Chicago Dermatological Society

June 2011
Monthly Educational Conference

Program Information
Continuing Medical Education Certification
Case Presentations

Wednesday, June 8, 2011

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

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Program

Conference Location

Stritch School of Medicine/Cuneo Center
Loyola University Medical Center
2160 South First Avenue, Maywood

Program Events

7:30 a.m.	Registration & Continental Breakfast *Main Lobby - Cuneo Center*
8:00 a.m. - 10:30 a.m.	**General Session – Dermoscopy Course** *Tobin Hall Room 190 (just off main lobby)* Lectures will cover terminology and evaluation of melanocytic lesions/unknowns. This course is open to all CDS members and residents. *HAROLD RABINOVITZ, MD AND MARGARET C. OLIVIERO, MS, RN*
10:00 a.m. - 11:30 a.m.	**Clinical Rounds** • Patient Viewing - *Clinical Skill Center Room 330* • Slide Viewing - *Leischner Hall Room 390* • Posters - *Seminar Rooms 363, 364, 375*
11:45 a.m. - 1:00 p.m.	**General Session** *Tobin Hall Room 190* "What's New and Old in Evaluation of Melanoma" *HAROLD RABINOVITZ, MD*
1:00 p.m. - 1:30 p.m.	**Lunch Break** *Main Lobby - Cuneo Center*
1:30 p.m. - 1:45 p.m.	**CDS Business Meeting** *Tobin Hall Room 190*
1:45 p.m. - 3:00 p.m.	**General Session** – Case Discussions *Tobin Hall Room 190*
3:00 p.m.	**Meeting adjourns**

Mark the Date!

Next CDS monthly meeting – Wednesday, September 21, 2011 at Northwestern University
PLEASE NOTE NEW SCHEDULE!

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

Guest Speaker

HAROLD RABINOVITZ, MD
Clinical Professor of Dermatology at University of Miami School of Medicine Private Practice; Plantation, FL

Harold Rabinovitz, MD is a board certified dermatologist practicing in Plantation, FL. He graduated Cum Laude from Princeton University and received his medical degree from the University of Miami School of Medicine in 1977. After his internship at Mt. Sinai Medical Center in Miami Beach, he completed a dermatology residency at New York University Medical Center (1981), where he also completed a fellowship in Mohs surgery (1982).

Dr. Rabinovitz served as Assistant Clinical Professor and as Associate Clinical Professor of Dermatology at University of Miami School of Medicine and presently, he serves there as Clinical Professor of Dermatology.

Dr. Rabinovitz is the author of many publications and has engaged in a variety of research projects. In his practice, he performs Mohs Micrographic Surgery and Skin Surface Microscopy.

CME Financial Disclosure: Dr. Rabinovitz has disclosed the following financial relationships: 3Gen: consultant, speaker; Canfield: grant/research support; DermTech: grant/research support; Lucid: grant/research support, consultant, speaker; Megasciences: consultant.

Margaret C. Oliviero graduated from Wagner College in Staten Island New York with a Bachelors of Science in Nursing Magna Cum Laude in August of 1977, and a Masters of Science in Nursing in the summer of 1993. She completed post graduate courses in nursing at Florida Atlantic University and became a board certified family nurse practitioner in the fall of 2000.

Ms. Oliviero has worked in dermatology since 1979, beginning as a registered nurse at NYU Skin and Cancer Clinic. She has been employed by Skin and Cancer Associates in Plantation Florida since July 1982, where she currently coordinates the FDA clinical trials and investigative studies regarding skin cancers. She is an expert with dermoscopy and confocal microscopy. She is also the current secretary to the International Confocal Working Group.

Margaret has co-authored over 50 peer reviewed articles and has lectured at international meetings as well as the AAD.

Continuing Education Credit

Chicago Dermatological Society

"Chicago Dermatological Society Monthly Conference"

June 8, 2011 *Maywood, IL*

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

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

Link address to evaluation form:
http://www.yourcesource.com/eval/?act=524!06082011

JOINT SPONSOR STATEMENT

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

GOAL / PURPOSE

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

SESSION OBJECTIVES

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

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

- Analyze the basic criteria and patterns of dermoscopy.
- Apply a dermoscopic approach for the classifications of benign and malignant lesions on the skin.
- Demonstrate the benefits from the application of dermoscopy in daily practice.

- Demonstrate the potential usefulness of other imaging techniques such as total body photography, mole monitoring, and confocal microscopy.
- Demonstrate some of the new devices that are currently in the research development.

CREDIT STATEMENTS

CME CREDIT

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

The Colorado Foundation for Medical Care designates this ***Live Activity*** for a maximum of ***6 AMA PRA Category 1 Credit*(s) ™**. Physicians should claim only the credit commensurate with the extent of their participation in the activity.

OTHER HEALTH CARE PROFESSIONALS

This educational activity has been planned and implemented following the administrative and educational design criteria required for certification of health care professions continuing education credits. Registrants attending this activity may submit their certificate along with a copy of the course content to their professional organizations or state licensing agencies for recognition for 6 hours.

DISCLOSURE STATEMENTS

The following faculty member has disclosed that they have the following financial relationships:

First	Last	Degree	Organization	Financial Disclosure
Harold S.	Rabinovitz	MD	University of Miami School of Medicine	Grant/Research Support: Lucid, DermTech, Canfield; Consultant: 3-Gen, Lucid, Melasciencies/ Speakers Bureau: 3-Gen, Lucid

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

Loyola University Medical Center
Division of Dermatology

Edward Hines, Jr. VA Hospital
Section of Dermatology

FACULTY

Rebecca Tung, MD, Director
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DERMATOPATHOLOGY

Madhu Dahiya, MD
Kelli Hutchens, MD

RESIDENTS

Third Year

Joshua Mandrell, MD
Aaron Pace, MD

Second Year

Loebat (Julia) Kamalpour, MD
Vanessa Lichon, MD
Anita Shetty, MD
Krisanne Sisto, MD

First Year

Allison Goddard, MD
Anjali Shah, MD

Thank you to Drs. Madhu Dahiya and Kelli Hutchens for their review of the dermatopathology portions of these presentations.

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CHICAGO DERMATOLOGICAL SOCIETY **CASE # 1**

Presented by Vanessa Lichon, MD, Joseph Clark, MD, Anthony Peterson, MD, Madhu Dahiya, MD, Brian Nickoloff, MD, PhD, and Kelli Hutchens, MD
Division of Dermatology and Division of Hematology-Oncology, Loyola University Medical Center

HISTORY OF PRESENT ILLNESS

This 62 year-old African American female presented to the dermatology clinic for evaluation of weeping lesions on her right leg in January 2011. She had a long-standing history of melanoma on her right plantar foot as follows: she was initially diagnosed with melanoma at an outside hospital in November 2000, Breslow 0.77mm. Due to personal circumstances she did not undergo wide local excision with a skin graft until February 2003 and had subsequent recurrence in December 2004 at which time the Breslow depth was 3.1mm. She was treated with a wide local excision, skin graft, and sentinel lymph node biopsy (1/3 with microscopic involvement) at that time and in April of 2005 had a right superficial inguinal lymph node dissection with 3/3 lymph nodes negative. She underwent adjuvant interferon-alpha 2b therapy in 2005 which was stopped due to toxicity (nausea, vomiting) and she was subsequently lost to follow-up.

In April 2010, she re-established care with hematology-oncology at Loyola and was noted to have two lesions suspicious for in-transit metastases on her right lower extremity which were confirmed by biopsy. In September 2010 she was started on high-dose IL-2 which was complicated by atrial fibrillation with rapid ventricular response and progression of disease with increased number of in-transit metastases and leg swelling. In November 2010, she was enrolled in an ipilimumab trial and was due for her fourth cycle in January 2011 but this was held due to poor pain control and significant progression of in-transit metastases. She was hospitalized for pain management and then referred to dermatology clinic for further assistance with wound care. At the time of her dermatology appointment she complained of difficulty walking, drainage around the lesions on her right leg, and pain to palpation. She expressed interest in potential limb-saving procedures as amputation had been discussed with general surgery.

PAST MEDICAL HISTORY

Hypertension

MEDICATIONS

Fentanyl
Morphine
Metoprolol
Prochlorperazine
Sennosides

ALLERGIES

Penicillin

FAMILY HISTORY

Patient denied family history of skin cancer including melanoma.

SOCIAL HISTORY

Patient was a ½ pack-per-day smoker for 25 years and quit in 1/2005.

PHYSICAL EXAM

The patient had a well-healed hyperpigmented skin graft on her right plantar foot. On her right distal extremity were many grouped firm, weeping, tender flesh-colored to hyperpigmented to erythematous exophytic nodules and tumors. She had palpable right inguinal lymphadenopathy.

HISTOPATHOLOGY

Punch biopsy, 4/2010, right medial leg
The mid-to-deep reticular dermis was infiltrated by atypical spindle cells with large and hyperchromatic nuclei and many of the cells were pigmented. The cells were S-100 positive and these findings were consistent with in-transit metastatic melanoma.

RADIOLOGY

1/2011 CT Chest/Abdomen/Pelvis
Impression: Enlarged right external iliac and common femoral lymph nodes, otherwise, stable findings.

10/2010 MRI Brain
Impression: No evidence for metastatic disease or other acute intracranial abnormality.

DIAGNOSIS

In-transit metastatic melanoma

TREATMENT AND COURSE

After initial evaluation in our clinic, the patient was started on unna boot therapy to her right lower extremity. She was referred to Northwestern for evaluation and possible enrollment in Dr. Murad Alam's clinical trial titled In Situ Photoimmunotherapy: A Tumor Directed Treatment for Advanced Melanoma with Cutaneous Metastases. Prior to evaluation, she had significant progression of disease, and was admitted to the medical intensive care unit at Northwestern for hypokalemia in February 2011. She was eventually discharged to a rehabilitation facility where, unfortunately, she died in April 2011.

DISCUSSION

In 2010, an estimated 68,130 adults in the United States were diagnosed with invasive melanoma and approximately 8,700 deaths occurred due to melanoma. About 5-7% of melanoma patients will develop in-transit metastases which are defined as cutaneous or subcutaneous deposits of melanoma trapped within the lymphatics between the primary tumor and the regional lymph node basin. Patients who develop in-transit metastases or local recurrences have a poorer prognosis, with 5-year survival rates reported between 3-28%.

Risk factors cited in the literature for in-transit metastases include age greater than 50 years, increased Breslow thickness, primary tumors on the extremities, ulceration and positive lymph node status. Treatment options depend on the severity of disease and include surgical excision, intralesional injections, laser ablation, chemotherapy, radiotherapy, electrochemotherapy, or immunotherapy. For advanced cases, isolated limb perfusion is a well-established approach to in-transit metastases.

This case is presented to highlight the current melanoma trials in the Chicago-land area, many of which are listed below. Thank you to many of the principal investigators and assistants involved in these trials who replied to my inquiries. A comprehensive list of ongoing clinical trials both locally and nationally can be accessed at http://clinicaltrials.gov/.

Loyola University Medical Center

1) S0933 - a Southwest Oncology Group sponsored phase II trial assessing the efficacy of RO4929097, a gamma secretase inhibitor, in the treatment of advanced cutaneous malignant melanoma.

2) LU 203466 - a randomized phase II trial of temozolomide versus Hyd-sulfate AZD6244, a MEK-inhibitor, in the treatment of advanced uveal melanoma.

3) Soon to open: A Phase IB pilot study of denileukin diftitox (Ontak) in combination with high-dose interleukin-2 in metastatic cutaneous melanoma, evaluating the efficacy of this combination and the role of regulatory T cells in this setting.

4) In the near future: The Southwest Oncology Group will be sponsoring a randomized phase III adjuvant trial comparing standard high dose alpha interferon versus ipilimumab in patients with resected high risk cutaneous malignant melanoma. Specifics on exact patient eligibility are still pending.

Rush University Melanoma Center

Therapeutic Trials

1) A Randomized Phase 3 Clinical Trial to Evaluate the Efficacy and Safety of Treatment with OncoVEXGM-CSF Compared to Subcutaneously Administered GM-CSF in Melanoma Patients with Unresectable Stage IIIb, IIIc and IV Disease

2) An Extension Protocol to Evaluate the Efficacy and Safety of Extended Use Treatment with OncoVEXGM-CSF for Eligible Melanoma Patients Participating in Study 005/05

3) A double-blind, randomized, placebo-controlled Phase III study to assess the efficacy of recMAGE-A3 + AS15 ASCI as adjuvant therapy in patients with MAGE-A3 positive resected stage III melanoma

4) A Randomized, phase III, open-label, multi-center, two-arm study to compare the efficacy of Tasigna versus dacarbazine (DTIC) in the treatment of patients with metastatic and/or inoperable melanoma harboring a c-Kit mutation

5) E1608: A Phase II Trial of GM-CSF Protein plus Ipilimumab in Patients with Advanced Melanoma

6) A Phase III, Randomized Trial of Surgical Resection With or Without BCG Versus Best Medical Therapy as Initial Treatment in Stage IV Melanoma

7) A Phase III Multicenter Randomized Trial of Sentinel Lymphadenectomy and Complete Lymph Node Dissection versus Sentinel Lymphadenectomy Alone in Cutaneous Melanoma Patients with Molecular or Histopathological Evidence of Metastases in the Sentinel Node

8) A Randomized Phase II Crossover Study of High-Dose IL-2 and Ipilimumab versus Ipilimumab Alone in Patient with Metastatic Melanoma

9) Phase I Study of an Anti-PD1 Monoclonal Antibody for Patients with Metastatic Melanoma (pending)

Non-therapeutic Trials

1) Melanoma Tissue Acquisition and Storage Protocol

2) A Prospective Tissue Collection Protocol to Investigate Predictive Models of Response to High Dose IL-2 Treatment in Patients with Advanced Melanoma (Prometheus SELECT study)

3) OncoVEX Registry Protocol

4) PROCLAIM InterLeukin-2 Registry Trial

Northwestern University, Robert H. Lurie Comprehensive Cancer Center

1) In Situ Photoimmunotherapy: A Tumor Directed Treatment for Advanced Melanoma with Cutaneous Metastases

2) Evaluation of a Simulation Training Tool to Identify Lesions Requiring Further Screening for Melanoma

3) A Double-Blind, Randomized, Placebo-Controlled Phase III Study to Assess the Efficacy of recMAGE-A3 + AS15 ASCI as Adjuvant Therapy in Patients with MAGE-A3 Positive Resected Stage III Melanoma

4) Phase Ib/II Study of ALT-801 with Cisplatin in Patients with Metastatic Melanoma

5) A Phase II Trial of GM-CSF Protein Plus Ipilimumab in Patients with Advanced Melanoma

6) A Phase I/II Study of High-Dose Calcitriol in Combination with Temozolomide for Patients with Metastatic Melanoma

7) No Worries? Adaptation and Health Behaviors among Young Adult Cancer Survivors

8) Multicenter Selective Lymphadenectomy for Melanoma Trial II: A Phase III Multicenter Randomized Trial of Sentinel Lymphadenectomy and Complete Lymph Node Dissection versus Sentinel Lymphadenectomy Alone in Cutaneous Melanoma Patients with Molecular or Histopathological Evidence of Metastases in the Sentinel Node

University of Chicago Comprehensive Cancer Center

1) Randomized Phase II Study of Multipeptide Vaccination with or without Regulatory T Cell Depletion using Ontak in Patients with Metastatic Melanoma

2) Phase II Study of the Anti-Ganglioside GD3 Mouse/Human Chimeric Antibody KW2871 Combined with High Dose Interferon-a2b in Patients with Metastatic Cutaneous Melanoma

3) A double blind, randomized, placebo-controlled Phase III study to assess the efficacy of recMAGE-A3 + AS15 ASCI as adjuvant therapy in patients with MAGE-A3 positive resected stage III melanoma

4) A Phase II Study of Nilotinib (AMN107) in TKI resistant or intolerant patients with metastatic mucosal, acral, or chronically sun damaged melanoma

5) A Phase II Open-Label, Multicenter Study of ONTAK in Patients with Stage IIIC and Stage IV Melanoma

6) A Phase I, Open-Label, Dose-Escalation Study to Determine the Safety, Tolerability, Pharmacokinetics and Pharmacodynamics of INCB024360 in Patients with Advanced Malignancies

7) Identification of cancer/testis (CT) antigens from plasma in locally advanced patients

8) S0933: Phase II Study of RO4929097 (NSC-749225) in Advanced Melanoma

9) A Phase Ib, Open label, Dose-Escalation Study evaluating the Safety, Tolerability and Pharmacokinetics of RO5185426 in Combination with GDC-0973 when Administered in Patients with BRAFV600E-Positive Metastatic Melanoma who have Progressed after treatment with RO5185426

10) Randomized Phase II Trial of Temozolomide versus Hyd-sulfate AZD624 [NSC 748727] in Patients with Metastatic Uveal Melanoma.

