Chicago Dermatological Society

June 2009
Monthly Educational Conference

Program Information
Continuing Medical Education Certification
and
Case Presentations

Wednesday, June 10, 2009

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

LOYOLA MEDICINE
We also treat the human spirit.®

Program

Committees & Registration

8:00 a.m. - 9:00 a.m.	IDS Board of Directors *Room 150*
9:00 a.m. - 10:00 a.m.	CDS Plans & Policies Committee *Room 150*

Program Activities

9:00 a.m. - 10:00 a.m.	RESIDENT LECTURE "The Use of the Immunodermatology Laboratory in Evaluation and Management" John Zone, MD *Tobin Hall Room 190*
9:30 a.m. - 11:00 a.m.	CLINICAL ROUNDS Patient Viewing *Clinical Skill Center Room 330* Slide Viewing *Leischner Hall Room 390* Posters *Seminar Rooms 363, 364, 375*
11:00 a.m. - 12:15 p.m.	GENERAL SESSIONS *Tobin Hall Room 190*
11:00 a.m.	CDS Business Meeting
11:15 a.m.	"The Celiac Epidemic and the Practice of Dermatology" John Zone, MD
12:15 p.m. - 1:00 p.m.	Lunch & visit with exhibitors *Room 160*
1:00 p.m. - 2:30 p.m.	Case Discussions *Tobin Hall Room 190*
2:30 p.m.	MEETING ADJOURNS

Future Meeting Schedule – check the CDS meeting calendar on our website:
www.ChicagoDerm.org

CME Information

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

Accreditation Statement: 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 the joint sponsorship of the Chicago Medical Society and the Chicago Dermatological Society. The Chicago Medical Society is accredited by the ACCME to provide continuing medical education for physicians.

Designation Statement: The Chicago Medical Society designates this educational activity for a maximum of 4 AMA PRA Category 1 Credits™. Physicians should only claim credit commensurate with the extent of their participation in the activity.

Commercial Support: There is no commercial support associated with this meeting.

Guest Speaker

John Zone, MD is professor and chairman of the Department of Dermatology at the University of Utah School of Medicine, Salt Lake City. He also is a consultant and investigator for the Utah Clinical Trials, and is head of the Section of Dermatology at the Veteran's Administration Medical Center, Salt Lake City. He received his B.S. from the University of Notre Dame in 1967 and his M.D. in 1971 at SUNY, Upstate Medical Center, Syracuse, NY. He completed a residency in Internal Medicine, 1971-1974, SUNY, Upstate Medical Center, Syracuse, NY; and a residency in Dermatology, 1975-1978, SUNY at Buffalo. Dr. Zone's clinical practice involves primarily medical dermatology with special interests in disorders of the immune system including dermatitis herpetiformis, linear IgA bullous dermatosis, bullous pemphigoid, pemphigus and celiac disease. Dr. Zone has had a long-term interest in melanoma and was a member of the team that discovered p16, the melanoma risk gene. Dr. Zone's research interests include the autoimmune blistering diseases and celiac disease. He has extensive experience as the author, co-author, editor or reviewer of journal articles, books, book chapters, and many other publications.

Speaker CME Disclosure of Financial Interests

Dr. Zone has no significant financial relationships to disclose.

CME Credit Documentation

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

Evaluation Forms

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

TABLE OF CONTENTS

Presented by Tricia Hultgren MD, and Edward Keuer MD
Division of Dermatology, Loyola University Medical Center

HISTORY OF PRESENT ILLNESS

A 1-day old baby boy was transferred to our institution after normal spontaneous vaginal delivery to a healthy 27-year old Polish woman at 36 weeks and 6 days gestation. His mother had history of 2 prior miscarriages but had sustained an uncomplicated pregnancy with regular prenatal care.

PAST MEDICAL HISTORY

None

MEDICATIONS

None

ALLERGIES

No known drug allergies

FAMILY HISTORY

No history of ichthyosis in family members
Parents are non-consanguineous

SOCIAL HISTORY

Non-contributory

PHYSICAL EXAM

The patient's body was encased in a shiny, transparent membrane. He had prominent ectropion and eclabium, as well as hypoplastic auricular cartilage and low set ears. Fissures and maceration were present in the groin and axillae, and his fingers were contracted. The baby's nails were normal without dystrophy and there was no evidence of cleft palate.

