or the use of non-treponemal tests (anti-cardiolipin) using either the venereal disease research laboratory assay (VDRL) or the rapid plasma regent (RPR). Confirmatory testing using either of the anti-treponemal tests which include the *T. pallidum* hemabsorbtion test (TPHA), microhemagglutination assay for antibodies to *T.pallidum* test (MHA-TP), or the fluorescent treponemal antibody absorption assay (FTA-ABS) is recommended following a positive non-treponemal test. The quantified titers of the non-treponemal tests correlate with disease activity and can be used to monitor treatment response, although the VDRL and RPR titers cannot be used interchangeably. In HIV positive patients, non-treponemal antibody tests may be falsely negative in primary and secondary syphilis due to the prozone effect. Furthermore, post therapy, HIV co-infected patients have an increased rate of having persistent positive non-treponemal serological tests (i.e. serofast) and negative treponemal antibody tests.

Parenteral penicillin remains the mainstay therapy for all stages of syphilis, although the CDC recommends different dosages and treatment durations depending on the stage of disease. Some experts recommend three doses of 2.4 million units of penicillin in HIV infected patients with primary or secondary disease. There is limited data supporting the use of penicillin alternatives in the treatment of early syphilis.

References:

1. Sexually transmitted Disease Surveillance 2005 Supplement. Syphilis Surveillance Report, 2006. CDC and Prevention, Atlanta, GA. Dec. 2006. (www.cdc.gov/std/Syphilis2005)
2. Centers for Disease Control and Prevention. Genital ulcers –STD treatment Guidelines 2006. www.cdc.gov/std/treatment/2006/genital-ulcers.htm#syphamonghiv.
3. Lynn WA, Lightman S. Syphilis and HIV: a dangerous combination. *The Lancet Infectious Diseases*. July 2004; 4: 456-466.
4. Musher DM, et al. Effect of human immunodeficiency virus (HIV) infection on the course of syphilis and on the response to treatment. *Ann Int Med* 1990;113: 872-881.

Key Locations: trunk and extremities **Case # 17**

Presented by Giacomo Maggiolino, MD, Warren Piette, MD, and Jerry Feldman, MD

History of Present Illness:
This 9 year old Hispanic boy was diagnosed with epidermolytc hyperkeratosis as an infant. A limited history was obtained by the patient's stepfather, who stated that erythema and blisters began within the first few months of life. As the patient grew older, the erythema and blisters were replaced with thicker skin. Throughout the years, the patient had been treated with various treatments, including isotretinoin and loratadine, which helped relieve the associated pruritus. In addition, the patient had been applying a combination of 40% urea cream, 2.5 % hydrocortisone ointment, and petroleum jelly to his skin. For the past three years, the patient has not followed up with any dermatologist and has obtained his medications through his grandfather in Mexico.

Past Medical History:
No other medical problems

Medications/Allergies:
Isotretinoin, 40% urea cream, 2.5% hydrocortisone ointment, and petroleum jelly/ no known drug allergies

Physical Exam:
Trunk and extremities: generalized mottled hyperpigmented and hyperkeratotic plaques in a corrugated pattern
Dorsal hands: hyperkeratosis in a cobblestone pattern

Laboratory Data:
The following were normal or negative:
Complete blood count, basic metabolic pattern, liver function tests, and triglycerides

Histopathology:
Not available

Diagnosis:
Epidermolytic hyperkeratosis

Treatment and Course:.
After checking appropriate baseline labs, the patient was continued on isotretinoin 10 mg daily, loratadine 10 mg daily, and topical therapy with emollients and 40% urea cream.

Discussion:
Epidermolytic hyperkeratosis (EHK), also known as bullous congenital ichthyosiform erythroderma or bullous icthyosis, is a rare genetic disorder of keratinization associated with mutations in keratin 1 and/or keratin 10. Inheritance has been shown to be autosomal dominant, with 50% of cases representing spontaneous mutations.