University of Illinois at Chicago

1) DERMA Protocol 111482, A double-blind, randomized, placebo-controlled Phase III study to assess the efficacy of recMAGE-A3 + AS15 ASCI as adjuvant therapy in patients with MAGE-A3 positive resected stage III melanoma.

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9. Deroose JP, et al. Isolated limb perfusion for melanoma in-transit metastases: developments in recent years and the role of tumor necrosis factor alpha. Curr Opin Oncol. 2011 Mar;23(2):183-8.
10. http://www.clinicaltrials.gov/

CHICAGO DERMATOLOGICAL SOCIETY **CASE # 2**

Presented by Anita Shetty, MD, Rama Vaitla, MD, Anthony Peterson, MD, Madhu Dahiya, MD, and Kelli Hutchens, MD
Division of Dermatology, Loyola University Medical Center

UNKNOWN #1

CHICAGO DERMATOLOGICAL SOCIETY **CASE # 3**

Presented by Anjali Shah, MD, Anthony Peterson, MD, Brian Nickoloff, MD, PhD, and Kelli Hutchens, MD
Division of Dermatology, Loyola University Medical Center

HISTORY OF PRESENT ILLNESS

A 39 year-old female presented to the hospital with a two-day history of left lower quadrant abdominal pain in October 2010. The pain was severe, and subjectively localized by the patient as both superficial and deep. She also complained of mild itching and swelling in the area. Prior to admission, a CT abdomen at an outside hospital showed extensive inflammation involving the subcutaneous tissue of the abdominal wall with small lobules of gas. She was evaluated by general surgery and was not believed to have an acute abdomen or underlying infectious process. She denied fevers, chills, night sweats, nausea, vomiting, or diarrhea.

During the ten months prior to admission she had been evaluated numerous times for intermittent left lower quadrant pain. CT abdomen in January 2010 showed numerous foci of subcutaneous air. She was treated with surgical debridement and antibiotics (piperacillin/tazobactam and vancomycin), despite all cultures being negative. Subsequent CT three months later revealed pockets of subcutaneous air worrisome for fat necrosis without abscess, again wound cultures returned negative. Of note, she was previously injecting enoxaparin for a remote history of pulmonary embolism until April 2010, but denied any abdominal injections or trauma to the area since that time. She was up to date on her age appropriate malignancy screenings.

PAST MEDICAL HISTORY

Cholecystectomy 1999, chronic pain, depression, gastric bypass 2002, hernia repair with mesh placement 2003, hysterectomy 2007, obesity, pulmonary embolus 2006

MEDICATIONS

Clindamycin
Clonazepam
Duloxetin
Gabapentin
Hydrocodone/acetaminophen

ALLERGIES

No known drug allergies

FAMILY HISTORY

No family history of malignancy

SOCIAL HISTORY

Single, on disability since 3/2010. No tobacco or illicit drugs. Occasional alcohol.

PHYSICAL EXAM

Physical exam of the abdomen was notable for scattered striae distense. The left lower quadrant showed very subtle edema, more visible within the striae, and several exquisitely tender, subcutaneous indurated nodules.

HISTOPATHOLOGY

A punch biopsy of an indurated, subcutaneous nodule showed an unremarkable epidermis, with a marked eosinophilic infiltrate in the subcutaneous adipose tissue, with predominantly

septal involvement. A superficial and deep dermal lymphoeosinophilic infiltrate and perivasculitis was also noted. There was no evidence of vasculitis, granuloma formation, or flame figures. Periodic acid-Schiff diastase and acid-fast bacilli stains were negative.

Bacterial and acid-fast bacilli tissue cultures were negative.

LABORATORY RESULTS

Abnormal or positive:
WBC differential: 47% eosinophils with a normal WBC count (8.3), hemoglobin 10.2, CRP 1.4
Normal or negative:
Complete metabolic panel, serum platelets, blood cultures, alpha-1-antitryptase, amylase, lipase, ANA, ENA-5, ANCA, RF, Hepatitis panel, HIV, stool ova and parasites

DIAGNOSIS

Eosinophilic panniculitis

TREATMENT AND COURSE

Prednisone 60mg daily was initiated and the patient experienced rapid resolution of her peripheral eosinophilia within 48 hours, however, her abdominal pain persisted. The primary service discharged the patient home on oxycodone. Hematology was consulted to evaluate the eosinophilia and felt it unlikely to be a primary process such as hypereosinophilic syndrome given her rapid resolution. They recommended bone marrow biopsy and additional studies should the eosinophilia recur. The patient was lost to follow up until recently when she presented again with abdominal pain. She has been following with rheumatology at an outside hospital and is in the process of obtaining her records for our review.

DISCUSSION

Eosinophilic panniculitis (EP) is a rare form of panniculitis considered to be a nonspecific reactive inflammatory pattern. Less than fifty cases have been reported in the literature. The term was initially coined by Burket and Burket in 1985. They described a patient with a 'distinctive panniculitis' presenting clinically as inflammatory nodular lesions that had the 'histologic changes of Well's syndrome'. They speculated that streptococcus was implicated as an antigenic stimulus for the disease process.

Eosinophilic panniculitis is considered a reactive process because most patients have an associated local or systemic condition. Case series have reviewed diverse patterns of associated systemic disease, including Wells' syndrome, vasculitis, atopy, arthropod bite reaction, contact dermatitis, bacterial infections, and erythema nodosum. Parasitic infection, specifically with *Gnathostoma spinigerum* larve (deep larva migrans) and *fasciola hepatica* have produced findings of EP. One series found a strong association with psychiatric disease as well as narcotic dependency with injection granulomas. In some instances, EP has been observed as a local phenomenon induced by subcutaneous or intramuscular drug injections. Isolated cases secondary to apomorphine, calcium heparin or intramuscular penicillin have been reported. Associated hematologic malignancy has been described, however in the majority of patients these conditions were diagnosed before the onset of eosinophilic panniculitis.

Histologically, eosinophilic panniculitis shows a septal or mixed septal and lobular panniculitis with a dense subcutaneous inflammatory infiltrate composed predominantly of eosinophils. Neutrophils, lymphocytes, or monocytes can be present, and prominent

eosinophilia may also be seen within the dermis. No consistent pattern of laboratory data has been described. Concurrent peripheral eosinophilia has been reported in a small number of cases. The clinical spectrum of lesions that display the pathologic changes of eosinophilic panniculitis is diverse. Nodular lesions are most commonly seen, but plaques, vesicles, and macular erythema can also be the presenting cutaneous findings.

The systemic evaluation of a patient with EP should be based on the potential associated conditions. Prognosis is dependent on the underlying etiology, however many patients have spontaneous resolution of their symptoms. In addition, reports have shown eosinophilic panniculitis to be responsive to steroids.

REFERENCES

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CHICAGO DERMATOLOGICAL SOCIETY **CASE # 4**

Presented by Loebat Julia Kamalpour, MD, David Eilers, MD, Brian Nickoloff, MD, PhD, and Kelli Hutchens, MD
Section of Dermatology, Edward Hines, Jr. VA Hospital

HISTORY OF PRESENT ILLNESS

A 63 year-old Caucasian male with a history of rheumatoid arthritis on methotrexate and prednisone, presented to the emergency room for evaluation of diffuse rash and painful oral lesions. The patient denied significant associated pruritus. He reported a four to five day history of fever, malaise, and myalgias, with subsequent development of diffuse rash. The lesions initially developed on his trunk and then became widespread. Of note, the patient was exposed to herpes zoster two weeks prior to admission. He denied ever having had a history of chickenpox.

PAST MEDICAL HISTORY

Rheumatoid arthritis, degenerative joint disease, gout, hyperlipidemia

MEDICATIONS

Hydrocodone/ acetaminophen PRN
Hydroxychloroquine sulfate 200 mg BID
Methotrexate 20 mg weekly
Prednisone 5 mg daily
Simvastatin 20 mg at bedtime

ALLERGIES

No known drug allergies

FAMILY HISTORY

Father with leukemia. Mother with history of COPD and CVA.

SOCIAL HISTORY

Divorced. Salesman. Denied alcohol or illicit drug use. Positive history of tobacco use (50 pack-year history).

PHYSICAL EXAM

Vitals T 97.5 P 109 RR 20 BP 128/99 O2 sat: 99% on 4L O2 NC

Numerous erythematous papules and vesicles on an erythematous base scattered over the face, neck, trunk, and bilateral upper and lower extremities. Clear fluid-filled vesicles over an erythematous base were seen over the hard palate and buccal mucosa.

LABORATORY RESULTS

Abnormal or positive:
Viral culture was positive for varicella zoster
Normal or negative:
Urinalysis, urine cultures, blood cultures

RADIOLOGY

Chest x-ray showed bilateral fluffy infiltrates, more prominent in the lower lobes

DIAGNOSIS

Varicella in an immunocompromised patient

TREATMENT AND COURSE

The patient was started immediately on high dose IV acyclovir (10 mg/kg/dose q8 hours). Within hours after admission, he developed worsening shortness of breath and hypoxia, necessitating intubation. The patient then developed multisystem organ failure, went into asystole and passed away 43 hours after initial presentation. Post-mortem examination revealed disseminated varicella zoster infection involving the skin, lungs and spleen. Acute necrotizing and organizing bronchopneumonia with viral inclusions was found within the lungs. The patient's spleen showed sinusoids with viral inclusions.

DISCUSSION

Primary varicella has a global distribution and is typically acquired during childhood in temperate regions of the world. The lifetime incidence of zoster is between 20 and 30%, rising to 50% of those living to 85 years of age.

Although varicella zoster infection is generally self-limiting, severe illness and death do occur, particularly in adults and the immunocompromised. Primary infection is via the respiratory tract and is presumably followed by a period of local replication within the mucosa prior to the development of viremia, resulting in fever, malaise and the pruritic vesicular rash. Dissemination favoring the skin appears to be due to infection of T lymphocytes and a hijacking of their normal trafficking pathways. The incubation period from exposure to development of rash is around 14 days. The patient is infectious to others from 48 hours prior to rash onset until crusting of all vesicles has occurred.

The case fatality rate of varicella is approximately 1 per 100,0000 in children but is at least twenty times higher in adults. Severe or complicated illness is more likely to occur in those with defective cell-mediated immunity but the majority of deaths still occur among previously healthy patients. Varicella in seronegative immunocompromised patients may have an atypical presentation and is often devastating, with about one-half of children developing hepatitis, pneumonitis, or encephalitis with a mortality rate of up to 20%. There has been firm evidence of benefit from intravenous acyclovir in the prevention of visceral complications of varicella in these patients.

Post-exposure prophylaxis of seronegative patients who have primary or iatrogenic immunocompromise, pregnancy, or HIV infection and are exposed to VZV has conventionally been with varicella-zoster immune globulin administered within 10 days of exposure. Patients who have (or are at particular risk for) severe disease or life-threatening complications, including neurological syndromes and pneumonitis, should initially receive intravenous acyclovir at a dose of 10 mg/kg three times daily. Some authorities also recommend the use of oral acyclovir 800 mg five times daily x 7 days (only if within 24 hours of rash onset) in uncomplicated cases of varicella for groups of individuals at higher risk of severe disease including otherwise healthy non-pregnant patients over age 13.

Methotrexate is among the most commonly used drugs for the treatment of rheumatoid arthritis. A major constraint on the use of methotrexate is the occurrence of adverse events. In a review of 673 patients with inflammatory arthritis who were treated with methotrexate between 1986 and 1999, there was one reported case of disseminated varicella zoster. In a systematic review of the long-term safety of methotrexate monotherapy in patients with RA including 88 published studies, long-term use of methotrexate did not appear to be a risk factor for serious infections including herpes zoster.

A review of the literature did not reveal any reports of severe varicella infection in patients on chronic low-dose prednisone therapy. While the additive impact of low-dose prednisone in patients on methotrexate is unknown, we believe it was unlikely to have been a significant factor in our patient's disease course.

In some contradiction to the prior studies that showed no increased risk for serious infections with methotrexate use, we believe our case shows that caution is advised prior to initiation of methotrexate (or other forms of immunosuppression) in patients without a clear history of primary VZV infection or VZV immunization. Previous studies showed a high positive predictive value (ranging from 95-100%) and a low negative predictive value of a self-reported history of primary VZV infection, suggesting that a positive history of disease is a reliable marker for immunity. We recommend serological testing of patients without a clear history of infection prior to the commencement of immunosuppressive therapy and vaccination of patients with negative serology.

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CHICAGO DERMATOLOGICAL SOCIETY **CASE 5**

Presented by Allison Goddard, MD, David Eilers, MD, and Madhu Dahiya, MD
Section of Dermatology, Edward Hines, Jr. VA Hospital

PATIENT A

HISTORY OF PRESENT ILLNESS
A 69 year old Caucasian male with history of chronic lymphocytic leukemia (CLL) presented with a three month history of intensely pruritic, erythematous dermal papules. The eruption appeared soon after initiation of chemotherapy for progressing CLL. The patient denied new medications other than the chemotherapy, no recent travel and had no recollection of exposure to insect bites. Biopsies were taken at an outside facility and various treatment modalities were carried out in our clinic. The condition severity waxed and waned, both on and off chemotherapy, with pruritus as the prominent symptom.