LABORATORY RESULTS

The following were negative or normal:
Sodium, potassium, calcium, blood culture

The following were abnormal or positive:

Chloride 108	(96-106 mm/L)
Hemoglobin 13.9	(15.0-24.0 g/dL)
Hematocrit 40.1	(44-70%)

DIAGNOSIS

Collodion baby associated with an autosomal recessive congenital ichthyosis versus self-healing collodion phenotype

TREATMENT AND COURSE

The baby was placed in a 70% humidified incubator, and his fluids and electrolytes were monitored closely. He received aquaphor to the entire body four times daily and

puralube to the eyelids daily. Empiric treatment with ampiciliin and gentamycin was initiated and was discontinued after seven days with no signs of infection. Genetics was consulted, and chromosomal analysis showed a normal 46 XY karyotype.

The baby's membrane desquamated within the first week of life. His ectropion and eclabium resolved, and his hand contractures improved. He was gradually weaned from the humidified environment and was discharged home after 21 days. At his five-month follow-up, the infant was developing well and reaching appropriate milestones. Exam revealed mild xerosis with desquamation in the bilateral axillae and on the scalp. His mother continues to apply petrolatum to his entire body once to twice daily.

Molecular analysis for transglutaminase 1 gene mutation proved negative. Unfortunately, further genetic testing was deferred secondary to financial limitations. Tele-consultation with Dr. Masashi Akiyama and Dr. Hiroshi Shimizu, both experts in inherited keratinization disorders from Hokkaido University, Japan was obtained. They hypothesized the diagnosis to be a mild form of non-bullous congenital ichthyosiform erythroderma.

DISCUSSION

Collodion baby refers to the clinical presentation of a neonate with a parchment-like membrane covering the entire body. Collodion baby is a phenotype rather than a disease entity, with most patients eventually developing one of the autosomal recessive congenital ichthyoses (ARCI). ARCI include lamellar ichthyosis (LI), non-bullous congenital ichthyosiform erythroderma (NBCIE) and harlequin ichthyosis (HI). The taut skin created by the collodion membrane often leads to ectropion, eclabium, and hypoplastic nasal and auricular cartilage. The membrane fissures and peels off within 12 weeks, and transition to the underlying phenotype ensues. The most commonly associated conditions are LI and NBCIE. Rare cases of Sjogren-Larsson syndrome, trichothiodystrophy with ichthyosis, neutral lipid storage disease, infantile Gaucher disease, Conradi-Hunermann-Happle syndrome, or ectodermal dysplasia may present with a collodion membrane at birth. In some patients, normal skin or very mild ichthyosis develops and has been termed '"self-healing collodion phenotype".

Collodion babies are often premature and suffer increased morbidity and mortality rates. Improved neonatal care, however, has led to decreased mortality rate from 50% in 1960 to 11% in 1986. A 2002 prospective study showed 0% mortality related to skin conditions in 17 collodion babies. The most common complications include hypernatremic dehydration due to excessive transepidermal water loss, hypothermia, and cutaneous infection and sepsis due to impaired barrier function. Placement in a humidified incubator soon after birth may prevent dehydration and hypothermia.

In one of only two studies evaluating the outcome of 17 collodion babies, 41% of the patients developed NBCIE, 18% developed LI, 24% eventually developed normal skin, and 18% developed other disorders (including one case each of Sjogren-Larsson, epidermolytic hyperkeratosis, and a fatal variant of Gaucher disease). Diagnoses were made solely on clinical findings in all cases.

Skin biopsy of the collodion membrane is usually nonspecific and shows diffuse orthohyperkeratosis. Marked parakeratosis and an inflammatory cell infiltrate has been reported as more characteristic of NBCIE, whereas hyperkeratosis is usually more prominent in LI. Findings on electron microscopy, which including cholesterol clefts and

lipid droplets, cannot reliably distinguish between ARCI phenotypes.

