Wednesday - NOVEMBER 15, 2006

University of Chicago (*Map attached)*

- ***Plans & Policy Committee Meeting: M - 137 / Lectures: Frank Billings Auditorium P-117***
  Enter through Wyler Children's Hospital (the old Children's Hospital) at 5841 S. Maryland Ave., Chicago, IL

- ***Patient and slide viewing – (DCAM) Duchossois Center for Advanced Medicine: 5758 S. Maryland Ave., Chicago, IL***

****Parking spaces in the main parking garage are limited. Valet parking is highly recommended. Please see maps for details.****

8:00 a.m. – 10:00 a.m. Plans & Policy Committee Meeting	**Room M-137** *Enter thru Wyler Children's Hospital main entrance* *5841 S. Maryland*
9:00 a.m. – 11:00 a.m. Registration Derm Clinic DCAM 6C will also have attendance check in, badge pick-up at P-117 auditorium	**P-117** Frank Billings Auditorium *Enter thru Wyler Children's Hospital main entrance* *5841 S. Maryland*
9:00 a.m. – 10:00 a.m. Resident Lecture – Dr. Thomas N. Darling	**P-117** (Frank Billings Auditorium)
9:30 a.m. – 11:00 a.m. Patient Viewing	**DCAM 6C** *Duchossois Center for Advanced Medicine* *5758 S. Maryland Ave.*
9:30 a.m. – 11:00 a.m. Slide Viewing	**DCAM 1402** *5758 S. Maryland Ave.*
11:00 a.m. – 11:15 a.m. CDS Business Meeting	**P-117** (Frank Billings Auditorium)
11:15 a.m. – 12:00 p.m. Guest Lecture – Dr. Thomas N. Darling	**P-117** (Frank Billings Auditorium)
12:00 a.m. – 12:30 p.m. Lunch	**P-117** (Frank Billings Auditorium)
12:30 p.m. – 2:00 p.m. Case discussions	**P-117** (Frank Billings Auditorium)

Allan Lorincz Lecture

Guest Speaker
Thomas N. Darling, M.D., Ph.D.

Resident's Lecture
"Oncogenes and Tumor Suppressor Genes in Skin Disease"

General Membership Lecture
"***Tuberous Sclerosis Complex and Hamartoma Syndromes"***

The American Academy of Dermatology certifies that this educational activity has been recognized for 4 hours of AAD Category 1 and may be used toward the American Academy of Dermatology's continuing Medical Education Award. (119-300)

Nominees to be considered for membership:

Ashish C. Bhatia, MD; Amy J. Derick, MD; Vassilious A. Dimitropoulos, MD; Animesh A. Sinha, MD, PhD; Rama Vaitla, MD

Please direct any comment on these nominees to Dr. Herrmann - Phone: (630) 871-6690 or Email: jherrmann@aol.com

TABLE OF CONTENTS

CHICAGO DERMATOLOGICAL SOCIETY CASE 1

PRESENTERS
Leslie E. Bernstein, MD, Vesna Petronic-Rosic, MD, and Christopher R. Shea, MD

HISTORY OF PRESENT ILLNESS
A 34-year-old black woman initially presented in 2002 to the dermatology clinic with asymptomatic papules and pits on her palms and soles for one year. She expressed concern that the lesions were spreading, particularly to the tops of her fingers. She received a prescription for lactic acid 12% cream but instead applied Eucerin cream daily to her hands and feet. She refused a skin biopsy until 2006.

REVIEW OF SYSTEMS
The patient denied fever, cough, or pain in the abdomen or joints.

PAST MEDICAL HISTORY
The patient reported multiple allergies including to eggs, milk, cheese and latex.

PAST SURGICAL HISTORY
Cesarean sections in 1998 and 2002

MEDICATIONS
None

ALLERGIES
No known drug allergies

FAMILY HISTORY
Four children with eczema, son with asthma, aunt with psoriasis, grandmother with breast cancer

SOCIAL HISTORY
The patient denied tobacco or alcohol use. She works as a secretary.

PHYSICAL EXAMINATION
Multiple cup-shaped, hyperpigmented, 1-2 mm papules with central keratotic plugs were present on the palms and soles. The distribution included the thenar eminences, palmar and ventral digital creases, dorsal interphalangeal digits, lateral and medial plantar areas, and metatarsal regions. There was longitudinal splitting and hyperkeratosis of her toenails.

DERMATOPATHOLOGY
Biopsy of a papule on the left hand revealed acral skin with focal hyperkeratosis overlying well-defined depressions of the epidermis. The dermis was unremarkable.

DIAGNOSIS
Keratosis Punctata Palmoplantaris

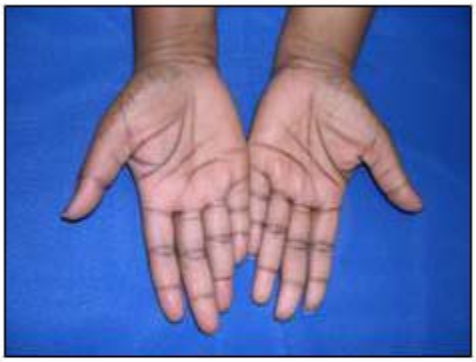
TREATMENT & CLINICAL COURSE
The patient has tried salicylic acid 4% and urea 40% cream without improvement. Her case is presented to the Chicago Dermatological Society to generate discussion regarding other treatment modalities.

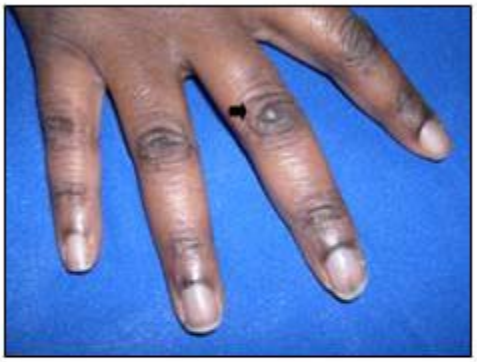
DISCUSSION
Palmoplantar keratoderma represents excess keratin on the palms and soles. Keratosis punctata palmoplantaris of Buschke-Fischer-Brauer (MIM 148600) is rare and commonly affects black men, beginning around the second or third decade. It is characterized by multiple, 1-5 mm papules and pits on the palms and soles, particularly in the metatarsal area, where pressure may be increased. Lesions are generally asymptomatic and can become confluent. Keratosis punctata palmoplantaris of Buschke-

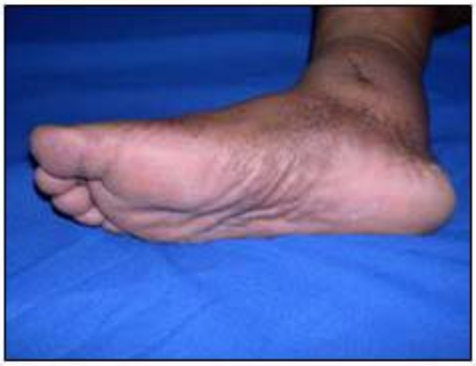
Fischer-Brauer has been associated with numerous disorders, including various nail dystrophies and malignancies of the breast, lung and colon. It also has been documented in patients with psoriasis, spastic paralysis, anodontia, HLA-B27-associated arthropathy and knuckle pads. Histopathologic findings include acanthosis and hyperkeratosis overlying a depressed epidermis. Biopsy specimens also may demonstrate parakeratosis, basal spongiosis, and occluded vasculature or acrosyringia. An autosomal dominant inheritance pattern with variable penetrance has been reported in this condition. Gao *et al*. identified a punctate palmoplantar keratoderma locus on chromosome 15 in a study of affected members in four generations of a family from Zhejiang province after Zhang *et al*. localized the disease to chromosome 8. Treatment options, including keratolytics, calcipotriol, and mechanical debridement or excision have not been reported to be highly effective. Case reports of punctate palmoplantar keratoderma successfully treated with low-dose oral retinoids have been published.

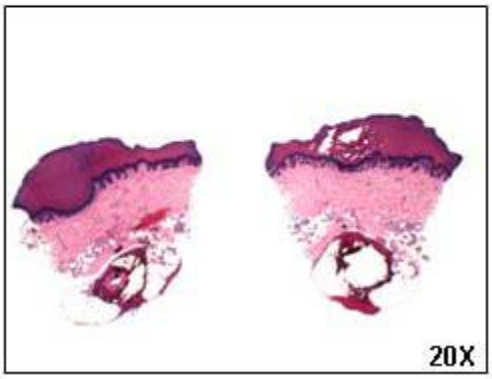
REFERENCES

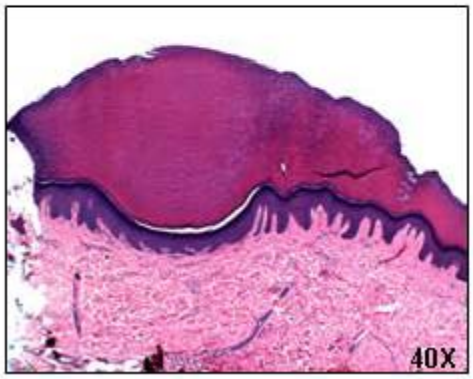
1. Gao M, Yang S, Li M, Yan KL, Jiang YX, Cui Y, Xiao FL, Shen YJ, Chen JJ, Liu JB, Xu SJ, Huang W, Zhang XJ. Refined localization of a punctate palmoplantar keratoderma gene to a 5.06-cM region at 15q22.2-15q22.31. Br J Dermatol 2005;152:874-8.
2. Zhang XU, Ming L, Gao TW, He PP, Wei SC, Liu JB, Li CR, Cui Y, Yang S, Yuan WT, Li CY, Liu YF, Xu SJ, Huang W. Identification of a locus for punctate palmoplantar keratodermas at chromosome 8q24.13-8q24.21. J Invest Dermatol 2004;122:1121-5.
3. Emmert S, Kuster W, Zutt M, Hanssle H, Hallermann C, Kretschmer L, Neumann C. A new family with the rare genodermatosis keratosis punctata palmoplantaris Buschke-Fischer-Brauer. J Am Acad Dermatol 2003; 49:1166-9.








20X


40X

CHICAGO DERMATOLOGICAL SOCIETY CASE 2

PRESENTERS
Yaohui Gloria Xu, MD, PhD, Christopher R. Shea, MD, and Sarah L. Stein, MD

HISTORY OF PRESENT ILLNESS
This 20-year-old, otherwise healthy, Caucasian woman presented with a minimally pruritic rash on her left arm that had persisted over the past two years and recently had spread to her right arm and face. She was initially seen by an outside dermatologist who had performed two biopsies from lesions on her left arm. One biopsy specimen showed a ruptured folliculitis, and the other a superficial and deep lymphocytic dermatitis with eosinophils. Evaluation for lupus was negative. The rash was treated with fluticasone propionate and tacrolimus ointments without improvement; lesions receiving intralesional triamcinolone injection did show some improvement with associated atrophy. The patient does not feel that there is any relation of the rash to sun exposure.

PAST MEDICAL HISTORY
Seasonal allergies; childhood atopic dermatitis; Giardia infection seven years ago

MEDICATIONS
Oral contraceptive pill (Ethinyl estradiol and norethindrone) initiated seven months ago; ibuprofen as needed for cramps associated with menstruation

ALLERGIES
No known drug allergies

FAMILY HISTORY
Non-contributory

SOCIAL HISTORY
The patient is a college student.

PHYSICAL EXAMINATION
On examination, there were ill-defined, erythematous patches and thin plaques with dry scale, with intermingled deep papules and nodules scattered on the face and upper arms. Over time, the nodules seemed to resolve in some locations and appear in nearby areas. Surrounding hypopigmentation developed at sites of improvement. Generalized facial erythema was also notable. The remainder of the physical exam was unremarkable.

LABORATORY DATA & DIAGNOSTIC STUDIES
The following were negative or within normal limits:
CBC with differential, complete metabolic panel, ANA, anti-dsDNA, complement profile, SS-A and SS-B antibody, creatinine kinase, aldolase, lactic dehydrogenase, and serum protein electrophoresis.

The following were abnormal:
Borderline decreased complement level of 174 U/mL (180-320), and total globulin of 2.3 g/dL(2.5-3.5).

DERMATOPATHOLOGY
A punch biopsy specimen from a lesion on the right upper arm revealed parakeratosis, serous crust, reactive hyperplasia and mild spongiosis of the epidermis. There was a superficial and deep perivascular infiltrate of lymphocytes and eosinophils in the dermis. Some of lymphocytes had enlarged, irregular, or angulated nuclei but high-grade atypia was not identified. A hair follicle had lucencies among follicular keratinocytes. The periodic acid-Schiff stain failed to demonstrate fungi or basement membrane thickening. The colloidal iron stain demonstrated increased mucin within both the dermis and the follicular epithelium. A direct immunofluorescence test was negative.

DIAGNOSIS
Idiopathic Benign Follicular Mucinosis (Alopecia Mucinosa)

TREATMENT & CLINICAL COURSE
The patient was started on desonide lotion for the face and mometasone ointment for the arms, and strict sun avoidance was recommended. Serologic tests for lupus and dermatomyositis were negative. The patient was unable to tolerate oral minocycline due to gastrointestinal side effects. After a normal baseline eye examination therapy with hydroxychloroquine at 200 mg bid was initiated, and has been continued for about four months. A trial of clobetasol ointment under occlusion was also recommended for limited areas of the arms for up to two weeks. The lesions have continued to wax and wane. We are in the process of obtaining blocks of previous biopsies for re-evaluation.

DISCUSSION
The term "alopecia mucinosa" was introduced by Hermann Pinkus in 1957 to describe six patients with localized alopecia characterized histopathologically by follicular degeneration with accumulation of mucin within hair follicles. In retrospect, this condition had been recognized decades before Pinkus's description, and in 1959, Jablonska *et al.* proposed the term "follicular mucinosis (FM)." Since then, although both terms have been used interchangeably, some authors propose that "alopecia mucinosa" refers to a clinical condition in which hair loss secondary to follicular mucinosis is seen in areas bearing terminal hairs, whereas "follicular mucinosis" is a distinctive histologic pattern of epithelial mucinosis that occurs incidentally in a host of conditions, being characterized by deposits of mucin mainly in infundibular and sebaceous epithelium.

Histologic findings of FM can be seen in idiopathic, benign settings, associated with malignancy (particularly in association with cutaneous T-cell lymphoma [CTCL]), or with a wide range of conditions including eosinophilic folliculitis, angiolymphoid hyperplasia, lupus, sarcoid, or even nevi and even lentigo maligna. The deposition of mucin, which predominantly consists of hyaluronic acid, is best appreciated with a colloidal iron or Alcian Blue stain. The source of the mucin is not well understood; it might be produced by follicular keratinocytes, or be a product of cell-mediated immunity.

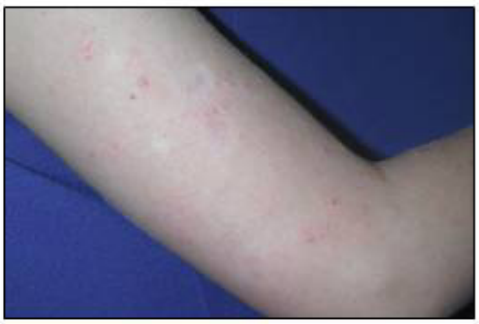
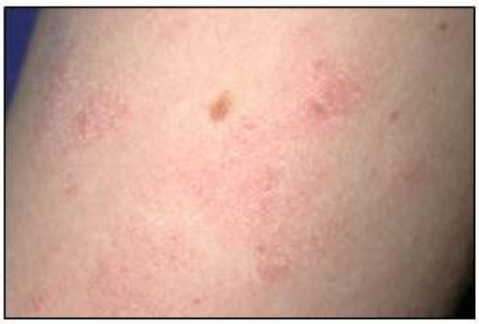
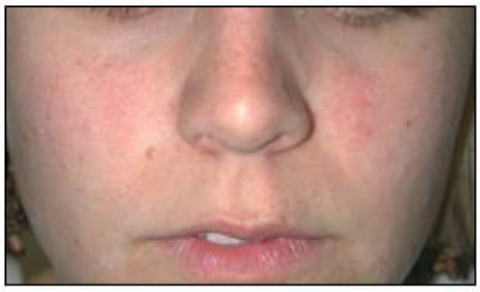
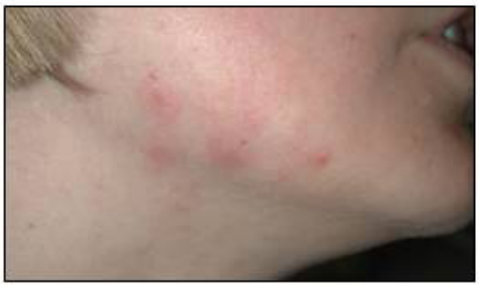
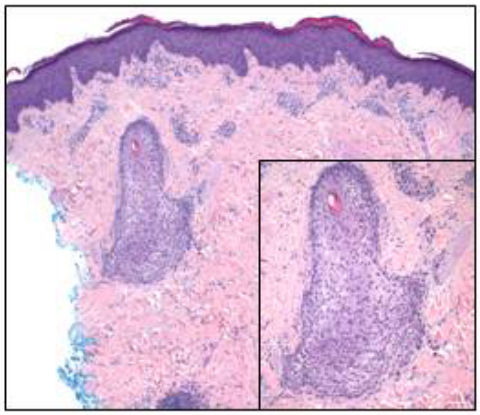
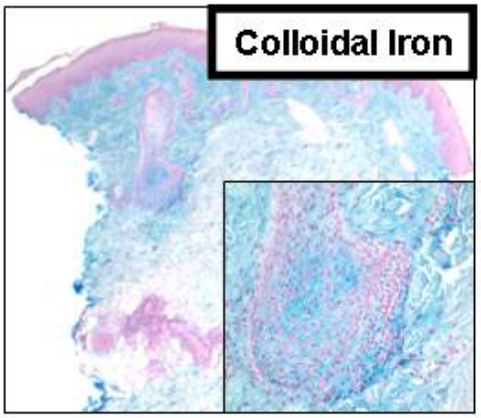
Clinically FM typically presents with erythematous, scaly, infiltrated plaques with scaling and sometimes follicular prominence on the head and neck. Two main types of FM have been recognized. The first type occurs in young patients in the absence of concomitant cutaneous or extracutaneous disorders and shows localized lesions mainly on head and neck with a tendency to resolve within a few years (idiopathic FM). The second type occurs in elderly patients usually with widespread papules and plaques and a relapsing course and is associated with mycosis fungoides or Sézary syndrome, or less commonly, other malignancies (secondary FM). A third type of FM presenting with clinicopathologic features of both main groups has also been reported (the so-called persistent or chronic benign FM). However, the existence of this distinct third type is questionable as it may be an early presentation of malignancy-associated FM.

Remarkably, studies of clinicopathologic features of 44 patients with FM in the absence or presence of CTCL by Cerroni *et al.* revealed no reliable criteria allowing differentiation of idiopathic from malignancy-associated FM, for there is a considerable overlap in patients' age, lesion location, the number of lesions, histopathologic analysis, or even the molecular analysis of TCRγ gene rearrangement. Some authors thus believe that so-called idiopathic FM is a variant of indolent CTCL with localized disease and good prognosis. Therefore, in cases of idiopathic or benign FM, long term follow-up with repeated biopsies is warranted. The incidence of cutaneous lymphoma occurring in association with FM varies between studies, but approximately 15-30% of patients with FM will have mycosis fungoides, which may precede FM, present with FM, or develop years after the diagnosis of FM.

Treatment for malignancy-associated FM is directed toward the underlying malignancy. For idiopathic FM, a wide range of therapeutic options have been tried with inconsistent results: topical and oral antibiotics, topical, intralesional or oral steroids, topical or oral retinoids, dapsone, methotrexate, nitrogen mustard, PUVA, UVA, excision, electron beam, or X-ray therapy.

REFERENCES

1. Anderson BE, Mackley CL, Helm KF. Alopecia mucinosa: report of a case and review. J Cutan Med Surg 2003; 124-8.
2. Brown HA, Gibson LE, Pujol RM, Lust JA, Pittelkow MR. Primary follicular mucinosis: long-term follow-up of patients younger than 40 years with and without clonal T-cell receptor gene rearrangement. J Am Acad Dermatol 2002;47:856-62.
3. Cerroni L, Fink-Puches R, Back B, Kerl H. Follicular mucinosis. A critical reappraisal of clinicopathologic features and association with mycosis fungoides and Sézary syndrome. Arch Dermatol 2002;138:182-9.
4. Rupnik H, Podrumac B, Zgavec B, Lunder T. Follicular mucinosis in a teenage girl. Acta Dermatovenerol Alp Panonica Adriat 2005;14:111-4.

CHICAGO DERMATOLOGICAL SOCIETY CASE 3

PRESENTERS
Elaine F. Kung, MD and Christopher R. Shea, MD

HISTORY OF PRESENT ILLNESS
A 61-year-old Caucasian man, with myelodysplastic syndrome (MDS) diagnosed in 2004, presented with recurrent eruptions of multiple, subcutaneous non-tender nodules on his upper and lower extremities, flank and lower back since 2005. The nodules disappeared completely after four to five months without specific treatment. Histopathologic evaluation of a nodule at another institution revealed neutrophilic granulomatous panniculitis. Since he had MDS, a presumptive diagnosis (prior to immunohistochemical and molecular analysis) of Sweet's panniculitis was made.

REVIEW OF SYSTEMS & PAST MEDICAL HISTORY
He has had complaints of bilateral symmetric lower extremity arthralgias, arthritis, and edema since 2001. A rheumatologist at another institution treated him for seronegative rheumatoid arthritis initially with prednisone 5 to 20 mg (2001 to present), methotrexate 2.5 mg (2001 to 2004), nonsteroidal anti-inflammatory agents, and opioids. Methotrexate was discontinued when he developed severe anemia and it was replaced by adalimumab for 6 months in 2004.

An investigation of his severe anemia in 2004 led to a diagnosis of MDS with refractory anemia (MDS-RA), which has progressed to multi-lineage bone marrow dysplasia with excessive blasts (MDS-RAEB) by 2006. He has required epoietin alfa weekly and packed red blood cell transfusions periodically.

In addition, he has experienced progressive fatigue and weight lost in the last six months.

MEDICATIONS
Prednisone (2001 to present), methotrexate (2001 to 2004), adalimumab (2004), erythropoetin alfa (2005 to present), pentoxifylline (2006), alendronate (2006), valacyclovir (2006), oxycodone (2006), trimethoprim-sulfamethoxazole (2006)

ALLERGIES
No known drug allergies

FAMILY HISTORY & SOCIAL HISTORY
His mother had lymphoma in her 80s and his brother had liver cancer. He lives with his wife and works as an automobile mechanic.

PHYSICAL EXAM
General examination revealed a frail and thin man without acute distress. Skin examination showed multiple, 1 to 2 cm, non-tender, non-ulcerated, erythematous to violaceous nodules scattered over the flexor and extensor aspects of the upper and lower extremities, flanks, and lower back. There were purpuric patches over the dorsal forearms and ill-defined brawny patches over the shins. Bilateral, tense, 3+ pitting edema from feet to mid-calf obscured the ankles' bony contours and limited their range of motion.

Musculoskeletal examination demonstrated mild synovial thickening of the right elbow with full range of motion and bilateral warm knees with effusions. Lymph node examination was unremarkable.

LABORATORY DATA & DIAGNOSTIC STUDIES

The following were negative or within normal limits:
Complete metabolic panel including uric acid, liver function test, lactic dehydrogenase; tissue culture did not grow bacterial, atypical mycobacterial, or fungal organisms; computed tomography of the body did not demonstrate lymphadenopathy.

The following were abnormal:
Hemoglobin 9.1 K/uL (normal range 13.5 to 17.5), platelet count 14 K/uL (150-450), bands 11% (0-6), lymphocytes 4% (0 to 6), monocytes 20% (4 to 12), myelocyte 2 (0%); mildly prolonged PT and PTT , elevated Factor VIII at 270% (57-152); sedimentation rate > 150 mm/hr (0-33); C-reactive protein 74 mg/L (< 5)

Synovial fluid from a knee effusion showed inflammatory cells without evidence of crystals, microorganisms, or malignant cells.