PAST MEDICAL HISTORY
Chronic lymphocytic leukemia, prostate adenocarcinoma, rosacea, coronary artery disease, hypertension, diabetes mellitus, hyperlipidemia, esophageal reflux, degenerative disc disease

MEDICATIONS
Aspirin
Acyclovir
Allopurinol
Atenolol
Cetirizine
Clopidogrel
Cyclophosphamide
Diltiazem
Glipizide
Insulin glargine
Lansoprazole
Metformin
Metronidazole gel
Pentostatin
Prednisone (pre-medication for chemo)
Rituximab
Simvastatin

ALLERGIES
Penicillin, IV contrast, shellfish

FAMILY HISTORY
Non-contributory

SOCIAL HISTORY
Former smoker 15 pack years – quit 1993. Occasional alcohol. No drugs. Retired truck driver and stagehand.

PHYSICAL EXAM
Indurated pink papules, many with central excoriation over the face, upper back, bilateral upper arms.

HISTOPATHOLOGY
*Note, all biopsies were obtained and read at Northwestern Medical Faculty Foundation. The patient receives his oncologic care at Northwestern.

12/02/2008 Back: Acute suppurative and eosinophilic folliculitis.

A DPAS demonstrated numerous intrafollicular pityrosporum yeast forms. Within the dermis there was a dilated follicular infundibulum with abundant neutrophils and occasional eosinophils. Atypia was not identified.

12/17/2009 Right shoulder: Perivascular dermatitis with eosinophils.
The changes were most consistent with a CLL associated dermal hypersensitivity reaction. A drug eruption could present with a similar pattern. There was a mild superficial perivascular mononuclear cell infiltrate with scattered eosinophils. Margination of neutrophils was noted and DIF was negative.

LABORATORY RESULTS

Positive or abnormal:
8/2008: WBC 20.3 K/UL [ref 4.0-11.0], PMN 5% [ref 50-60], Lym 81% [ref 15-40], Atypical lymphocytes 6, Absolute neutrophil count 1218 [ref 1500-8000]
Negative or normal:
Hbg, Hct, Plt, % Eosinophils, % monocytes, LFT, BMP

DIAGNOSIS

Eosinophilic dermatosis of myeloproliferative disease

TREATMENT AND COURSE

Initial outside biopsy demonstrated many pityrosporum yeast forms within the follicles. The patient was treated with systemic diflucan and ketoconazole shampoo without improvement. He was then started on narrow band UVB twice weekly, sulfacet and topical pimecrolimus with some improvement after 2-3 months. Trials of topical steroids and acitretin were not effective. He continued to have flares of various degrees but never total clearance of lesions, despite completing a full course of chemotherapy, placing the underlying CLL in remission. Subjectively the phototherapy, as well as natural sunlight, in combination with topical pimecrolimus cream have been most beneficial at controlling associated pruritus and severity of lesional flares.

PATIENT B

HISTORY OF PRESENT ILLNESS

A 61 year old Caucasian male with history of chronic lymphocytic leukemia (CLL) presented with a two week history of dozens of small, intensely pruritic papules on the face and neck. The eruption appeared after a fourth cycle of bendamustine chemotherapy for progressing CLL. The patient denied recent travel or new medications other than the chemotherapy. He did not recall exposure to insect bites. All systemic medications were held per patient preference due to concern for possible drug eruption but failed to yield clinical improvement.

PAST MEDICAL HISTORY

Chronic lymphocytic leukemia, hypertension, esophageal reflux, gout, degenerative disc disease

MEDICATIONS

Allopurinol
Bendamustine
Hydrochlorothiazide-Valsartan
Meloxicam
Ranitidine

ALLERGIES
No known drug allergies

FAMILY HISTORY
Non-contributory

SOCIAL HISTORY
Drinks 2-4 alcohol beverages daily. Never smoker. No drugs. Retired appliance repairman. Married with four children. Volunteers weekly providing food to the homeless population.

PHYSICAL EXAM
Dozens of small, 2-5 mm, indurated, flesh colored to pink papules on the forehead, cheeks and posterior auricular neck. No scale. Few excoriations.

HISTOPATHOLOGY
09/30/2010 Right neck: Subacute spongiotic dermatitis with dermal lympho-eosinophilic infiltrate, and acutely inflamed scale crust. PAS stain negative for fungal organisms.

10/20/2010 Forehead: Dermal lympho-eosinophilic infiltrate and isolated follicular spongiosis/mucinosis.

LABORATORY RESULTS
Positive or abnormal:
9/2009: WBC 46.71 K/UL [ref 4.0-11.0], Lym 85% [ref 15-40], PMN 6% [ref 50-65], Atypical lymphocytes 4, Hbg 11.4 g/dL [ref 13-17], Hct 34.7 [ref 40-51], Plt 103 [ref 130-400]
Negative or normal:
Monocytes, Eosinophils, Absolute neutrophil count, LFT, BMP

DIAGNOSIS
Eosinophilic dermatosis of myeloproliferative disease

TREATMENT AND COURSE
The facial eruption was treated with topical steroids and subsequent cessation of bendamustine with near complete resolution. A few months later when the eruption flared again, but to lesser degree, topical steroids were not felt to be beneficial to the patient. He applied topical terbinafine to individual lesions with subjective relief of pruritus. However, a trial of oral antifungal therapy was not clinically beneficial. Recently he was started on doxycyline 100 mg twice daily and the severity of flares has remained mild and stable. He currently reports 3-4 lesions per month, each lasting 1-2 weeks.

DISCUSSION
Eosinophilic dermatosis of myeloproliferative disease is a term proposed by Byrd, et al in 2001 to describe a specific pruritic cutaneous eruption seen in patients with various hematologic malignancies. Prior reports identified as insect bite-like reactions, exaggerated arthropod bites, itchy vesiculobullous eruption in chronic lymphocytic leukemia (CLL) and possibly even eosinophilic pustular folliculitis in the setting of hematologic malignancy or human immunodeficiency virus (HIV), are likely all on a spectrum of the same condition.

Exaggerated reaction to mosquito bites in patients with CLL was first described in 1965 by Weed. Since that time various authors pointed out that although these patients may indeed demonstrate a hypersensitivity reaction to insect assault, a separate entity exists in which the clinical and histopathological picture of individual lesions is suggestive of arthropod bite,

however, patients with this condition rarely recall insect assault, and clinically no punctum is visible, therefore evidencing the need for alternate terminology.

Eosinophilic dermatosis of myeloproliferative disease is an eruption characterized by persistent, erythematous, pruritic, papulonodules and distinctive lymphocytic and eosinophilic infiltrates. Onset can occur at any time during the course of the hematologic dyscrasia, and has even been reported to preclude the laboratory evidence of malignancy. Byrd et al proposed criteria for the diagnosis as: (1) pruritic papules, nodules and/or a vesiculobullous eruption resistant to conservative treatment; (2) eosinophil-rich dermal lymphohistiocytic infiltrate (superficial and deep) on histopathologic examination; (3) exclusion of other causes of tissue eosinophilia, including immunobullous diseases, parasitic infections, known insect bite, or drug reactions; and (4) pre-existing diagnosis of a hematologic malignancy or dyscrasia or its subsequent development.

Treatment of this condition is characteristically difficult. In efforts to provide relief to patients from the associated pruritus and lesional flares, a number of treatment modalities have been anecdotally reported with marginal success. Phototherapy, including natural sunlight, narrow band UVB and Dead Sea salt plus UVA may be helpful in some patients. Others report improvement of the skin condition with chemotherapeutic treatment of the underlying malignancy, however, a number of patients report their first flare of skin lesions shortly after chemotherapy initiation. Other isolated reports of chlorambucil, interferon alpha, systemic and topical corticosteroids, dapsone, and intravenous immunoglobulin demonstrate isolated success. Palliative therapy with oral antihistamines and other anti-pruritic agents are common.

In our clinic, patient A has tried topical steroids, topical calcineurin inhibitors, sulfacet, short-term acitretin, narrow band UVB and cautious natural sunlight. He states that the topical calcineurin inhibitor is most efficacious for him as well as natural sunlight. Patient B has tried topical steroids with variable improvement. Oral doxycyline has provided stabilization of lesion flares. As mentioned above, our patient reports more relief from symptoms with terbinafine cream when compared to topical steroids, however systemic terbinafine was not clinically beneficial.

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CHICAGO DERMATOLOGICAL SOCIETY **CASE # 6**

Presented by Joshua Mandrell, MD and David Eilers, MD
Section of Dermatology, Edward Hines, Jr. VA Hospital

HISTORY OF PRESENT ILLNESS

This 28 year-old Caucasian male presented to dermatology clinic with a recurrent, mildly pruritic eruption predominately on his trunk and distal extremities. This rash had spontaneous onset and remission and was unresponsive to antihistamines and topical betamethasone cream. There were no associated upper respiratory or viral symptoms. The patient had received intravenous steroids in the emergency department which improved the eruption in a prompt, but partial, manner. The patient reported three to four episodes where, upon waking up, the rash spontaneously appeared and then incompletely regressed after one hour. The patient admitted to a significant amount of emotional stress and to consumption of at least a large coffee daily. The patient also had a coexistent allergic contact dermatitis from known contact to poison ivy.

PAST MEDICAL HISTORY

Post-traumatic stress disorder

MEDICATIONS

Propranolol

ALLERGIES

No known drug allergies

FAMILY HISTORY

Non-contributory

SOCIAL HISTORY

Stopped smoking two months prior to presentation (after approx 12 pack years), no illicit drugs, social alcohol.

PHYSICAL EXAM

Physical examination revealed numerous 2-4 mm erythematous blanchable macules and faint papules, each surrounded by a narrow rim of pallor on the lower back, buttocks, bilateral arms and hands, and bilateral ankles and feet.

DIAGNOSIS

Adrenergic urticaria

TREATMENT AND COURSE

At the initial visit in July 2010, the patient was prescribed a 15-day course of oral prednisone for the coexistent allergic contact dermatitis to *Toxicodendron radicans* and counseled on avoiding known physical urticarial triggers including pressure and excess sweating. At two-week follow-up, he noted recurrence of the urticarial lesions despite antihistamine and prednisone therapy. The patient was prescribed propranolol (20mg twice daily). The patient has remained clear and symptom-free with propranolol monotherapy over a follow-up period of ten months. He states that the rash remains under control with propranolol without side effects from treatment. He reported one instance when the rash briefly reoccurred during a three-day period while he was waiting for a propranolol refill.

DISCUSSION

Adrenergic urticaria (AU) is a rare subtype of stress-induced physical urticaria. First described by Shelley and Shelley in 1985, adrenergic urticaria is distinguished from the more common cholinergic urticaria by the presence of pallid, vascoconstricted skin surrounding small red or pink wheals. Unlike cholinergic urticaria, adrenergic urticaria is not induced by exercise or increases in body temperature; rather, known triggers include emotional upset, coffee, tea, chocolate, and ginger.

Limited medical literature available on adrenergic urticaria identifies the involvement of norepinephrine, degranulated mast cells, and histamine, though precise mechanisms have yet to be elucidated. In AU, serum catecholamines, norepinephrine, dopamine and epinephrine become elevated, while histamine and serotonin levels remain normal. Diagnosis of adrenergic urticaria can be confirmed via an intradermal injection of 3 to 10mg of norepinephrine, which induces the characteristic lesions. Of note, cholinergic urticaria, comparatively, is induced by the action of acetylcholine on mast cells, which then release histamine on capillaries, causing dermal edema and cutaneous wheals surrounded by a distinctive red halo. Cholinergic urticaria can be confirmed by intradermal injection of nicotine.

Oral propranolol and trigger avoidance are currently the best-known treatments for adrenergic urticaria. Propranolol, a non-selective beta-adrenoreceptor antagonist, blocks mast cell beta-2 receptors, thus regulating degranulation. Selective beta-blockers, including atenolol and bisoprolol, do not successfully treat AU. Non-specific therapies, including tranquilizers and antihistamines, also ease symptoms.

(A special thanks to Sara Hogan, Loyola Stritch School of Medicine medical student, for her assistance in this case.)

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CHICAGO DERMATOLOGICAL SOCIETY **CASE # 7**

Presented by Loebat Julia Kamalpour, MD, Anthony Peterson, MD, Brian Nickoloff MD, PhD, and Kelli Hutchens, MD
Division of Dermatology, Loyola University Medical Center

UNKNOWN #2

CHICAGO DERMATOLOGICAL SOCIETY **CASE # 8**

Presented by Vanessa Lichon, MD, Aaron Pace, MD, Paul Getz, MD, Steven Goulder, MD, Brian Nickoloff, MD, PhD, and Kelli Hutchens, MD
Dundee Dermatology, West Dundee, IL
Division of Dermatology, Loyola University Medical Center

HISTORY OF PRESENT ILLNESS

A 51 year-old Hispanic female presented to an outside dermatologist for evaluation of melasma. During her visit she noted a lesion on her left thumb that had been present for approximately twenty years. She stated the lesion was stable in size and was asymptomatic. The lesion was biopsied and sent for consultation and management.

PAST MEDICAL HISTORY

Gastroesophageal reflux disease, hypertension

MEDICATIONS

Hydrochlorothiazide Omeprazole

ALLERGIES

No known drug allergies

FAMILY HISTORY

Non-contributory

SOCIAL HISTORY

Non-contributory

PHYSICAL EXAM

On the left distal thumb approximating the distal nail fold was a 0.6cm x 0.6cm hyperkeratotic, non-tender, firm, slightly verrucous periungual papule. No nail plate deformity was seen.

HISTOPATHOLOGY

Biopsy, by shave technique, left distal thumb (outside pathology report)
Biopsy revealed a spindle cell neoplasm with focal storiform growth pattern and a small area of sclerosis. The tumor was positive for CD34, negative for factor XIIIa and negative for S100. These features and immunoprofile were consistent with dermatofibrosarcoma protuberans

Skin, left distal thumb, first Mohs stage – H&E frozen sections examined during Mohs micrographic surgery and tissue block thawed for immunostains and permanent H&E
Immunostains revealed spindle-shaped tumor cells to be positive for CD34 and negative for factor 13a, P63, MART-1, S100, and smooth muscle actin, confirming the diagnosis of dermatofibrosarcoma protuberans.

Nail plate avulsion
Consistent with unremarkable appearing nail plate with no evidence of malignancy.