To date, ARCI have been linked to five genes, including *TGM1, ABCA12, ALOXE3, ALOX12B* and *ichthyin.* Defective formation of the intercellular lipid layers with subsequent loss of epidermal barrier function is thought to underlie the pathogenesis of all forms of ACRI. Specific mutations cannot reliably determine phenotype, as LI and NBCIE have been reported in association with all of the above mutations. An exception exists in specific ABCA12 deletion mutations leading to harlequin ichthyosis. ABCA12 is a lipid transporter protein that when mutated causes defective lipid secretion into lamellar granules. TGM1 mutations cause malformation of the cornified envelope, which serves as a scaffold for accumulation of the lipid layer. The lipid layer does not develop properly, leading to the ichthyosis phenotype. ALOXE3 and ALOX12B are non-heme iron containing dioxygenases expressed in the epidermis. Their exact function of these genes is unknown, but they may be associated with lipid metabolism in the lamellar granule and/or intercellular lipid layers. Ichthyin is a plasma membrane protein whose function remains unknown but has been linked to the ichthyosis phenotype.

As mutations in the above genes may lead to both LI and NBCIE phenotypes, the diagnosis is often made on clinical grounds. In classic LI, patients develop thick, brown scales over the entire body, including the face. Ectropion and eclabium are common but often mild. Palmoplantar keratoderma is common, while hair and teeth appear normal. Skin manifestations seldom improve with age, although patients have a normal lifespan. In contrast, NBCIE patients demonstrate erythroderma and fine white scaling. Symptoms often become more mild with age. Ectropium and eclabium are frequent but not severe. As in LI, PPK is variably present and hair and nails appear normal. Although the classic presentations of LI and NBCIE demonstrate distinct differences, patients often present with clinical features intermediate between the two classic phenotypes.

The self-healing collodion phenotype has been linked to mutations in TGM1 and recently, two novel mutations in ALOX12B. The exact mechanism behind the rapid improvement in the skin is not known. Recent functional analysis of mutated TGM1 in 2 patients with self-healing collodion phenotype suggest that the enzyme is non-functional in utero, but then undergoes a conformational change to become partially active after birth due to environmental change.

REFERENCES

1. Van Gysel D, Lijnen RL, Moekti SS, de Laat PC, Oranje AP. Collodion baby: a follow-up study of 17 canses. J Eur Acad Dermatol Venereol. 2002;16:472-75.

2. Akiyama M, Sawamura D, Shimizu H. The clinical spectrum of nonbullous congenital ichthyosiform erythroderma and lamellar ichthyosis. Clin and Exp Dermatol. 2003;28:235-40.

3. R Raghunath M, Hennies HC, Ahvazi B, *et al.* Self-healing collodion aby: a dynamic phenotype explained by a particular transglutaminase-1 mutation. J Invest Dermatol. 2003;120:224-28.

4. Akiyama, M. Harlequin ichthyosis and other autosomal recessive congenital ichthyosis: The underlying genetic defects and pathomechanisms. J Dermato Science. 2006;42:83-89

5. Harting M, Brunetti-Pierri N, Chan S *et al.* Self-healing collodion membrane and mild nonbullous congenital ichthyosiform erythroderma due to two novel mutations in the ALOX12B gene. Arch Dermatol. 2008;144:351-56

CHICAGO DERMATOLOGICAL SOCIETY **CASE # 2**

Presented by Joshua Mandrell MD, Stacy McClure MD, and Madhu Dahiya MD
Division of Dermatology, Loyola University Medical Center

HISTORY OF PRESENT ILLNESS

This 63-year old female with a past medical history of estrogen receptor-positive, ductal carcinoma in situ of the right breast presented to the dermatology clinic for evaluation of a purple spot on the right breast that had been present for six months. She stated that the lesion was asymptomatic and had not changed in size, shape, or color. The patient had a history of right breast lumpectomy with axillary node dissection and adjuvant chemotherapy and radiation four years prior to presentation.

PAST MEDICAL HISTORY

Ductal carcinoma in situ of the right breast with lumpectomy, axillary node dissection, adjuvant chemotherapy, and radiation four years prior to presentation
Hypercholesterolemia
Hypertension

MEDICATIONS

Anastrozole (estrogen antagonist)
Atorvastatin
Lisinopril
Ibuprofen

ALLERGIES

Penicillin

FAMILY HISTORY

Mother with lung cancer

SOCIAL HISTORY

Widowed
No tobacco, alcohol, or illicit drug use

PHYSICAL EXAM

A 6mm violaceous macule was present on the right breast.

HISTOPATHOLOGY

There was a diffuse dermal proliferation of well-formed capillary structures with mild endothelial atypia. Staining was positive for the CD34 vascular marker and negative for the D2-40 lymphatic marker.