Most patients present before the first year of life (usually at birth) with erythroderma, widespread bullae, and denuded skin. Newborns are particularly at risk for secondary sepsis and electrolyte imbalance. Widespread blistering usually resolves after the neonatal period. In later infancy and childhood, the erythroderma is replaced by hyperkeratosis, either localized or generalized, with or without palmoplantar kerataderma. Secondary bacterial infections are common. The presence of hyperkeratosis is usually lifelong, although generalized involvement usually improves to localized disease after puberty.

Case #17 continued

Mutations in the keratin 1 and keratin 10 genes result in defective keratin filaments with subsequent tonofilaments clumping at the suprabasal level within the epidermis which can be seen by electron microscopy. Hyperkeratosis, hypergranulosis, and epidermolysis are histologic features.

Clinical management consists of symptomatic treatment since a cure is not yet available. In the newborn period, it is recommended to transfer patients into the neonatal intensive care unit to closely monitor fluids and electrolytes and work up for sepsis. Later in infancy and through adulthood, topical emollients are used. Topical maxacalcitol, a vitamin D3 analogue, has been recently reported to be effective in treating the hyperkeratosis. Topical keratolytics are used with caution as they may remove too much stratum corneum and leave the skin denuded and raw. Use of anti-bacterial soaps or antibiotic coverage may be used to control malodor associated with bacterial overgrowth. Oral and topical retinoids are used in severely affected individuals and are effective in reducing hyperkeratosis. Retinoids should be used with caution as they may cause worsening of desquamation and blistering. Teratogenicity and skeletal toxicities are also a concern with retinoids. Multiple nonmelanoma skin cancers in a patient with EHK on long-standing retinoid therapy was recently reported.

References;

1. Spitz, JL. Genodermatoses: A clinical guide to genetic skin disorder. 2005. 6-9.
2. Kucharekova M, Mosterd K, Winnepenninckx V, Van Gel M, Sommer A, Van Steensel AM. Bullous congenital ichtyosiform erythroderma of Brocq. International Journal of Dermatology 2001. 46 (Suppl.3), 36-38.
3. Umekoji K, Fukai K, Ishii M. A case report of mosaic-type bullous congenital ichtyosiform erythroderma successfully treated with topical maxacalcitol, a vitamin D3 analogue. Clinical and experimental dermatology 2008. 33; 501-502.
4. Sarnoff D and Saini R. Multiple nonmelanoma skin cancers in a patient with epidermolytic hyperkeratosis on long-standing retinoid therapy. Journal of drugs in dermatology. 2008. 475-477.
5. DiGiovanna JJ and Bale, SJ. Clinical Heterogeneity in Epidermolytic Hyperkeratosis. Archives of Dermatology. August 1994; 130: 1026-1035.

Key Locations: primarily sun-exposed areas **Case #18**

Presented by Jordan Carqueville, MD and Jerry Feldman, MD

History of Present Illness:
The patient is a 48 year old male who presented with a pruritic eruption located on sun-exposed skin of the face, chest, arms, hands, and legs for 5 years. His condition is exacerbated by heat and sun exposure, and improves in the winter. The eruption first appeared when he began working at a printing press. He has used 1% hydrocortisone cream, which alleviates the pruritus.

Past Medical History:
None

Medications/Allergies:
None/ no known drug allergies.

Social History:
The patient currently works at a printing press and used to work in a shoe manufacturing factory.

Review of Symptoms:
He denied fatigue, weight loss, fever, shortness of breath, chest pain, arthralgias, and hematuria.

Physical Exam:
Face: scaly, lichenified papules and plaques, sparing eyelids and posterior auricular surfaces
Hands, wrists and feet: dorsal surfaces with widespread, severely lichenified, red-brown, scaly plaques with several deep fissures
Forearms, upper chest, lower abdomen and distal>proximal legs: scaly plaques with mottled pigmentation and scattered linear erosions mostly in photo-exposed areas

Laboratory Data:
The following were normal or negative:
Complete blood count and differential, basic metabolic panel, liver function tests, thyroid function tests, hepatitis B and C, anti-nuclear antibody, rheumatoid factor

Diagnostic Procedures and Tests:
1/09 T.R.U.E. Allergen Patch Test: positive for potassium dichromate, colophony, colbalt dichloride
2/09 Photopatch test: negative to oxybenzone

Histopathology:
2/09 Wrist: There is epidermal hyperplasia with marked compact orthokeratosis and a collection of plasma in the lower cornified layer. The dermis shows superficial perivascular lymphocytic infiltrate. There is no evidence of mycoses fungoides.