DIAGNOSIS

Dermatofibrosarcoma protuberans on the left distal thumb

TREATMENT AND COURSE

A biopsy by shave technique was performed by the patient's primary dermatologist and the pathology demonstrated dermatofibrosarcoma protuberans. The patient was referred to Loyola for evaluation and management options. A decision was made to perform Mohs micrographic surgery due to the location, clinically ill-defined borders, need for tissue conservation and desire to have full histologic confirmation of margins to ensure complete tumor resection. Immediately prior to Mohs surgery, a nail plate avulsion was performed to facilitate tumor extirpation. The nail plate was sent to pathology for H&E. An initial Mohs layer was taken with a 3mm margin. Evaluation of the first stage demonstrated positive deep and peripheral margins for a spindle cell tumor consistent with dermatofibrosarcoma protuberans. The tissue block was thawed and sent to pathology for immunostains. Ultimately, the tumor was cleared in four stages. The resultant defect measured 1.7cm x 1.6cm and was repaired with a full-thickness skin graft. To facilitate wound care at home and per patient's request, the graft was taken from the patient's left shoulder. At the patient's three month follow-up the surgical site was well-healed with no signs of local recurrence and the nail plate demonstrated good re-growth. There was no palpable left axillary, olecranon, or intercalated lymphadenopathy at the time of follow-up. The patient was encouraged to continue to monitor for signs of recurrence and to maintain close follow-up with her primary dermatologist.

DISCUSSION

Dermatofibrosarcoma protuberans (DFSP) is a locally aggressive tumor of intermediate malignancy that accounts for <2% of soft-tissue sarcomas. The tumor most commonly occurs on the trunk (50-60%), followed by the upper limbs (20-30%), and the head and neck (10-15%). The tumor is rarely reported occurring on the distal extremities, and less than five cases are reported in the literature involving a digit. Adults aged 30-50 years old are most likely to develop DFSP, and the annual incidence is approximated at 0.8 cases per million per year.

Clinically, DFSP usually presents as an asymptomatic, firm slow-growing nodular or plaque-like growth which is frequently indurated. Over time, these lesions may become symptomatic due to deeper tissue invasion into the fascia, muscle, and even bone. Often, there may be a delay in diagnosis due to low clinical suspicion for disease. Despite this delay, DFSP rarely metastasizes, with a reported rate of less than 2-5%.

Histologically, DFSP is characterized by a dense collection of spindle cells with whorled, storiform, or cartwheel configurations. In early lesions, a Grenz zone may be seen. The spindle cells may course throughout the dermis and invade the subcutaneous fat, creating a honeycomb or lace-like appearance. Irregular projections of tumor cells may deeply invade fascia and muscle. There is low mitotic activity in these lesions.

DFSP may be difficult to distinguish from dermatofibroma, dermatomyofibroma, fibrosarcoma, leiomyosarcoma, malignant fibrous histiocytoma (MFH), or atypical fibroxanthoma (AFX) and immunohistochemistry is often utilized to establish the diagnosis. Generally, DFSP stains positive for CD34 and negative for factor XIIIa, unlike dermatofibroma (CD34 negative, factor XIIIa positive). DFSP can be distinguished from desmoplastic melanoma, neurofibroma, schwannoma and malignant peripheral nerve sheath tumor as it is almost always S-100 negative. DFSP is CD68 negative, helping to distinguish from MFH and AFX.

While surgical excision remains the gold standard for treatment of DFSP, specific surgical modalities have been debated in the literature. Some advocate the use of wide local

excision (WLE) with margins ranging from 2.5cm – 4cm, while others have begun to recommend Mohs micrographic surgery (MMS) as the treatment of choice. DFSP, due to its invasive nature, has a high recurrence rate after WLE, with ranges in the literature between 20-70%. As MMS examines 100% of the histological border of a tumor, recurrence rates have been much lower, with a recent review noting 6 recurrences of 474 cases treated with MMS (1.27% recurrence rate).

Radiation therapy is considered for patients with metastatic or recurrent DFSP, especially in areas of non-resectable tumor. Most recently, targeted molecular therapy has emerged in the management of DFSP. Over 90% of DFSPs have detectable chromosomal rearrangements that lead to the excessive production of platelet-derived growth factor receptor (PDGFR) ligand. Imatinib mesylate (Gleevac), a selective tyrosine kinase inhibitor, has efficacy against the tyrosine kinase receptor PDGFR, thereby inhibiting the ability for tumor cells to divide and expand. In 2006, imatinib was approved by the US Food and Drug Administration as a single agent or adjuvant treatment for patients with non-resectable, recurrent, or metastatic DFSP. Off-label use of imatinib includes preoperative use to decrease tumor burden prior to surgical removal.

Few case reports exist in the literature describing DFSP on the digits. Our case highlights the use of MMS as a tissue-sparing process, thereby preserving full function of our patient's digit and avoiding amputation. To date, our patient remains tumor-free although long-term follow up is warranted and was emphasized.

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CHICAGO DERMATOLOGICAL SOCIETY **CASE # 9**

Presented by Anita Shetty, MD, Rama Vaitla, MD, Anthony Peterson, MD, Brian Nickoloff MD, PhD, and Kelli Hutchens, MD
Division of Dermatology, Loyola University Medical Center

HISTORY OF PRESENT ILLNESS

A 42 year-old African-American female presented with a six-month history of dark discoloration of the skin on the face, shoulders, and back. She denied any pain or pruritus associated with the lesions. She denied starting any new oral or topical medications prior to the onset of the lesions, and denied previous or current therapy with minocycline, antimalarials, amiodarone, silver, hydroquinone, or over-the-counter topical preparations or supplements. She had no treatment of the lesions prior to presentation.

PAST MEDICAL HISTORY

Hypertension, pituitary microadenoma, toxic thyroid nodule s/p lobectomy in 2009 with subsequent hypothyroidism, vitamin D deficiency

MEDICATIONS

Amlodipine
Ergocalciferol
Levothyroxine

ALLERGIES

Sulfamethoxazole

FAMILY HISTORY

Thyroid disease, son with multiple endocrine neoplasia type I; no history of pigmentary abnormalities

SOCIAL HISTORY

The patient had a 7-pack-year smoking history but quit several years prior to presentation. She denied use of alcohol or illicit drugs.

PHYSICAL EXAM

Physical exam revealed blue-gray, well-demarcated, symmetrical patches on the bilateral lower eyelids and zygoma, bilateral shoulders, and midline upper back. Wood's lamp examination of the lesions did not reveal any pigment enhancement.

HISTOPATHOLOGY

A 4 mm punch biopsy of the upper back demonstrated scattered elongated pigmented cells in the dermis. The cells were positive for Melan-A, MITF, and S100 by immunohistochemistry, confirming their melanocytic nature. Fontana-Masson stain was positive and Prussian blue stain was negative, confirming the pigment to be melanin. Periodic acid-Schiff stain was also negative.

DIAGNOSIS

Multifocal acquired dermal melanocytosis

TREATMENT AND COURSE

The patient has been referred for treatment of the lesions with a Q-switched neodymium:yttrium-aluminum-garnet (Nd:YAG) laser.

DISCUSSION

Acquired dermal melanocytosis (ADM) comprises a variety of conditions that are characterized by abnormal cutaneous pigmentation. Many entities fall under the designation of ADM, and are defined by their clinical presentation. When occurring at or soon after birth, the lesions are known as Mongolian spots, are generally located on the lumbosacral back, and spontaneously regress during childhood. Nevus of Ota and Ito generally occur in infancy or at puberty and persist throughout life. Nevus of Ota classically is distributed adjacent to the eye and can involve the conjunctiva, while nevus of Ito almost always occurs on the shoulder, neck, supraclavicular, and/or upper arm.

Several types of ADM can appear in adulthood; most commonly, acquired bilateral nevus of Ota-like macules (ABNOM, or Hori nevus), acquired unilateral nevus of Ota (Sun's nevus), and extrafacial ADM on the trunk and extremities. Histologically, ADM entities are indistinguishable; all demonstrate dermal melanocytes, bipolar or oval in shape, scattered in the upper and middle portions of the dermis. Overlying epidermal hyperpigmentation has been described in ABNOM, but is usually not observed in nevus of Ota or Ito.

ABNOM, the most frequently seen of the ADM entities, is predominantly described in Japanese female patients, with onset in the third or fourth decade of life. There is often a positive family history. This case is unusual in the occurrence of bilateral facial and truncal lesions, as well as a midline lesion. In addition, ADM without preceding inflammation has only rarely been described in African-American patients.

The etiology of ADM is thought to involve ectopic placement of inactive, poorly melanized dermal melanocytes during embryological development. These dormant melanocytes are activated later in life in response to ultraviolet exposure, excessive sex hormones, chronic inflammation, or an unknown trigger. The persistence of these melanocytes is proposed to be secondary to a protective extracellular sheath enclosing the involved dermal melanocytes. These sheaths decrease in size with age and usually disappear in melanocytes of Mongolian spots; in contrast, extracellular sheaths of nevus of Ota melanocytes increase in thickness with advancing age. Spontaneous regression, malignant transformation, and association with systemic disease have not been described in ADM.

Treatment of ABNOM is difficult, but is sometimes accomplished with the use of Q-switched ruby, alexandrite, or Nd:YAG lasers. The response to treatment is generally not as complete as that seen in nevus of Ota or Ito; in addition, the risk of post-treatment hyperpigmentation is greater. Any overlying epidermal hyperpigmentation may respond to hydroquinone or superficial-to medium-depth chemical peels.

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CHICAGO DERMATOLOGICAL SOCIETY **CASE # 10**

Presented by Aaron Pace, MD, David Eilers, MD, and Madhu Dahiya, MD
Section of Dermatology, Edward Hines, Jr. VA Hospital

HISTORY OF PRESENT ILLNESS

A 75 year-old male with a recently diagnosed monoclonal gammopathy, described a 1-week history of red bumps on the left forearm. There was no associated bleeding, itching, or pain. The patient had been using nystatin cream without improvement.

PAST MEDICAL HISTORY

Monoclonal gammopathy of undetermined significance (with 2 monoclonal spikes), leukocytoclastic vasculitis, coronary artery disease, hyperlipidemia, obesity, hypertension, diabetes, atrial fibrillation, depression, obstructive sleep apnea, and glaucoma.

MEDICATIONS

Calcium
Digoxin
Docusate
Folic Acid
Gabapentin
Insulin
Magnesium
Omeprazole
Potassium
Simvastatin
Tramadol
Travaprost Oph Solution

ALLERGIES

Cholestyramine and niacin

FAMILY HISTORY

Non-contributory

SOCIAL HISTORY

Non-contributory

PHYSICAL EXAM

Exam of the bilateral forearms revealed scattered red shiny papules, violaceous ulcerated nodules, and occasional telangiectasias. The left forearm was worse than the right. A few of the lesions had a faint yellow hue or a pale atrophic center.

On the temples there were faint violaceous arcuate and annular plaques.

HISTOPATHOLOGY

Biopsy of the left forearm revealed palisading granulomas throughout the dermis with central necrobiotic zones. Within these zones were some acute inflammatory cells. Xanthoma cells were rarely noted; however, multinucleate giant cells were present and there were clusters of plasma cells, which were more prominent at the base of the lesion. Special stains including PAS, GMS, Gram, AFB and colloidal iron were negative. Polarization did not reveal foreign material.

Bone marrow biopsy in 8/2009 showed slight hypercellularity at 30% with trilineage hematopoiesis with 5% plasma cells and 11% lymphocytes. FISH studies were normal.

Repeat bone marrow biopsy in 11/2010 showed a slight hypercellularity at 30% but the plasma cell component had increased to 8% (still within normal limits, <10%). These cells

showed a decreased CD128 staining pattern (which may indicate a shift toward myeloma cells). FISH showed a new abnormality, a CCND1 (11q13) deletion of which the significance is unclear.

LABORATORY RESULTS

Serum protein electrophoresis has on multiple occasions demonstrated 2 monoclonal bands, a monoclonal IgG kappa band in the beta-gamma region and a monoclonal IgG lambda band in the gamma region.

Serum immunoglobulin levels			
Date	IgG (nl 700-1600mg/dL)	Kappa light chains (nl 74-295 mg/dL)	Lambda light chains (nl 32-156 mg/dL)
7/2009	3380	976	352
12/2009	4500	867	513
6/2010	2400	690	381
9/2010	1870	579	332
11/2010	1670	490	273
4/2011	1580	437	268

Normal or negative: IgA and IgM levels, CBC, iron studies, thyroid, and liver function tests.

Abnormal or positive: elevated creatinine (1.46 mg/dL), elevated triglycerides (186 mg/dL), elevated LDL (101 mg/dL), decreased HDL (36 mg/dL), decreased albumin (3 g/dL)

RADIOLOGY

CT of the chest, abdomen, and pelvis in 2009 revealed axillary, mediastinal, and abdominal lymphadenopathy. A repeat CT in 2010 demonstrated resolution of the lymphadenopathy, which was thus thought to be a reactive process.

August 2010 – Skeletal survey for lytic lesions was normal.

DIAGNOSIS

Necrobiotic xanthogranuloma (NXG)

TREATMENT AND COURSE

The patient was first diagnosed with a monoclonal gammopathy of undetermined significance in 7/2009 and with NXG in 5/2010. Since then he has had close follow up with dermatology, hematology/oncology, and ophthalmology. Initially his lesions were treated with topical clobetasol twice a day with steroid holidays, and the patient did well. At one point, when the clinical photos were taken, he developed ulcerations after his small dog scratched his left forearm. Several of these ulcerations did not improve with clobetasol. Mechlorethamine was added to his regimen with some improvement of the ulcerations but the lesions persisted. His course continued waxing and waning without progression; however, several months ago he began to flare and he developed scattered lesions on the rest of his body. Concurrently mechlorethamine was no longer available and he was switched to carmustine. Since then his disease has continued to progress. Ophthalmology follows the patient, and treats his glaucoma and chronic uveitis. Hematology/oncology has been reluctant to treat his gammopathy since his IgG levels have continued to decrease.

DISCUSSION

Necrobiotic xanthogranuloma (NXG) is a rare and chronic granulomatous disease. It was recently described, being first clearly delineated in 1980 by Kossard and Winkelmann. There is debate in the literature about the "classic" clinical presentation. In general, the disease involves periocular skin in 80 to 85 percent of patients and it occurs equally in men and women. Typically, it occurs in the sixth or seventh decade but NXG has occurred in people as young as 17. The lesions often ulcerate and heal with atrophy. The face, trunk, and limbs may all be affected. Some authors argue that the majority of patients first develop lesions on the trunk and extremities and only later have periorbital involvement. The clinical appearance can vary from a classic yellow xanthomatous appearance to violaceous or red with only a hint of a xanthomatous hue. The severity of either the hematologic or the granulomatous systemic involvement cannot be predicted by the extent of skin disease. Systemic granulomatous involvement occurs in less than 15% of patients; granulomatous lesions may involve the heart, lungs, kidneys, liver, spleen, intestines, skeletal muscle, central nervous system, myocardium, larynx, pharynx, and ovary. The eye may also be affected; findings include iritis, uveitis, conjunctivitis, and keratitis.