Bone marrow aspirate revealed multi-lineage dysplasia with 7% blasts (MDS-RAEB).

DERMATOPATHOLOGY

A skin biopsy from a nodule on the left medial thigh showed a polymorphous dermal and subcutaneous lobular and septal granulomatous infiltrate composed of lymphocytes, atypical large cells, macrophages, lipophages, neutrophils with karyorrhexis as well as occasional eosinophils and plasma cells. There was also a lymphocytic infiltrate surrounding large subcutaneous vessel wall without necrotizing vasculitis

A skin biopsy from a nodule on the right forearm revealed a hyperplastic epidermis and elastotic dermis with a superficial and deep perivascular mixed cell infiltrate. A dense, polymorphous granulomatous infiltrate of subcutaneous lobules was composed of small lymphocytes, neutrophils, and atypical large cells with nuclear enlargement, prominent nucleoli, and abundant cytoplasm. Extensive necrosis and mitotic figures were seen in the subcutaneous fat.

Immunohistochemical and molecular analysis was notable for CD3+, CD8+ and TCR-β+ (labeling 50% of the subcutaneous lymphoid infiltrate), CD45+ (leukocyte common antigen) lymphocytes that rimmed individual adipocytes. CD4+ (labeling another 50% of the subcutaneous lymphoid infiltrate) lymphocytes did not rim individual adipocytes, A few CD20+ (L26) B-cells and CD56+ (NK cells) surrounded nerves in the reticular dermis. CD68+ foamy cells formed collections in the dermis and subcutaneous fat.

DIAGNOSIS

Subcutaneous Panniculitis-like T-cell lymphoma (SPTCL)

TREATMENT & CLINICAL COURSE

Our patient reported complete clearance of subcutaneous nodules after 4 to 5 months without specific therapy. He experienced less arthritic pain in his lower extremities after the initiation of pentoxifylline although the pitting edema remained. For MDS-RAEB, he received a second round of azacitibine, which post-dated the disappearance of his nodules and the improvement of joint symptoms.

DISCUSSION

The appearance of cutaneous lesions in patients with myelodysplastic syndrome (MDS) is a poor prognostic sign often linked to disease progression into acute myeloid leukemia (AML). Skin lesions specific to MDS result from dermal infiltration of malignant hematopoietic cells. Non-specific skin lesions are more common and are secondary to cutaneous infections, especially in those who are neutropenic, cutaneous vasculitis, and neutrophilic dermatoses (Sweet syndrome, pyoderma

gangrenosum, subcorneal pustular dermatosis of Sneddon-Wilkinson, or erythema elevatum diutinum). However, SPTCL has not to our knowledge been reported in patients with MDS.

Our patient developed recurrent, self-remitting, eruptive, subcutaneous nodules one year after initiation of adalimumab, a recombinant human IgG_1 monoclonal antibody specific for human tumor necrosis factor (TNF)-α. Among 2468 patients treated with adalimumab in clinical trials, 10 of the 48 malignancies observed were lymphoma. A case of mycosis-fungoides-associated follicular mucinosis reportedly developed within months after the start of adalimumab. In addition, two cases of aggressive cutaneous lymphomas were attributed to other TNF-α inhibitors, namely etanercept and infliximab. Due to the chronology and sudden onset of SPTCL following adalimumab administration, it is reasonable to suspect that the immunosuppressive nature of TNF-α inhibitors may be contributory.

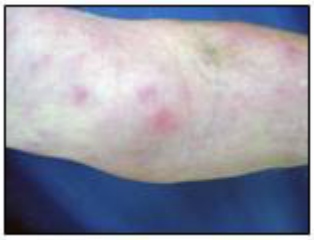
SPTCL is a rare form of peripheral T-cell lymphoma with fewer than 100 cases reported worldwide. Patients with SPTCL develop multiple, erythematous, subcutaneous nodules or plaques on the extremities or trunk along with constitutional symptoms of fever, fatigue, and weight loss. Most cases occur in young adults with a slight female preponderance. As in our patient's case, SPTCL may be indolent, self-remitting, and recurrent. The aggressive type of SPTCL can run an acute course, especially in those who develop hemophagocytic syndrome (HPS), characterized by pancytopenia, hepatic dysfunction, hemorrhagic diathesis, hepatosplenomegaly, serositis, and mucous membrane ulceration.

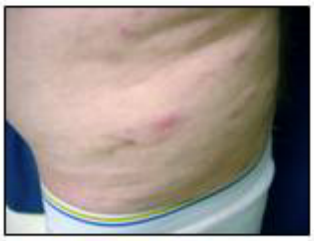
The diagnosis of SPTCL requires clinical suspicion correlated with histopathologic, immunohistochemical, and molecular analysis. SPTCL is often mistaken for malignant histiocytosis, histiocytic cytophagic panniculitis, Weber-Christian disease, inflammatory panniculitis, and systemic lymphoma. Histologically, SPTCL mimics panniculitis due to involvement of fat lobules and focal areas of the septa. Rimming of individual adipocytes with atypical clonal lymphocytes is characteristic but not specific for SPTCL. Cytologically, small to medium-sized lymphocytes with atypia are often admixed with reactive histiocytes and rarely neutrophils. Prominent karyorrhectic debris, necrosis, and erythrophagocytosis by histocytes are common features of SPTCL. Immunohistochemically, the neoplastic cells usually express CD2, CD3, and CD45RO, demonstrating T-cell lineage. Approximately two-thirds of the cases show CD8 cytotoxic phenotype with T-cell-restricted intracellular antigen (TIA) and granzyme B. Most cases reported in the United States express T-cell receptor rearrangement (TCR)-α/β, which portends a better prognosis than the γ/δ-type. SPTCL with TCR-γ/δ often have cells expressing the natural killer (NK) cell marker CD56+, and are CD4- and CD8-. The cases reported in Europe and Asia suggest a higher prevalence of the γ/δ variant of SPTCL, which has a high mortality rate due to HPS.

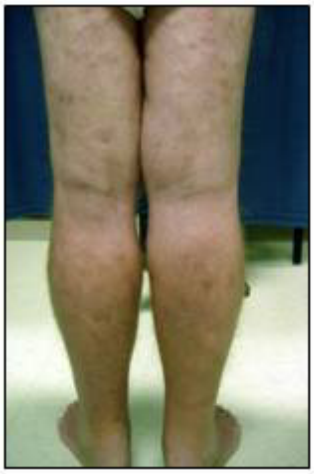
The onset of our patient's signs and symptoms, consistent with remitting symmetric seronegative synovitis with pedal edema (RS3PE syndrome), heralded both MDS and SPTCL. RS3PE syndrome comprises (1) bilateral pitting edema of both hands; (2) sudden onset of polyarthritis; and (3) seronegativity for rheumatoid factor. Nevertheless, polyarthritis involving knees and ankles is quite common. RS3PE may be the initial manifestation of rheumatic diseases of the elderly, such as rheumatoid arthritis, Sjögren syndrome, late-onset spondyloarthropathies, polymyalgia rheumatica, and giant-cell arteritis. However, as in the case of our patient, a paraneoplastic condition preceding or concurrent with malignancies such as MDS should be suspected if the clinical findings do not improve within a few days of initiating corticosteroids.

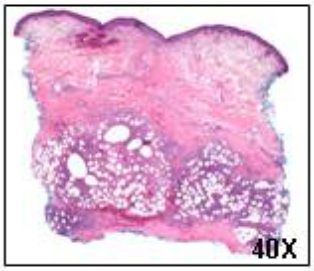
REFERENCES

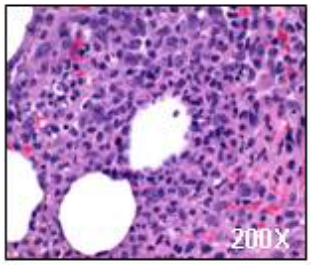
1. Go RS, Wester SM. Immunophenotypic and molecular features, clinical outcomes, treatments, and prognostic factors associated with subcutaneous panniculitis-like T-cell lymphoma. Cancer 2004; 101: 1404-1408.
2. Hogue SR, Child FJ, Whittaker SJ, Ferreira S, Orchard G, Jenner K, Spittle M, Russell-Jones R. Subcutaneous panniculitis-like T-cell lymphoma: a clinicopathological, immunophenotypic and molecular analysis of six patients. Br J Dermatol 2003; 148: 516-522.
3. Manganelli P, Delsante G, Bianchi G, Fietta P, Quaini F. Remitting seronegative symmetrical synovitis with pitting oedema in a patient with myelodysplastic syndrome and relapsing polychondritis. Clin Rheumatol 2001; 20: 132-135.
4. Scheinfeld N. A comprehensive review and evaluation of the side effects of the tumor necrosis factor alpha blockers etanercept, infliximab, and adalimumab. J Dermatol Treatment 2004; 15: 280-294.

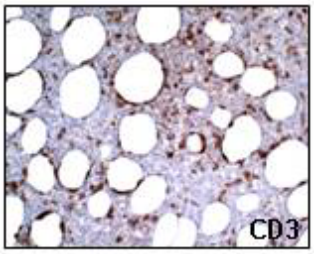


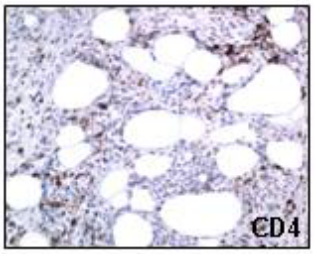


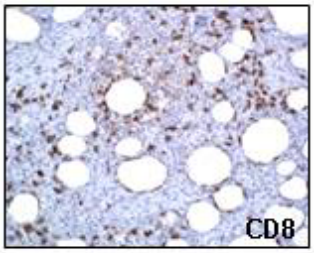


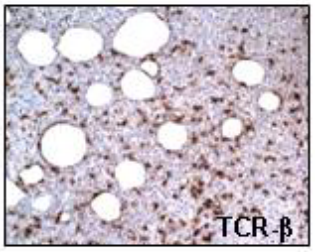

40X


200X


CD3


CD4


CD8


TCR-β

CHICAGO DERMATOLOGICAL SOCIETY CASE 4

PRESENTERS
Olga Ulitsky, MD, Vesna Petronic-Rosic, MD, and Christopher R. Shea MD

HISTORY OF PRESENT ILLNESS
A 53-year-old African American woman with a history of hypertension was admitted to University of Chicago Hospitals with extensive subarachnoid hemorrhage after being found unconscious at home. Dermatology was consulted for evaluation of hemorrhagic vesicles on the right forearm and breast, which were originally attributed to trauma from the fall.

PAST MEDICAL HISTORY
Hypertension

MEDICATIONS
Medications initiated on admission:
Senna, docusate sodium, phenytoin, lansoprazole, ciprofloxacin, metoprolol, fentanyl, enoxaparin, nystatin, vancomycin, ferrous sulfate, regular human insulin, acetaminophen.
Medications initiated after patient was seen by dermatology service: amphotericin, posaconazole

ALLERGIES
No known drug allergies

FAMILY HISTORY
Cerebrovascular accident in father

SOCIAL HISTORY
No history of illicit drug use

PHYSICAL EXAMINATION
Grouped hemorrhagic vesicles were present on the extensor right forearm. Grouped vesicles and pustules on an erythematous base were under the right breast. A superficial erosion with yellow crust was noted on the right cheek.

LABORATORY DATA & DIAGNOSTIC STUDIES
The following were negative or within normal limits:
Toxicology screen, basic metabolic panel, HIV ELISA, HIV-1 viral load, IgG, IgM, IgA, urinalysis

The following were abnormal:
Abnormal labs: Total CK 3809 (9-185), WBC 20.7(3.5-11), spinal fluid with 16600 RBCs (0) and 111 WBC (0-5), absolute CD3 577 (828-2328), absolute CD4 370 (515-1642), absolute CD8 170 (212-887), SGOT 54 (8-37), SGPT 55 (8-35), ferritin 282 (10-220)

MRI of brain: intraventricular hemorrhage, increased signal density in left occipital and temporal cortex, consistent with stroke.

DERMATOPATHOLOGY:
There is subepidermal and intraepidermal blister formation with overlying epidermal necrosis. Broad-branching hyphae with bulbous extensions are present associated with thrombi in the dermal vasculature, while fibrin deposits and neutrophils are noted within the vessel walls. The PAS stain highlights non-septate hyphae with ninety-degree branching. The Gram and Fite stains are negative for bacteria. Fungal culture from the biopsy grew *Rhizopus* organisms. Skin biopsy cultures for bacteria and mycobacteria were negative.

CHICAGO DERMATOLOGICAL SOCIETY CASE 4

DIAGNOSIS
Cutaneous Mucormycosis

TREATMENT & CLINICAL COURSE
The patient was started on amphotericin and posaconazole. Complete resolution of skin lesions occurred within two weeks. The patient's mental status improved and she was eventually transferred to the general floor and later discharged. Although limited by a near-complete Broca's aphasia, she presently is interactive with the environment.

DISCUSSION
Cutaneous mucormycosis is an infrequent, aggressive, potentially lethal fungal infection, which occurs predominantly in immunocompromised hosts. It involves members of the class Zygomycetes, order Mucorales. *Rhizopus, Mucor, Absidia*, and *Rhizomucor* are the four genera of this order that can be pathogenic. The clinical patterns of the disease produced by different species of Mucorales are virtually identical. These agents are saprophytes found in soil, corn, and rotten fruits and vegetables. They have also been identified in air samples and dust from air conditioning systems.

After aspergillosis, mucormycosis is the second most common mycosis caused by filamentous fungi with *Rhizopus* and *Absidia* being the most frequent pathogens isolated from infected patients. Mucormycosis carries an overall mortality of about 75-80%, with the mortality rate in cases of disseminated mucormycosis exceeding 95%.

Several factors allow these organisms to survive, including their vasculotropic nature, ability to grow at or above body temperature, production of destructive enzymes, and resistance to destruction of spores at extremes of temperature. The organism has an active ketone reductase system, allowing its growth in the acidic, glucose-rich environment of diabetic ketoacidosis.

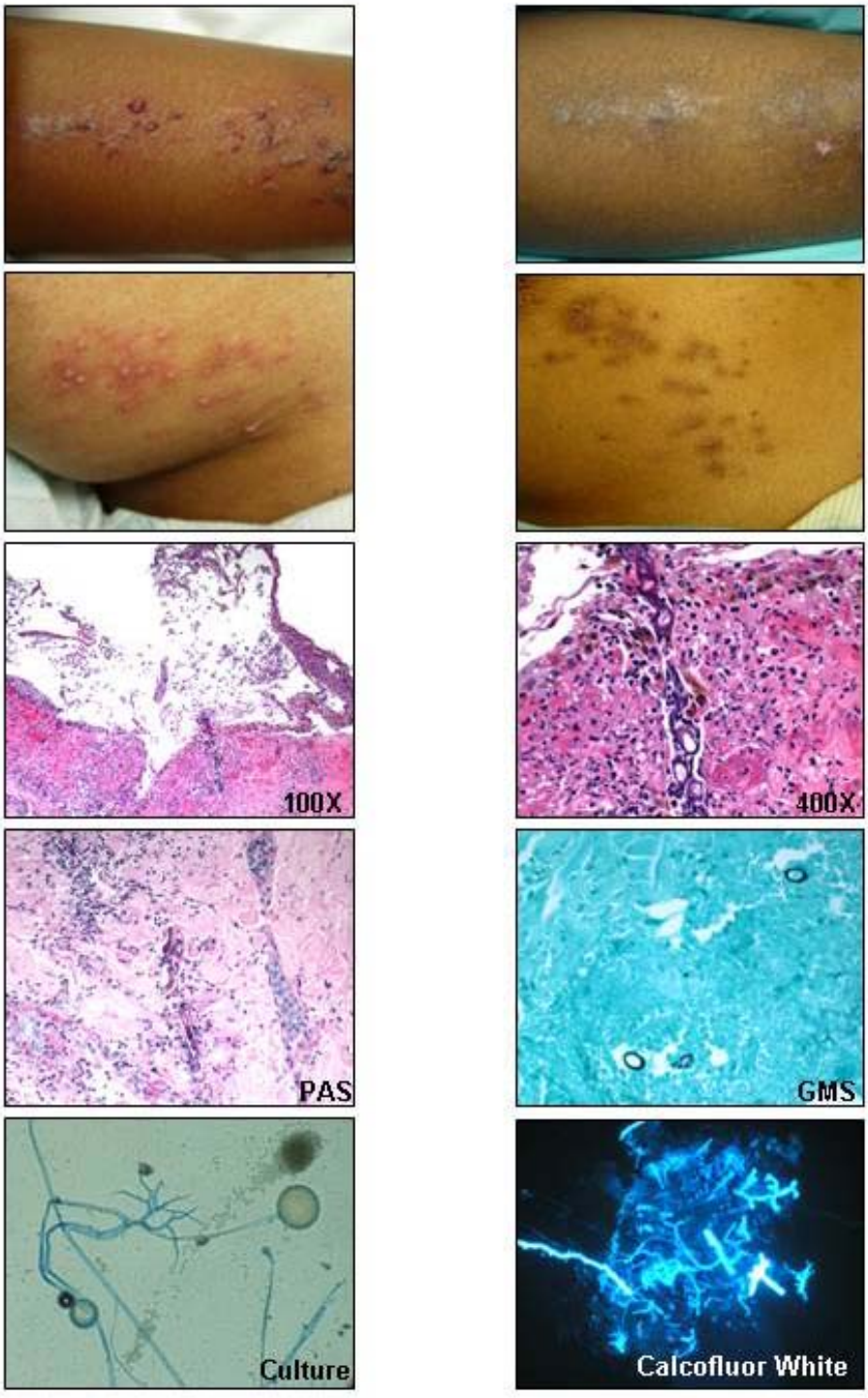
Most cases of mucormycosis occur in immunocompromised hosts. Risk factors include diabetes mellitus, neutropenia, sustained immunosuppressive therapy, broad-spectrum antibiotic use, severe malnutrition, and breakdown in skin barrier integrity. Only the latter factor was present in our patient. Several classical forms of mucormycosis are recognized: rhino-orbitocerebral, pulmonary, disseminated, gastrointestinal, cardiac, and cutaneous. Common to all forms is vascular invasion with production of necrotic tissue. The clinical presentation is variable, including black vesicles, indurated lesions with necrosis, erythematous plaques with central eschars, etc. There are several reports of distinctive morphology, coined as "bulls-eye infarct of cutaneous zygomycosis," which may aid with clinical diagnosis of this condition.

The definitive diagnosis of zygomycosis requires both the visualization of the characteristic broad, non-septate hyphae with right-angle branching in tissue as well as fungal culture. Successful treatment requires a combination of early diagnosis, surgical debridement, antifungal therapy, and medical management of any predisposing condition. Amphotericin B has been used successfully. With the liposomal formulation, one can achieve higher concentrations of drug with less risk of nephrotoxicity. One report demonstrated posaconazole, an experimental oral antifungal agent with good CNS penetration and anecdotal efficacy against Rhizopus, to be effective after failure of amphotericin B therapy in a human heart-kidney transplant recipient with zygomycosis. Recently, Mohs micrographic surgery has been used as treatment for cutaneous zygomycosis.

Considering the potentially fulminant and fatal course of this condition, awareness and a high index of suspicion for mucormycosis are required.

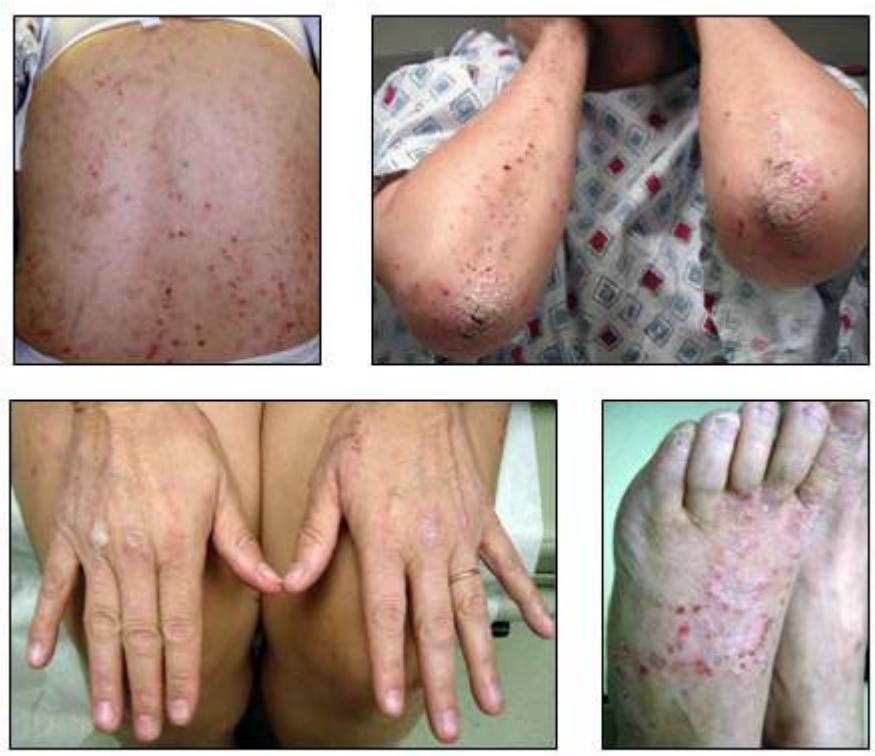
REFERENCES:

1. Eucker J, Sezer O, Graf B, Possinger K. Mucormycoses. Mycoses 2001;44:253-60.
2. Fujimoto A, Nagao K, Tanaka K, Yamagami J, Udagawa S, Sugiura M, The first case of cutaneous mucormycosis caused by Rhizopus azygosporus. Br J Dermatol 2005;153:428-30.
3. Roden M. Zaoutis T., Buchanan W. et al. Epidemiology and outcome of zygomycosis: a review of 929 reported cases. Clin Inf Dis 2005:41:634-53.
4. Rubin A, Grossman M. Bull's-eye cutaneous infarct of zygomycosis:a bedside diagnosis confirmed by touch preparation. J Am Acad Dermatol 2004;51:996-1001.


100X
400X
PAS
GMS
Culture
Calcofluor White

PRESENTERS
Bernhard Ortel, MD, Vishakha Sharma, MD, and Vesna Petronic-Rosic, MD

UNKNOWN CASE



CHICAGO DERMATOLOGICAL SOCIETY CASE 6

PRESENTERS
Vishakha Sharma, MD, Bernhard Ortel, MD, and Sarah L. Stein, MD

HISTORY OF PRESENT ILLNESS
A 16-year-old Caucasian male presented for evaluation of a long-standing eczematous skin condition characterized by dry, red, pruritic, and scaling skin that has been present from two months of age. He had been treated in the past with multiple topical agents, including topical corticosteroids and petrolatum based emollients without significant improvement. The patient felt that the use of ointment-based products always seemed to exacerbate his skin condition. The only treatment in the past that has helped is oral corticosteroids. During the short courses of oral steroids, his skin would improve significantly only to flare severely upon discontinuation. In addition to his "eczema," he has suffered from significant asthma, allergies, and frequent upper respiratory and skin infections.

PAST MEDICAL HISTORY
- Born at 36wga via SVD; pregnancy was complicated by premature labor
- Atopic dermatitis: diagnosed at 2 months of age
- Failure to thrive/growth delay: diagnosed at 6 months; chronological age < bone age at 3 yo
- Chronic diarrhea: diagnosed at 6 months
- Allergies: diagnosed at 13 months; RAST strongly + for eggs and peanuts
- Hypothyroidism: diagnosed at 18 months
- Asthma: diagnosed at 18 months
- GERD: diagnosed at 15 years old; EGD performed with esophageal biopsy showing mild chronic inflammatory infiltrate

REVIEW OF SYSTEMS
Positive for pruritus, burning, and pain all over skin; headaches; and a foul odor accompanied by GI distress with most foods, currently only able to tolerate Neocate (100% amino acid based hypoallergenic formula)

MEDICATIONS
Theophylline, levothyroxine, cetirizine, montelukast sodium, lansoprazole, zaleplon, pirbuterol inhaler, fluticasone and salmeterol, hydrocortisone, levalbuterol, iodine tablets, culture-lactobacillus

ALLERGIES
No known drug allergies

FAMILY HISTORY
Sisters with asthma and atopic dermatitis, mom with asthma and allergies, cousin with cystic fibrosis, cousin with thyroid disease, maternal grandfather with SLE, maternal aunt with JRA

SOCIAL HISTORY
Lives with parents and four siblings, home schooled and currently in the 9th grade

PHYSICAL EXAMINATION
Severe scaling, fissuring, and crusting were present on the skin of this 16-year-old male of short stature with erythroderma. His skin exuded a significant odor. His scalp hair consisted of short, blonde, brittle hair, and his eyebrow hairs were fine and somewhat sparse. The palmar surface of his hands displayed scaling and fissuring, but his soles were unaffected. Mild nail dystrophy was present.