Diagnosis:
Chronic actinic dermatitis

Treatment and Course:
The patient was started on a prednisone taper, tacrolimus ointment twice daily to the affected areas on face, chest and arms, and clobetasol 0.05% ointment twice daily under occlusion at night for thick areas on hands and feet, and hydroxyzine 25mg at bedtime. He was instructed to wear sun protective clothing and use sunscreen liberally and hourly with SPF greater than 30. After months of therapy, the patient showed only mild improvement, still having occasional flares of dermatitis requiring prednisone

tapers. He was therefore started on azathioprine 100mg daily. After approximately 5 months of azathioprine and sun protection, the pruritus improved and he had no exacerbations requiring prednisone. The patient did have an exacerbation in the summer and was treated with a prednisone taper, topical corticosteroids, and the azathioprine was increased to 150mg daily. He is currently stable on this present dose.

Discussion:

Chronic actinic dermatitis (CAD) is hypothesized to be an immunologic photodermatitis to sunlight-induced endogenous cutaneous antigen rather than an external agent. It may occur on previously normal skin, skin with preceding allergic contact dermatitis, atopic dermatitis, or after an oral drug photosensitivity. Only 10% of patients report no previous dermatitic condition or contact allergy prior to developing CAD. We confirmed contact allergies in our patient to potassium dichromate, colophony, and colbalt dichloride. Further patch and phototesting may be beneficial in identifying other possible triggers. The inciting wavelength is UVB (280-315 nm) and UVA (315-400 nm) in the majority of patients with CAD, and visible light in the minority.

CAD occurs on sun-exposed skin, often with well-demarcated edges at clothing, and spares the upper eyelids, folds in the face and neck, and behind the earlobes. The dermatitis is extremely pruritic and lichenification is a common finding in long-term disease. Hyper- and hypopigmentation occurs late in the disease. Some lesions may mimic cutaneous T-cell lymphoma (CTCL) as shiny, infiltrated plaques.

Histopathology is not diagnostic, as it demonstrates a non-specific dermatitis with epidermal spongiosis, acanthosis and a dermal lymphohistiocytic infiltrate that is usually perivascular. On occasion, leukocyte epidermotropism may be observed, giving rise to the concern of cutaneous T-cell lymphoma. This association, however, has not been proven, and use of T-cell receptor rearrangement studies along with immunohistochemistry will aid in differentiating between chronic actinic dermatitis and CTCL. A predominance of CD8+ lymphocytes occur in CAD, while CD4+ cells predominate in CTCL. Close follow-up, however, is still advised.

Treatment of chronic actinic dermatitis includes accurate diagnosis by phototesting and patch testing, along with patient presentation and history of relevant dermatitic conditions, i.e. atopic or allergic contact dermatitis. Education regarding sunlight avoidance including behavioral measures, protective clothing, environmental filter protection, and sunscreens should be given. CAD should be treated like other eczematous dermatitis, with regular application of emollients and potent topical corticosteroids, with intermittent oral prednisone for flares. Topical tacrolimus and pimecrolimus have demonstrated efficacy, and offer an alternative to avoid steroid atrophy. In resistant cases, oral immunosuppressive agents have been used successfully, as in our patient who received azathioprine. Other systemic immunomodulators include: cyclosporine 3.5 to 5.0 mg/kg and mycophenolate mofetil 15 to 40 mg/kg. Gradual resolution by 10 years will occur in 20% of patients.