Almost all patients have an underlying hematologic disorder. The vast majority (80%) have a monoclonal IgG kappa gammopathy. Cases have been reported to have two monoclonal spikes, as in our patient, but this is much less common. Ten percent go on to develop multiple myeloma, which emphasizes the need for life long follow up. Other underlying hematologic processes that have been associated include multiple myeloma, Hodgkin's and non-Hodgkin's lymphoma, and chronic lymphocytic leukemia. Other abnormalities that are seen but not thought to be causative are leukopenia, C4 deficiency, elevated ESR, and cholesterol. Bone marrow biopsy frequently reveals a plasmacytosis. NXG may precede or follow the diagnosis of the underlying hematologic disorder by as much as a decade.

The mechanism of this disease process is poorly understood. The inflammatory cell infiltrate of lymphocytes, plasma cells, and histiocytes is polyclonal. One theory suggests that the monoclonal protein may be binding lipoprotein receptors and stimulating xanthoma formation. Another hypothesis is that deposition of the circulating paraprotein in the skin elicits a granulomatous response. Investigational data points at a polyclonal process whereas one would expect a monoclonal process if paraprotein deposition was indeed responsible. Recently, a European study of multiple myeloma patients with NXG demonstrated *Borrelia sp.* in several patients' lesions using focus-floating microscopy, where sections are scanned both vertically and horizontally at the same time. Clearly, further exploration of the mechanism of this disease needs to be performed to better elucidate the disease process and perhaps result in more effective treatments.

On histopathology, distinct changes are seen. There are extensive granulomatous changes in both the dermis and subcutis, broad areas of collagen necrobiosis and granulomas. Touton type multi-nucleated giant cells are common. The xanthomatous component can be variable. The xanthomatous histiocytes may extend to the papillary dermis and be present in an ulceration. The histiocytes are CD68 positive and CD1a negative confirming a non-Langerhans cell process. Cholesterol clefts may be present as well as lymphocytes, lymphoid follicles, and the rare eosinophil. Compared to necrobiosis lipoidica, the process appears more cellular, cholesterol clefting is much more common, and more atypical giant cells. Colloidal iron may reveal only scant mucin.

Treatment is primarily directed at any underlying hematologic abnormality. There is no single best therapy for NXG. Topical, oral, and intralesional steroids and chlorambucil are the most reported treatments and have been reported to clear the cutaneous lesions. The

other alkylating agents, melphalan and cyclophosphamide, have been used with more varying degrees of success than chlorambucil. Nitrogen mustard, azathioprine, localized radiotherapy, PUVA, cyclosporine, antimicrobials, retinoids, interferon α-2a, intravenous immunoglobulin, and plasmapheresis with hydroxychloroquine have all been utilized with varying degrees of success. Interestingly, a recent case series of treatment of NXG with IVIG showed no effect on one patient's monoclonal gammopathy, but completely cleared the cutaneous lesions. Surgical excision has been tried as well, but recurrence rates approach 40%.

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CHICAGO DERMATOLOGICAL SOCIETY **CASE # 11**

Presented by Krisanne Sisto, MD, David Eilers, MD, Madhu Dahiya, MD, and Kelli Hutchens, MD
Section of Dermatology, Edward Hines, Jr. VA Hospital

HISTORY OF PRESENT ILLNESS

A 34 year-old Hispanic man presented to the emergency room with a six week history of painful, non-healing skin lesions and was admitted to general medicine for further evaluation. According to the patient, the lesions began as small pink bumps that evolved into persistent draining sores. He had been seen in the emergency room for the same complaint four days prior to this encounter and had been started on a nine day 60 mg prednisone taper by the emergency room physician. He did not report improvement with this therapy and complained of malaise, low grade fever and night sweats for the past several weeks. Of note, in 2003 the patient had been injured in a shrapnel explosion while on military duty in Baghdad. He stated that multiple pieces of shrapnel were still embedded in his skin and that the lesions only occurred in areas where shrapnel was present. Prior to his admission to the ward and prior to evaluation by dermatology, the patient received 125 mg of methylprednisolone and 1g of vancomycin in the emergency room.

PAST MEDICAL HISTORY

Traumatic injury while on military duty in 2003.

MEDICATIONS

None

ALLERGIES

No known drug allergies

FAMILY HISTORY

Non-contributory

SOCIAL HISTORY

The patient denied use of alcohol, tobacco or illicit drugs. No history of high risk sexual behaviors. He was on active military duty in Iraq in 2003.

PHYSICAL EXAM

On physical exam several large depressed pink papules with serous and hemorrhagic crust were present on the left central cheek. Small pink papules, some with central umbilication, were scattered over the left cheek and left temple. A few indurated pink papules were present on the left nasal rim and there was a cluster of depressed pink scars on the lower left cheek. There were several indurated crusted pink papules on the left ear as well as multiple grey papules, representing shrapnel. On the left anterior lower leg there was a large cluster of erythematous crusted papules and nodules, several with central ulceration or eschar. Several tender erythematous nodules with central crust were present on the bilateral volar surfaces of the hands and fingers. Shrapnel remnants were noted on both palms. The trunk, right side of the face, right leg and right arm were clear.

Lymph node exam revealed prominent bilateral inguinal lymphadenopathy, greater on the left than on the right.

HISTOPATHOLOGY

An initial incisional biopsy was obtained from a crusted nodule on the left anterior lower leg. It showed a partially ulcerated epidermis with adjacent pseudoepitheliomatous hyperplasia. The entire dermis and a superficially sampled part of the subcutis were filled with non-caseating epithelioid granulomas with a mild associated lymphocytic infiltrate. There were areas of necrosis and fibrinoid changes between granulomas. Polarizable foreign material was identified on some slides. Gram, periodic acid-Schiff, acid fast bacilli, Giemsa and Grocott's methenamine silver stains were negative for microorganisms.

Additional punch biopsies were obtained from the left leg nine days later. Hematoxylin and eosin staining again showed pseudoepitheliomatous hyperplasia and sarcoidal granulomas, nearly identical to the original biopsy. Special staining for microorganisms was negative. Additional tissue was sent to the Walter Reed Army Institute of Research Leishmania Diagnostic Laboratory. No amastigotes were seen and PCR for leishmania was negative.

A left inguinal lymph node obtained by general surgery also revealed well formed epithelioid granulomas, infiltrating lymphocytes and foci of necrosis between granulomas. Again, no microorganisms were identified with special staining. Leishmania genome amplification performed by the Armed Forces Institute of Pathology was negative. No foreign material was identified.

LABORATORY RESULTS

Abnormal or positive:

WBC 2.68 x 10^3 m/L [ref 4-11], 85% neutrophils [ref 40-80], 11.6% lymphocytes [15-45], 1.5% monocytes [ref 2-12], ALT 102 U/L [ref 10-65], AST 115 U/L [ref 10-37], total bilirubin 1.7 mg/dL [ref 0.2-1.0]

Normal or negative:

Bacterial, fungal and AFB tissue culture (performed on three separate specimens), Hgb, platelets, BMP, HIV, RPR, hepatitis B & C, CRP, ESR, PT, PTT, C-ANCA, P-ANCA, ACE level, EBV IgM (IgG positive), CMV, lyme polyvalent, quantiferon gold, *Erlichicha chafensis* IgM, IgG, urine *Histoplasma* antigen, *Blastomyces* antibodies, *Coccidiodes* antibodies, *Leishmania donovani, braziliensis, mexicana* and *tropicalis* IgM & IgG

RADIOLOGY

Abnormal or positive:

Chest x-ray: bilateral hilar lymphadenopathy

CT chest and abdomen: bilateral hilar, mediastinal and bilateral axillary lymphadenopathy; mild non-specific reticulonodular opacities in the left upper lobe.

Left femur, tibia and fibula x-ray: Multiple small metallic particles in the soft tissues of the thigh and the leg.

Right hand x-ray: Soft tissue swelling. Metallic foreign body near the soft tissue of the first metacarpal and right thumb.

Left hand x-ray: Soft tissue swelling. Small metal fragments in distal part of the middle finger. A few metal fragments were also seen in the ring and index fingers.

DIAGNOSIS

Sarcoidosis

TREATMENT AND COURSE

Extensive work-up by the infectious disease service revealed no evidence of infectious etiology. Rheumatology evaluated the patient and did not find an autoimmune explanation for his condition. Pulmonary function tests were within normal limits. The patient was followed closely while the etiology of his condition was being worked up but therapeutic

measures were not instituted during this time. Within a week of his initial encounter with dermatology it was clear that his skin lesions were starting to improve. The improvement was attributed to the four days of prednisone and one dose of methylprednisolone he had received early in his presentation.

Given the findings of hilar lymphadenopathy, extensive peripheral lymphadenopathy, a negative infectious work up and sarcoidal granulomas on skin and lymph node biopsies, a diagnosis of sarcoidosis was made. After an extensive discussion of the risks and benefits of immunosuppressive therapy the patient was started on prednisone 40 mg daily. After several weeks of therapy he has not developed any new lesions and has had slow improvement of existing lesions. His white blood cell count has increased into the normal range and transition to a steroid sparing agent such as methotrexate is being considered.

DISCUSSION

Cutaneous lesions present in 20-35% of patients with systemic sarcoidosis. A variety of morphologies are seen. Papular lesions, typically occurring on the periorbital skin or the nose, are the most frequently encountered type of lesion. Infiltrative plaques on the face or extensor surfaces may be distinctive but occur less commonly. Even less common presentations include hypopigmented patches, subcutaneous nodules and cicatricial sarcoidosis. Ulcerative lesions are rare and when present often represent an early manifestation of systemic disease. The pretibial area is reported as the most frequently involved site of ulcerative cutaneous sarcoidosis, although lesions occurring on the face, trunk and extremities have been reported.

Making a diagnosis of sarcoidosis is often challenging. There is no definitive diagnositic criteria; diagnosis is based on a constellation of clinical and radiologic findings, histologic pattern and the exclusion of other diagnoses.

Clinically, patients often present with complaints of fatigue, malaise and low grade fever. Sarcoidosis can affect any organ system and the severity of disease varies widely. Ninety percent of patients have lung and hilar lymph node involvement. Forty percent have peripheral lymphadenopathy. Ocular involvement occurs in 20-40% of patients and cardiac involvement in approximately 25%. Up to 75% of patients will have liver involvement if biopsied and clinically these patients may have abnormal liver function tests. A lesser proportion of patients have hematopoietic, neurologic, musculoskeletal or gastrointestinal involvement. The most classic and earliest radiographic finding is hilar lymphadenopathy. Reticular lung opacities, more often in the upper lobes than the lower, may appear with advancement of disease.

The prototypical sarcoidal granuloma is a non-caseating epithelioid granuloma with scant mononuclear cell infiltrate found within the dermis and sometimes extending into the subcutis. Asteroid and Schaumann bodies may be found within multinucleate giant cells but are relatively non-specific. Epidermal changes are seen in approximately half of cases. Epidermal atrophy is the most frequent epidermal change observed. Rare cases of sarcoidosis with the finding of pseudoepitheliomatous hyperplasia have been reported. Necrosis is uncommon but does not exclude the diagnosis of sarcoidosis in the correct setting.

The main histologic differential diagnosis is infection and granulomatous foreign body reaction, particularly in cases with necrosis or pseudoepitheliomatous hyperplasia. Mycobacterial infections, deep fungal infections, leishmaniasis and syphilis are highly suspect and need to be carefully ruled out. Foreign bodies identified in biopsy specimens

were once thought to exclude the diagnosis of sarcoidosis, however the frequency of foreign matter in cutaneous sarcoidosis appears to be much greater than once thought. Foreign bodies can be identified in 22-77% of skin specimens obtained from patients with a granulomatous dermatitis and a known diagnosis of systemic sarcoidosis, and there is at least one report of a patient with probable systemic sarcoidosis who developed cutaneous granulomas on the face 14 years after shrapnel wounds to the area. Foreign body granulomas, which are classically described as sarcoidal, cannot be distinguished from sarcoidosis based on histology alone and need to be evaluated within the context of the clinical scenario. It seems improbable that such a high number of isolated foreign body reactions would be present in the setting of systemic sarcoidosis. Rather, it is probable that the presence of foreign material often acts as a nidus for granuloma formation in patients with sarcoidosis.

Once a diagnosis of sarcoidosis is established corticosteroids are the mainstay of treatment. Methotrexate appears to be an effective steroid sparing agent. Hydroxychloroquine, thalidomide, isotretinoin, minocycline and allopurinol have all been reported to improve cutaneous disease. Topical or intralesional steroids may be of benefit in cases with limited skin involvement.

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CHICAGO DERMATOLOGICAL SOCIETY **CASE # 12**

Presented by Joshua Mandrell, MD and David Eilers, MD
Section of Dermatology, Edward Hines, Jr. VA Hospital

HISTORY OF PRESENT ILLNESS

This 72 year-old Caucasian male presented to the dermatology clinic in September 2006 with a 26-year history of a thickened right third fingernail which started after a baseball injury in 1980. The patient stated the lesion was asymptomatic. He noted no improvement with a three month treatment with topical clotrimazole.

PAST MEDICAL HISTORY

Prostate cancer s/p radiation treatment, lung nodules and chronic recurrent bronchitis, hypertension, hyperlipidemia, impaired fasting glucose, lower back pain, obstructive sleep apnea, obesity, anxiety and depression

MEDICATIONS

Albuterol/Ipatropium inhaler
Aspirin
Calcium/Vitamin D
Citalopram
Fish oil
Flunisolide nasal spray
Goserelin
Guafenesin
Hydrochlorothiazide
Multivitamin
Nifedipine
Vardenafil
Simvastatin

ALLERGIES

No known drug allergies

FAMILY HISTORY

Non-contributory

SOCIAL HISTORY

Social alcohol, history of tobacco use (stopped January 2006), no illicit drug use.

PHYSICAL EXAM

The right third nail plate was thickened and displayed yellow discoloration and transverse over-curvature with longitudinal ridging.

HISTOPATHOLOGY

On microscopic examination, a benign-mixed epithelial and stromal proliferative lesion was noted. The basaloid epithelium, lacking a granular layer, arose from the surface epithelial layer and formed a reticulated pattern extending into the stromal component. The stromal component was moderately cellular with spindle to fusiform nuclei dissecting between collagen bundles arranged in parallel arrays. The stromal component predominated over the epithelial component in this neoplasm. The processed nail was thickened and grossly showed filiform fibrous projections extending into the nail plate. The nail histologically displayed prominent oval, clear channels. Periodic acid-Schiff stain was negative for fungal organisms.