DIAGNOSIS

Atypical vascular lesion, vascular type

TREATMENT AND COURSE

The patient underwent wide local excision with 1cm margins, with pathologic examination confirming the complete excision of the residual atypical vascular proliferation.

DISCUSSION

Atypical vascular lesions (AVLs) develop as one or more, small erythematous to violaceous macules or papules following radiation therapy for breast carcinoma. The latency period ranges from one to twenty years following radiation, though presentation within three to six years is most common. Hyalinization of dermal collagen fibers, swelling of endothelial cells, telangiectatic dilation of dermal vessels, and proliferation and hyalinization of deeper vessels are typical late radiation-induced changes seen within the skin. Because such skin changes usually stop within three years of radiation therapy, observed changes after this period should alert the clinician.

The term “atypical vascular lesion” was coined in 1994 by Fineberg and Rosen, who described four women with cutaneous vascular proliferations following lumpectomy and radiation for breast carcinoma. They believed these lesions to be benign and related to lymphatic obstruction after surgery and/or radiation-induced dilation of vascular channels. Others have used the terms “atypical hemangiomas,” “acquired progressive lymphangioma,” “benign lymphangiomatous papules” (BLAP), “lymphangioma circumscriptum,” and “benign lymphangioendothelioma” to describe the presumptive benign nature of the same entity.

However, in their review of 42 cases, Brenn and Fletcher concluded that atypical vascular lesions were part of a continuum and were in fact precursors to angiosarcomas which warranted more aggressive treatment. This opinion was based primarily on a patient with a classic atypical vascular lesion in whom serial biopsies showed slow development of angiosarcoma over the next five years. Other cases of malignant transformation to angiosarcomas are also reported in the literature. However, despite such contradictory reports, the predominant consensus in the literature remained that atypical vascular lesion represented a benign entity.

The natural course and malignant potential of AVLs remains controversial as evidenced by a 2008 report by Patton *et al.* who reviewed 32 cases of atypical vascular lesions (AVLs) after surgery and radiation of the breast. The authors divided these into two histiologic types: the less common vascular type (VT) was observed to have a higher risk of development into angiosarcoma, while the more common lymphatic type (LT) had a lower risk. VT lesions were characterized by irregular dispersed, pericyte-invested, capillary-sized vessels within the superficial or deep dermis, which were often associated with erythrocytes or hemosiderin. These lesions resembled capillary hemangiomas, with vessels displaying a vascular immunophenotype (CD 31^{+}, CD 34^{+}, and C2-40 -) though lacking a lobular organization. Although four of the ten VT lesions showed endothelial atypia, they differed from angiosarcomas in that the vessels did not intercommunicate and did not display endothelial multilayering. The lymphatic subtype AVLs displayed thin-walled, variably anastomosing lymphatic vessels lined by attenuated or slightly protuberant endothelial cells. These vessels displayed a lymphatic immunophenotype (CD 31^{+}, CD2-40 +, and CD $34^{+/-}$). Most of the original descriptions of atypical vascular lesions seem to describe this LT entity with a discontinuous endothelial lining, absence of pericytes, and smooth muscle actin and Ki67-negative. Of note, six of the vascular type AVLs displayed some overlap with lymphatic type histology.

Of the 21 patients with lymphatic type AVLs who had follow-up in the clinicopathologic study by Patton *et al.,* five patients developed local recurrences, and one developed several additional lymphatic AVLs and eventually a multifocal angiosarcoma. Of the

eight patients with vascular type AVLs who had follow-up, one had local recurrences of vascular type AVLs and another developed high-grade epithelioid angiosarcoma. The authors conclude that vascular-type AVLs have the highest risk for angiosarcoma transformation based on the degree of endothelial atypia. This opinion seems to be congruent with the observation of recurrences and fatalities in patients with vascular lesions of the breast with a capillary lobular pattern but with moderately atypical endothelium reported as "postirradiation angiosarcomas." Although the risk may be smaller, it should be remembered that lymphatic-type AVLs with unusual histologic features also have a risk of malignant transformation. It remains to be seen whether LT AVLs are precursors to VT AVLs as part of a continuum to angiosarcoma, or instead distinct entities with their own inherent risk.