LABORATORY DATA & DIAGNOSTIC STUDIES

The following were negative or within normal limits:
Tissue transglutaminase Ab, duodenal biopsy to evaluate for celiac disease (preservation of villous architecture), zinc level, Vitamin A, Vitamin E, PT, PTT, INR, 25-hydroxyvitamin-D, liver function tests, CF gene mutation

The following were abnormal:
Slightly increased antigliadin IgG Ab of 25 (normal is < 11); low IgA of 27 (normal 57-300); IgE markedly elevated; complete blood count with peripheral eosinophilia of 17%

DERMATOPATHOLOGY

A punch biopsy of skin from the left axilla was performed in 1991 at Wright-Patterson Air Force Base in Ohio. The biopsy was interpreted as "consistent with atopic dermatitis [with] hyperkeratosis and acanthosis." More recently, hair mounts obtained from eyebrows show several examples of trichorrhexis nodosa, and changes suggestive of trichorrhexis invaginata.

DIAGNOSIS

Netherton syndrome

TREATMENT & CLINICAL COURSE

Given the above constellation of abnormalities, the patient was suspected to have Netherton syndrome. A buccal swab was obtained and sent for genetic analysis to evaluate for a SPINK5 mutation, the results of which are pending. In the meantime, he was started on fluocinolone in an oil vehicle to apply to his body daily, cyproheptadine 4-6mg orally three times daily, and a course of cephalexin for MSSA infection. After initial dramatic improvement, then relapse on the above regimen, he was started on narrow-band UVB therapy. An initial slowly tapering course of corticosteroids was started concurrently with phototherapy to prevent a severe flare.

A minimal erythema dose was obtained prior to initiation of phototherapy and found to be less than 100mJ/cm^2. As such, phototherapy was begun conservatively with exposure at 30mJ/cm^2 and continued with five treatments a week with ten percent daily dose increases eventually reaching 220mJ/cm^2. At this dose, his skin was improving with resolution of many of the fissures and a noticeable improvement in the pruritus. He is now receiving phototherapy three times a week with dose increases as tolerated and continues to improve.

DISCUSSION

Netherton syndrome (NS) is a rare, autosomal recessive disorder characterized by a triad of ichthyosis, hair shaft abnormalities, and an atopic diathesis. The classic lesion of NS is ichthyosis linearis circumflexa (ILC) consisting of erythematous, polycyclic, migratory plaques with double-edged scales at the border. This peculiar finding was first reported by Comel in 1949 and then later paired with the pathognomonic hair finding of trichorrhexis invaginata by Netherton in 1958. Although ILC is the best known cutaneous finding of Netherton syndrome, it is only thought to be present in 75% of cases with others showing a clinical picture similar to congenital ichthyosiform erythroderma (CIE). Other hair shaft defects have been noted in NS including trichorrhexis nodosa (as seen in our patient), pili torti, and helical hair. Completing the triad is a strong predisposition to atopy with allergies, asthma, elevated IgE and hypereosinophilia predominating. Other associated conditions that have been reported in NS include failure to thrive, growth delay, frequent infections, and enteropathy, all of which are present in our patient. Mental retardation, which is not seen in our patient, has also been variably reported in NS.

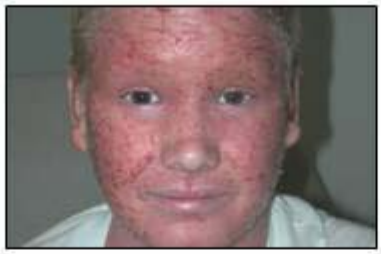
Netherton syndrome is caused by mutations in the secretory serine protease inhibitor Kazal-type 5 (*SPINK5*) gene located on chromosome 5q32. This gene encodes a lympho-epithelial Kazal-type related inhibitor (LEKTI) which is predominantly expressed in stratified epithelial tissue layers and in the granular layer of the epidermis. Almost all identified *SPINK5* mutations in NS involve premature termination codons, leading to complete loss of LEKTI expression in the epidermis. Loss of LEKTI results in increased stratum corneum tryptic enzyme, which through a variety of mechanisms is thought to lead to premature cornification, degradation of corneodesmosomes, and premature desquamation of the stratum corneum, all of which contribute to the high degree of epidermal barrier dysfunction invariably seen in NS. Premature lamellar body secretion is now thought to be a partially compensatory mechanism in NS providing a limited barrier to transcutaneous water loss.

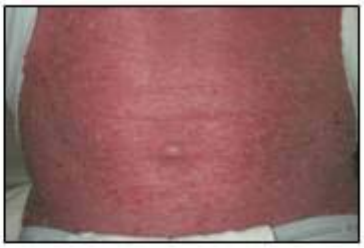
Many therapeutic options have been proposed for the ILC and erythroderma seen in NS. Topical treatments have included 12% ammonium lactate lotion, 10% urea, topical calcipotriol ointment, and topical calcineurin inhibitors all with varied success. The use of topicals in general is limited by risks of systemic toxicity due to the impaired barrier function consistently seen in NS, with topical calcineurin inhibitors posing the greatest risks. Systemic therapies for NS thus far have included retinoids and phototherapy. Oral retinoids have been found to be successful for the more ichthyotic component of NS but often worsen the erythroderma or accompanying atopic dermatitis, making this an unfavorable choice in our patient. Both PUVA and UVA-1 have been reported to be successful in NS, but narrow-band UVB has not been explicitly mentioned. If our patient continues to improve with narrow-band UVB, we propose this as another therapeutic option in this difficult to treat condition.

REFERENCES

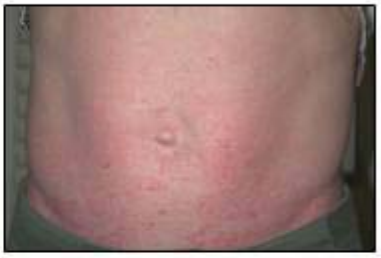
1. Allen A, Siegfried E, Silverman R, Williams ML, Elias PM, Szabo SK, Korman NJ. Significant absorption of topical tacrolimus in 3 patients with Netherton Syndrome. Arch Dermatol 2001;137:747-50.
2. Bens G, Boralevi F, Buzenet C, Taieb A. Topical treatment of Netherton's syndrome with tacrolimus ointment without significant systemic absorption. Br J Dermatol 2003;149:224-5.
3. Capezzera R, Venturini M, Bianchi D, Zane C, Calzavara-Pinton P. UVA1 phototherapy of Netherton Syndrome. Acta Derm Venereol 2004;84:69-94.
4. Descargues P, Deraison C, Prost C, Fraitag S, Mazereeuw-Hautier J, D'Alessio M, Ishida-Yamamoto A, Bodemer C, Zambruno G, Hovnanian A. Corneodesmosomal cadherins are preferential targets of stratum corneum trypsin-and chymotrypsin-like hyperactivity in Netherton Syndrome. J Invest Dermatol 2006;126:1622-32.
5. Godic A, Dragos V. Successful treatment of Netherton's syndrome with topical calcipotriol. Eur J Dermatol 2004;14:115-7.
6. Nagata T. Netherton's Syndrome which responded to photochemotherapy. Dermatologica 1980;161:51-6.

Initial Presentation

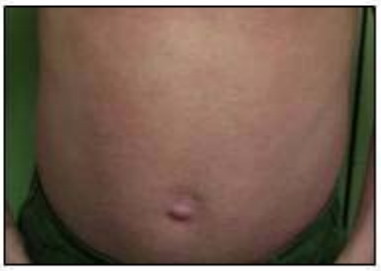




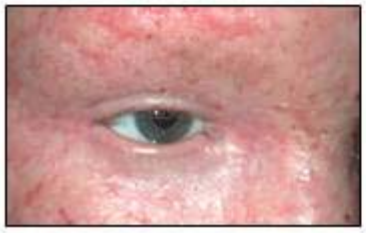
After 1 month of Derma-Smoothe oil and course of cephalexin



After 3 weeks of NB-UVB and short course of corticosteroids

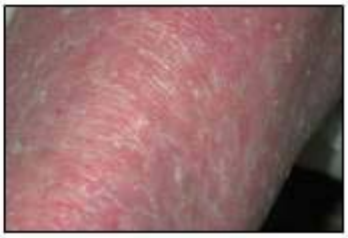


Sparse eyebrow hairs



Trichorrhexis nodosa

Ichthyotic Scale



CHICAGO DERMATOLOGICAL SOCIETY CASE 7

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

HISTORY OF PRESENT ILLNESS
Patient A was first seen on her day of birth for evaluation of a rash over the scalp and face. The infant was born at term and was uncompromised in the neonatal period.
Patient B is the mother of patient A. She is a 33-year-old Caucasian female who was seen in dermatology urgent care clinic 6 weeks after the birth of her baby due to a recurrence of her "psoriasis". According to the patient she had a history of hand and foot psoriasis about 6 yrs ago, which resolved and reappeared during her recent pregnancy. The rash had resolved with delivery of the infant until approximately 2 to 3 weeks post partum when she noticed the return of her hand lesions this time with a rash on her face, chest, and arms.

PAST MEDICAL HISTORY
Patient A: Full term infant, uncomplicated pregnancy and delivery.
Patient B: Recurrent papulosquamous rash, previously called eczema and psoriasis.

MEDICATIONS
Patient A and B: None

ALLERGIES
Patient A and B: No known drug allergies

FAMILY HISTORY
Patient A and B: Psoriasis, atopy only reported in patient B (mother)

SOCIAL HISTORY
Patient A: Lives with parents and sister
Patient B: She does not smoke, use illicit drugs, or drink alcohol

REVIEW OF SYSTEMS
Patient A: No fevers or chills, eats and drinks well, many wet diapers, many bowel movements of normal consistency, sleeps well
Patient B: No fevers, chills, weight change, chest pain, SOB, abdominal pain, or joint pains

PHYSICAL EXAM
Patient A:
Day 1: Numerous large white thin-walled inclusions were found on the scalp containing a greasy waxy material. On the face there was periorificial erythema with desquamation. The trunk and extremities were spared.

Subsequently the rash slowly evolved into increased erythema of the face with papular lesions more peripherally and greasy scale in scalp. By 3 months of age, the scalp and face were clearing, with new small blanching erythematous papules appearing on the chest and abdomen.

Patient B: Diffuse erythematous-orange hued rash with perifollicular 1-2 mm papules on the upper chest and upper extremities with facial involvement most prominent periorbitally.

LABORATORY DATA & DIAGNOSTIC STUDIES
Patient A: Neonatal blood screen was within normal limits.
Patient B: Labs obtained on the day of Patient B's birth were within normal limits.

DERMATOPATHOLOGY
Patient A: A biopsy was obtained of the left pre-auricular area showing focal horizontal and vertical parakeratosis alternating in a "checkerboard" pattern and involving the hair follicle infundibula. Some psoriasiform hyperplasia of the epidermis and diffuse mild spongiosis was present. The granular layer was intact. Occasional isolated necrotic keratinocytes were present as well as some keratinocytes in mitosis. The dermis contained dilated blood vessels and a sparse perivascular and interstitial chronic inflammatory cell infiltrate.
Patient B: Biopsies were obtained of the shoulder and wrist both showing horizontal and vertical parakeratosis in a "checkerboard" pattern. Parakeratosis was present at the shoulders of adnexal ostia on the wrist biopsy. Both contained hyperplasia of the epidermis with focal hypergranulosis and scant exocytosis of lymphocytes. The dermis contained a moderately dense perivascular mononuclear cell infiltrate. Extravasated red blood cells were present in the dermal papillae.

DIAGNOSIS
Patient A: Congenital Pityriasis Rubra Pilaris
Patient B: Pityriasis Rubra Pilaris (PRP)

TREATMENT & CLINICAL COURSE
Patient A: The patient was discharged home soon after birth with the rash but otherwise healthy. On day 9 the patient was started on 2.5% hydrocortisone ointment. While on treatment her papular lesions continued to progress. However, the lesions remitted almost completely by 3 months. The truncal rash was first noted on the 11 week visit. Currently the only treatment is with emollients.
Patient B: After the first visit the patient was started on 0.005% calcipotriene/0.064% betamethasone ointment and 0.025% fluocinolone acetonide ointment with little to no improvement over the subsequent week. After the biopsy results returned a diagnosis of PRP, the patient was started on topical 20% urea to help with the keratoderma, and preparations for starting isotretinoin were initiated.

DISCUSSION
Pityriasis rubra pilaris is a rare skin condition affecting men and women equally and has an incidence of 1:5,000 to 1:50,000 with some variability depending on ethnic background. Nearly all cases are acquired with only occasional reports of a familial form. Most commonly it is inherited in an autosomal dominant pattern with variable penetrance, but an autosomal recessive pattern has been decribed.

The etiology of PRP is poorly understood. Several hypotheses have been considered, including a possible dysfunction in keratinization and vitamin A metabolism. The role of a physical trigger or superantigen is supported by cases where a preceding trauma, UV exposure, or infection occurred. An autoimmune etiology is supported by associated instances of myasthenia gravis, celiac sprue, myositis, inflammatory arthritis, hypothyroidism, and HIV.

Five forms of PRP have been described and classified according to Griffiths scheme. Type I (classic adult, 55%) is the most common with red-orange plaques, islands of sparing, perifollicular keratotic papules, waxy palmoplantar keratoderma, erythema with fine diffuse scale on the scalp, and caudal spread. Early on, PRP of the scalp can be difficult to distinguish from seborrheic dermatitis. Type II (atypical adult, 5%) is similar to type I, but with more icthyosiform scale of the legs, a keratoderma with coarse lamellated scale, and occasional alopecia. Type III (classic juvenile, 10%) usually occurs in the first 2 years of life and is similar to type I clinically. Type IV (circumscribed juvenile, 25%) occurs

before puberty and is much more circumscribed, occurring on elbows and knees, with erythema and follicular papules. Type V (atypical juvenile, 5%) is similar to type II clinically, with occasional scleroderma-like changes of the hands and feet. It presents in the first few years of life. The familial forms of PRP that have been reported, have presented as type II or V.

Treatment is empiric due to low number of patients available for randomized studies and propensity for spontaneous resolution in many cases. Systemic retinoids have met with some success. Methotrexate has also been reported to improve clinical outcomes. Other treatments such as vitamin D analogues, immunosuppressives, and UV light have produced variable results. Congenital presentation of PRP is extremely rare and in the few reported cases tends to resolve without treatment in 3 to 6 months.

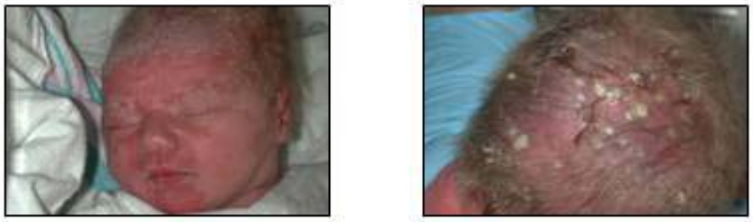
Patient B is a typical example of type I PRP; however patient A is not so easily categorized. Clinically patient A fits best into type III PRP in terms of symptoms and course of the disease.

REFERENCES

1. Albert MR, Mackool BT. Pityriasis rubra pilaris. Int J Dermatol 1999;38:1-11.
2. Griffiths WAD. Pityriasis rubra pilaris. Clin Exp Dermatol 1980;5:105-12.
3. Dicken CH. Treatment of classic pityriasis rubra pilaris. J Am Acad Dermatol 1994;31:997-9.
4. Gelmetti C, Schiuma A, Cerri D, Gianotti F. Pityriasis rubra pilaris in childhood: a long-term study of 29 patients. Pediatr Dermatol 1986;3:446-51.

PATIENT A

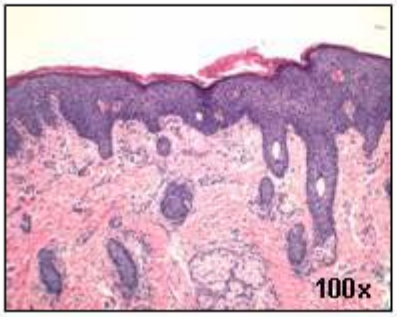
Day 1

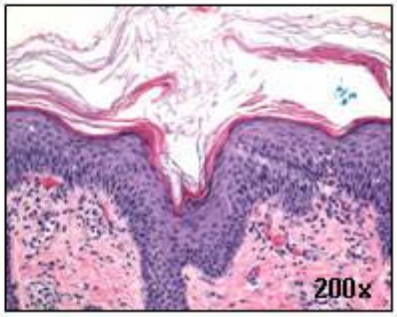


Day 9

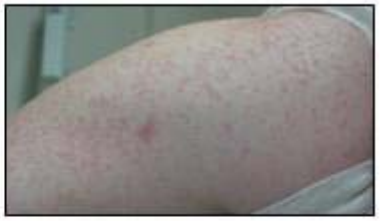
Week 6

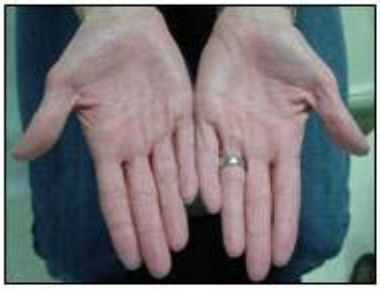
Week 11

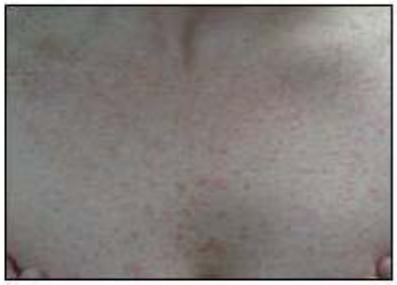


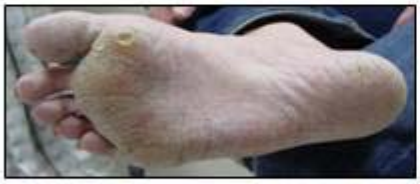


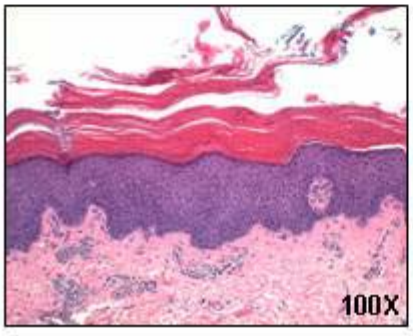
PATIENT B

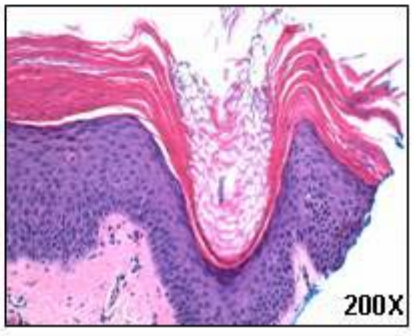












CHICAGO DERMATOLOGICAL SOCIETY CASE 8

PRESENTERS
Irene J. Vergilis-Kalner, MD, Rebecca Satoskar, MD, Vesna Petronic-Rosic, MD, and Christopher R. Shea, MD

HISTORY OF PRESENT ILLNESS
A 62-year-old Caucasian male presented with a two-year history of a painful eruption that started on his distal fingertips and progressed to a diffuse rash involving the trunk, legs, and scalp. Associated symptoms were burning, pruritus, and hypersensitivity over the shins. He also complained of a two-year history of diffuse pain of the proximal interphalangeal and metacarpophalangeal joints, elbows, knees, and occasionally of the metatarsphalangeal joints.

REVIEW OF SYSTEMS
The patient complained of joint pains in both hands and both knees, recurrent inflammation of fingers, and fatigue. He denied fever, weight loss, and nasal or oral ulcers, or other symptoms.

PAST MEDICAL HISTORY
Recurrent episcleritis, plantar fasciitis

PAST SURGICAL HISTORY
Arthroscopic surgery of the left knee in 2004 for torn meniscus

MEDICATIONS
Naproxen, glucosamine/chondroitin

FAMILY HISTORY
Osteoarthritis in mother and father, gout in brother

SOCIAL HISTORY
No tobacco or alcohol use

PHYSICAL EXAMINATION
Approximately 35% of the skin surface was covered with erythematous to pink, well-demarcated papules and plaques, with some white scale involving both arms (especially the dorsal aspects). Scattered pink papules were found on the lower extremities, and extensive confluence of the lesions was noted over the back, neck, scalp, and temple areas. Blisters were noted on the dorsal aspects of the patient's hands. The fourth left digit was erythematous, swollen, and tender to palpation with a "sausage" appearance. There was no lymphadenopathy

LABORATORY DATA & DIAGNOSTIC STUDIES
The following were negative or within normal limits:
CMP, lipids, liver function tests and thyroid function tests, RPR, Lyme abs, and hepatitis C and B panel were negative.

The following were abnormal:
Hemoglobin 11.7 g/dl (> 13.5 g/dl), hematocrit 34.6% (> 41%); monocytes 16% (< 12%), absolute monocytes 1.17 K/UL (< 0.92 K/UL); serum iron 18 mcg/dL (> 40 mcg/dL), % saturation 6.1% (> 14%), B12 serum level 952 pg/ml (< 900 pg/ml), rheumatoid factor 17 IU/ml (< 14 IU/ml); ESR 98 MM/HR (<33 MM/HR), C-reactive protein 152 mg/L (<5 mg/L)

On electrophoresis, globulin, beta globulin, and gamma globulin were elevated at 4.2 g/dl, 1.33 g/dl, and 1.65 g/dl (reference values < 3.5 g/dl, 1.2 g/dl, and 1.5 g/dl) but no monoclonal spike. Anti-DNA ds Ab and Anti-nuclear IFA were borderline normal with a speckled pattern;

CT of the chest abdomen and pelvis: few small nodes, enlarged prostate but no CT findings highly worrisome for malignancy
CT Head: normal
X-rays of hands/feet: Focal soft tissue prominence along the ulnar aspect of left 4th finger, a non-specific finding in MRH

DERMATOPATHOLOGY
Skin biopsy specimens from the left arm and back contained several collections of mononuclear and multinucleated histiocytes within the dermis. Histiocytes, especially the multinucleated ones, had eosinophilic, finely granular, "ground glass" cytoplasm. Some of the multinucleated giant cells had numerous nuclei that were arranged mostly at the cell periphery and some contained PAS-positive granules within their cytoplasm. Other giant cells and histiocytes had foamy cytoplasm. Elastin stain showed scant, thin, ropy fragments within some of the multinucleated cells. PAS, GMS, GRAM and FITE stains were negative for microorganisms. Immunohistochemistry showed that the tumor cells were negative for CD1A and S100 and positive for CD68 and CD14.

DIAGNOSIS
Non-Langerhans Cell Histiocytosis consistent with Multicentric Reticulohistiocytosis

TREATMENT & COURSE
After the diagnosis of multicentric reticulohistiocytosi, the patient was started on methotrexate (MTX) on 2/06 at 10 mg weekly together with folate 1 mg daily except for the day when MTX was taken. This led to marked cutaneous improvement, with skin lesions becoming flatter and less scaly, and with a reduction in pruritus. However, the joint symptoms showed minimal improvement and the patient continued to develop blisters and swelling of his fingers. The MTX was subsequently increased to the current dose of 15 mg weekly in 3/06. By 6/06 progressive development of new subcutaneous 2cm nodules on trunk were noted which resolved on their own. The patient was seen by rheumatology for the joint symptoms and planned to start etanercept 50 mg weekly – however, he has been unable to do so as of yet, because of insurance problems.