References:

1. Dawe RS, Ferguson J. Diagnosis and treatment of chronic actinic dermatitis. Dermatologic Ther 2003; 16: 45-61.
2. Hawk JL. Chronic actinic dermatitis. Photodermatol Photoimmunol Photomed 2004; 20:312-314.
3. Hawk JL, Lim HW. "Chronic Actinic Dermatitis." Photodermatology. New York: Informa Healthcare USA, Inc., 2007. 169-83.
4. Murphy, GM, Maurice PM, Norris PG, et al. Azathioprine in the treatment of chronic actinic dermatitis: a double-blind controlled trial with monitoring of exposure to ultraviolet radiation. Br J Dermatol 1989; 121:639-646.

Key Locations: axilla and groin **Case #19**

Cases presented by Robert Lieberman, MD and Warren Piette, MD

History of Present Illness:
The patient is a 54 year old Indian man who presented with a three-day history of asymptomatic red papules in his axillae and groin.

Past Medical History:
None

Medications/Allergies:
None/ no known allergies

Review of Systems:
The patient reports a three-day history of dyspnea on exertion and weakness. He denies fever, chills, chest pain, or abdominal pain.

Physical Exam:
General: alert and oriented x 3
Vitals: afebrile, pulse 90, respiratory rate 22, blood pressure 70/40 (on norepinephrine), oxygen saturation 92% (on 100% non-rebreather mask)
Lungs: inspiratory crackles at the bases
Axillae, left groin, inner arms: erythematous, monomorphic, 2-3mm, folliculocentric papules, some forming annular configurations

Laboratory Data:
The following were abnormal or positive:

White blood count	14.5 k/μL	[4.2-10.0 k/μL]
Neutrophils	12%	[40-82%]
Lymphocytes	46%	[12-44%]
Monocytes	14%	[2-12%]
Metamyelocytes	1%	[0%]
Myelocytes	11%	[0%]
Blasts	8%	[0%]
Hemoglobin	10.1 g/dL	[13.0-16.8 g/dL]
Platelets	134 k/μL	[185-395 k/μL]
Prothrombin time	18.2 sec	[11.8-13.8 sec]
Partial Thromboplastin time	38.8 sec	[25.6-34.4 sec]
Fibrinogen	697mg/dL	[196-457 mg/dL]
INR	1.59	
D-dimer	6.10	[0.22-0.43]
Urinalysis	small blood	[negative]

The following were normal or negative:
Comprehensive metabolic panel, % bands, basophils, eosinophils, liver function tests, hepatitis B surface antigen, hepatitis C antibody, HIV antibody, antinuclear antibody, anti-centromere antibody, C3 level, C4 level, urine legionella antigen, blood cultures, sputum culture for AFB, and cultures of bronchial washings for AFB, fungus, bacteria, pnuemocystis, and legionella

Case #19 continued

Radiology:

10/08 CT scan, chest: mediastinal and right hilar adenopathy measuring up to 12 mm; bilateral airspace consolidation within lower lobes

Cytology:

Bronchial alveolar lavage fluid: numerous poorly preserved bare nuclei suspicious for degenerated blasts. No fungal elements or pneumocysts identified on GMS stain.

Bone marrow aspirate: acute myelogenous leukemia (AML) with maturation (FAB-M2).

Histopathology:

10/08 Chest: Superficial perivascular and interstitial lymphohistiocytic infiltrate with marked subepidermal edema and blister formation. The infiltrate is located within the blister and upper dermis. Immunohistochemical studies show that the inflammatory cells are mainly T lymphoctyes (CD3 positive) and histiocytes (CD68 positive) and rarely B lymphocytes (CD20 positive). No atypical forms of hematopoietic cells are seen.

Diagnosis

Lymphohistiocytic Sweet syndrome with associated acute myelogenous leukemia

Treatment and Course:

The patient was admitted to the medical ICU for treatment of sepsis initially believed to be secondary to bilateral pneumonia, although all cultures were negative and the patient responded poorly to broad-spectrum antibiotic therapy. Leukemic infiltration could not be excluded. He subsequently developed multiorgan failure, including acute renal failure necessitating hemodialysis. Chemotherapy was initiated for treatment of his AML, however the patient developed worsening pulmonary infiltrates consistent with acute respiratory distress syndrome. Two weeks after admission, he passed away.