In a study by the French Sarcoma Group, 20% of patients with AVLs experienced recurrence, after biopsy or excision with varying margins. The authors concede that these new vascular lesions may not represent true recurrences but rather new lesions within the same irradiated field or "field-effect phenomenon." Other studies have observed that up to 31% of patients develop further lesions within the radiation field. However, it should be noted that despite the over 100 diagnosed cases of atypical vascular lesions reported in the literature, no more than five have progressed to angiosarcoma.

Histologically, atypical vascular lesions do display unique features that separate them from the typical angiosarcoma. Fineberg and Rosen used these histological findings to differentiate AVLs from low-grade angiosarcoma. In contrast to angiosarcoma, AVLs typically lack infiltration into the subcutis, multilayering of endothelial cells, prominent nucleoli, mitoses, and hemorrhage. Others have observed that AVLs histologically display dilated vascular spaces within the papillary dermis with plump endothelial cells, differentiated from angiosarcoma by lack of destruction of adnexa, localized growth, and little penetration into reticular dermis or subcutaneous tissue. While angiosarcomas usually lack chronic inflammation, circumscription, and stromal projections into the lumen, these features are commonly seen in AVLs. Dissection of dermal collagen can be present in both entities. However, the clinical and histological overlap causes the diagnosis to remain challenging. In fact, in a series of 11 patients with atypical vascular lesions on biopsy, five were reclassified as angiosarcoma after complete excision.

Atypical vascular lesions remain challenging and enigmatic entities in terms of diagnosis, natural history, and appropriate therapy. Histologic features or immunophenotypic markers that could more specifically predict which AVLs will develop into angiosarcomas would be valuable. More research and controlled studies with careful long-term follow up are needed to further delineate this risk. In addition, guidelines for treatment including recommendations regarding surgical margins would be beneficial, as current treatments have ranged from wide local excision with 1 cm margins to mastectomy. In breast cancer patients with a previous history of surgery and radiation therapy, close monitoring of the skin for new vascular eruptions, including macular lesions resembling a bruise (as in our patient), and a low threshold for biopsy should be emphasized.

REFERENCES

1. Patton KT, Deyrup AT, Weiss SW. Atypical Vascular Lesions After Surgery and Radiation of the Breast: A Clinicopathologic Study of 32 Cases Analyzing Histologic Heterogeneity and Association with Angiosarcoma. *Am J Surg Pathol.* 2008;32(6):943-50.

2. Gengler C, Coindre JM, Leroux A, et al. Vascular proliferations of the skin after radiation therapy for breast cancer: clinicopathologic analysis of a series in favor of a benign process: a study from the French Sarcoma Group. *Cancer.* 2007;109(8):1584-98.
3. Weedon D. Skin pathology. 2nd edition. Edinburgh: Churchill Livingstone, 2002.
4. Brodie C, Provenzano E. Vascular proliferations of the breast. *Histopathology*. 2008; 52(1):30-44.
5. West JG, Qureshi A, West JE, et al. Risk of angiosarcoma following breast conservation: a clinical alert. *Breast J*. 2005;11:115-123.
6. Fineberg S, Rosen PP. Cutaneous angiosarcoma and atypical vascular lesions of the skin and breast after radiation therapy for breast carcinoma. *Am J Clin Pathol.* 1994;102:757-63.
7. Hoda SA, Cranor ML, et al. Hemangiomas of the breast with atypical histological features. Further analysis of histologic subtypes confirming their benign nature. *Am J Surg Pathol*. 1992; 16(6):553-60.
8. Rosso R, Gianelli U, Carnevali L. Acquired progressive lymphangioma of the skin following radiotherapy for breast carcinoma. *J Cutan Pathol.* 1995;22:163-67.
9. Wagamon K, Ranchoff RE, Rosenberg AS, et al. Benign lymphangiomatous papules of the skin. *J Am Acad Dermatol.* 2005;52(5):912-13.
10. Diaz-Cascajo C, Borghi S, Weyers W, et al. Benign lymphangiomatous papules of the skin following radiotherapy: a report of five new cases and review of the literature. *Histopathology.* 1999;35(4):319-27.
11. Martin-Gonzalez T, Sanz-Trelles A, et al. Benign lymphangiomatous papules and plaques after radiotherapy. *Actas Dermosifiliogr.* 2008;99(1):84-6.
12. Brenn T, Fletcher CD. Radiation-associated cutaneous atypical vascular lesions and angiosarcoma: clinicopathologic analysis of 42 cases. *Am J Surg Pathol*. 2005;29:983-96.
13. Guillou L, Fletcher CD. Benign lymphangioendothelioma (acquired progressive lymphangioma): a lesion not to be confused with well-differentiated angiosarcoma and patch stage Kaposi's sarcoma: clinicopathologic analysis of a series. *Am J Surg Pathol.* 2000; 24(8):1047-57.
14. Hildebrandt G, Mittag M, et al. Cutaneous breast angiosarcoma after conservative treatment of breast cancer. *Eur J Dermatol.* 2001;11(6):580-3.
15. Di Tommaso L, Fabbri A. Cutaneous angiosarcoma arising after radiotherapy treatment of a breast carcinoma. Description of a case and review of the literature. *Pathologica.* 2003;95(4):196-202.
16. Moskaluk CA, Merino MJ, Danforth DN, et al. Low-grade angiosarcoma of the skin of the breast: a complication of lumpectomy and radiation therapy for breast carcinoma. *Hum Pathol.* 1992;23:710-14.
17. Requena L, Kutzner H, Mentzel T, Duran R, Rodriguez-Peralto JL. Benign vascular proliferations in irradiated skin. *Am J Surg Pathol.* 2002;26:328-37.
18. Bodet D, Rodriguez-Cano L, et al. Benign lymphangiomatous papules of the skin associated with ovarian fibroma. *J Am Acad Dermatol.* 2007;56(2 Suppl):S41-4.
19. Mattoch IW, Robbins JB, et al. Post-radiotherapy vascular proliferations in mammary skin: a clinicopathologic study of 11 cases. *J Am Acad Dermatol*. 2007;57(1):126-33.
20. Grunwald MH, Amichai B. Acquired progressive lymphangioma. *J Am Acad Dermatol.* 1997;37(4):656-7.
21. Kim HS, Kim JW, et al. Acquired progressive lymphangioma. *J Eur Acad Dermatol Venereol.* 2007;21(3):416-7.