DISCUSSION
Multicentric reticulohistiocytosis (MRH) is a rare, granulomatous, multisystemic disease of unknown etiology, which occurs mostly in the fifth decade, with a female-male ratio of 3:1. Less than 200 cases have been reported. MRH is characterized by a cutaneous and mucous membrane reticulohistiocytomas, seronegative polyarthritis, and involvement of multiple internal organs. Mycobacterial infection has been suggested as a possible trigger for MRH, and MRH has been reported in association with antituberculous therapy. It is also suggested that MRH may be a reactive response to an unknown agent causing an inflammatory macrophage disorder, histiocytic proliferation, and an immunologic response to a possible underlying autoimmune disease, such as lupus erythematosus, Sjögren syndrome, diabetes mellitus, hypothyroidism, primary biliary cirrhosis, systemic sclerosis, celiac disease, dermatomyositis, or rheumatoid arthritis. MRH can also be a paraneoplastic condition and 15%-28% of patients have a solid organ or hematologic malignancy including bronchial, breast, pancreas, stomach, ovarian, colon, cervical carcinomas, malignant melanoma, mesothelioma, sarcoma, lymphoma, leukemia, and metastases from unknown primary. Therefore, detailed evaluation for underlying malignancy needs to be performed on presentation. MRH is also associated with hyperlipidemia, pregnancy, systemic vasculitis, IgG hypergammaglobulinemia and cryoglobulinemia. A positive RF, ANA Ab, hypergammaglobulinemia, elevated ESR, C-reactive protein, and anemia have been reported.

Typical skin manifestations are asymptomatic, gradually enlarging, skin-colored to red, brown, gray, or yellow papules and nodules, ranging in size from a few millimeters to 2 cm and in number from a few to a hundred. Lesions tend to be acral, favor upper body and overlying joints, and coalesce into large plaques. Small papules along proximal nail folds may form a typical "coral bead" appearance.

Vermicular erythematous lesions around the nostril are also seen. Many patients develop papules and nodules of the oropharyngeal, ocular, and nasal mucosa. Twenty-five percent develop xanthelasma. Rarely, "leonine facies" disfigurement from severe MRH, periarticular rheumatoid-like nodules, or nail changes can be seen. MRH may also present with photodistributed diffuse erythematous patches or severe pruritus that can precede the more characteristic nodules. All lesions repeatedly appear and regress on their own or with therapy.

Symmetric, painful, erosive and destructive polyarthritis with stiffness and swelling may precede (in 61%), accompany (in 21%), or follow (in 18%) the skin lesions. It waxes and wanes for years, eventually evolving into crippling arthritis and, if untreated, 45% progress to arthritis mutilans. In interpahalgeal joints MRH can cause disabling "opera-glass" hand deformity. Peripheral joints of the hands and fingers (particularly distal and proximal interphalangeal joints) are most commonly affected. On radiology, peri-articular erosions that reflect the infiltrative, granulomatous process progress to involve entire articular surfaces, causing prominent, osteolytic, punched-out damage to bones and joints, widening of joint spaces, loss of cartilage, and resorption of subchondral bone with disfigurement. Arthritis can remit spontaneously in 5-10 years after its onset but patients are often left with disability and significant disfigurement. Histiocytic involvement of the bone, muscle, liver, thyroid, larynx, liver, kidney, salivary glands, pleura, lung, stomach, pericardium, myocardium, lymph nodes, lead to a myriad of symptoms including pericarditis, hypertension, polyadrenomegally, pulmonary infiltrates and effusions, heart failure, myopathy, carpal tunnel syndrome, muscle weakness, ocular, and neurologic symptoms. Systemic complaints like fever, malaise, weakness, and weight loss have been reported, and in severe cases MRH can be fatal.

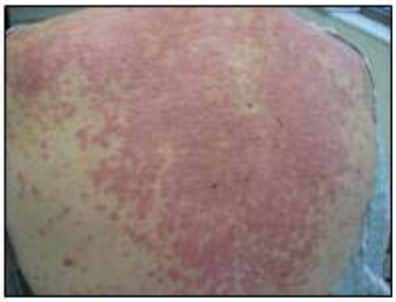
Diagnosis is based on the biopsy of the of skin nodules or synovial tissue showing dense dermal infiltrates of lymphocytes, histiocytes, and multinucleated 80-100μm foreign body giant cells, of monocyte–macrophage origin, with eosinophilic, homogenous, finely granulated or ground-glass appearing cytoplasm, and with few plasma cells and eosinophils. The early lesions have more eosinophils, lymphocytes, and histiocytes and fewer giant cells, while the later ones show large number of giant cells. Collagen fragmentation and its strands in cytoplasm and accumulation of lipids and other PAS-positive material are also seen. Multicentric reticulohistiocytes are positive for lysozyme, alpha1-antitrypsine, and often for CD68, CD45, CD3, CD11b, CD14, and HAM56. S100, CD1a, CD30, CD43 are usually negative indicating that these cells are not Langerhans cells. RANKL-positive cells may induce histiocytes to differentiate into osteoclast-like giant cells.

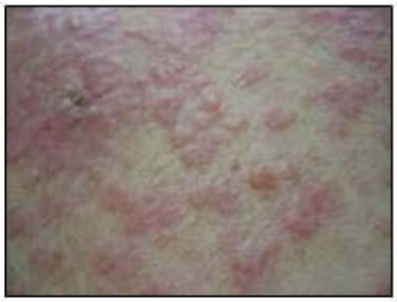
NSAIDs may help symptoms in mild inactive disease but to prevent irreversible damage, early and aggressive therapy is necessary. Although the specific treatment of MRH has not yet been established, corticosteroids alone or with immunosuppressive agents (cyclophosphamide, methotrexate, or azathioprine) have been shown to be effective. Great improvement in cutaneous nodule size and joint symptoms has also been reported with methotrexate, either alone or with systemic steroids or cyclophosphamide. Chlorambucil and hydroxychloroquine, with or without pulse methylprednisolone therapy can be attempted. Immunohistochemical studies of the MRH lesions show macrophage activation with increased release of proinflammatory monokines and cytokines, including TNF-α, IL-1β, IL-6, and IL-12, with both TNF- α and interleukins having proinflammatory effects that promote macrophage proliferation, phagocytosis and destructive proteases production, causing cartilage, peri-articular, and bone erosion and resorption. These findings support use of TNF-α antagonists in MRH and etanercept, infliximab, or adalimumab, with or without other immunosuppressants, have shown great

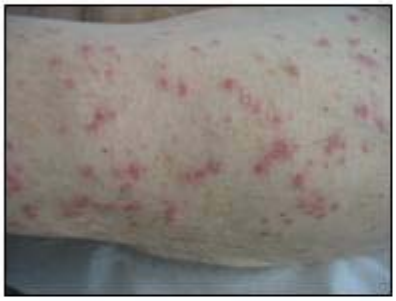
improvement in joint symptoms, regression of skin lesions, halting of erosive changes on X-Rays, and normalization of ESR and CRP. Alendronate (aminobisphosphonate) and bisphosphonates can also improve both joint symptoms and skin manifestations of MRH probably via direct effect on the mononuclear cells.

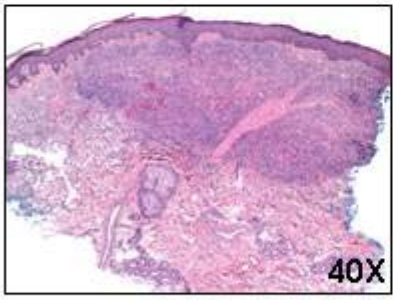
REFERENCES

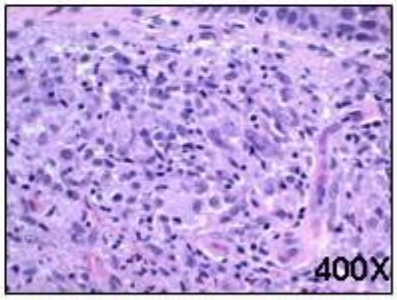
1. Chen CH, Chen CH, Chen HA, Liao HT, Lin HY. Multicentric reticulohistiocytosis presenting with destructive polyarthritis, laryngopharyngeal dysfunction, and a huge reticulohistiocytoma. J Clin Rheumatol 2006;12:252-4.
2. Levin J, Werth VP. Skin disorders with arthritis. Best Pract Res Clin Rheumatol 2006; 20: 809-26.
3. Shannon SE, Schumacher HR, Self S, Brown AN. Multicentric reticulohistiocytosis responding to tumor necrosis factor-alpha inhibition in a renal transplant patient. J Rheumatol 2005,32:565-7.
4. Trotta F, Castellino G, Lo Monaco A. Multicentric reticulohistiocytosis. Best Pract Res Clin Rheumatol 2004;18:759-72.

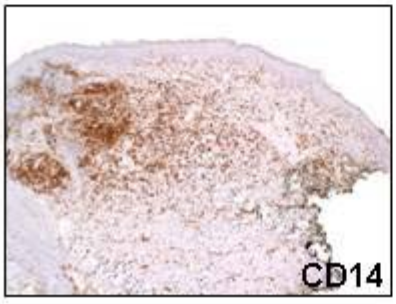


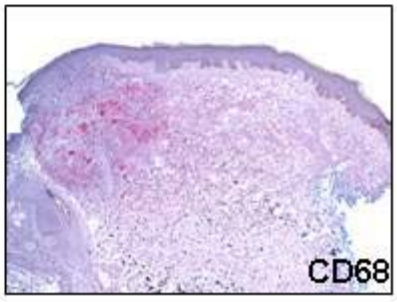





40X


400X


CD14


CD68

CHICAGO DERMATOLOGICAL SOCIETY CASE 9

PRESENTERS
Jessica Maddox, MD, Vesna Petronic-Rosic, MD, and Sarah L. Stein, MD

Case A
HISTORY OF PRESENT ILLNESS
This is a 13-year-old African American boy who presented to the clinic for evaluation of bumps on his lower back. The lesion was first noted at approximately six or seven years of age as a single lesion about the size of a dime that slowly grew. There were no other sites of involvement, and the area was asymptomatic.

PAST MEDICAL HISTORY
Asthma, developmental delay

MEDICATIONS
Albuterol

ALLERGIES
No known drug allergies

PHYSICAL EXAMINATION
There was a six by seven centimeter area of soft, fleshy, exophytic, slightly hyperpigmented papules, coalescent on right lower back. Remainder of physical exam was unremarkable.

DERMATOPATHOLOGY
A shave biopsy of an isolated papule from the lower back revealed dermis containing mature adipose tissue.

DIAGNOSIS
Nevus Lipomatosus Cutaneous Superficialis (NLCS)

TREATMENT & CLINICAL COURSE
The patient and mother were reassured that the lesion was benign. However, his mother remained concerned that the nevus was unsightly and a source of teasing by the patient's peers. Surgical excision versus shave removal of the remaining lesions was discussed.

Case B
HISTORY OF PRESENT ILLNESS
This is a 12-year-old Hispanic boy who presented for evaluation of skin-colored bumps on the lower aspect of the left buttock and thigh. The bumps appeared approximately one year earlier and have remained stable. The patient believes that the bumps swell with rubbing, but are not itchy.

PAST MEDICAL HISTORY
Non-contributory

MEDICATIONS
None

ALLERGIES
No known drug allergies

CHICAGO DERMATOLOGICAL SOCIETY CASE 9

PHYSICAL EXAMINATION
Multiple skin-colored, papillomatous, soft, exophytic papules were segmentally distributed on the left lower buttock and upper thigh.

DERMATOPATHOLOGY
A 4mm punch biopsy of a papule revealed hyperkeratosis and irregular acanthosis of the epidermis. Within the dermis, at the level of the superficial vascular plexus, there were collections of irregularly sized mature adipocytes and numerous small blood vessels, proliferations of endothelial cells, and some extravasated red blood cells. The adjacent dermis had increased numbers of fibroblasts.

DIAGNOSIS
Nevus Lipomatosus Cutaneus Superficialis

TREATMENT & CLINICAL COURSE
The patient and mother were reassured that the lesion was benign. No intervention was planned.

DISCUSSION
Nevus lipomatosus cutaneus superificialis was first reported in 1921 by Hoffmann and Zurhelle. NLCS is considered a rare idiopathic hamartomatous anomaly characterized by ectopic mature adipose tissue or isolated adipocytes in the dermis without connection to the subcutis. It is classified into two clinical types. The classic, and most common, is the multiple type of NLCS, in which lesions appear at birth or within the first two decades of life. The distribution is often in a linear or segmental pattern in the gluteal region, lower back, or upper thighs, although a few cases have been reported in other locations. The solitary form of NLCS can exist at any site and usually appears in the third to sixth decade. There is no genetic transmission.

Clinically, NLCS lesions are soft skin-colored to yellow papules that often coalesce into plaques. These lesions are described as smooth, verrucoid, cerebriform, wrinkled, sessile or pedunculated. While most are stable, some do enlarge over time. NLCS is differentiated from lipoma by clinical history, as well as histopathologically. Lipomas are slow-growing, benign fatty tumors that form lobulated soft nodules. Typical features include a soft rubbery feel, lobulation, and the mobility of overlying skin, which is typically unremarkable. Histologically, there is proliferation of normal-appearing adipocytes, often enclosed by a thin fibrous capsule.

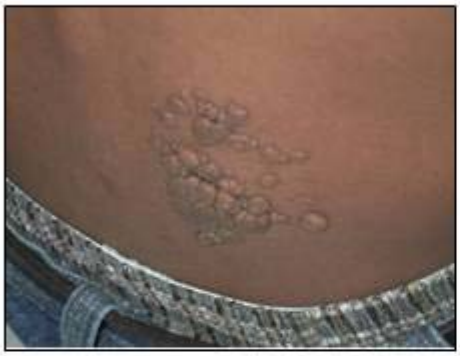
The origin of the anomaly is not clear. It was originally postulated that the ectopic adipose tissue was a result of degenerative change in the connective tissue. Subsequent theories included metaplasia of connective tissue or heterotopic development of adipose tissue. The predilection for the pelvic girdle and buttocks has been hypothesized to be a result of pressure to the area during fetal development.

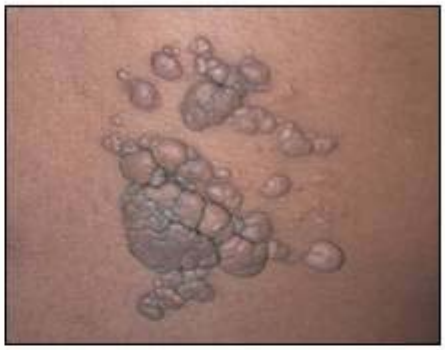
Treatment is usually not necessary except for cosmesis. A shave or elliptical surgical excision may be performed with infrequent recurrence.

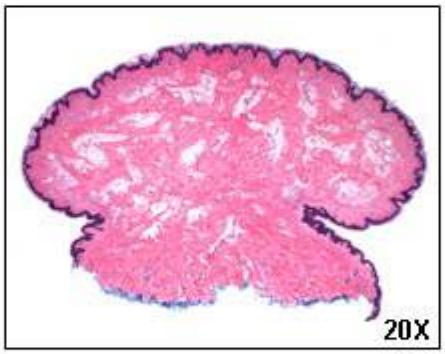
REFERENCES

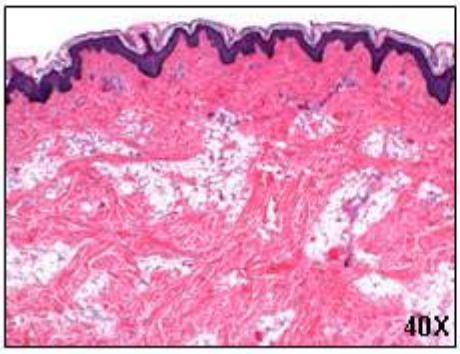
1. Dotz W, Prioleau PG. Nevus lipomatosus cutaneous superificialis, Arch Dermatol 1984; 120:121-133.
2. Finley, AG, Musso LA. Nevus lipomatosus cutaneous superificialis (Hoffman-Zurhelle), Br J Dermatol 1972; 87:557-63.
3. Hoffmann E, Zurhelle E. Uber einen Naevus lipomatodes cutaneus superificalis der linken Glutaal gegend. Arch Dermatol Syphilol 1921;130:327-33.
4. Wilson-Jones E, Marks R, Ponnsehirum D. Naevus superficialis lipomatosus: a clinicopathological report of twenty cases. Br J Dermatol 1975;93:121-33.

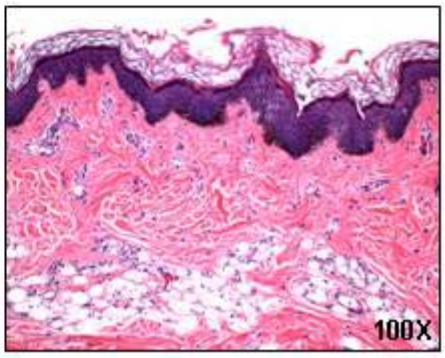
PATIENT A



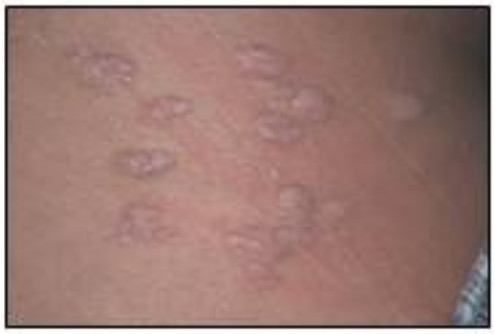


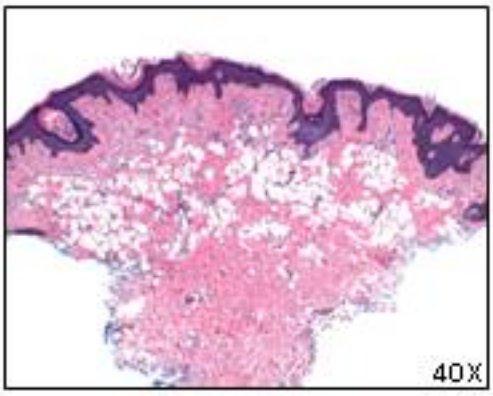


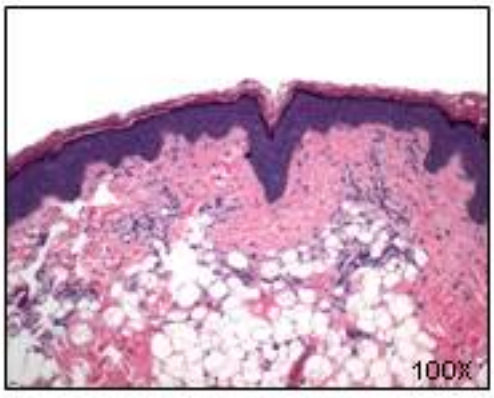


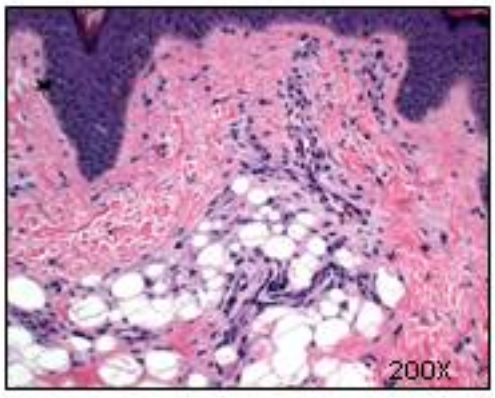


PATIENT B









CHICAGO DERMATOLOGICAL SOCIETY CASE 10

PRESENTERS
Arlene C. Molino, MD, MPH, Christopher Shea, MD, and Aisha Sethi, MD

HISTORY OF PRESENT ILLNESS
This patient is a 64-year-old Caucasian male with a history of multiple knee replacements who presented for evaluation of discolorations on his arms and legs. He had been treated with minocycline at a dose of 100 mg twice daily for the previous 18 months for a chronic methicillin-resistant staphylococcus aureus (MRSA) infection of his left knee. No treatment had been given for his skin condition.

PAST MEDICAL HISTORY
Multiple left knee replacements, asthma, hypertension

ALLERGIES
Amoxicillin/clavulanate

MEDICATIONS
Minocycline, fluticasone inhaler, ipratropium bromide/albuterol sulfate inhaler, albuterol inhaler, lansoprazole, fentanyl patch, alprazolam

PHYSICAL EXAMINATION
Well-circumscribed blue-gray coalescent patches were distributed over his forearms, extending from his dorsal hands to approximately 10 centimeters proximal to the elbows. Similar patches were found on his anterior and posterior lower legs. Of note, there is relative sparing of the scars on his arms and legs. There was no evidence of blue-gray patches on his nails, teeth, oral mucosa, or ocular mucosa.

LABORATORY DATA & DIAGNOSTIC STUDIES
A biopsy from his right arm revealed an atrophic epidermis and solar elastosis in the papillary dermis. There were focal brown deposits throughout the dermis. Extracellular pigmentation was noted around eccrine glands and several dermal blood vessels. Perl's stain for iron demonstrated hemosiderin deposits within the pigmented foci. Fontana-Masson stain demonstrated normal amounts of epidermal melanin pigment as an intrinsic control and also stained the brown pigment in the dermis.

DIAGNOSIS
Minocycline Induced Cutaneous Hyperpigmentation

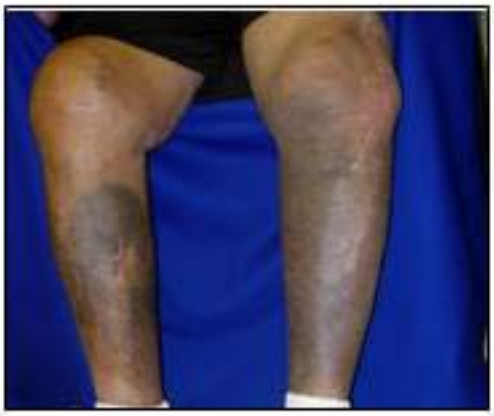
DISCUSSION
Cutaneous adverse reactions to minocycline include pruritus, urticaria, photosensitivity, and hyperpigmentation. Of these, hyperpigmentation, usually asymptomatic, is the most commonly observed cutaneous side effect. Similar pigmentation change has also been seen in nails, bones, oral mucosa, eyes, and the thyroid gland. The incidence of minocycline induced pigmentation is variable, ranging from 3 to 14%. Three types of minocycline hyperpigmentation are well characterized. Type I consists of blue-black macules occurring within sites of scarring or inflammation. In type II hyperpigmentation, blue-black, brown, or slate-grey patches appear on normal skin, with predilection for the arms, shins, and ankles. Type III hyperpigmentation occurs as muddy-brown coloration in a generalized and symmetric distribution, with increased prominence in sun-exposed areas. Histologically, type I pigment is primarily located in the dermis, type II in the dermis and subcutis, and in type III there is increased melanin in the basal layer and in macrophages in the upper dermis. Perl's iron stain is usually positive in type I and type II minocycline hyperpigmentation, and may be negative

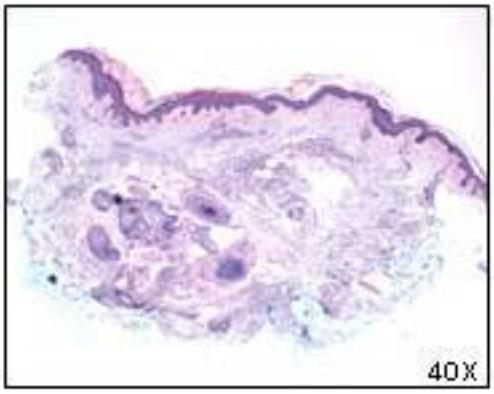
in type III. Positive staining with Fontana-Masson is usually seen in types II and III, and may be negative in type I hyperpigmentation.