LABORATORY RESULTS

Abnormal or positive:

August 2009 - Moderate colonies of Chaetomium species

DIAGNOSIS
Onychomatricoma (OM), unguioblastic fibroma type

TREATMENT AND COURSE
The patient first presented in September 2006 and was lost to follow-up after his initial visit. When he presented again in August 2009, a culture of the nail plate revealed Chaetomium species. Lack of response to a 6-week course of terbinafine prompted the patient to consent to a nail avulsion with nail matrix incisional biopsy in August 2010. After receiving a diagnosis, the patient was offered conservative surgical excision but preferred clinical monitoring.

DISCUSSION
Onychomatricoma (OM) is a rare tumor originating from the nail matrix. Less than 50 cases have been reported in the literature with the majority of these being from Europe. It appears to affect men and women equally but is more common in adults (mean age of 48) and Caucasians. Fingernail involvement is twice as common as toenail involvement. Onychomatricoma is the only tumor that actively produces a nail plate.

Clinically, it presents with yellow discoloration along the entire nail plate, proximal splinter hemorrhages, and a tendency towards transverse over-curvature of the nail plate with prominent longitudinal ridging. Trauma has been associated with three cases reported in the literature. Our case makes the fourth. Xanthonychia and onychodystrophy of the nail are common. Pterygium, melanonychia, nail bleeding, and cutaneous horns have been reported but are rare. The tumor is typically painless with no radiographic bone involvement. Onychomycosis can be present which may serve as a predisposing factor or be secondary due to the deformed nail plate.

When the nail plate is avulsed and the proximal nail fold is turned back, the matrix tumor is exposed. This polypoid and filiform tumor has characteristic fingerlike fibrokeratogenous projections extending from the nail matrix into the nail plate.

Histologically, the tumor is fibroepithelial or biphasic with stromal and epithelial components. It has a lobulated and papillary growth pattern with two distinct areas that correspond to two anatomic zones. The base of the tumor corresponds to the proximal anatomic zone which begins at the root of the nail and extends to the cuticle. This area is composed of V-shaped keratinous zones similar to that of the normal matrix. If the nail is removed prior to excision, these areas can be avulsed leaving clear clefts. The superficial aspect of the tumor corresponds to the distal anatomic zone which is located in the region of the lunula. This area is composed of multiple digitate or fingerlike projections with a fibrous core and a thick matrix epithelial covering. These digitations extend into small cavities into the nail plate which can be visualized as clear channels or woodworm-like holes in processed specimens. A biphasic fibrous stroma is also observed with the superficial dermis being cellular with fibrillary collagen and the deep dermis more hypocellular with thicker collagen bundles. Angioproliferative areas as well as mast cells can be observed in some specimens.

Due to the histological differences among the described cases of onychomatricoma in the literature, a new classification based on the spectrum of epithelial to stromal ratio of stromal cellularity and the extent of nuclear pleomorphism was proposed in 2004. The unguioblastoma is an onychomatricoma tumor with a predominant epithelial component. The unguioblastic fibroma is a tumor where the cellular stroma is the prominent feature.

Atypical unguioblastic fibroma is the term applied to a tumor with increased mitotic activity and nuclear pleomorphism among the stroma.

The differential diagnosis is vast and includes acquired digital fibrokeratoma, periungual fibroma, onycholemmal horn, low-grade fibrosarcoma, superficial angiomyxoma, Bowen's disease, eccrine syringofibroadenoma, superficial acral fibromyxoma, neurofibroma, perineuroma, dermatofibrosarcoma protuberans, subungual keratoacanthoma, subungual squamous cell carcinoma, subungual and periungual porocarcinoma, subungual exostoses, and subungual and periungual verruca.

Most onychomatricoma tumors follow a benign clinical course. However, complete excision is advised to include the normal nail matrix proximal to lesion. This will prevent recurrence and serves as primary treatment. Some authors speculate a possible malignant potential for a subset of these tumors with cytological atypia, although no malignant cases have been reported.

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CHICAGO DERMATOLOGICAL SOCIETY **CASE # 13**

Presented by Loebat Julia Kamalpour, MD, Anthony Peterson, MD, Brian Nickoloff MD, PhD and Kelli Hutchens, MD
Division of Dermatology, Loyola University Medical Center

HISTORY OF PRESENT ILLNESS

A 57 year-old female presented for follow-up of biopsy-proven sclerodermatous graft-versus-host disease (GVHD) of the bilateral lower extremities. The patient was status-post allogeneic bone-marrow transplant in January 2007 for myelodysplastic syndrome. She reported steady progression of "bound-down" skin on the lower extremities with interim leg pain and tingling (worse at bedtime). The patient also had gastrointestinal involvement with six loose bowel movements per day and intermittent melena, which required frequent blood transfusions. Cutaneous treatment included intermittent topical clobetasol, however she had not noticed significant improvement in its appearance or associated symptoms.

Review of systems was significant for chronic fatigue and a six-month history of dry cough of unknown etiology.

PAST MEDICAL HISTORY

Ovarian cancer, myelodysplastic syndrome, GVHD of the gastrointestinal tract, ocular GVHD

MEDICATIONS

Acyclovir
Erythromycin ophthalmic ointment
Furosemide
Mycophenolate mofetil
Prednisone
Sulfa-trimethoprim
Tacrolimus

ALLERGIES

Calcipotriene, iodine penicillin G, prochlorperazine, tape

FAMILY HISTORY

Positive for non-melanoma skin cancer (mother and father)

SOCIAL HISTORY

Patient denied alcohol or illicit drug use. Prior 17 pack-year history of tobacco use, quit in 1988.

PHYSICAL EXAM

Examination of the bilateral lower extremities revealed woody, indurated erythematous plaques with a rippled appearance. Scarring and dyspigmentation were also apparent.

HISTOPATHOLOGY

Punch biopsy of the right lower extremity revealed increased fibrosis of the reticular dermis with a slight deep perivascular lymphocytic inflammation without plasma cells. Punch biopsy of the left lower extremity revealed increased dermal fibrosis.

LABORATORY RESULTS

Normal or negative:
PPD

DIAGNOSIS
Sclerodermatous graft-versus-host disease

TREATMENT AND COURSE
After multidisciplinary consultation with oncology and gastroenterology, infliximab 10mg/kg qweekly x 3 infusions was initiated. Despite our suggestion, the patient deferred concurrent use of methotrexate to prevent antibody formation.

Prior to initiation of infliximab, our patient was asked to rate both her pain and pruritus on scale of 0 to 9, with 0 representing no pain (no pruritus) and 9 representing worst pain (worst pruritus) imaginable. Our patient's subjective leg pain was 2-3 on average, with a peak of 8 and minimum of 1 over the course of the preceding week. Her average pruritus was 2-3 with a peak of 8 and minimum of 2. Her Dermatology Life Quality Index Score (DLQI) was 8, indicating that her GVHD had a "moderate effect" on her life.

The patient was seen in follow-up one week after completion of her 3rd infliximab dose. She reported a significant decrease in pruritus as well as decreased leg and knee pain. Her average pain level over the past week was 0 with a maximum pain level of 2, and her pruritus averaged 1 with a maximum of 4. The patient's DLQI score had decreased to 3, now indicating a "small effect" on patient's life.

She reported the same frequency of bowel movements (six per day) but a fewer number of these were now "loose". She reported no further melena since initiating the infliximab. Her chronic cough also resolved after 2 doses of Infliximab.

Physical exam revealed erythematous indurated plaques over her lower extremities with overlying erythema and mottled dyspigmentation secondary to prior chronic inflammation. Physical therapy and massage therapy were recommended.

DISCUSSION
Sclerodermatous GVHD is a rare form of chronic GVHD with a prevalence of approximately 3% in patients receiving allogeneic bone marrow transplants. It may be generalized or localized and is characterized by cutaneous features including sclerosis, atrophy, telangiectasias, hyper- or hypopigmentation, erythema, contractures, ulceration, hair loss and nail changes. Mucocutaneous features include xerophthlamia and xerostomia. Generalized forms of sclerodermatous GVHD cause significant functional disability due to reduced mobility. Mortality may be approximately 20-40% due to extracutaneous involvement, although some series show reduced mortality in sclerodermatous GVHD due to enhanced graft vs. tumor effect.

Skin biopsy in sclerodermatous GVHD may show a normal or atrophic epidermis, basal cell layer vacuolar degeneration, inflammation and eosinophilic body formation. Fibrosis and destruction of adnexal structures are commonly seen in the dermis and fibrosis may extend to the subcutaneous fat. Pigmentary incontinence may also be seen in the dermis.

Oral corticosteroids and immunosuppressants such as cyclosporine are standard treatments for sclerodermatous GVHD. Unfortunately, good clinical responses are rarely seen, adverse drug events are frequent, and overall mortality remains high.

In murine bone marrow transplant models, host-derived TNF-alpha has been shown to play an integral role in the development of GVHD and treatment with anti-TNF antibodies has

been found to decrease disease progression. Increased TNF-alpha levels have also been reported in human studies of patients with chronic GVHD.

In their initial study, Couriel *et al.* described 22 patients with chronic GVHD treated with a median of four weekly 10 mg/kg infusions of infliximab in addition to prednisone and other immunosuppressive therapy. They observed a response rate of 57% for skin disease and 92% for GI tract disease in these patients. Eleven patients died, with GVHD identified as the cause of death in 7 patients.

In a series of 8 patients with chronic GVHD who received infliximab salvage therapy (with a median of four weekly 10 mg/kg infusions), responses were observed in 7 of 8 patients with skin disease, 6 of 7 patients with GI tract disease, and no response was seen in 4 patients with liver disease.

There were many infections among the treated patients. In most cases, it was not possible to determine whether infections were related to infliximab or to prior and concurrent immunosuppressive therapies.

A retrospective cohort study concluded that infliximab was associated with an increased risk of invasive fungal infections and suggested that the possibility of increased infections with infliximab should be further evaluated. TNF-antagonists appear to be most effective for skin and GI tract manifestations and less effective for liver involvement and high-grade acute disease.

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CHICAGO DERMATOLOGICAL SOCIETY **CASE # 14**

Presented by Krisanne Sisto, MD, James Swan, MD, Brian Nickoloff, MD, PhD, and Kelli Hutchens, MD
Division of Dermatology, Loyola University Medical Center

HISTORY OF PRESENT ILLNESS

A 62 year-old woman presented with a five year history of tender, red lesions on her legs. Both the upper and lower legs were affected, and she reported at least one lesion occurring in the sacral area. Some lesions had ulcerated and many had healed with scarring or discoloration. An outside dermatologist had made a clinical diagnosis of erythema nodosum, although the underlying cause of her condition was not able to be identified. Past treatment included potassium iodide 15 drops twice daily, colchicine 0.6 mg twice daily and intralesional kenalog without improvement.

PAST MEDICAL HISTORY

Coronary artery disease, depression, diverticulosis, hypercholesterolemia

MEDICATIONS

Aspirin
Atorvostatin
Cholecalciferol
Loratidine
Multivitamin
Omega-3 fatty acid
Vitamin C
Vitamin D-3

ALLERGIES

No known drug allergies

FAMILY HISTORY

Non-contributory

SOCIAL HISTORY

The patient was an office worker with no exposure to homeless shelters or prisons. She did not use alcohol, tobacco or illicit drugs.

REVIEW OF SYSTEMS

The patient denied weight loss, fever, chills, heat or cold intolerance, cough, shortness of breath, blood tinged sputum, fatigue, joint pain, diarrhea or abdominal pain.

PHYSICAL EXAM

On the anterior and posterior thighs and lower legs there were scattered erythematous to violaceous, tender indurated nodules. The lower legs, and to a lesser extent the thighs, had scattered hyperpigmented patches as well as a few atrophic and scarred plaques.

LABORATORY

Normal or negative:
Tissue culture for bacteria, fungus and acid fast bacilli, BMP, AST, bilirubin, total protein, CBC, TSH, free T3 & T4, quantiferon gold, PPD, hepatitis panel, antinuclear antibody, rheumatoid factor, ESR, G6PD, urine analysis

RADIOLOGY

Normal or negative:
Chest x-ray, renal ultrasound

HISTOPATHOLOGY
Punch biopsy of the left thigh demonstrated a florid septolobular panniculitis with dense infiltration of lymphocytes, neutrophils and plasma cells. A mixed inflammatory infiltrate was present within vessel walls and vessel lumen. Periodic acid-Schiff and acid fast bacteria stains were negative for microorganisms. No polarizable foreign material was seen.

DIAGNOSIS
Nodular vasculitis

COURSE AND THERAPY
The patient had thorough evaluations by her primary care physician as well as by an infectious disease specialist. No potentially contributory underlying medical condition, infectious process or causative medication was identified. She was started on dapsone 25 mg twice daily for symptomatic relief. She is tolerating the mediation well and has experienced a marked improvement in her condition.

DISCUSSION
Nodular vasculitis, which is synonymous with erythema induratum of Whitfield, is a panniculitis with a classic predilection for the posterior lower legs of young women. The term erythema induratum was coined by Bazin in the 1800's to describe the violaceous nodules he observed on the posterior legs of women infected with tuberculosis. However, by the early 20th century there were reports of patients with similar clinical findings but no evidence of tuberculosis infection. In order to distinguish between the two groups, tuberculous associated cases were given the designation erythema induratum of Bazin and non-tuberculous associated cases became known as erythema induratum of Whitfield. The term nodular vasculitis has in recent years replaced erythema induratum of Whitfield as the preferred terminology for the non-tuberculous associated variant of erythema induratum.

Nodular vasculitis is characterized by recurrent crops of erythematous to violaceous nodules on the posterior lower legs. Patients may also have more widespread skin involvement with nodules occurring on the thighs, buttocks or arms. Ulceration and drainage often develops within nodules and lesions tend to heal with scarring and dyspigmentation. The main differential diagnosis in such a setting includes tuberculosis associated erythema induratum, erythema nodosum, other forms of panniculitis, subcutaneous T cell lymphoma, and polyarteritis nodosa.

The histological hallmark is a diffuse lobular or septolobular panniculitis with accompanying vasculitis. The inflammatory infiltrate is mixed, composed of lymphocytes, neutrophils, histiocytes and multinucleated giant cells. In some cases the infiltrate is granulomatous. Granulomas, if present, may be well formed and tuberculoid but are more often poorly developed. The vascular changes of nodular vasculitis involve all size arteries and veins and is characterized by endothelial swelling and a mixed inflammatory infiltrate within vessel walls. A necrotizing vasculitis may also be found. There are no definitive histological findings that distinguish nodular vasculitis from tuberculous associated erythema induratum other than visualization of microorganisms.

Nodular vasculitis, like erythema induratum and erythema nodosum, is a reactive process. A number of underlying conditions have been associated with it, although a significant percentage of cases are idiopathic. Initial work-up often focuses on eliminating a diagnosis of erythema induratum of Bazin by ruling out tuberculosis infection. Careful screening with PPD, serum quantiferon gold, chest x-ray, histological stains for microorganisms and tissue

culture is indicated. If clinically warranted identification of mycobacteria using polymerase chain reaction may be performed on a tissue specimen. Once a diagnosis of nodular vasculitis has been established an underlying trigger should be sought. Reported infectious causes include nocardia, pseudomonas, fusarium, hepatitis B and hepatitis C. Non-infectious associations include superficial thrombophlebitis, hypothyroidism, rheumatoid arthritis, Crohn's disease, chronic lymphocytic leukemia, renal cell carcinoma and the use of propylthiouracil.