22. Brenn T, Fletcher CD. Postradiation vascular proliferations: an increasing problem. *Histopathology.* 2006;48(1):106-14.
23. Di Tommaso L, Rosai J. The capillary lobule: a deceptively benign feature of post-irradiation angiosarcoma of the skin: report of three cases. *Am J Dermatopathol.* 2005;27:301-05.

CHICAGO DERMATOLOGICAL SOCIETY **CASE #3**

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

HISTORY OF PRESENT ILLNESS

This 60-year old Caucasian male presented to clinic for routine skin cancer screening. He had a long-standing history of multiple asymptomatic skin lesions on the trunk and extremities. Past medical history was significant for IgA nephropathy status post renal transplant in September 2005. Immunosuppressive medications included prednisone, mycophenolate mofetil, and cyclosporine. He had a distant history of basal cell carcinoma of the eyelid.

PAST MEDICAL HISTORY

Maffucci's syndrome
Hallux valgus status post bunionectomy with first metatarsal phalangeal joint arthrodesis
Coronary artery disease status post coronary artery bypass graft
Hypercholesterolemia
Colonic polyps
Gout
Prostate cancer status post prostatectomy
Gastroesophageal reflux disease
Essential hypertension
Myocardial infarction
Right nephrectomy secondary to renal artery stenosis
Diabetes mellitus type II
Overactive bladder
Osteopenia
Fracture of right forearm (childhood)

MEDICATIONS

Acetaminophen
Amiloride
Aspirin
Clonidine
Clopidogrel
Cyclosporine
Fenofibrate
Glipizide
Lansoprazole
Lisinopril
Metoprolol
Multivitamin
Mycophenolate mofetil
Nifedipine
Omega- 3 fatty acids
Prednisone
Simvastatin

Tolterodine
Vitamin D

ALLERGIES
Atorvastatin, tramadol, acetylcysteine

FAMILY HISTORY
No family history of Maffucci's syndrome.

SOCIAL HISTORY
The patient had a 75 pack year history of smoking; quit 20 years ago. Also with history of heavy alcohol abuse; quit 15 years ago. The patient lives with his wife and two children.

PHYSICAL EXAM
There were multiple 2-8 mm compressible venous papules on the trunk and extremities. There was a lateral deformity of the right forearm.