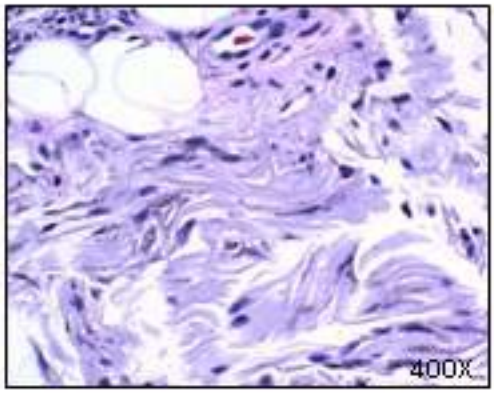
The relationship of hyperpigmentation to duration and total dosage of minocycline remains controversial. In general, it is thought that the occurrence of type I pigmentation is dose independent, while type II and type III often develop after prolonged treatment with cumulative doses greater than 50g. The degree of hyperpigmentation does not appear to be related to the duration or total dosage. In many cases type I and II hyperpigmentation will resolve upon discontinuation of the medication, while type III may persist indefinitely. Management includes the discontinuation of minocycline, and use of sunscreen in cases exacerbated by sunlight. Several types of lasers have been reported to be of benefit in cases where pigmentation failed to resolve after stopping minocycline. These include the Q-switched ruby, Q-switched Nd:YAG, Q-switched frequency doubled Nd:YAG, and Q-switched alexandrite lasers. It is felt that the Nd:YAG laser may be of benefit in cases where the pigment lies deeper in the dermis due to the longer wavelength, while the alexandrite induces less splatter intra-operatively. Improvement in pigmentation has been found with these lasers after 4 to 6 treatments separated by 4 to 6 weeks.

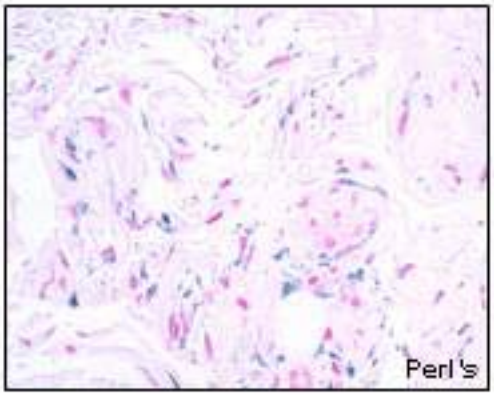
REFERENCES

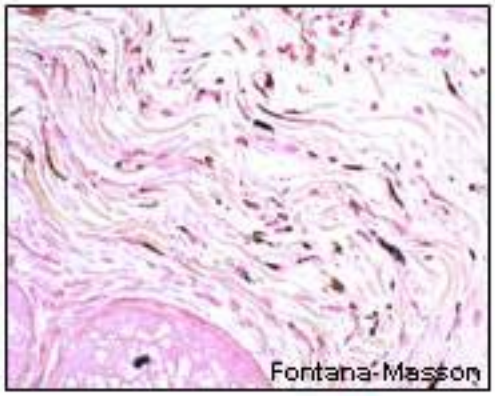
1. Alster T, Gupta S. Minocycline-induced hyperpigmentation treated with a 755-nm Q-switched alexandrite laser. Dermatol. Surg. 2004;30:1201-4.
2. Eisen D, Hakim MD. Minocycline-induced pigmentation: incidence, prevention, and management. Drug Saf. 1998;18:431-440.
3. Goulden V, Glass D, Cunliffe WJ. Safety of long –term high dose minocycline in the treatment of acne. Br J Dermatol. 1996;134:693-5.
4. Green D, Friedman KJ. Treatment of minocycline-induced cutaneous pigmentation with the Q-switched alexandrite laser and a review of the literature. J Am Acad Dermatol. 2001:44:342-7.
5. Mouton RW, Jordaan HF, Schneider JW. A new type of minocycline-induced cutaneous hyperpigmentation. Clin Exp Dermatol. 2004;29:8-14.




40X


400X


Perl's


Fontana-Masson

CHICAGO DERMATOLOGICAL SOCIETY CASE 11

PRESENTERS
Arlene C. Molino, MD, MPH, Vesna Petronic-Rosic, MD, and Sarah L. Stein, MD

HISTORY OF PRESENT ILLNESS
The patient is currently an 11-month-old African American female who was transferred to the neonatal intensive care unit from an outside hospital at age 4 days. Shortly after birth, bullous lesions and erosions were noted on her upper and lower extremities. Her mother had a history of a blistering disorder at birth restricted primarily to her right side and with resolution by 4 years of age. A maternal cousin also had a similar history. The patient's sibling was healthy.

PAST MEDICAL HISTORY
Born at 40 weeks gestation via uncomplicated vaginal delivery, unremarkable prenatal course

MEDICATIONS
Morphine sulfate

ALLERGIES
No known drug allergies

PHYSICAL EXAMINATION
Confluent erosions, some with yellow-brown or hemorrhagic crusting, were distributed over the patient's hands, feet, and ankles bilaterally. Circular patches of hypopigmentation were interspersed among erosions and bullae on her trunk and extremities. Milia were present at sites of healing. An Epstein's pearl was noted on the right upper gingiva. No oral or ocular mucosal lesions were observed. The patient's hair and nails were unremarkable.

LABORATORY DATA & DIAGNOSTIC STUDIES
Biopsy at 4 days of age of an induced bulla from the right upper arm for immunoflourescence revealed patterns consistent with EBS. Another biopsy of a lesion from her right lower leg showed a milium. Biopsy at 5 months of age for immunoepitope mapping performed at Indiana University Medical Center was consistent with EBS-DM.

DIAGNOSIS
Epidermoloysis Bullosa Simplex, Dowling-Meara Variant

TREATMENT & CLINICAL COURSE
On further examination, the patient's mother had mild dystrophy of her fingernails and toenails, some with subungual debris. She had isolated hyperkeratotic plaques on the palms and the soles, and an area of figurate hyperpigmentation on the right arm. Although biopsy of linear blisters at birth appeared consistent with incontinentia pigmenti, the mother's clinical presentation was felt to be consistent with EBS-Koebner type, given the course of her disease with resolution.

The importance of wound care has been discussed with the family. The dressings applied include an initial layer of Vaseline gauze, followed by a light gauze wrap, and elastic dressing, with topical antibiotic to open wounds and areas of superficial skin infections. In addition, due to the restrictive nature of the dressings, physical and occupational therapists have been working with the patient to facilitate proper musculoskeletal development. Nail care is a persistent issue as they are dystrophic and difficult to trim, and contribute to her EBS via scratching and trauma. Treatment with topical salicylic acid has been somewhat helpful in reducing the thickness of the nails and facilitating trimming. At each visit, her family has noted a decrease in new blistering.

DISCUSSION

Clinically, the manifestations of epidermolysis bullosa simplex (EBS) may range from localized blistering to severe, generalized blistering including mucosal involvement. The Dowling-Meara variant (EBS-DM, OMIM 131760) classically presents at or shortly after birth. Patients commonly have widespread cutaneous blistering and erosions, and may have mucosal involvement. Palmoplantar keratoderma, nail dystrophy, and milia occur during the course of the disease, as well as secondary skin infections, and possible sepsis. The lesions may heal with residual hyper- or hypopigmentation, and minimal to no scarring.

In the neonatal period the diagnosis may be based on family history, physical exam, and degree of cutaneous involvement. Routine histopathology reveals intraepidermal blister formation at the level of the basement membrane. On immunoflourescence antibodies to intracellular hemidesmosomal componenents, including BP230 and type IV collagen would localize to the floor. Intermediate filament clumping may be shown on electron microscopy.

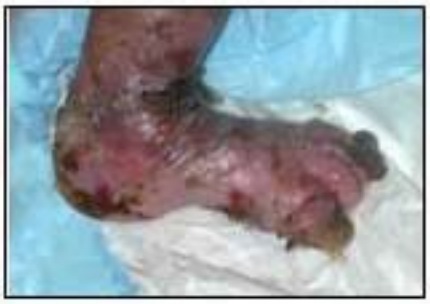
EBS-DM is usually inherited in an autosomal dominant fashion. The most common mutation is a heterozygous missense mutation in the helix initiation motif in the helix 1A domain of the K14 polypeptide. Our patient is interesting in that her mother and her mother's cousin both had a mild localized blistering condition at birth that resolved early in life without significant subsequent sequelae. Genetic mosaicism in the form of somatic mosaicism, gonadal mosaicism, as well as gonosomal mosaicisim has been described. Gonosomal mosaicism may occur when a mutational event in the parent occurs early enough that gonadal as well as somatic tissue carry the abnormal genetic material. The parent may express a mild, perhaps localized form of the disease, and subsequently have offspring that have full expression of the abnormal phenotype. This has been described in neurofibromatosis type I, osteogenesis imperfecta, and generalized epidermolytic hyperkeratosis. In addition, revertant mosaicism, which refers to the reversal of a mutation, has been described with EBS-DM, and may contribute to the mechanism whereby patients with EBS-DM may experience decreased blistering with age.

The mainstay of treatment of EBS-DM is wound management. Typically, the skin is protected with a non-adherent dressing, followed by a layer to add cushioning, and then surrounded by an elastic layer for security. Cleansing of the wounds should be done gently and regularly. Monitoring for signs or symptoms of infection is critical with prompt appropriate management should such complications occur. Keratolytics may be helpful for hyperkeratosis. Nutritional counseling and physical therapy should strongly be considered to facilitate proper development. Access to appropriate wound care supplies can be hindered by lack of insurance coverage, and can dramatically affect a patient's ultimate course, and thus early involvement of social services may be critical.

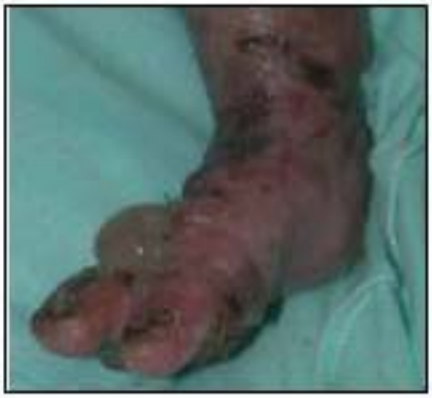
REFERENCES

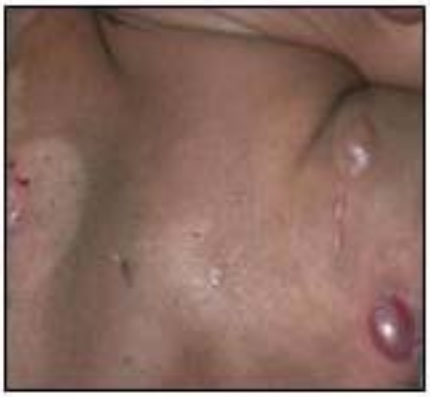
1. Pai S, Marinkovich P. Epidermolyisis bullosa: new and emerging trends. Am J Clin Dermatol 2002;3:371-80.
2. Paller A. The Complexities of Epidermolysis bullosa "simplex." J Invest Dermatol 2004 Jan;122:vi-vii.
3. Siegel DH, Sybert VP. Mosaicism in genetic skin disorders. Pediatr Dermatol 2006 Jan-Feb;23:87-92.
4. Smith FJD, Morley SM, McLean WHI. Novel mechanism of revertant mosaicism in Dowling Meara epidermolysis bullosa simplex. J Invest Dermatol 2004 Jan;122:73-7.

2 months old

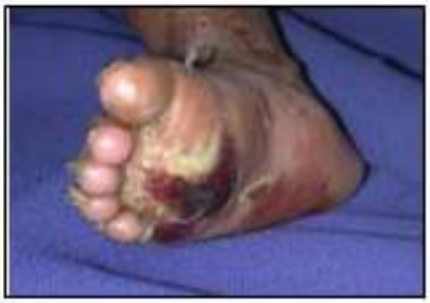


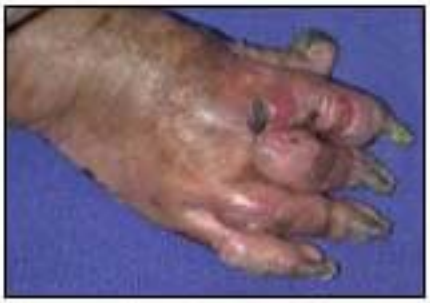
3 months old





11 months old





CHICAGO DERMATOLOGICAL SOCIETY CASE 12

PRESENTERS
Leslie E. Bernstein, MD, Vesna Petronic-Rosic, MD and Christopher R. Shea, MD

HISTORY OF PRESENT ILLNESS
A 21-year-old black woman presented with a two and a half week history of itchy blisters on the right hand, particularly in the ulnar distribution, approximately one year after injuring the right ulnar nerve. She had been experiencing pain, numbness and tingling in the exact location of the skin eruption for roughly three months, for which she received multiple corticosteroid injections. Her orthopedic surgeon referred her to the dermatology clinic for clearance before an ulnar nerve repair operation. She completed a week of valacyclovir therapy prior to her initial dermatology evaluation.

REVIEW OF SYSTEMS
The patient denied fever or chills.

PAST MEDICAL HISTORY
Migraine headaches, genital herpes, cholelithiasis

PAST SURGICAL HISTORY
Laparoscopic cholecystectomy

MEDICATIONS
Ipuprofen, gabapentin, tramadol

ALLERGIES
No known drug allergies

FAMILY HISTORY
Sister with migraine headaches

SOCIAL HISTORY
The patient denied tobacco use. She was in the process of applying for a job in retail sales.

PHYSICAL EXAMINATION
On the right hand, in the ulnar distribution of the hypothenar eminence and fourth and fifth digits, there were numerous 2 mm vesicles and papules.

LABORATORY DATA & DIAGNOSTIC STUDIES
The following were negative or within normal limits:
Basic metabolic panel , complete blood count, tzanck smear of right hand vesicle, vesicle direct fluorescent antibodies to herpes simplex virus and varicella-zoster virus, vesicle culture for herpes simplex virus and varicella-zoster virus, Herpes simplex virus type 1 and 2 IgG serum antibodies right hand radiograph

DERMATOPATHOLOGY
Biopsy of a right hand vesicle revealed an epidermis with intercellular edema and spongiotic vesicle formation. There was a superficial perivascular infiltrate of lymphocytes. The periodic acid-schiff and Gram stains did not reveal microorganisms.

DIAGNOSIS
Spongiotic Dermatitis in the Ulnar Nerve Distribution Following Traumatic Injury

TREATMENT & CLINCAL COURSE

The patient was given gentle skin care instructions. She applied fluocinonide 0.05% ointment twice daily to the lesions for two weeks, and the eruption resolved. Subsequently, she was lost to follow-up.

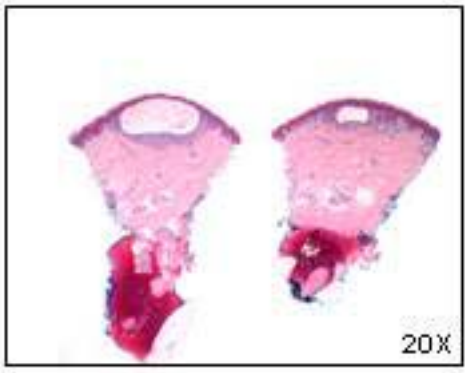
DISCUSSION

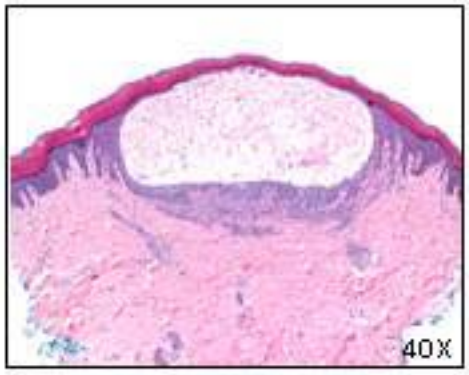
The association between the nervous and immune systems has been described, as well as its impact on chronic inflammatory diseases such as spongiotic dermatitides, including atopic, nummular and contact dermatitis. Hosoi *et al*. demonstrated the approximation of calcitonin gene-related peptide staining axons to the bodies of CD1+ Langerhans cells in the epidermis and dermis of human skin *via* confocal laser scanning microscopy. In addition, preincubation of murine epidermal cell populations with calcitonin gene-related peptide inhibited alloantigen presentation as well as delayed-type hypersensitivity. This suggests a possible role of neurotransmitters in modifying Langerhans cell antigen presenting activity, downregulating the TH1 response, and promoting the TH2 pathway which could favor conditions allowing for the development of chronic inflammatory processes. Ohmen *et al*. similarly published data that support this hypothesis. They highlighted the increased production of IL-10 mRNA in skin lesions of patients with atopic dermatitis by polymerase chain reaction assay. In contrast, patients with pulmonary tuberculosis, with an elicited purified protein derivative positive response, produced greater quantities of IFN-gamma mRNA. Jarvikallio *et al*. suggested that increased epidermal neuropeptides, such as calcitonin gene-related peptide and substance P, in cutaneous lesions of atopic dermatitis and nummular dermatitis, might promote keratinocyte cytokine release, causing inflammation.

We present this case for clinical interest, as it appears to be a spongiotic dermatitis mimicking herpes zoster or herpetic whitlow. It further supports the possibility of neurotransmission-stimulated immunomodulation leading to inflammatory cutaneous disease.

REFERENCES

1. Hosoi J, Murphy GF, Egan CL, Lerner EA, Grabbe S, Asahina A, Granstein RD. Regulation of Langerhans cell function by nerves containing calcitonin gene-related peptide. Nature 1993; 363:159-63.
2. Jarvikallio A, Harvima IT, Maukkarinen A. Mast Cells, nerves and neuropeptides in atopic dermatitis and nummular eczema. Arch Dermatol Research 2003; 295:2-7.
3. Ohmen JD, Hanifin JM, Nickoloff BJ, Rea TH, Wyzykowski R, Kim J, Jullien D, McHugh T, Nassif AS, Chan SC, Modlin RL. Overexpression of IL-10 in Atopic dermatitis: contrasting cytokine patterns with delayed-type hypersensitivity reactions. *J Immunology* 1995; 154:1956-1963.


20X


40X

CHICAGO DERMATOLOGICAL SOCIETY CASE 13

PRESENTERS
Yaohui Gloria Xu, MD, PhD and Vesna Petronic-Rosic, MD

HISTORY OF PRESENT ILLNESS
The patient is a 49-year-old Caucasian female who presented to the Dermatology clinic complaining of an asymptomatic, bright-red eruption on the lower extremities that had been present for two days without known precipitating factors. The patient denied any change in skin care products, history of insect bites, ill contacts, or recent travel.

PAST MEDICAL HISTORY
Hypertension, diabetes mellitus, hepatitis, atopic dermatitis

MEDICATIONS
Insulin, metformin, pioglitazone, lisinopril, aspirin

ALLERGIES
No known drug allergies

PHYSICAL EXAMINATION
There were about fifteen violaceous, nonblanchable, annular macules and patches ranging from 4mm to 2.5cm in diameter on the distal lower extremities. Some had pinpoint petechiae at the outer rim.

DERMATOPATHOLOGY
A punch biopsy from a representative lesion on the right leg revealed compact parakeratosis and spongiosis of the epidermis. In the dermis, there were dilated blood vessels, perivascular lymphocytic infiltrates, numerous extravasated red blood cells, and rare eosinophils.

LABORATORY DATA & DIAGNOSTIC STUDIES
A complete blood count with differential and urine analysis were within normal limits

DIAGNOSIS
Purpura Annularis Telangiectodes Majocchi

TREATMENT & CLINICAL COURSE
It was recommended that the patient discontinue aspirin if it was agreeable with her primary care physician, wear compression stockings with a pressure of 20-30mmHg, and initiate fluticasone propionate 0.05% ointment for one to two weeks. The patient was not able to tolerate compression stockings. Instead, she started to exercise regularly by jogging 3 to 4 miles three times weekly and her lesions gradually disappeared within three months, leaving a brownish discoloration.

DISCUSSION
First described in 1896 by Majocchi, purpura annularis telangiectodes is an uncommon subtype of pigmented purpuric dermatoses that comprise at least four other variants including progressive pigmented purpuric dermatosis of Schamberg, pigmented purpuric lichenoid dermatitis of Gougerot and Blum, eczematid-like purpura of Doucas and Kapetanakis, and lichen aureus. Clinical overlap between various subtypes may occur. Purpura annularis telangiectodes Majocchi or Majocchi's disease is characterized by symmetric, annular, purpuric, telangiectatic patches most commonly seen on the bilateral lower extremities in adolescents and young adults. Occasionally these lesions may appear linear, stellate, or serpinginous in shape. Most are asymptomatic, although pruritus can be present. The lesions may persist for years and often develop dark-brown discoloration and atrophy over time.

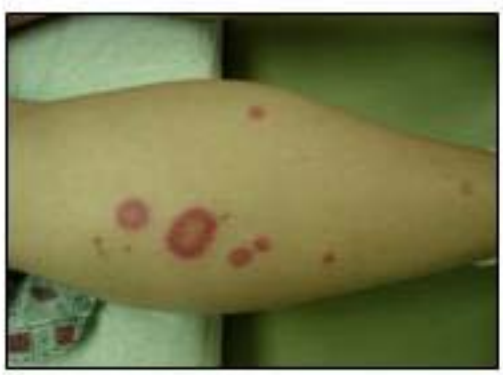
All variants of pigmented purpuric dermatoses share similar histological features, which include red cell extravasation, endothelial cell swelling, a perivascular lymphocytic infiltrate and hemosiderin-containing macrophages. The reason that we did not appreciate hemosiderin deposits in our patient might be due to the recent onset of the lesions.

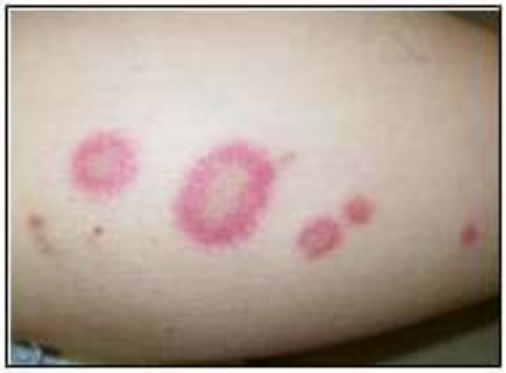
Pigmented purpuric dermatoses all have minimal inflammation and hemorrhage around superficial papillary dermal capillaries, without any systemic association in most cases. The etiology of purpura annularis telangiectodes is not well known. Given that it has predilection for the lower extremities, it is postulated that the effect of gravity and elevated venous pressures might be triggering factors. It is also hypothesized that a cellular immune reaction might play a role, or Langerhans-cell mediated injury and immune-complex deposition might result in capillary leakage. Additionally, genetic predisposition has been described. A case of Majocchi's disease was reported in a two-month-old boy born to a mother with diagnosed Majocchi's disease 8 years prior to the delivery, suggesting that there might be a genetically determined trait that has yet to be determined.

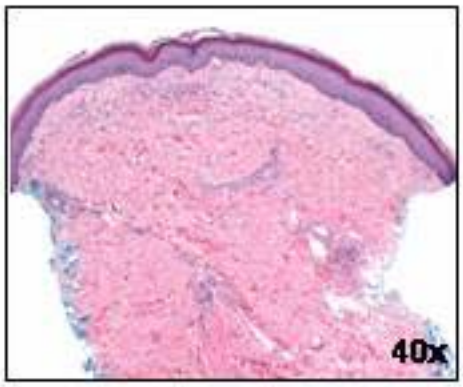
For asymptomatic purpura annularis telangiectoides, reassurance and observation might be sufficient. A work-up to rule out thrombocytopenia and a biopsy to exclude vasculitis are performed to confirm the benign nature of the disease. Supportive measures to decrease venous stasis, such as leg elevation and compression stockings, may be helpful. Topical steroids are used if the lesions are pruritic. Other anecdotal treatments include griseofulvin, pentoxifylline, ascorbic acid, and PUVA

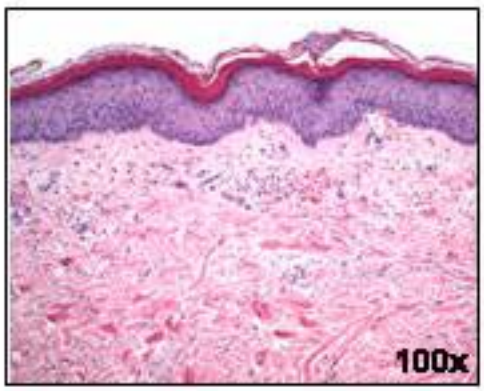
REFERENCES

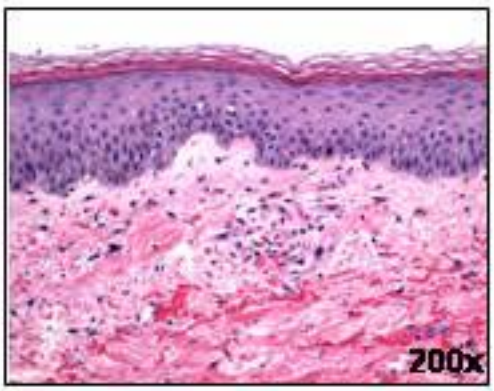
1. Hale EK. Purpura annularis telangiectodes of Majocchi. Dermatol Online J 2003;9:17.
2. Honda M, Saijo S, Tagami H. Majocchi's disease in a newborn baby: a familial case. Br J Dermatol 1997;137:655-6.
3. Kim HJ, Skidmore RA, Woosley JT. Pigmented purpura over the lower extremities: purpura annularis telangiectodes of Majocchi. Arch Dermatol 1998;134:1477.