The mainstay of treatment is identification and management of the inciting cause. In idiopathic cases or cases that do not respond to modification of a suspected triggering factor additional therapy is warranted. Elevation, compression of the affected area, and the administration of non-steroidal anti-inflammatory agents may prove beneficial. Potassium iodide and gold have been reported to be effective in many patients. Colchicine or dapsone may be tried. For patients in whom more conservative management has failed, a systemic immunosuppressant such as prednisone or mycophenolate mofetil may be helpful.

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CHICAGO DERMATOLOGICAL SOCIETY **CASE # 15**

Presented by Joshua Mandrell, MD, James Swan, MD, and Kelli Hutchens, MD
Division of Dermatology, Loyola University Medical Center

HISTORY OF PRESENT ILLNESS
This 33 year-old Pakistani female presented in January 2011 to the dermatology clinic with complaints of a red rash on her bilateral cheeks and brown pigment on her lower face and neck for the past year. The eruption was asymptomatic and facial redness was unrelieved by metronidazole topically. The patient reported that she occasionally felt bumps on her cheeks. She had no family history of similar facial findings.

PAST MEDICAL HISTORY
Hypothyroidism

MEDICATIONS
Levothyroxine

ALLERGIES
No known drug allergies

FAMILY HISTORY
No similar facial pigment changes

SOCIAL HISTORY
No smoking, alcohol, or illicit drug use reported

PHYSICAL EXAM
Erythematous to hyperpigmented patches were present on the cheeks and lateral neck bilaterally. Some telangectasias were present. On diascopy, the reddish component faded with the brown pigmentation persisting. There were a few, less than 1mm, slightly keratotic papules present on the bilateral cheeks. Her arms were clear.

HISTOPATHOLOGY
A punch biopsy of the right preauricular cheek showed increased epidermal pigmentation (Fontana stain) without nevomelanocytic proliferation (MART-1 immunostain). Pigment incontinence without interface change was noted. There was a lack of follicular hyperkeratosis. Mild perifollicular and perivascular inflammation as well superficial vascular dilatation was also present.

LABORATORY RESULTS
ANA positive at 1:40

DIAGNOSIS
Erythromelanosis follicularis faciei et colli

TREATMENT AND COURSE
At the initial presentation in January 2011, the patient was prescribed topical fluticasone cream daily for one month which resulted in no improvement. After biopsy in February 2011 confirmed the diagnosis, she began tretinoin 0.1% cream in April 2011. Improvement has not yet been noted.

DISCUSSION

Erythromelanosis follicularis faciei or erythromelanosis follicularis faciei et colli (EFFC) was first described in 1960 by Kitamura *et al.* with the triad of background erythema, hyperpigmentation, and follicular papules on the lateral face and neck. Telangectasias are occasionally observed. Initially, EFFC was thought to be more common in men, however, women are increasingly being reported with the condition. EFFC usually begins in the second decade and is bilateral but can be unilateral in rare cases. It was originally described in Japanese men and is now known to affect all races. The condition still favors individuals of Asian descent. An association with keratosis pilaris is classically described. Less than 50 cases of EFFC have been reported in the literature likely due to underreporting or lack of recognition of the condition.

Erythromelanosis follicularis faciei et colli is considered a disorder of follicular keratinization, however, the etiology is unclear. Initially, autonomic nerve dysfunction was suggested. Familial reports have suggested autosomal recessive transmission in some cases.

Histologically, slight follicular hyperkeratosis with increased basal layer pigmentation but without an increase in melanocytes is classically observed. The thickness and compactness of the horny layer is increased. The diameter of the hair shaft, the diameter of the outer root sheath, and the thickness of the inner root sheath are all decreased. The adnexae and vasculature are often surrounded by a lymphocytic infiltrate. There is an increase in superficial blood vessels. In one study, the percent area of inner space of blood vessels directly correlated with the severity of clinical erythema. In addition, the degree of pigmentation in the basal layer correlated with the clinical severity of hyperpigmentation. Our patient did not display classic histology in that she lacked follicular hyperkeratosis. This also correlated to the very few keratotic papules noted on clinical exam. We attribute this, at least in part, to her prior use of moisturizers and a month of topical steroid prior to biopsy. The histology in our case also displays pigment incontinence, which has not previously been reported in this entity.

The differential diagnosis for EFFC includes melasma, Poikiloderma of Civatte, Riehl's melanosis, keratosis pilaris, ulerythema ophryogenes or keratosis pilaris atrophicans faciei, atrophoderma vermiculatum, and keratosis follicularis spinulosa decalvans.

Treatment is difficult as most reported therapies provide varied levels of improvement but not clearance. Treatment with urea cream, ammonium lactate lotion, topical retinoids, topical ammonium lactate combined with hydroquinone, and superficial peels have all been employed. Limited courses of isotretinoin have been used which have improved the condition in most cases, but many patients experienced recurrence after stopping the medication. Recently, promising results with long-pulsed dye laser and dual-wavelength (585-nm pulse dye laser and 1,064-nm neodymium-doped yttrium aluminum garnet laser) systems have been observed in a few patients.

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CHICAGO DERMATOLOGICAL SOCIETY **CASE # 16**

Presented by Anjali Shah, MD, Anita Shetty, MD, Anthony Peterson, MD, Brian Nickoloff, MD, PhD, and Kelli Hutchens, MD
Division of Dermatology, Loyola University Medical Center

HISTORY OF PRESENT ILLNESS

A 59 year-old woman presented for evaluation of a rash of two days' duration. The mildly tender lesions first appeared on her arms and then spread to her legs and abdomen. The patient denied pruritus. She noted especially prominent redness over the ankles after wrapping with ace bandages in an attempt to control lower extremity swelling. Associated symptoms included a low grade fever and upper respiratory tract infection-like symptoms a week prior to onset of rash. She denied any new medications or a history of herpes simplex.

PAST MEDICAL HISTORY

Depressive disorder, diabetes mellitus type 2, hyperlipidemia, hypertension

MEDICATIONS

Aspirin
Furosemide
Gabapentin
Glucosamine-chondroitin
Insulin
Lisinopril
Lorazepam
Magnesium
Metformin
Multivitamin
Simvastatin
Synthroid
Venlafaxine

ALLERGIES

Morphine

FAMILY HISTORY

Non-contributory.

SOCIAL HISTORY

Works as a 5th grade teacher. The patient denies alcohol, tobacco, or use of illicit drugs.

PHYSICAL EXAM

Physical exam revealed scattered purpuric papules on the arms, upper legs, and abdomen; some lesions were targetoid in appearance with a dusky center. The lower legs were edematous with mainly horizontally oriented, linear, non-palpable purpura in the distribution of skin pressure lines.

HISTOPATHOLOGY

A 4 mm punch biopsy of the right anterior thigh revealed a dermal neutrophilic infiltrate with extravasated red blood cells and fibrinoid necrosis, consistent with a leukocytoclastic vasculitis. Direct immunofluorescence revealed deposition of IgA and C3 (positive for kappa and lambda light chains) in the superficial vascular plexus. Immunostaining for IgG and IgM was negative, and staining for fibrinogen was nonspecific.

A kidney biopsy revealed IgA nephropathy with underlying features of diabetic nephropathy.

LABORATORY RESULTS

Abnormal or positive: C3 183 mg/dL [ref 79-152]; erythrocyte sedimentation rate 85 mm [ref 0-30], C-reactive protein 6.9 mg/dL [ref <0.8], WBC 11.9 K/UL [ref 4-10] glucose 226 mg/dL, BUN 34 mg/dL [ref 7-22], creatinine 2.95 mg/dL [ref 0.7-1.5], potassium 5.8 mm/L [ref 3.3-5.1]. Urinalysis was positive for 2+ protein, moderate blood, large leukocytes, 5 RBCs, and WBC >180.
Normal or negative: C4, ANA, cryoglobulins, the remainder of the complete blood count, hepatitis panel, the remainder of the basic metabolic panel, magnesium, anti-streptolysin.

DIAGNOSIS

Henoch-Schönlein purpura with concurrent IgA nephropathy, occurring in an adult

TREATMENT AND COURSE

The patient was started on intravenous methylprednisolone for treatment of acute renal failure in the presence of leukocytoclastic vasculitis and IgA nephropathy. The patient's renal function and skin lesions improved with IV steroids, and she was soon transitioned to oral steroids and discharged from the hospital. Several of the lower extremity skin lesions became ulcerated and were slow to heal, requiring Unna boots for compression therapy and local wound care. The patient continues to follow with podiatry for wound care.

DISCUSSION

Henoch-Schönlein purpura (HSP) is a small vessel systemic vasculitis characterized by tissue deposition of IgA-containing immune complexes. Although typically a disease of childhood, with over 90% of cases arising before the age of fifteen, HSP can also be seen in adults. The classically described tetrad of presenting symptoms includes palpable purpura, polyarthralgias, abdominal pain, and renal disease. In a retrospective cohort study of 250 adults diagnosed with HSP, palpable purpura were noted at presentation in 96% of patients, arthritis in 61%, gastrointestinal involvement in 48%, and renal insufficiency in 32% of patients.

Laboratory findings may include increased erythrocyte sedimentation rate, elevated circulating immune complexes and IgA, elevated complement, and hematuria. The main histopathologic features of HSP are leukocytoclastic vasculitis (LCV) on hematoxylin-eosin stained tissue and vascular IgA and complement 3 (C3) deposits on direct immunofluorescence (DIF). Similar histopathological studies of the kidney are often essential in confirming the diagnosis.
The exact cause of HSP is unknown, but it is hypothesized that various triggers, including bacteria, viruses, and drugs, stimulate the formation of IgA immune complexes that are deposited in the small blood vessels. While bacterial and viral infections are the most frequently identified triggers in children, in adults the main instigators are drugs and toxins. More recently, malignancy has been reported as a rare causative factor of HSP.

A recent review found 31 cases of adult HSP associated with malignancy. The patients were mostly male (94%) with a mean age of 60 and had predominantly solid tumors. Most of the patients developed HSP within one month of cancer diagnosis or detection of metastasis. The most frequent tumors were lung cancer, multiple myeloma, prostate cancer, and non-Hodgkin's lymphoma.

Although HSP in adults generally has a poorer prognosis than in children, it often has a benign course with complete spontaneous resolution. In one study, renal insufficiency and proteinuria > 1g/24 hours at presentation were found to be the risk factors for long-term renal dysfunction. Supportive treatment is the main therapeutic intervention for a large

percentage of adults with HSP. Dapsone has been shown to have beneficial effects on cutaneous, gastrointestinal and articular manifestations in adults, especially those with chronic forms. The benefits of corticosteroid and cyclophosphamide therapy in relation to reducing the risk of renal involvement have not yet been established.

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CHICAGO DERMATOLOGICAL SOCIETY **CASE # 17**

Presented by Anjali Shah, MD, James Swan, MD, Brian Nickoloff, MD, PhD, and Kelli Hutchens, MD
Division of Dermatology, Loyola University Medical Center

HISTORY OF PRESENT ILLNESS

A 79 year-old female presented to clinic with asymptomatic papules on her trunk and posterior neck. She first noted the papules on her abdomen and flanks approximately six months prior to presentation. She later noticed new papules on her posterior neck and occipital scalp. They were stable in size. She denied pruritus, pain, or preceding inflammation in the area. There was no family history of similar lesions.

PAST MEDICAL HISTORY

Aortic stenosis, hypertension, hypothyroidism, osteoarthritis

MEDICATIONS

Alprazolam
Amlodipine
Ibuprofen
Levothyroxine
Multivitamin

ALLERGIES

No known drug allergies

FAMILY HISTORY

Mother with arthritis

SOCIAL HISTORY

Tobacco ½ pack per day, occasional alcohol

PHYSICAL EXAM

On the occipital scalp and posterior neck were soft, nonfollicular, flesh-colored dermal papules. Her bilateral flanks and abdomen had multiple, flesh-colored, soft papules coalescing into cobblestone nevoid plaques.

HISTOPATHOLOGY

A punch biopsy from the left occiput showed an unremarkable epidermis with a localized reduction of elastic fibers and normal collagen within the underlying dermis. Elastic Van Gieson (EVG) stain highlighted the fragmented elastic fibers, which coursed throughout the reticular dermis. Trichrome stain highlighted unremarkable collagen fibers. Congo Red stain was negative for amyloid deposition. Colloidal iron stain showed scant mucin deposition in the reticular dermis. Polarization of the biopsy was negative for the presence of foreign material.

LABORATORY RESULTS

Normal or negative:
Baseline CBC, CMP, TSH on file per her primary care physician were all within normal limits

DIAGNOSIS

Papular elastorrhexis

TREATMENT AND COURSE

The patient continues to do well and her cutaneous lesions remain asymptomatic without progression. She has declined radiographic imaging to rule out Buschke-Ollendorff syndrome.

DISCUSSION

Connective tissue nevi are a group of cutaneous disorders that display an imbalance in the relative amount and distribution of collagen bundles and elastic fibers. Papular elastorrhexis is a rare type of elastic tissue nevus first described in 1987 by Bordas and colleagues. The clinical lesions of papular elastorrhexis are usually acquired, asymptomatic nonfollicular papules on the trunk and upper extremities. They typically present in females during the second decade, however cases of adult onset have been reported. The differential diagnosis includes nevus anelasticus, anetoderma, mid-dermal elastolysis, papular acne scars, and pseudoxanthoma elasticum.

Histopathology shows a decrease and/or fragmentation of elastic fibers in the reticular dermis. Intense fragmentation of elastic fibers can be seen. There is usually no inflammation, however a perivascular lymphohistiocytic infiltrate in dermis has been reported. Collagen bundles in the dermis can be thickened and homogenized, or normal. Electron microscopy may reveal an absolute reduction of the elastic tissue, with a relative increase in the fibrillar component of elastic fibers in comparison with normal fibers.

At present, because of the small number of reported cases, the nature of this disease is not entirely clear. Some authors consider the term nevus anelasticus to be a synonymous disease state with papular elastorrhexis, while others consider these terms to be distinct entities. Although the histology is similar in both nevus anelasticus and papular elastorrhexis, the lesions of the former are usually perifollicular in nature and predominantly located on the chest. Other authors believe papular elastorrhexis to be an incomplete or abortive form of Buschke-Ollendorff syndrome that manifests only skin lesions without skeletal changes. In these reports, familial patterns have been described.