RADIOLOGY
X-Ray, AP Lateral feet (2/08): Two standing views of the left foot demonstrated abnormality of the distal tibial cortex, likely an enchondroma. Two standing views of the right foot demonstrated developmental shortening of the fourth and fifth metatarsals and midshaft deformity of the third proximal phalynx. Enchondromas are seen at the distal tibia and fibula.

X-Ray, Right femur (5/04): On the right femur, there were multiple hereditary exostoses with metaphyseal deformity and small sessile and pedunculated enchondromas. There were no dominant aggressive lesions or focal bone destruction. There were enchondromas at the right iliac wing.

DIAGNOSIS
Muffucci's syndrome with cutaneous hemangiomas and enchondromas of the bone

TREATMENT AND COURSE
The hemangiomas and osteochondromas have been asymptomatic thus far and have not required treatment.

DISCUSSION
In 1881, Maffucci described a new clinical syndrome characterized by the association of multiple skeletal lesions and cutaneous hemangiomas. In the past ten years, a gene defect has been discovered in the type I receptor for parathyroid hormone and parathyroid hormone-related protein, which allows for constitutively activated hedgehog signaling, resulting in the formation of enchondromas of the bone. Maffucci's syndrome is inherited sporadically and onset is generally in childhood or adolescence, although approximately 25% of patients will have evidence of radiographic or cutaneous findings at birth. There are less than 200 case reports of Maffucci's syndrome in the English literature. According to these case reports, the syndrome has no racial or gender predilection.

The differential diagnosis of Maffucci's syndrome includes Ollier's disease (multiple enchrondromas), blue rubber bleb nevus syndrome, Klippel-Trenaunay syndrome, Gorham's syndrome (angiomas of bone and adjacent soft tissue), and Kaposi's sarcoma. It can be difficult to distinguish between Ollier's disease and Maffucci's syndrome, as Maffucci's syndrome may have subtle cutaneous hemangiomas. It has also been suggested that these conditions are the same disorders in different periods of development, with different phenotypic expression of the same gene.

The hemangiomas in Maffucci's syndrome appear as reddish-blue, soft, compressible, subcutaneous nodules. Controversy exists regarding the nomenclature of the vascular skin lesions, as they often behave unlike typical hemangiomas and show more features of vascular malformations. This is demonstrated by the fact that the vascular lesions tend to grow over the course of one's life and show no tendency for spontaneous resolution. In several case reports, they are referred to as venous malformations. Histologically, the hemangiomas are the venous type, but capillary or mixed venous/ capillary types have been reported. The hemangiomas show a predilection for the extremities and are often unilateral, but involvement of the leptomeninges, eyes, pharynx, tongue, trachea, and intestines has been reported. Also reported are the rare presence of lymphangiomas. Successful treatment with surgical excision has been documented for both hemangiomas and lymhangiomas.

It is hypothesized that the bone lesions in Maffucci's syndrome are secondary to generalized dyschondroplasia. During ossification of the bone, the normal degenerating cartilage may persist and proliferate to form cartilaginous tumors, or enchondromas. There is also decreased activity in the proliferation zone of the epiphyseal plate, resulting in shortening and deformity of the affected bone. Pathologic fractures with resulting nonunion or malunion may lead to debilitating deformities. Enchondromas are often multiple and most commonly involve the hands, but may also involve the long bones of the limbs or flat bones of the skull, pelvis, and scapulae. Surgical removal of enchondromas is not indicated.

Malignant transformation of the benign skeletal lesions is observed in approximately 25% of lesions, and early diagnosis of the disease is therefore an important factor for prognosis. The most common malignancies include chondrosarcoma (15%) and osteosarcoma (5%). Although less common, hemangiosarcomas, lymphangiosarcomas, and fibrosarcomas have been reported and behave more aggressively. The average age for development of chondrosarcoma is 40 years. Despite newer surgical therapies for chondrosarcomas, the prognosis for patients with these tumors remains poor.

Although Maffucci's syndrome is believed to be a mesodermal dysplasia, the number of both benign and malignant nonmesodermal tumors appears high (30%). Common tumors include astrocytomas, pituitary adenomas, thyroid adenomas, pancreatic adenocarcinomas, ovarian sarcomas, and breast fibroadenomas. Periodic imaging of the brain, abdomen, and pelvis is suggested for patient with Maffucci's syndrome.

REFERENCES

1. Hyde, GE et al. Head and neck manifestations of Maffucci's syndrome: Chondrosarcoma of the nasal septum. *Am J Otolaryngology.* 1995; 16(4): 272-275.