40x


100x


200x

CHICAGO DERMATOLOGICAL SOCIETY CASE 14

PRESENTERS
Elaine F. Kung, MD, Christopher R. Shea, MD, Vesna Petronic-Rosic, MD, Keyoumars Soltani, MD, and Aisha Sethi, MD

PATIENT A
HISTORY OF PRESENT ILLNESS
A 54 year-old white woman with a history of metastatic rhabdomyosarcoma developed a generalized pruritic macular rash 10 days after taking sorafenib dosed at 400mg twice daily. She denied hand and foot pain, gastrointestinal symptoms, swelling of lips or tongue, or difficulty breathing.

PAST MEDICAL HISTORY
Her medical history is significant for metastatic adult rhabomyosarcoma involving the right lung and adrenal gland. Her tumor burden has decreased with 3 cycles of doxorubicin and ifosfamide 3 months previously. She enrolled in the phase I clinical trial of sorafenib for sarcomas because the previous chemotherapy caused intolerable side effects.

MEDICATIONS
Sorafenib, fentanyl patch, oxycodone, hydrocodone/acetaminophen, senna, docusate sodium, multivitamins, and fluticasone/salmeterol

ALLERGIES
No known drug allergies

PHYSICAL EXAMINATION
Skin examination revealed a generalized eruption of blanchable erythematous coalescing macules, sparing the mucosae, genitalia, and intertriginous areas. In addition, there were erythematous plaques found on pressure areas of palms and soles and blue-grey hyperpigmented patches on his forehead, cheeks, and chin.

DERMATOPATHOLOGY
Skin biopsy specimen from the right upper thigh revealed focal exocytosis of lymphocytes in the epidermis. A perivascular infiltrate composed of lymphocytes and eosinophils was noted in the papillary and mid-dermis.

DIAGNOSIS
Sorafenib Induced Drug Eruption

TREATMENT & CLINICAL COURSE
She reported dramatic improvement in the appearance of her eruption 5 days after discontinuing sorafenib and symptomatic relief with pramasoine/1% hydrocortisone lotion used three times daily. Ten days after discontinuing the medication, she was re-challenged with sorafenib at 200mg twice daily without cutaneous side effects.

PATIENT B
HISTORY OF PRESENT ILLNESS
A 67-year old white woman with a history of Stage IIIC ovarian cancer, developed facial redness and a generalized non-pruritic papular eruption, which occurred 9 and 10 days, respectively, after initiating sorafenib 400mg twice daily. Concurrently, she developed acral redness and pain, fever, and malaise. She denied diarrhea, lip or tongue swelling, or difficulty breathing.

CHICAGO DERMATOLOGICAL SOCIETY CASE 14

PAST MEDICAL HISTORY
Her medical history is significant for stage IIIC serous papillary carcinoma of the ovaries surgically treated with hysterectomy, bilateral salpingo-oophorectomy, omentectomy, and lymph node dissection 22 months previously. She received six cycles of carboplatin and paclitaxel 17 months previously with good response. However, after 9 months of tumor control, she developed enlargement of peritoneal nodules causing vague abdominal pain and an elevation of CA-125. Hence, she was enrolled in a multi-targeted tyrosine kinase inhibitor (XL-999) trial. Because she developed angioedema of the face and lips after XL-999, she was removed from that trial, but enrolled in the phase IV clinical trial of sorafenib for ovarian cancer.

MEDICATIONS
ASA, metoprolol, atorvastatin, coenzyme Q-10, docusate sodium, and senna

ALLERGIES
No known drug allergies

PHYSICAL EXAMINATION
Skin examination revealed facial erythema in rosacea-like distribution sparing facial folds, peeling of the lips, and erythema of genitalia without erosions One to two millimiter erythematous follicular papules were distributed on her extremities. Coalescent non-follicular papules were found on her trunk, sparing the intertriginous areas.

LABORATORY DATA & DIAGNOSTIC STUDIES
The following were abnormal:
Hemoglobin 9.0 g/dL (normal range 11.5-15.5), bands 36% (0-6), potassium 2.9 mEq/L (134-149), inorganic phosphate 2.2 mg/dL (2.5-4.4), calcium 6.5 mg/dL (8.4-10.2), albumin 3.3 g/dL (3.5-5.0), total protein 5.5 g/dL (6.0-8.3); CA-125 40 U/mL (<35); lactic dehydrogenase 258 U/L (116-245)

CT of the body revealed prominent lymph nodes anterior to left hepatic lobe and right common femoral chain as well as a mass on the surface of the liver and at the anterior peritoneum.

Blood and urine cultures did not grow aerobic or anaerobic organisms.

DERMATOPATHOLOGY
A skin biopsy specimen of the back and right arm was obtained. The epidermis and follicular infundibulum were spongiotic, and had single necrotic keratinocytes. There was exocytosis of lymphocytes and a few neutrophils. The dermis had a sparse superficial and deep infiltrate comprised of lymphocytes, neutrophils, and eosinophils.

DIAGNOSIS
Sorafenib Hypersensitivity

TREATMENT & CLINICAL COURSE
The patient was admitted to the hospital for fever, electrolyte abnormalities, and a generalized skin eruption, which were attributed to sorafenib by the oncology service. She improved with electrolyte supplementation, hydrocortisone 2.5% cream for the face, and triamcinolone 0.1% ointment for the body. Twelve days after discontinuation of sorafenib, she was re-challenged with half the initial dose at 200mg twice daily, but developed a similar eruption. Hence, she was discontinued from the phase IV clinical trial.

DISCUSSION

Epidermal growth factor (EGFR) inhibitors such as sorafenib (BAY 43-9006), are revolutionizing cancer therapy by targeting kinase activity involved in oncogenesis. Sorafenib was originally developed as an inhibitor of the RAF serine/threonine kinases, which are important in regulating normal cellular growth, differentiation, and apoptosis. In addition, *in vitro* studies have shown sorafenib to be a potent multikinase inhibitor, targeting receptor tyrosine kinases associated with tumor angiogenesis (VEGFR-2, VEGFR-3, and PDGFR-β) and tumor progression (c-KIT and FLT-3). Sorafenib monotherapy (400mg twice daily) has a manageable side effect profile in Phase I/II/III studies conducted on over 900 patients with solid tumors, such as renal cell carcinoma, melanoma, soft tissue sarcoma, thyroid carcinoma, and hepatocellular carcinoma.

Despite the promise of EGFR inhibitors as mono- or adjuvant therapy for solid tumors, the activity of these agents is not specific for tumor cells. The most common adverse reactions, which are considered dose-limiting toxicities, are fatigue (73%) hand-foot skin reaction (HFS 62%), rash or desquamation (66%), pain (58%) and diarrhea (58%). These are mostly mild to moderate and easily managed.

Besides HFS or palmar plantar dyesthesia, most of sorafenib's dermatologic toxicities consist of nonspecific maculopapular eruptions, alopecia, and xerosis. In addition, inflammation of previously undetected actinic keratoses (AK) with precipitous development of invasive squamous cell carcinoma (SCC) was reported in the literature. Since sorafenib targets dysregulated Ras pathways found in SCC, it may cause an inflammatory response in AK and SCC that have not been identified on the patient prior to treatment. Furthermore, the inflammatory response to epidermal atypia may be a function of sorafenib's inhibiting VEGFR and PDGF-β, which are necessary for angiogenesis, progression and invasion of SCC. Atypical cells in the epidermis are more susceptible to inflammation and apoptosis since proliferating cells are redistributed into S and M phases of the cell cycle with epidermal growth factor inhibitors.

At our institution, patients on sorafenib have been noted present generalized, erythematous, macular eruption sparing mucosal surfaces, a generalized erythematous follicular-based papular eruption sparing intertriginous areas, hand-foot syndrome, and facial erythema. These cutaneous side effects, which are asymptomatic or mildly pruritic, often develop 8 to 10 days after starting sorafenib at the dose of 400mg twice daily. Multiple dosing for 7 days results in a 2.5- to 7-fold accumulation compared to single-dose administration. Steady-state plasma concentrations are achieved within 7 days, which explains the timing of the cutaneous side effects occurring 8 to 10 days after administration of sorafenib. The mean elimination half-life of sorafenib is approximately 25 to 48 hours, which correlates with the patients' observations of their rashes fading within two days and almost completely gone within two weeks of discontinuing the medication.

Patient A, who had a drug eruption without other systemic side effects or other drug allergies, was re-challenged with sorafenib at half the initial dose without complications. However, Patient B had a hypersensitivity to sorafenib as evidenced by fevers, bandemia, and electrolyte disturbances as well as previous history of angioedema with XL-999, a multi-targeted tyrosine kinase inhibitor. She experienced recurrent cutaneous side effects upon re-challenge of sorafenib at the lower dose. Perhaps this signifies that those who experienced systemic side effects and/or previous type 1 hypersensitivity with other medications directed at kinase activity cannot tolerate re-challenge despite a dose reduction.

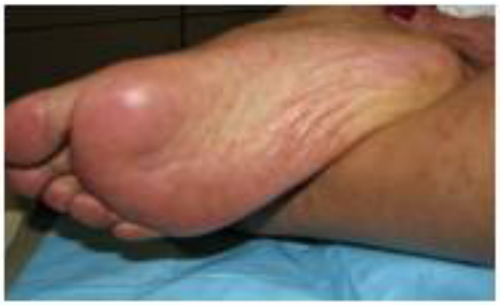
In conclusion, systematic dermatological evaluation of oncologic patients treated with EGF-R inhibitors is important for multiple reasons: 1) Prompt intervention of drug eruptions will prevent further deterioration of the patient's quality of life and maintain compliance with their chemotherapy; 2) Cutaneous side effects may be good surrogate markers of treatment efficacy because they are easy to

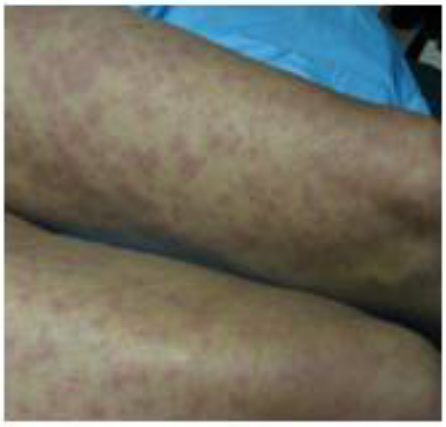
monitor; and 3) The association of targeted kinases with cutaneous side effects might help elucidate normal mechanisms of epidermal and/or hair development.

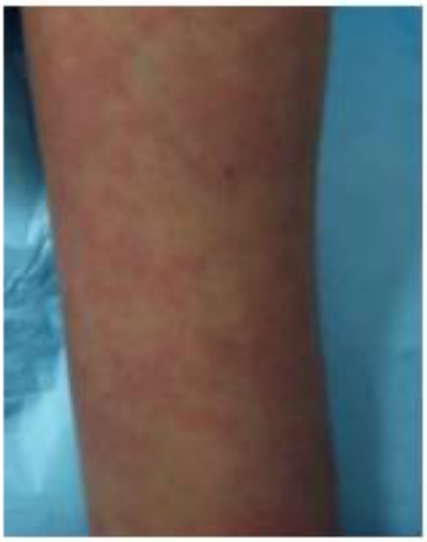
REFERENCES

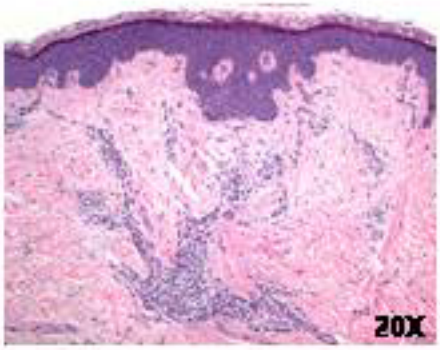
1. Eisen T, Ahmad T, Flaherty KT, Gore H, Kaye S, Marais R, Gibbens I, Hackett S, James M, Schuchter LM, Nathanson KL, Xia C, Simantov R, Schwartz B, Poulin-Costello M, O'Dwyer PJ, Ratain MJ. Sorafenib in advanced melanoma: a phase II randomized discontinuation trial analysis. BJ Cancer 2006; 95:581-6.
2. Lacoutour ME, Sesai A, Soltani K, Petronic-Rosic V, Laumann AE, Ratain MJ, Stadlert WM. Inflammation of actinic keratoses subsequent to therapy with sorafenib, a multitargeted tyrosine-kinase inhibitor. Clin Exp Dermatol 2006;31:783-5.
3. Ratain MJ, Eisen T, Stadler WM, Flaherty KT, Kaye SB, Rosner GL, Gore M, Desai AA, Patnaik A, Xiong HQ, Rowinsky E, Abbruzzese L, Xia C, Simantov R, Schwartz B, O'Dwyer J. Phase II placebo-controlled randomized discontinuation trial of sorafenib in patients with metastatic renal cell carcinoma. J Clin Oncology 2006;24(16):2505-11.
4. Richly, H, Henning BF, Kupsch P, Passarge K, Grubert M, Hilger A, Christensen O, Schwartz B, Ludwig M, Flashar C, Voigtmann R, Scheulen ME, Seeber S, Strumbert D. Annals of Oncology 2006;17:866-73.
5. Robert C, Sorio JC, Spatz A, Le Cesne A, Malka D, Pautrier P, Wechsler J, Lhomme C, Escudier B, Boige V, Armand JP, Le Chevalier T. Cutaneous side-effects of kinase inhibitors and blocking antibodies. Lancet 2005; 6: 491-9.
6. http://www.rxlist.com

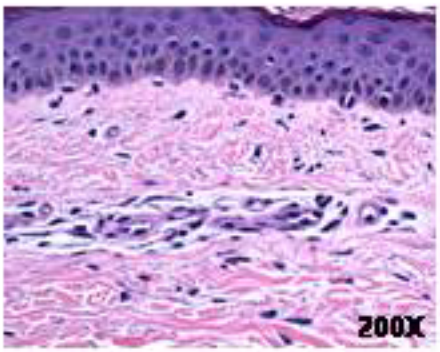
PATIENT A



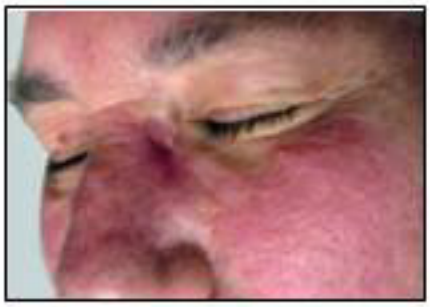


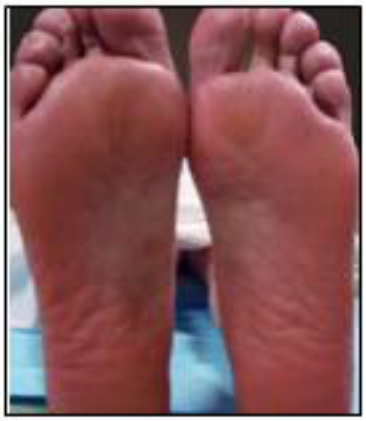


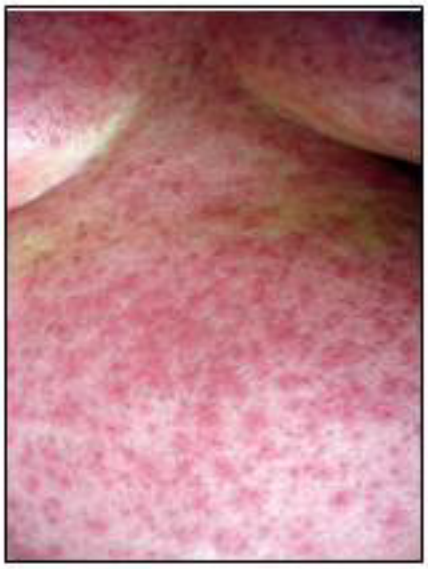


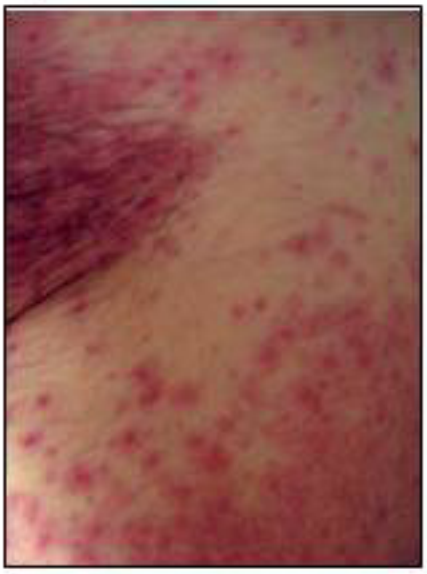


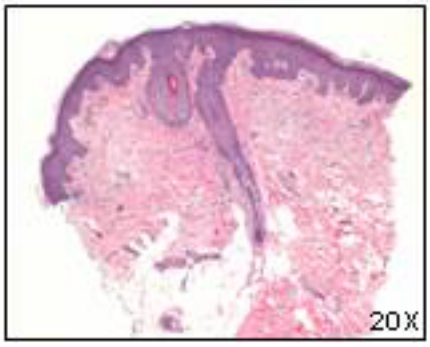
PATIENT B

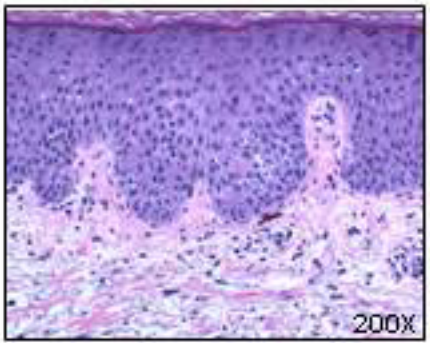












CHICAGO DERMATOLOGICAL SOCIETY CASE 15

PRESENTERS
Bernhard Ortel, MD, Vesna Petronic-Rosic, MD, Sonya Chawla, and Vivek Iyengar, MD

HISTORY OF PRESENT ILLNESS
This 35-year-old female complained of a mildly itchy rash in both axillae and a history of hyperhidrosis in the past. After treatment with topical corticosteroids the symptoms subsided but the localized papules persisted. The patient presented for diagnosis of the lesions. She had used different methods of axillary hair removal, none of which had given her unusual or persistent irritation. She used antiperspirant-free deodorants for several years. A change of brands after one month without any deodorants did not alter the course of her condition.

PAST MEDICAL HISTORY
Following a fortuitous finding of hypercalcemia in 2000 the patient had repeatedly elevated serum calcium levels and was eventually diagnosed with hyperparathyroidism and osteopenia. Her medical history was otherwise insignificant.

PAST SURGICAL HISTORY
In November 2004 the patient underwent minimally invasive surgery for a single left lower parathyroid adenoma. An intraoperatively discovered ectopic left cervical thymus remnant was removed in the same session. Postoperatively the patient was put on a prolonged oral calcium supplement regimen.

MEDICATIONS
None

ALLERGIES
No known drug allergies

PHYSICAL EXAM
The axillae exhibited scant hair growth and regularly scattered 1 mm skin colored papules in the central vaults.

LABORATORY DATA & DIAGNOSTIC STUDIES
Preoperative serum calcium levels were 11.5 and 12.8 mg/dL (normal 8.8-10.3) on separate occasions.

DERMATOPATHOLOGY
Multiple step sections reveal hair follicles with large sebaceous glands, apocrine glands, and layers of concentric perifollicular fibrosis. There is compact, well-cicumscribed bone with vascular channels at the level of the pilosebaceous-apocrine unit. Some ducts in the vicinity have papillary projections with no cellular atypia.

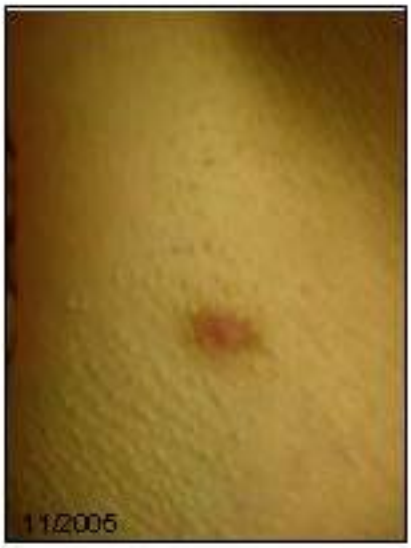
DIAGNOSIS
Osteoma Cutis Associated with the Pilo-Sebaceous-Apocrine Unit

DISCUSSION
The clinical presentation of the axillary lesions reminded of apocrine miliaria as described by Fox and Fordyce in 1902. The gender, age, localization of lesions and scarcity of axillary hair matched typical findings in patients with this condition, but the indolent nature and rapid symptomatic response to topical steroids in our patient was less compatible with this diagnosis. In addition, the biopsy did not show features of apocrine duct obstruction but deep-seated tiny osteomas in association with the pilo-sebaceous-apocrine unit.

Cutaneous osteomas are found in association with inflammation, such as in acne, and in benign as well as malignant cutaneous neoplasms. They are also found associated with hyperparathyroidism. We were unable to find reports of osteomas associated with apocrine glands in the dermatologic literature, but found single reports of calcifications associated with eccrine and apocrine sweat glands.
In our patient we tried to harmonize the clinical and histopathological features with the only significant temporally associated history of a parathyroid adenoma with hypercalcemia, which preceded the development of the axillary skin findings. We were evaluating the role of metal salt antiperspirants in the setting of elevated calcium concentrations in the apocrine secretions. However, the patient had been using deodorants free of such components for several years preceding her cutaneous changes.
We suggest the following pathogenetic sequence. The patient had an initial inflammatory episode affecting her apocrine glands that responded symptomatically to topical corticosteroids. Although we have no data from this period we can safely assume postoperative variations of PTH and calcium levels. The localized inflammation resulted in calcium deposits that eventually were remodeled to form osteomas. Osteoblasts are rather sensitive to changes in tissue calcium levels. An alternative explanation is the formation of calcium deposits before surgery when increased PTH levels resulted in high levels of ionized calcium. Postoperatively, these crystalline deposits caused an inflammatory reaction that eventually resulted in remodeling of the deposits to osteomas. We report these findings because of the unusual presentation and unique histopathology.