Discussion:

Sweet syndrome, or acute febrile neutrophilic dermatosis, is characterized by tender, red or purple-red pseudovesicular papules or nodules that frequently occur on the upper extremities, face, and neck. These skin lesions usually occur in the context of fever, leukocytosis, arthralgias, and malaise. Originally described by Dr Robert Douglas Sweet in 1964, Sweet syndrome classically occurs in women between the ages of 30 and 50. Idiopathic Sweet syndrome is associated with infection (usually an upper respiratory tract or gastrointestinal tract infection), inflammatory bowel disease, or pregnancy. Certain medications, including granulocyte-colony stimulating factor and all-trans retinoic acid among others, may also induce Sweet syndrome. However, 20 percent of cases are associated with malignancy, the most common of which is AML. These cases may be clinically atypical, in that they are relapsing or chronic, may lack systemic symptoms, or be histologically atypical.

Classic histologic findings in Sweet syndrome include dermal edema and typically a dense neutrophilic infiltrate with leukocytoclasia, endothelial cell swelling, but no primary leukocytoclastic vasculitis. Less commonly, biopsies of early lesions may demonstrate predominantly lymphocytes and histiocytes, and these cases have usually been associated with myelodysplasia. Evans et al describes two patients with underlying myelodysplasia and classic lesions of Sweet syndrome whose initial biopsies demonstrated a perivascular lymphohistiocytic infiltrate - with a mixture of CD68+, CD4+, and CD8+ cells – but whose subsequent biopsies two to eleven months later reflected more classic findings of a dense dermal neutrophilic infiltrate and edema. These observations were confirmed by Vignon-Pennamen et al, who identified nine patients with chronic recurrent lymphocytic Sweet syndrome who subsequently developed myelodysplasia, seven of whom had sequential biopsies two to eight years apart in which a lymphocytic infiltrate preceded a neutrophilic infiltrate. Five of these cases also demonstrated atypical medium-sized mononuclear cells with eccentric, kidney-shaped nuclei in the first biopsy, the

etiology of which was unclear given that none of the patients had evidence of myelodysplasia at that time. It should be noted that all patients, including those lacking atypical mononuclear cells on biopsy, eventually developed myelodysplasia. While the biopsy of our patient did not demonstrate atypia, it did demonstrate the other features of a lymphohistiocytic Sweet syndrome.

References:

1. Cohen P, et al. Sweet's syndrome revisited: a review of disease concepts. *Int J Dermatol* 2003; 42:761-78.
2. Evans A, et al. Lymphocytic infiltrates as a presenting feature of Sweet's syndrome with myelodysplasia and response to cyclophosphamide. *Br J Dermatol* 2002; 146:1087-90.
3. Vignon-Pennamen M, et al. Chronic recurrent lymphocytic Sweet syndrome as a predictive marker of myelodysplasia. *Arch Dermatol* 2006; 142:1170-1176.

Key Locations: face & right extremities **Case #20**

Presented by Lauren Fine, MD, Lissette Ortiz-Ferrer, MD. and Warren Piette, MD

History of Present Illness:
This is a 41 year old Hispanic male admitted to the hospital with a 10 day history of progressively worsening headaches. Three days prior he also had nausea, vomiting, and subjective fevers. The dermatology service was consulted to evaluate 3 asymptomatic lesions on the right upper eyelid, right forearm, and right knee that the patient first noticed approximately 3 months ago. Recently the lesion near the eyelid started to bleed and is currently crusted.

Past Medical History:
HIV diagnosed in 1990 and off HAART therapy since 2004
Hodgkin's lymphoma status post ABVD chemotherapy

Medications/ Allergies:
Acetaminophen/ no known drug allergies

Social History:
The patient is a homosexual male, currently unemployed and living with his partner. He has smoked one pack of cigarettes a day for the past 10 years.

Physical Exam:
Superior right medial canthus: there was a cluster of well demarcated, hypopigmented-to-skin-colored waxy umbilicated papules ranging in size from 4-10 mm. The largest papule has central crust and minimal hemorrhage. No telangictasias were appreciated.
Right forearm & right knee: there are two well-demarcated hypopigmented waxy umbilicated papules ranging in size from 8-12mm.