There is no reliable treatment for papular elastorrhexis. Case reports have shown some improvement after intralesional injection of triamcinolone, however this may result in temporary exaggerated dermal atrophy. Oral antibiotics, oral isotretinoin, topical tretinoin, and benzoyl peroxide have also been tried without success. Management of papular elastorrhexis should include radiographic imaging to rule out Buschke-Ollendorff syndrome. In this autosomal dominant syndrome, a mutation in the LEMD3 gene leads to numerous connective tissue nevi and the classic bone findings of osteopoikilosis. Osteopoikilosis is characterized by several bone islands in the skeleton and is most common in the epiphysis and the metaphysis of the long bones, especially in the fingers, the ulna, and the radius. The connective tissue nevi in this syndrome are usually juvenile elastomas or collagen-type connective tissue nevi (dermatofibrosis lenticularis disseminata). Less commonly, nevi with decreased elastin, such as papular elastorrhexis, have been reported. As our patient declined radiographic imaging, we cannot entirely exclude Buschke-Ollendorff syndrome. However, her negative family history makes the diagnosis of Buschke-Ollendorff syndrome unlikely.

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CHICAGO DERMATOLOGICAL SOCIETY **CASE # 18**

Presented by Allison Goddard, MD, Kathleen Remlinger, MD, and Madhu Dahiya, MD
Section of Dermatology, Edward Hines, Jr. VA Hospital

HISTORY OF PRESENT ILLNESS

A 50 year-old Caucasian male presented to the clinic with a 6 year history of asymptomatic, flesh colored, coin shaped, soft plaques on the trunk and upper extremities. Past medical history was significant for primary cutaneous b-cell marginal zone lymphoma (PCMZL), diagnosed and treated with surgical excision and unknown monoclonal anti-body chemotherapy seven years prior. The patient reported that the current lesions appeared approximately 1 year after clearance of the PCMZL and have remained stable. He stated that the current lesions were not sites of prior lymphoma nodules, but developed spontaneously. He had recently transferred care to Hines VA and we were consulted to rule out recurrent lymphoma. Review of systems was unremarkable.

PAST MEDICAL HISTORY

Primary cutaneous marginal zone lymphoma

MEDICATIONS

Aspirin

ALLERGIES

No known allergies

FAMILY HISTORY

Non-contributory

SOCIAL HISTORY

Drinks 1-2 beers per day. Never smoker. Denied drugs.

PHYSICAL EXAM

On the back and upper arms, few scattered, well demarcated, coin shaped, flesh colored, soft plaques with redundant and wrinkled surface. No scale or erythema. Slight button-hole effect. Also on the back and arms were scattered healed, linear scars.

HISTOPATHOLOGY

11/08/2010, 4 mm punch biopsy of the right posterior upper arm: Skin with focally decreased elastic fibers and focal mild perifollicular lymphoplasmacytic infiltrate. No atypical lymphocytes. Adnexal structures appeared diminished. No increase in dermal mucin as demonstrated by colloidal iron stain. Elastic stains showed focal decrease and straightening of elastic fibers.

LABORATORY RESULTS

None

DIAGNOSIS

Anetoderma

TREATMENT AND COURSE

The lesions were asymptomatic and stable for many years per patient history. He remained free of any signs of recurrent lymphoma. The association of anetoderma and antiphospholipid antibodies was discussed with the patient. He denied prior history of thrombotic events. He takes low dose aspirin daily for cardiac prevention, and since prophylactic aspirin would be the only likely intervention implicated if the test in fact resulted positive, he declined testing. No further treatment was required.

DISCUSSION

Anetoderma (anetos, Greek for slack) is a benign condition characterized by limited, circumscribed areas of flaccid or herniated saclike skin, relating to underlying focal loss of elastic tissue. It is currently classified into two forms. Primary, idiopathic anetoderma develops in clinically normal skin, and secondary anetoderma, which arises at or near the site of various preceding skin lesions including tumorous, inflammatory or infectious etiology. Both types may be associated with systemic disease.

In 1993 Jubert et al described a patient with primary cutaneous B-cell lymphoma, which manifested as indurated typical lymphomatous plaques and nodules resolving as anetodermic lesions. A handful of similar reports have since been described in the literature. The majority of reported cases were primary cutaneous marginal zone lymphoma (PCMZL), similar to our patient. The majority of anetodermic lesions in patients with cutaneous lymphomas are considered secondary anetoderma, arising in areas of prior lymphomatous lesions. There have been at least 2 patients reported to have developed primary anetodermic plaques years prior to any cutaneous lymphoma lesions. Our patient recalls that his anetodermic lesions developed after treatment of his PCMZL, in areas of previously normal skin, suggesting primary anetoderma.

The etiopathogenesis of anetoderma is largely unknown. Postulations have been made regarding the underlying mechanism of loss of elastic tissue and include; destruction of elastic fibers mediated by uncontrolled production of elastolytic enzymes such as elastase or loss of their inhibitors, elastophagocytosis, release of matrix metalloproteinases, secretion of cytokines, especially interleuken-6, by tumoral cells or other inflammatory cascades, or degeneration of elastic fibers secondary to local ischemia induced by microthrombosis of small dermal vessels.

There is increasing evidence linking anetoderma to antiphospholipid antibodies (aPL), which may play a role in elastolysis by means of immunologic pathways. Hodak, et al suggest that aPL may bind directly to elastic fiber via antigenic epitopes that are phospholipid related. In their recent series of 5 patients with what they described as anetodermic primary cutaneous b-cell lymphoma, 4 of 5 patients had aPL present without signs of aPL syndrome.

The management of the presence of aPL without signs or symptoms of aPL syndrome is an area of debate. In the past, the standard of care was starting daily aspirin, even if the patient had no history of thrombotic event. A recent large randomized, double blind, placebo-controlled trial (APLASA trial) looking at outcomes of patients with aPL with and without prophylactic aspirin, failed to show benefit in prevention of thrombotic events.

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CHICAGO DERMATOLOGICAL SOCIETY **CASE # 19**

Presented by Aaron Pace, MD, David Eilers, MD, and Madhu Dahiya, MD
Section of Dermatology, Edward Hines, Jr. VA Hospital

HISTORY OF PRESENT ILLNESS

A 70 year-old male presented to clinic for evaluation of a growth in the right groin. It had been present and slowly enlarging for the last 20 years. The patient reported occasional malodor but with good hygiene and talcum powder was able to control this issue. The patient denied any local irritation, pain or discomfort, bleeding, or weakness. The patient denies any history of sexually transmitted diseases and reports being monogamous with his wife.

PAST MEDICAL HISTORY

Inguinal hernia on the ipsilateral side, diabetes, high cholesterol, DVT, hypertension, peripheral vascular, and coronary artery disease

MEDICATIONS

Clopidogrel
Metoprolol
Simvastatin
Temazepam
Warfarin

ALLERGIES

No known drug allergies

FAMILY HISTORY

Non-contributory

SOCIAL HISTORY

No history of sexually transmitted diseases.

PHYSICAL EXAM

Exam revealed a 5 x 12cm exophytic, cauliflower-like inguinal verrucous tumor extending from the medial thigh toward the perineum, scrotum, and base of penis. Smaller but similar appearing lesions were noted on the distal dorsal shaft of the penis and the perineum.

HISTOPATHOLOGY

Initial biopsy was a shave and only sampled a small portion of the lesion. It revealed a superficial portion of a pedunculated seborrheic keratosis. Due to clinical suspicion the entire lesion was excised and this revealed hyperkeratosis, hypergranulosis, and prominent koilocytosis. On higher power, in the epidermis, there were some atypical appearing keratinocytes and few mitoses.

LABORATORY RESULTS

The patient has declined any lab workup for other sexually transmitted diseases.

DIAGNOSIS

Giant condyloma of Buschke-Lowenstein

TREATMENT AND COURSE

Due to the clinicopathologic discord with the initial biopsy and after discussion with the patient, the decision was made to pursue excision of the large inguinal lesion. The patient had an underlying hernia that complicated the planning of the excision. The patient underwent excision in August of 2010 and repair of hernia at the same time was considered, however, given the large size of the cutaneous repair, there would be an increased infection risk and it was postponed. The patient has since done well and not had a recurrence, although he has untreated treated condyloma on both the penile tip and perineum. The patient was referred to urology for removal of the remaining condyloma, but a urothelial carcinoma was discovered due to the patient developing hematuria. Their efforts have been focused on eradicating the new malignancy, which is thought to be unrelated to the condyloma.

DISCUSSION

Abraham Buschke described a large penile lesion in 1896 and later with the help of Ludwig Lowenstein described benign carcinoma-like condyloma acuminatum in 1925. Lauren Ackerman, referring to similar oral lesions and later coined the term verrucous carcinoma in 1948. Now the term is applied to several of these lesions based on their location and they are thought to be a well-differentiated variant of a squamous cell carcinoma. Their specific names based on location include the giant condyloma of Buschke-Lowenstein (genital), epithelioma cuniculatum (foot), papillomatosis cutis carcinoides of Gottron (lower calf), and oral florid papillomatosis. This discussion will focus primarily on the genital giant condyloma of Buschke-Lowenstein.

The giant condyloma of Buschke-Lowenstein is most commonly found on the penis but may occur anywhere on the anogenital skin. Historical investigation frequently reveals slow growth over a decade or more. On exam, a fetid smell may be appreciated due to bacterial overgrowth in the numerous crypts. If left untreated, the lesions may invade the dermis and even underlying muscle, bone, and peritoneal structures. As the course progresses, they may become less differentiated, but distant metastasis has not been reported.

The etiology of giant condyloma of Buschke-Lowenstein is related to the human papilloma virus (HPV) whereas oral florid papillomatosis is related to chewing tobacco. The associated HPV types usually are low risk HPV-6 and 11, but less frequently, the high risk HPV-16 and 18 may also be causative. These tumors can be more aggressive in immunosuppressed patients, particularly in HIV/AIDS patients. CD4 positive lymphocytes are known to predominate in regressing condyloma acuminatum and the lack of these cells is thought to allow for the tumors increased growth in immunosuppressed patients.

Histopathology reveals a surprisingly benign appearance when compared to the clinical appearance and size of the lesion. The pathology is usually contained completely within the epidermis as it is rarely invasive. A recent article and letter to the editor in Dermatologic Surgery by Livaoglu and Roos underscore the paramount importance of thorough histologic evaluation of large portions of the lesion to get a good idea of the nature of the growth. Under the microscope it tends to be both endophytic and exophytic with papillomatosis, hyperkeratosis and parakeratosis. The lesions may extend into the deep reticular dermis with regular acanthotic rete. The deeply penetrating rete are usually contained within an intact basement membrane. Invasive areas are sometimes identified. Mitotic activity if present will be minimal. These lesions are thought to be on a continuum between benign viral changes and carcinoma.

For treatment, surgical excision or Mohs are considered treatments of choice. Traditional surgical excision can have a recurrence rate between 40 and 70 percent. Many other therapies have varying degrees of success. Topically, imiquimod, podophylin, and 5-fluorouracil have been used. Intralesional injections of bleomycin and interferon alpha can induce regression. Intralesional interferon alpha is used 3-5x/week and often results in regression within about 6 months when used as monotherapy. In one case, it was used 3 times per week for 12 months and induced complete regression, the course was continued for a total of 28 months to ensure complete resolution. Biopsy one year later continued to demonstrate complete resolution. Liquid nitrogen cryotherapy, photodynamic therapy, and systemic chemotherapy have been used as well. Systemic chemotherapy plays a roll when used in an adjuvant manner. The tetravalent HPV vaccine against serotypes 6, 11, 16, and 18 has been shown to reduce recurrence of cervical HPV related lesions in women after surgical removal, but its utility with a giant condyloma of Buschke-Lowenstein has not been investigated. Radiation of these lesions is usually avoided. It is thought to increase the chance of a high-grade anaplastic transformation. In circumstances where other treatment modalities are impractical, radiotherapy may be combined with chemotherapy and surgical debulking.

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CHICAGO DERMATOLOGICAL SOCIETY **CASE # 20**

Presented by Vanessa Lichon, MD, David Eilers, MD, and Madhu Dahiya, MD
Section of Dermatology, Edward Hines, Jr. VA Hospital

HISTORY OF PRESENT ILLNESS

A 62 year-old African American male presented for evaluation of lesions on his palms and soles. He noted the presence of these lesions for the past few years. He stated that the areas were occasionally pruritic, but otherwise asymptomatic. He was a golfer, but upon presentation had not golfed in months. He denied any other hobbies involving his hands and feet.

PAST MEDICAL HISTORY

Chronic myelogenous leukemia, gout, hypertension

MEDICATIONS

Allopurinol
Amlodipine
Atenolol
Hydrocodone/acetaminophen
Imatinib mesylate

ALLERGIES

No known drug allergies

FAMILY HISTORY

Non-contributory

SOCIAL HISTORY

Patient is retired. Hobbies include golfing.

PHYSICAL EXAM

On the bilateral palms and web-spaces of hands were scattered 1-2mm black non-blanchable macules. On the bilateral feet, primarily over pressure points, were hyperkeratotic plaques with 1-2mm black non-blanchable macules.

HISTOPATHOLOGY

Left palm, 3mm punch biopsy
Hyperkeratosis with intracorneal hemorrhage

DIAGNOSIS

Tache and Talon Noir

TREATMENT AND COURSE

A 3mm punch biopsy was obtained from the left palm to establish the diagnosis. The patient was informed of the biopsy results and reassured of the benign nature of this condition.

DISCUSSION

Talon noir (or black heel) is a condition classically associated with athletes and was first described in 1961 by Crissey & Peachey in basketball players. Clinically, the lesions are usually asymptomatic and present as grouped or linear blue-black macules, most commonly on the convex aspect of the heel. Adolescents and young adults are most frequently affected. Lesions develop from traumatic shearing forces secondary to repetitive

movement, causing rupture of blood vessels in the papillary dermis, with subsequent extravasation into the cornified layer of the epidermis.

Tache noir (or black palm) is also classically associated with athletes and has been described in gymnasts, golfers, weightlifters, racket sports players and mountain climbers. Clinically, the lesions normally appear on the thenar aspect of the palms. Pathogenesis is identical to talon noir.

Sometimes, these lesions should be differentiated from melanoma. The diagnosis can be established by paring the affected areas with a blade, by examining the lesions with a dermatoscope, or by performing a biopsy. Classic histopathologic examination reveals intracorneal hemorrhage. Dermoscopy may be of value by looking for features of subcorneal hematoma including red-black homogenous pigmentation, often combined with satellite globules. Treatment is not necessary for tache or talon noir and reassurance should be provided to the patient. Normally, these lesions resolve with time.

Of interest, other names used to describe these conditions in the literature include: calcaneal petechiae, post-traumatic punctuate hemorrhage of the skin, purpura traumatica pedis, basketball heel, tennis heel, tennis toe, hyperkeratosis haemorrhagica, disseminated punctuate intraepidermal hemorrhage, subcorneal hematoma, pigmented palmar petechiae, black palmar macules, Playstation thumb, plantar chromhidrosis, and pseudochromhidrosis.

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