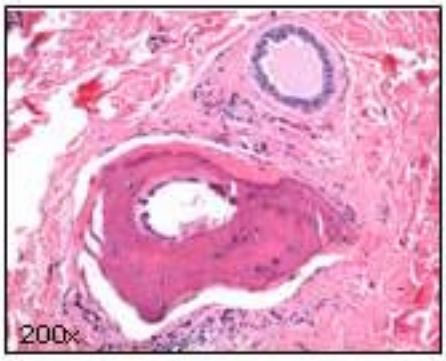
REFERENCES

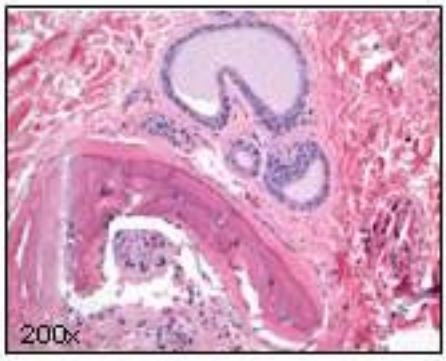
1. Conlin PA, Jimenez-Quintero LP, Rapini RP. Osteomas of the skin revisited: a clinicopathologic review of 74 cases. Am J Dermatopathol. 24:479-83 (2002)

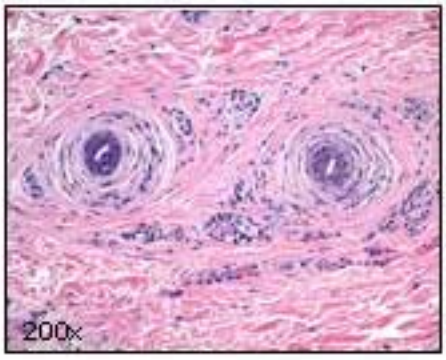

11/2006

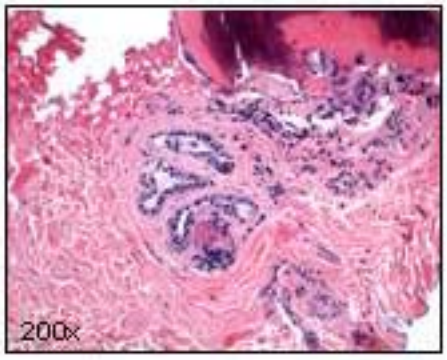

11/2006


20x


200x


200x


200x


200x

CHICAGO DERMATOLOGICAL SOCIETY CASE 16

PRESENTERS
Vishakha Sharma, MD, Arlene C. Molino, MD, and Sarah L. Stein, MD

HISTORY OF PRESENT ILLNESS
A 16-day-old African American female presented to the Dermatology Clinic for evaluation of "skin changes" on her cheeks and neck that had been present since birth. Per mom, these areas were asymptomatic and did not seem to be spreading or worsening. Of note, the patient had also failed her initial hearing test on the left.

PAST MEDICAL HISTORY
Born preterm at 34 weeks gestational age via Cesarean section secondary to decreased fetal heart rate. No neonatal complications; discharged home with mom in the first few days of life.

MEDICATIONS
None

ALLERGIES
No known drug allergies

FAMILY HISTORY
Family history negative for any skin conditions.

SOCIAL HISTORY
Patient lives with her mom.

PHYSICAL EXAMINATION
Linear, pink, depressed plaques following Blaschko's lines were present along the left cheek, extending laterally to the ear and inferiorly to the chin, neck, and upper chest. A few scattered similar lesions were also present on the right cheek and neck. A preauricular pit was present on the left side. The remainder of her skin examination was unremarkable. Her limbs displayed rhizomelia (proximal shortening) and mesomelia (shortening of the middle portion of bones). Ophthalmologic exam revealed a right corneal opacity and numerous foci of hypopigmentation of the choroid deep to the retinal epithelium. Examination of the left eye was unremarkable. Cardiologic exam was also unremarkable with no evidence of a murmur.

LABORATORY DATA & DIAGNOSTIC STUDIES
EKG and renal ultrasound were unremarkable. Chromosomal analysis revealed a deletion at Xp22.2.

DIAGNOSIS
MLS Syndrome (Microphthalmia with Linear Skin Defects; MIM 309801)

TREATMENT & CLINICAL COURSE
The patient is being followed by dermatology, ophthalmology, and genetics. Management of her skin condition has been mainly supportive, with application of topical bacitracin to areas on the neck which had become eroded. At nine months of age, her skin defects have healed significantly, leaving behind faintly hypopigmented patches. A repeat hearing test was normal.

DISCUSSION

MLS syndrome, which stands for microphthalmia with linear skin defects, was first described in 1988. It was initially given the name "MIDAS" syndrome to describe the triad of microphthalmia, dermal aplasia, and sclerocornea. Since 1994, the term MLS syndrome has been felt to be more appropriate in light of the fact that dermal aplasia has not been found in histological samples. The primary characteristics of MLS syndrome include microphthalmia and other ocular anomalies, as well as linear, jagged skin defects typically involving the scalp, face, neck, and in some cases the upper trunk. Other associated characteristics of MLS syndrome include congenital heart defects, diaphragmatic hernia, short stature, agenesis of the corpus callosum, anencephaly, hydrocephalus, seizures, and developmental delay. As in our patient, preauricular pits and abnormal or failed hearing tests have also been reported. The described congenital heart defects include hypertrophic cardiomyopathy, atrial and ventricular septal defects, supraventricular tachycardia, ventricular fibrillation, and other arrythymias. Ocular abnormalities are many and varied, including microphthalmia (seen in 76% of cases), anophthalmia, sclerocornea, and cataracts. Similar to our patient, another patient with MLS syndrome was also found to have hypopigmented areas of the retinal epithelium.

The cutaneous manifestations of MLS syndrome include nail dystrophy (seen in 14% of cases) and the linear skin defects seen curiously only on the upper half of the body, limited predominantly to the face, scalp, neck, and upper trunk. This regional restriction to the head and neck area is thought to be due to involvement of neural crest cells. Skin biopsies of the linear, reticulated skin defects have yielded varied results including normal in appearance in one case, basal layer vacuolar changes with an interface infiltrate in another case, hypertrophied musculi arrectores pilorum in the deep dermis in two cases, and necrotic epidermis with an intact basement membrane and no sign of inflammation in the last case.

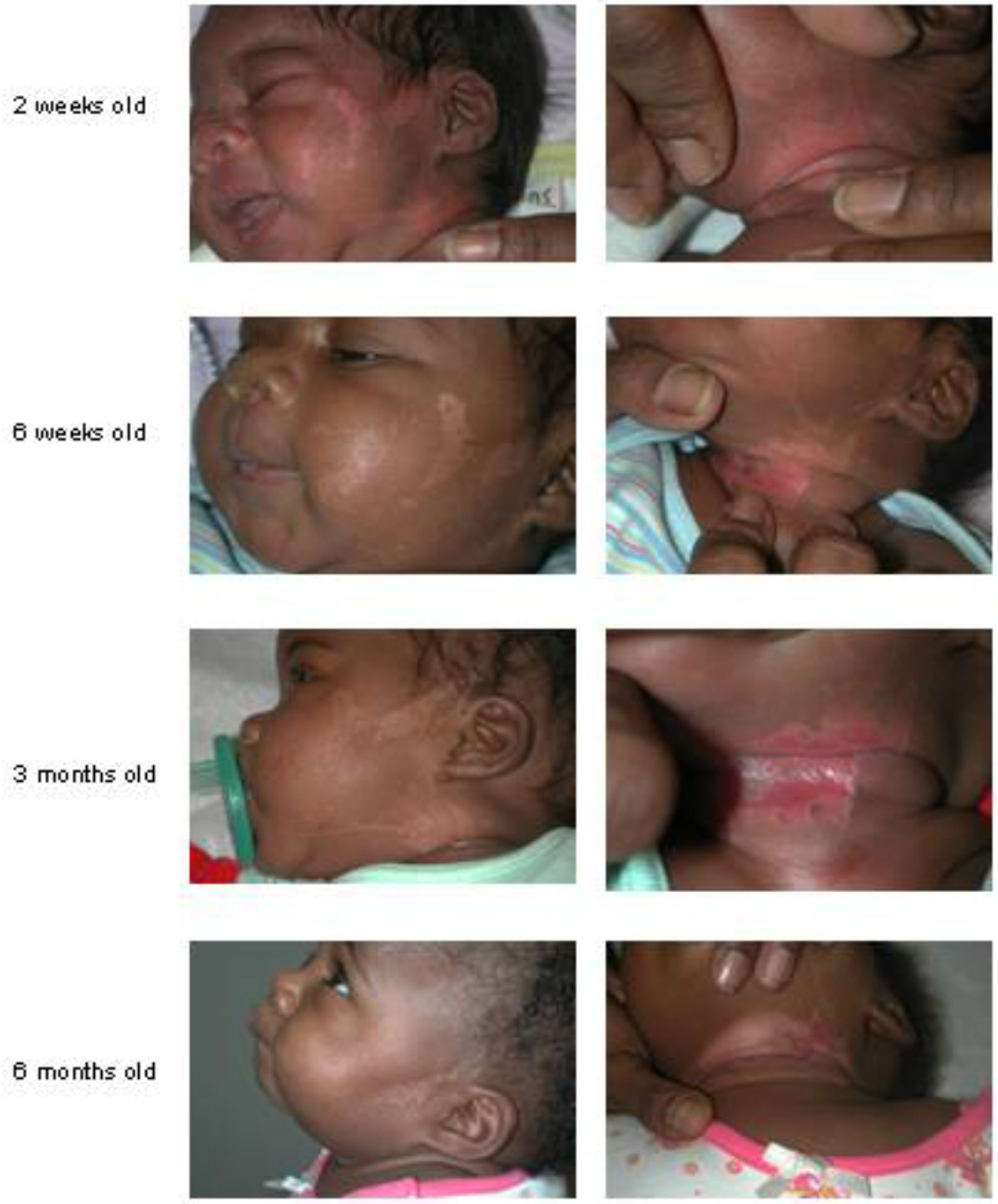
MLS syndrome is now known to be caused by a deletion or mutation in the Xp22 region. Similar to Goltz syndrome, this syndrome is X-linked dominant with lethality in the male hemizygous state. This is supported by the lack of reported XY males with this disorder. More recently, the microdeletion involved at Xp22.2 has been mapped to the *HCCS* gene which encodes a mitochondrial holocytochrome *c*-type synthase. Cytochrome *c*, the final product of the activity of this synthase, is thought to play a role in oxidative phosphorylation and apoptosis. It has been postulated that in MLS syndrome, the lack of cytochrome *c* disrupts the balance between apoptosis and necrosis, leading to necrosis of affected cells with damage to the neighboring cells, particularly in the areas of ocular and neuronal development.

The prognosis of individuals with MLS syndrome is highly dependent on the various extracutaneous abnormalities, with diaphragmatic hernia and cardiac defects carrying the highest rate of mortality. The linear skin defects have been reported to heal with and without scarring, becoming hardly noticeable in some by one to two years of age. Management of patients with MLS syndrome involves a multidisciplinary approach. This should incude referrals to ophthalmology, cardiology, genetics, and neurology if evidence of any neural involvement.

REFERENCES

1. Cape CJ, Zaidman GW, Beck AD, Kaufman AH. Phenotypic variation in ophthalmic manifestations of MIDAS Syndrome (microphthalmia, dermal aplasia, and sclerocornea). Arch Ophthalmol 2004;122:1070-4.
2. Happle R, Daniels O, Koopman RJJ. Midas Syndrome (microphthalmia, dermal aplasia, and sclerocornea): an x-linked phenotype distinct from Goltz Syndrome. Am J Med Genet 1993;47:710-3.
3. Paulger BR, Kraus EW, Pulitzer DR, Moore CM. Xp Microdeletion Syndrome characterized by pathognomonic linear skin defects on the head and neck. Pediatr Dermatol 1997;14:26-30.

4. Wimplinger I, Morleo M, Rosenberger G, Iaconis D, Orth U, Meinecke P, Lerer I, Ballabio A, Gal A, Franco B, Kutsche K. Mutations of the mitochondrial holocytochrome c-type synthase in X-Linked Dominant Microphthalmia with Linear Skin Defects Syndrome. Am J Hum Genet 2006;79:878-89.
5. Zvulunov A, Kachko L, Manor E, Shinwell E, Carmis R. Reticulolinear aplasia cutis congenita of the face and neck: a distinctive cutaneous manifestation in several syndromes linked to Xp22. Br J Dermatol 1998;138:1046-52.



CHICAGO DERMATOLOGICAL SOCIETY CASE 17

PRESENTERS
Olga Ulitsky MD, Vesna Petronic-Rosic MD and Christopher R. Shea MD

HISTORY OF PRESENT ILLNESS
A 49-year-old African American woman was admitted to the intensive care unit with shortness of breath and acute mental status changes. The patient was diagnosed with disseminated tuberculosis (acid fast bacilli present in sputum and bone marrow) and was started on a four drug anti-TB regimen. A rash that started on the right leg was diagnosed as cellulitis by the primary team and broad spectrum antibiotic treatment was initiated with vancomycin and piperacillin/tazobactam. The rash subsequently generalized in 48 hours, and dermatology was consulted to rule out a drug hypersensitivity reaction.

PAST MEDICAL HISTORY
Hemophagocytic syndrome, disseminated TB (AFB in sputum, bone marrow), systemic lupus erythematosus, hypertension, diabetes mellitus, cerebro-vascular accident, idiopathic thrombocytopenic purpura, chronic renal insufficiency, congestive heart failure

MEDICATIONS
Ganciclovir, isoniazid, rifampin, pyridoxine, pyrazinamide, caspofungin, metronidazole, folic acid, sertraline, citric acid, ferrous sulfate, prevacid, calcium acetate, darbepoetin alfa, labetolol, hydralazine, immune globulin, dacadron, acetaminophen, cepacol, regular insulin human, promethazine, clotrimazole cream

ALLERGIES
Piperacillin/tazobactam

SOCIAL HISTORY
No history of smoking or illicit drug use

PHYSICAL EXAMINATION
There are violaceous purpuric slightly elevated plaques generalized over the trunk, arms, and upper legs. These plaques are mildly scaly. Multiple superficial erosions were found on the buttocks.

LABORATORY DATA & DIAGNOSTIC STUDIES
The following were within normal limits:
Toxicology screen, hepatitis panel, WBC count, IgA, IgG, IgM levels, West Nile Virus IgG and IgM antibody

The following were abnormal:
CMV PCR from blood: 85000 copies/mL, Blood culture: Candida
Anti-nuclear Ab titer: 1:320 (0-80), anti-doublestranded DNA Ab: 1:640 (<10), CRP 39 (<5), ESR 73 (<5), C3: 68 (83-188), C4: 17 (18-45), alkaline phosphatase 378 (30-120), SGOT: 192 (8-37), SGPT 51 (8-35), bilirubin total: 8.5 (0.1-1.0), bilirubin conjugated 7.9 (0-0.3), hemoglobin 9.1 (11.5-15.5), hematocrit 28.0 (36-47), platelets 147 (150-450)

DERMATOPATHOLOGY
The epidermis has mild irregular hyperplasia. In the dermis, there is perivascular and intramural infiltrate composed of neutrophils and lymphocytes. Abundant intramural nuclear dust is present. Some endothelial cells have an epithelioid appearance with amphophilic cytoplasm and basophilic nuclear inclusions. Numerous extravasated red blood cells are seen in the dermis without evidence of thrombus formation. PAS is negative for fungi or thickening of the basement membrane. Gram, Fite, AFB, and

methenamine silver stain are negative for microorganisms. Anti-CMV antibody highlights numerous dermal endothelial cells with both a nuclear and cytoplasmic staining pattern.

DIAGNOSIS
Leukocytovlastic Vasculitis and Vascular Cytomegalovirus (CMV) Infection

TREATMENT & CLINICAL COURSE
The infectious disease team was consulted and the patient was started on ganciclovir. Subsequently she developed a lower gastrointestinal bleed, fever, and mental status deterioration and was transferred to the intensive care unit. Multiple lumbar punctures were performed seeking an infectious and/or inflammatory etiology for her mental status change, all negative to date.

DISCUSSION
Cutaneous leukocytoclastic vasculitis (LCV) most often manifests clinically as palpable purpura. Histologically LCV is defined as a predominantly neutophilic perivascular infiltrate affecting cutaneous postcapillary venules, with fibrinoid deposits in and around the vessel wall and extravasation of red blood cells. Cutaneous LCV is commonly associated with a wide spectrum of systemic inflammatory conditions, malignancies, infections, or drug hypersensitivities.

Cytomegalovirus (CMV) is a DNA-containing herpesvirus that can infect a wide range of mammalian species and organs. Most primary CMV infections are sublinical. Activation of latent virus results in viremia and organ-specific disease. A review of the literature revealed that cutaneous CMV infection is a rare clinical manifestation of this common opportunistic pathogen. There are no typical skin changes associated with this infection thus far in the reported cases. CMV has been identified in necrotic, ulcerated, vesiculobulous, and purpuric lesions. Eight cases of cutaneous CMV have been previously described, with only four showing evidence of cutaneous vasculitis. Three of these patients were chronically ill, one with alcoholic hepatitis, one was a renal transplant recipient, and one had acute myelogenous leukemia. The fourth case occurred in a woman with well-controlled insulin-dependent diabetes mellitus.

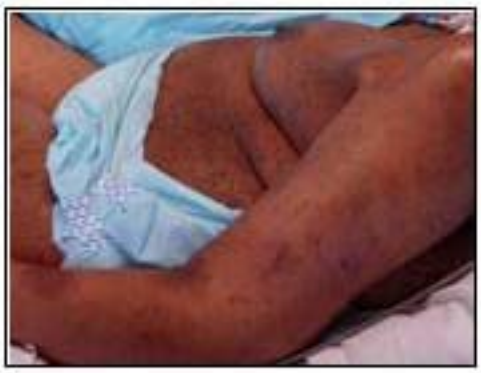
In the adult, CMV infection may present as *de novo* acquisition, usually from contaminated blood transfusion, or more frequently, from activation of latent virus. Both debilitated and healthy persons may be carriers of the virus without clinical manifestation. Because this patient has received numerous blood transfusions, it is impossible to delineate whether her infection arose from reactivation of latent virus or from exogenous sources. The diagnosis of CMV is made with identification of characteristic intranuclear and intracytoplasmic inclusions in affected tissues. Confirmation is possible by an immunoperoxidase technique with the use of a monoclonal antibody directed against CMV. Documentation of CMV in skin may reflect CMV involvement in other organs and therefore has important implications for patient care. The typical treatment of CMV is gancyclovir, which was intiated in our patient.

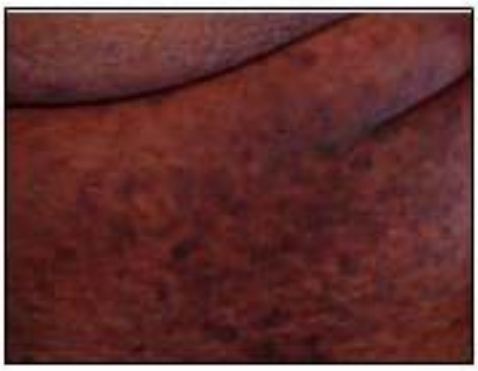
CMV-induced leucocytoclastic vasculitis is a rare entity and a rare manifestation of this common opportunistic pathogen and should be included in the differential diagnosis of purpuric lesions in immunocompromised, and, sometimes, even immunocompetent patients.

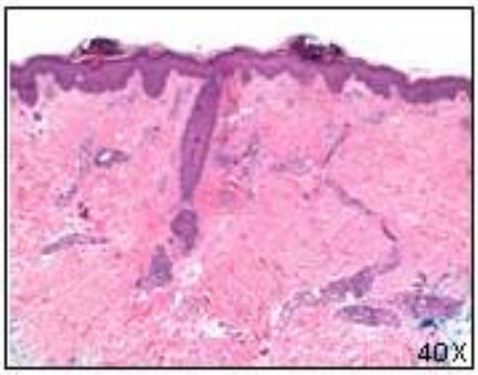
REFERENCES
1. Curtis J. Egbert B. Cutaneous cytomegalovirus vasculitis: an ususual clinical presentation of a common opportunistic pathogen. Hum Pathol 1982; 12: 1138-41.
2. Horn T, Hood AF. Clinically occult cytomegalovirus present in skin biopsy specimens in immunosuppressed hosts. J Am Acad Dermatol 1989; 21:781-4.

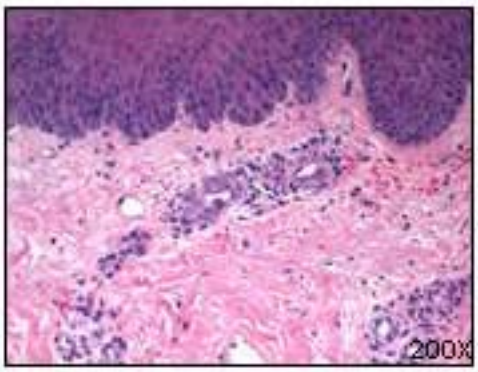
3. Horn T, Hood AF. Cytomegalovirus is predictably present in perineal ulcers from immunosuppressed patients. Arch Dermatol. 1990: 126:642-4.

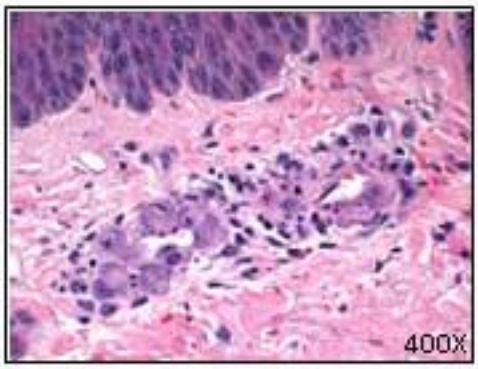
4. Russel J., Gibson L. Primary cutaneous small vessel vasculitis: approach to diagnosis and treatment. Inter J Derm 2006; 45: 3-13.

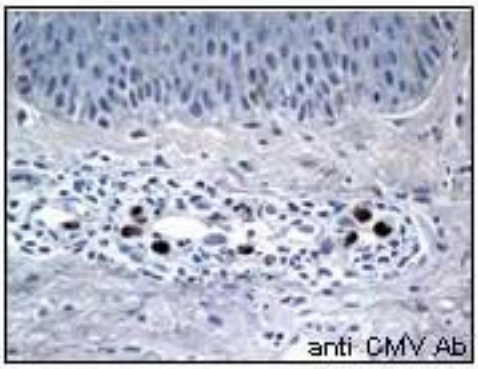












CHICAGO DERMATOLOGICAL SOCIETY CASE 18

PRESENTERS
Jessica Maddox, MD and Christopher R. Shea, MD

HISTORY OF PRESENT ILLNESS
This 29-year-old African-American woman presented to the clinic for evaluation of thickened and darkened skin on her feet and hands. The skin began changing on the backs of her hands and feet at about 8 years of age. She reported that it would get worse in the summer and never resolved completely. In addition, she complained of excessive sweating. She denied symptoms, such as pruritus or pain, or precipitating factors, such as rubbing or rash. There was no known exposure to irritants or allergens at onset of skin changes.

PAST MEDICAL HISTORY
Non-contributory

MEDICATIONS
None

ALLERGIES
No known drug allergies

FAMILY HISTORY
Possibly similar skin changes in a half-sister.

PHYSICAL EXAMINATION
Well-demarcated, hyperpigmented, hyperkeratotic plaques with accentuated skin lines were present on the distal dorsal surface of both hands and feet, extending laterally and medially to the insteps and involving the skin overlying the Achilles tendon. In addition, the plantar acral surfaces demonstrated well-demarcated erythematous plaques with thick scale.

DERMATOPATHOLOGY
A punch biopsy specimen of the edge of a plaque on the dorsal foot revealed a markedly thickened, orthohyperkeratotic stratum corneum and a prominent stratum lucidum. The granular layer was slightly thickened. The spinous layer was hyperplacstic. The basal layer exhibited physiologic pigmentation. The dermis had a very sparse, superficial, perivascular infiltrate of lymphocytes. The periodic acid-Schiff stain was negative for fungi or significant basement membrane thickening.

DIAGNOSIS
Keratoderma Palmoplantaris Transgrediens

TREATMENT & CLINICAL COURSE
Urea 40% ointment was prescribed. The patient deferred follow up.

DISCUSSION
The hereditary palmoplantar keratodermas (PPK) are a heterogeneous group of disorders characterized by hyperkeratosis of the palms and soles. Diagnosis is made on the basis of morphologic features, distribution of hyperkeratosis, presence or absence of extracutaneous anomalies, and inheritance pattern. Several mutations have been identified in various genes, often those for keratin. While many case reports have been published on series of findings within a family, spontaneous mutations have been noted in patients without family history of one of several of the familial PPKs.

Keratoderma palmoplantaris transgrediens, also known as Greither PPK or PPK of Sybert, is a diffuse PPK first described in 1952. It is an autosomal-dominant condition that typically manifests at the age of eight to ten years with variable expression. It is extremely rare, with only few cases appearing in the literature. Greither PPK is characterized by erythema, hyperkeratosis, and desquamation of the palms and soles with lateral and dorsal extension, which often extends up to the Achilles tendon. In addition, hyperkeratotic plaques frequently occur on the elbows and knees, and occasionally involve the thighs and axillae. The keratoderma may be mild or severe, and hyperhidrosis is a typical feature. Digital autoamputation has been reported. There are no associated extracutaneous anomalies.