Laboratory Data:
The following were abnormal or positive:

CD4 count	100	[359-1519/µl]
Lumbar puncture opening pressure	2800 mm of H_20	[60-200 mm of H_20]
Cerebrospinal fluid protein	77 mg/dL	[18-58 mg/dL]
CSF white blood cells	14 per mm3	[0-5 per mm3]
Platelet Count	72,000	[185,000-395,000 k/uL]

The following were normal or negative:
White blood cell count, hemoglobin, basic metabolic panel, liver enzymes, Hepatitis B and C antigens, and CSF glucose

Radiology:
12/25 chest CT: right middle lobe mass

Histopathology:
12/30/09 Right knee: Granulomatous inflammation within the dermis. PAS stain is positive for fungal elements. Mucicarmine stain shows rare positivity.
12/30/09 CSF: India Ink positive for encapsulated yeast

Diagnosis: Cutaneous cryptococcus infection

Case #20 continued

Treatment & Course:

The patient's clinical symptoms and cerebrospinal fluid findings were consistent with cryptococcal meningitis and he was started on IV flucytosine and IV amphotericin B. The fluid was later found to be positive for cryptococcal antigen. After a week of therapy his headaches and fevers resolved and he was discharged home on oral fluconazole. The lesion on the eyelid also improved within a week of treatment; however the other 2 lesions remained unchanged. He has plans to follow up with his HIV doctors to reinstitute HAART therapy as well as with Heme/Onc for possible recurrence of lymphoma.

Discussion:

Cryptococcus neoformans is the most common systemic fungal infection in patients with acquired immunodeficiency syndrome (AIDS), and most commonly presents with CNS involvement or meningitis. Skin lesions occur in about 10%-15% of all patients with Cryptococcal infection. Detection of these lesions can aid in early diagnosis of disseminated disease, as they can often precede or be the only clinical finding in disseminated Cryptococcal infection.

Cutaneous lesions are most commonly found on the head and neck and are characterized by multiple, discrete, flesh to red colored umbilicated papules varying in size from 4-6 mm. They are usually asymptomatic and may strongly resemble the lesions of molluscum contagiosum. Several factors can help to distinguish molluscum contagiosum lesions from cryptococcal lesions. A more acute onset of numerous papules is more common in disseminated cryptococcal infection. The umbilicated papules of disseminated Cryptococcus often have a tiny central hemorrhagic crust, which is uncommon in molluscum contagiosum. Similar to molluscum contagiosum, larger solitary lesions of cutaneous Cryptococcus infection may resemble basal cell carcinomas and keratoacanthomas. It is believed that the large polysaccharide capsule of the organism along with the sparse inflammatory infiltrate yields the morphologic findings. Other less common cutaneous manifestions of disseminated Cryptococcus have been reported and include follicular-based eczematous plaques, diffuse scaly nummular plaques, and lesions that mimic Kaposi's sarcoma. Co-infection of lesions with both Cryptococcus and Kaposi's sarcoma or other fungal or fusospirochetal organisms has also been reported.

Extraneural involvement of Crypotcoccus infection in patients with and without AIDS is associated with a poor prognosis, however intravenous amphotericin B alone or with flucytosine and oral fluconazole is a highly effective treatment. After primary treatment is completed, lifelong maintenance therapy with oral fluconazole is usually required.

This case illustrates how proper detection of these unique lesions can aid in the diagnosis of this important opportunistic infection that can have fatal implications if left untreated.

References:

1. Johnson R. Mucocutneous fungal infections in HIV disease. *Clinics in Dermatology*. 2000; 18: 411-422.
2. Murakawa GJ, Kerschmann R, Berger T. Cutaneous Cryptococcus infection and AIDS: report of 12 cases and review of the literature. *Archives of Dermatology*. 1996; 132(5): 545-548.
3. Vasanthi S, Padmavathy BK, Gopal R, Sundaram RS, Manoharan G. Cutaneous Cryptococcus among HIV infected patients. *Indian Journal of Medical Microbiology*. 2002; 20: 165-166.