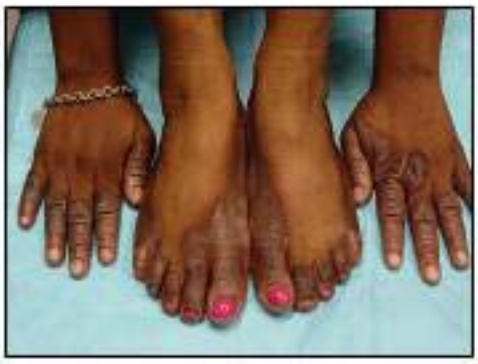
Histologic features include orthohyperkeratosis without epidermolysis and an absence of granular cell degeneration. Ultrastructural analysis reveals normal keratin filaments but abnormal keratohyaline granules. These abnormalities are reduced during treatment. The gene locus for Greither PPK is unknown, although mutations in the gene for keratin 1 have been identified.

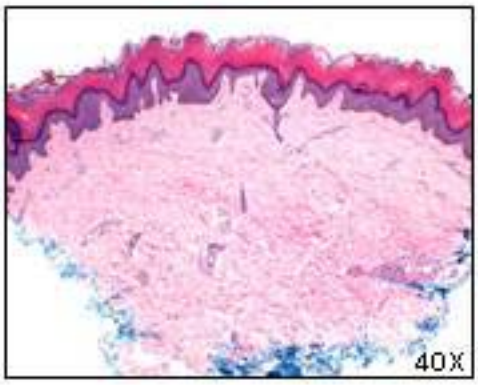
In mild cases, treatment with emollients, topical retinoids, keratolytics, and topical glucocorticoids has been used with some success. Treatment with oral isotretinoin has been tried in one case with clinical improvement.

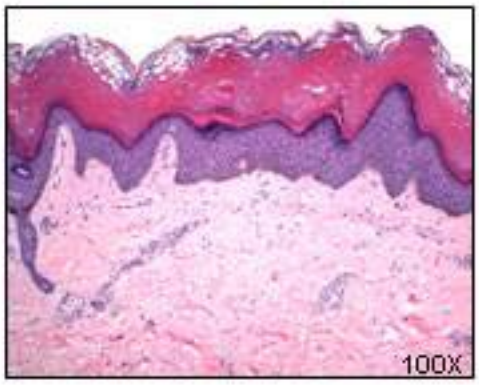
The differential diagnosis includes Mal de Meleda, otherwise known as keratosis extremitatum hereditaria trangrediens et progrediens. This is a rare congenital autosomal recessive PPK with onset in early infancy. Clinical features include diffuse, thick keratoderma with a prominent erythematous border. Lesions spread onto the dorsa of the hands and the feet. Patients may have severe hyperhidrosis, often accompanied by malodor. Molecular biology features include mutations in the gene encoding SLURP-1. Proteins of the SLURP family have been implicated in transmembrane signal transduction, cell activation, and cell adhesion.

REFERENCES

1. Gach JE, Munro CS, Lane EB, Wilson NJ, Moss C. Two families with Greither’s syndrome caused by keratin 1 mutation. J Am Acad Dermatol 2005; 53:S225-30.
2. Greither, A. Keratosis extremitatum hereditaria progrediens mit dominantem Erbgang. Hautarzt 1952; 3:198-203.
3. Grilli R, et al. Transgrediens et progrediens palmoplantar keratoderma (Greither's disease) with particular histologic findings. Cutis 2000; 65:141.
4. Sybert VP, et al. Palmar-plantar keratoderma: A clinical, ultrastructural, and biochemical study. J Am Acad Dermatol 1988;18:75.




40X


100X

CHICAGO DERMATOLOGICAL SOCIETY CASE 19

PRESENTERS
Irene J. Vergilis-Kalner, MD, Bernhard Ortel, MD, Vesna Petronic-Rosic, MD, and Christopher R. Shea, MD

HISTORY OF PRESENT ILLNESS
A 59-year-old African American man was admitted for chronic diarrhea and abdominal pain, with a 10-year history of asymptomatic, nodular, plate-like infiltrates involving both lower extremities.

PAST MEDICAL HISTORY
Hypertension, congestive heart failure, chronic renal failure, hyperlipidemia, pancreatitis, diverticulosis, tuberculosis, gout > 15 years, gouty arthritis, gouty nephropathy, bilateral renal artery stenosis, end-stage renal disease with failed renal transplant, on hemodialysis since 4/2006.

PAST SURGICAL HISTORY
Right lower lobectomy for pulmonary tuberculosis and surgery for spinal tuberculosis (1983)
Right kidney cadaveric transplant (5/1991); bilateral nephrectomies of native kidneys because of renin-dependent chronic renal hypertension (3/1992); Synovectomy of extensor tendon and excision of gouty tophi on left elbow in 5/2003; gouty nephropathy on biopsy (10/2005)

MEDICATIONS
Prednisone, colchicine, darbepoietin alfa

ALLERGIES
No known drug allergies

FAMILY HISTORY
Mother died of congestive heart failure; no other pertinent family history

SOCIAL HISTORY
Patient retired 19 years ago; on disability. Lives alone. History of chronic alcoholism until 10 years ago. Smokes 1 pack of cigarettes per week. Prior history of marijuana use and gambling addiction.

PHYSICAL EXAMINATION
Skin examination revealed multiple firm 1 cm subcutaneous nodules, most impressive on the distal legs but also on the thighs, arms, and elbows, with coalescence into large plates on the calves and shins. In addition, there were subcorneal, yellow-white papules on the left palmar aspects of several fingers. On the lower extremities the skin was dry and coarsely scaly. Deformity of the fingers and elbow joints was noted.

LABORATORY DATA & DIAGNOSTIC STUDIES
The following were negative or within normal limits:
Hepatitis C and B panel, liver function tests,

The following were abnormal:
Hemoglobin 11 g/dl (> 13.5 g/dl), hematocrit 33.6% (> 41%), total iron binding capacity 222 mcg/dl (> 230 mcg/dl), ferritin 2291 ng/ml (< 300 ng/ml). BUN, creatinine, and inorganic phosphate were elevated at 79 mg/dl (< 20 mg/dl) , 8.7 mg/dl (< 1.4 mg/dl), and 5.1 mg/dl (< 4.4 mg/dl), while GFR was low at 6 mL/min/B (> 59 mL/min/B). LDH, amylase, and plasma lactate were elevated at 269 U/L (< 245 U/L), 129 U/L (< 100 U/L), and 2.4 mEq/L (< 2.1 mEq/L).

Imaging: 8/2006 CXR normal; 7/2006 CT abdomen/pelvis: diverticulosis in descending colon, muscular thickening and hypertrophy in sigmoid colon; increased density of upper mesenteric fat.

On biopsy of transplanted kidney 10/2005: medullary uric acid microtophi consistent with gouty nephropathy and chronic transplant glomerulonephropathy with segmental glomerular sclerosis and widespread interstitial fibrosis; microscopic findings consistent with chronic rejection.

DERMATOPATHOLOGY
A skin biopsy from the right posterior calf demonstrated hyperkeratosis of the epidermis and large aggregations of needle-shaped crystals within the dermis and subcutaneous fat, which were refractile on polarization, surrounded by epithelioid histiocytes, mononuclear cells, and foreign body giant cells. Focal calcification was confirmed by Von Kossa stain.

DIAGNOSIS
Gout

TREATMENT & CLINICAL COURSE
The patient has not followed up with dermatology due to the time constraints of his current dialysis regimen.

DISCUSSION
This case demonstrates an unusual presentation of tophaceous gout involving the dermis and subcutis. Gout represents a heterogeneous group of metabolic diseases in which needle-shaped crystals of monosodium urate precipitate and are deposited in the tissue and within joints. It is the most common form of crystal-induced arthritis and typically occurs in the fifth and sixth decades, with a male-female ratio of 7:1 to 9:1.

Uric acid is the end product of purine metabolism. Normally, 65 to 75% of uric acid is excreted by the kidneys and the remainder primarily by the intestine. Hyperuricemia occurs when production of uric acid increases (idiopathically or due to hypoxanthine-guanine phsophoribosyl transferase deficiency, phosphoribosyl pyrophosphatase synthetase overactivity, excessive dietary purine or alcohol intake, obesity, or in association with high-grade lymphoma, leukemia, myeloma, tumor lysis syndrome, or with chronic hemodialysis) or when kidneys do not excrete sufficient amounts (as in renal insufficiency, dehydration, the use of thiazide and loop diuretics or cyclosporine for organ transplantation, exposure to toxins such as lead, or with acidosis). Urate crystals stimulate production of interleukin-1 by monocytes and macrophages. Subsequent migration and activation of neutrophils, complement activation, and ingestion of crystals by neutrophils trigger cell damage and leakage of lysosomes causing further inflammation and tissue damage.

Acute gouty arthritis presents as severely painful inflammation. Usually one joint at a time is affected but up to 40% of attacks may be polyarticular. In 75% of patients the first metatarsophalangeal joint is involved (podagra). Fever and other systemic symptoms may accompany acute attacks. Early attacks usually subside spontaneously after 3 to 10 days. Recurrent, often self-limited attacks may follow. Intervals between the attacks progressively shorten and on average 10 years after the onset of disease chronic tophaceous gout develops with monosodium urate deposits forming in cartilage, synovial membranes, tendons, and soft tissue.

Tophi can present as firm intradermal or subcutaneous papules and nodules or as fusiform swellings with smooth or multilobulated contours. Lesions vary from skin-colored to yellow-white to red. There may be ulceration with drainage of clear fluid with white flecks of urate or a thick, chalky material. The most common locations for tophi are the skin and subcutaneous tissue overlying the joints. Other sites

include the finger pads, penis, tongue, eyes, nose, larynx, breast, and heart valves. Excessive urate production and excretion cause uricosuria and predispose to uric acid nephrolithiasis. Renal insufficiency, proteinuria, or renal failure (uric acid nephropathy) can also occur when crystals precipitate and deposit within renal tubules and collecting ducts.

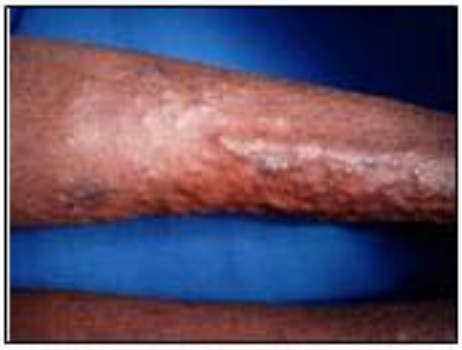
Initial diagnosis of gout is usually made in the setting of acute arthritis and it rests on the presence of monosodium urate crystals in the aspirate of joint fluid or in the tophus. Abnormal findings during acute attacks include hyperuricemia and elevated WBC count and ESR. Viewed with a polarizing filter, brightly refractile brown sheath of fine needle-shaped monosodium urate crystals in the skin or joint fluid aspirate vary from yellow to blue when the filter is turned and exhibit negative birefringence. When stained with silver nitrate, crystals appear black and surrounding tissue yellow, whereas with the De Galantha stain, crystals look brown to black. With recurrent attacks, radiographs of the involved joints show punched out erosions with sclerotic, overhanging margins. A 24-hour urinary uric acid collection allows for identification of the patients at risk for nephrolithiasis and helps to determine whether there is overproduction or underexcretion. In gouty tophi, the key histologic feature is dermal and subcutaneous deposits of amorphous material containing needle-like clefts, which represent dissolved urate crystals, surrounded by the infiltrate of histiocytes (including multinucleated giant cells) and lymphocytes. The epidermis may be intact or ulcerated and a fibrous capsule may surround tophi. Secondary calcification or even ossification can sometimes be seen. On ultrasound, tophi have central clear spaces. On MRI, tophi show low to intermediate signal intensity on the T1-weighted images and heterogeneous signal intensity on the T2-weighted images and on the gadolinium-enhanced MRI studies.

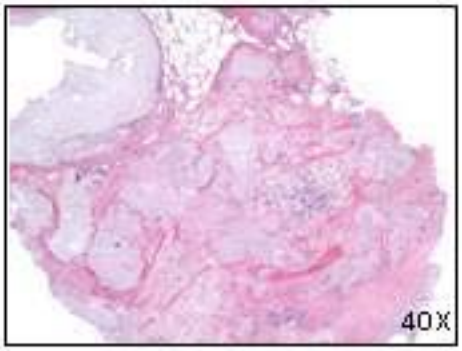
In acute gout, first-line therapy with short-acting NSAIDs, such as indomethacin, usually leads to marked symptomatic relief within 24 hours. Colchicine rapidly relieves pain and swelling when it is initiated within the first 24 hours, and can help to prevent future attacks. Colchicine binds to microtubules and inhibits them by inhibiting the transport of phagocytized urate crystals to the lysosomes in the neutrophils. Colchicine can also interfere with leukocyte migration, chemotaxis, and adhesion. Intraarticular injection of depot corticosteroids can also relieve symptoms within hours. Systemic corticosteroids can be used for 1-3 weeks if NSAIDs and colchicines are ineffective or contraindicated. Some patients may benefit from reduction in the purine-rich foods and avoidance of alcohol and diuretics. In addition, weight loss can improve insulin sensitivity and help to reduce uric acid in obese patients since insulin influences the renal urate excretion.

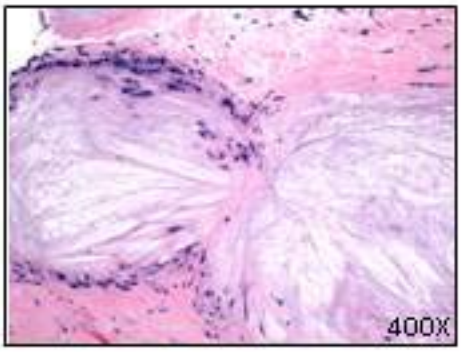
Effective long-term prophylaxis and treatment of gout aims to prevent recurrent acute attacks of arthritis and development of tophaceous disease These goals are achieved by lowering serum uric acid level to ≤0.36 mmol/l (60 mg/l), which dissolves monosodium urate deposits, monohydrate crystals and even tophi. When dietary treatment alone fails, urate-lowering drugs are added. The current mainstay of chronic therapy is allopurinol, a purine inhibitor of xanthine oxidase, which inhibits synthesis and production of uric acid. Allopurinol treats both urate overproduction and urate underexcretion. It is potent, rapid, and dosed once-daily based on the creatinine clearance. It should be reserved for severe gout with frequent attacks of gouty arthritis, presence of tophi, urate-induced arthropathy, or urinary lithiasis. However, it is contraindicated in organ transplant recipients. Other agents that lower uric acid are sulfinpyrazone and probenecid, which inhibits tubular reabsorption of uric acid, thus increasing renal urate clearance, and could be the first-line agent for patients with substantially decreased renal urate excretion. Losartan or fenofibrate, used to treat concomitant hypertension or dyslipidemia, respectively, can also lead to increased urinary excretion of uric acid, thus decreasing serum urate levels, and can control gout. Several xanthine oxidase inhibitors being studied are nonpurine inhibitor febuxostat and phenylpyrazole Y 100.

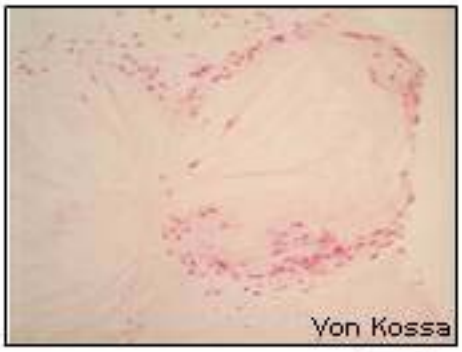
REFERENCES

1. Bardin T. Current management of gout in patients unresponsive or allergic to allopurinol. Joint Bone Spine 2004; 71: 481-5.
2. Gniadecka M, Wulf HC, Johansson CK, Ullman S, Halberg P, Rossen K. Cutaneous tophi and calcinosis diagnosed in vivo by Raman spectroscopy. Br J Dermatol 2001; 145: 672-4.
3. Kostler E, Porst H, Wollina U. Cutaneous manifestations of metabolic diseases: uncommon presentations. Clin Dermatol 2005; 23: 457-64.
4. Terkeltaub RA. Gout. N Engl J Med. 2003; 349: 1647-5.









CHICAGO DERMATOLOGICAL SOCIETY CASE 20

PRESENTERS
Justin Wasserman, MD and Sarah L. Stein, MD

HISTORY OF PRESENT ILLNESS
A 20-year-old white male presented to clinic for a general check-up and follow up on a skin condition present since birth. He was originally seen at the University of Chicago directly after birth and was found at that time to have a collodion membrane. The patient was cared for as an inpatient for a total of 2 weeks. He was treated with supportive care until stable and discharged home. During the patient's childhood he had few complains except for dry skin and redness of is face and trunk. When playing sports the patient found he became very hot and often needed to cool down. According to the patient he does not sweat very much. Otherwise his only complaint is of generalized, mildly itchy, fine, dry flaky skin, especially on the lower legs. He is otherwise healthy. He denies any hair loss or dryness of eyes.

PAST MEDICAL HISTORY
Collodion Baby

MEDICATIONS
None

ALLERGIES
No known drug allergies

FAMILY HISTORY
No history of ichthyosis

SOCIAL HISTORY
He does not smoke or use tobacco products, drink alcohol, or use illicit drugs.

REVIEW OF SYSTEMS:
He denies fevers, chills, chest pain, shortness of breath, abdominal pain, dizziness, nausea/vomiting, diarrhea, constipation, and weakness.

PHYSICAL EXAM
The patient is a well developed, well nourished, young man in no acute distress. He has generalized erythema of the head and trunk. The lower legs are dry with fine, powdery, white scale.

DIAGNOSIS
Congenital Ichthyosiform Erythroderma (CIE)

TREATMENT & CLINICAL COURSE
Moisturizers and sufficient nutrition were recommended. The patient was referred for genetic counseling to help answer questions on risk to potential children in the future.

DISCUSSION
CIE is a very heterogenous condition that appears to be transmitted in an autosomal recessive pattern, although a few cases of autosomal dominant inheritance have been reported. It has a prevalence of 1in 200,000 people and occurs much more often than lamellar ichthyosis.

The first sign of CIE presents at birth with the presence of a collodion membrane. Once the membrane resolves, the patient will typically have generalized erythema and persistent scaling throughout their

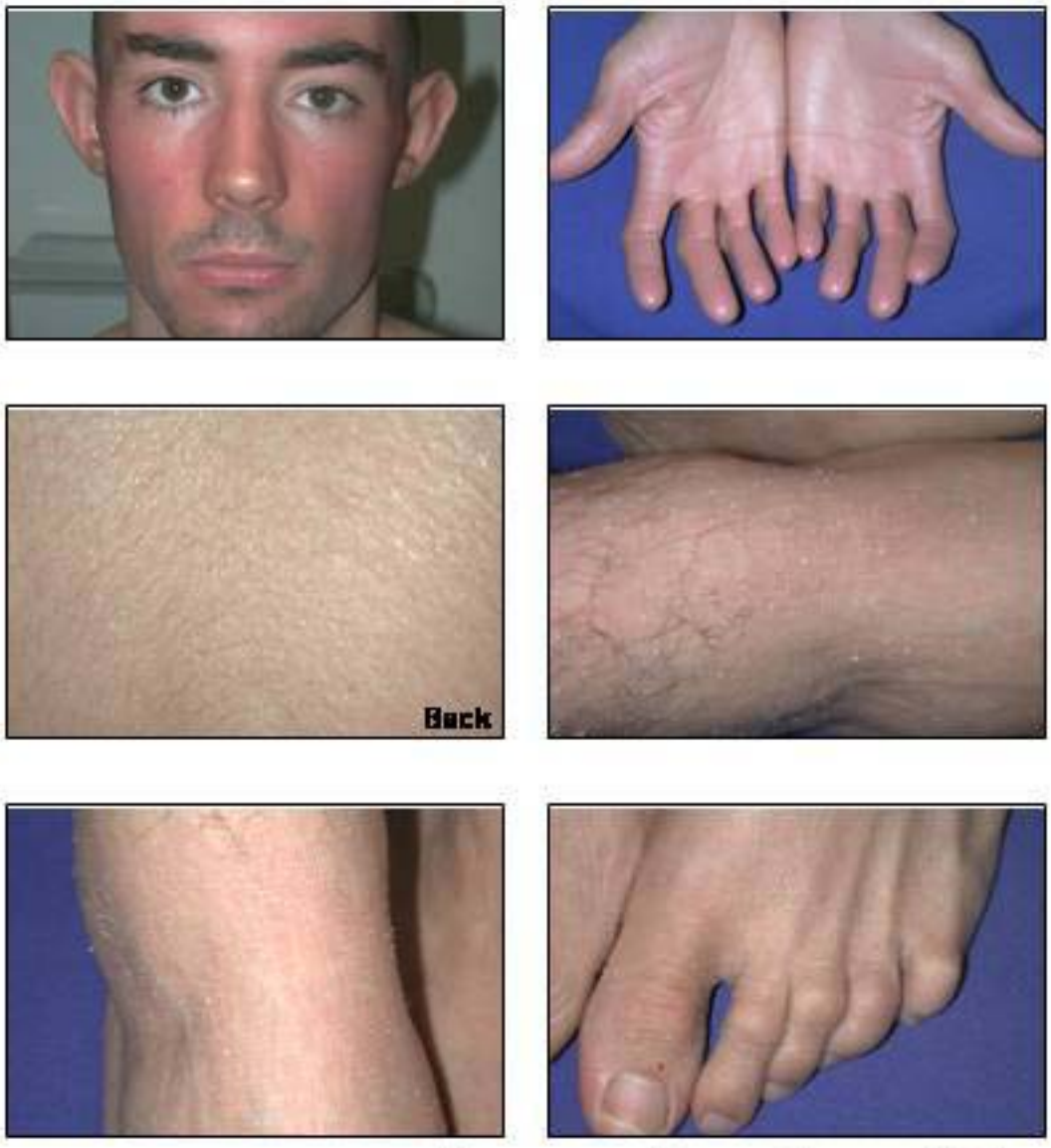
lifetime. The spectrum of the condition can vary significantly. More severe cases will present with generalized scale ranging from fine white powder to large dark plate-like scales, intense erythroderma, ectropion, fissuring keratoderma of palms and soles, and scarring alopecia. The milder forms will have generalized scaling, mild erythroderma, and variable involvement of the palms and soles. Hypohidrosis and heat intolerance can occur due to obstruction of pores and sweat ducts. In severe cases, where metabolic demand on the growing child is high, mild growth retardation may be present.

Histological features of CIE are non-diagnostic and overlap with features of lamellar ichthyosis and other hyperproliferative disorders. Typical features include acanthosis, hypergranulosis, parakeratosis, increased number of lamellar bodies, accumulation of lipid droplets in stratum corneum, and disorganized intercellular lipid lamellae.

Treatment is supportive in nature. At birth, babies should be carefully monitored for electrolyte, fluid and temperature imbalances. They should be placed in humidified incubators and treated with wet compresses, lubricants, and light emollients until the collodian membrane resolves. It is important to have sufficient nutritional intake in erythrodermic patients to make up for fluid, protein, iron and caloric losses. Use of oral retinoids may help with scaling, but usually does not improve erythroderma significantly.

REFERENCES

1. Ghadially R, Williams ML, Hou SY, Elias PM. Membrane structural abnormalities in the stratum corneum of the autosomal recessive ichthyosis. J Invest Dermatol 1992;99:755-63.
2. Hofmann B, Stege H, Ruzicka T, Lehmann P. Effect of topical tazarotene in the treatment of congenital ichthyosis. Br J Dermatol 1999;141:642-6.
3. Niemi KM, Kanerva L, Kuokkanen K, Ignatius J. Clinical, light, and electron microscopic features of recessive congenital ichthyosis type I. Br J Dermatol 1994;130:626-33.
4. William ML, Elias PM. Heterogeneity in autosomal recessive ichthyosis. Clinical and biochemical differentiation of lamellar ichthyosis and nonbullous congenital ichthyosiform erythroderma. Arch Dermatol 1985;121:477-88.


Back

CHICAGO DERMATOLOGICAL SOCIETY

Special thanks to

AMGEN

for their generous support of this event