2. Kaplan, RP et al. Maffucci's syndrome: Two case reports with a literature review. *JAAD.* 1993; 29(5): 894-899.
3. Ma, GY and Leung, PC. The management of the soft tissue hemagiomatous manifestations of Maffucci's syndrome. *Br J Plastic Surgery.* 1984; 37: 615-618.
4. Ramina, R et al. Maffucci's syndrome associated with a cranial base chondrosarcoma: Case report and literature review. 1997; 41(1): 269-272.
5. Shepherd, A et al. Maffucci's syndrome with extensive gastrointestinal involvement. *Aust J Derm.* 2005; 46: 33-37.

CHICAGO DERMATOLOGICAL SOCIETY **CASE # 4**

Presented by Jessica Kappelman MD, David Eilers MD, James Swan MD, and Scott Wickless, DO
Division of Dermatology, Hines Veterans Administration Hospital

HISTORY OF PRESENT ILLNESS

This 67-year-old Caucasian male presented to dermatology clinic in November, 2006 for evaluation and treatment of biopsy proven cicatricial pemphigoid (gingival mucosa). The patient complained of multiple painful blisters and erosions on the buccal mucosa and gingiva, as well as dry, pruritic, and burning eyes. The oral erosions had improved with triamcinolone 0.1% paste and dexamethasone swish and spit, which had been prescribed by the dental clinic. He denied any blisters on the skin or other mucous membranes, photophobia, or changes in vision.

PAST MEDICAL HISTORY

Spinal stenosis
Hepatitis C
Parkinson's disease
Orthostatic hypotension
Mild renal insufficiency
Benign prostatic hypertrophy
Seborrheic dermatitis
Blepharitis
Left knee replacement 2004
Right rotator cuff repair 2002
Fifth metatarsal fracture status post surgical repair 1968
Appendectomy 1960

MEDICATIONS

Carbidopa/ Levodopa
Carboxymethylcellulose sodium 0.5% ophthalmic solution
Clotrimazole 1% cream
Coal tar 2% cream
Coenzyme Q10
Docusate sodium
Erythromycin 0.5% ophthalmic ointment
Etanercept
Finasteride
Hydrocortisone valerate 0.2% cream
Psyllium oral powder
Tamsulosin
Tramadol

ALLERGIES
No known drug allergies

FAMILY HISTORY
No family history of bullous/ vesicular skin disease.

SOCIAL HISTORY
The patient is married and lives with his wife. He quit smoking in 1970. He admits to occasional social alcohol use, but denies any illicit drugs.

PHYSICAL EXAM
On initial presentation to dental clinic, the patient had mild involvement of the oral mucosa with small erythematous erosions on the right and left maxillary alveolar mucosa and right buccal mucosa. No intact blisters were present. On subsequent visits, he was noted to have small 1 mm vesicles along the upper and lower eyelid margins with conjunctival erosions and eventual symblepharon formation.

HISTOPATHOLOGY
A biopsy of the maxillary gingiva revealed acute and chronic inflammation with thickened, amorphous collagen.
Direct immunoflourescence microscopy of the maxillary gingiva showed linear deposits at the dermal-epidermal junction with IgG (3+) and IgA (2+). No intraepidermal or dermal deposits were seen. IgM, C3, and fibrinogen were negative.

LABORATORY RESULTS
The following were within normal limits or negative:
G6PD, sedimentation rate, complete blood count, liver function tests

DIAGNOSIS
Mucous membrane pemphigoid successfully treated with etanercept.

TREATMENT AND COURSE
At the initial consult, the patient was started on doxycycline 100 mg twice daily and niacinamide 500 mg three times daily. He was also followed by ophthalmology, who prescribed carboxymethylcellulose and lubricating eye drops. At his follow up two months later, his oral lesions had not improved and he had developed vesicles on the ocular mucosa. In addition, and after normal G6PD levels, he was started on dapsone 25 mg which was increased to 200 mg daily over the course of four months with excellent results. After nine months on dapsone, the patient went for routine colonoscopy and was found to have oxygen saturations in the mid eighties. He was sent to the emergency room, at which time he was noted to have pale skin and bluish discoloration of the lips, nail beds, and oral mucosa. He was otherwise asymptomatic and denied shortness of breath or fatigue. Labs revealed a methemoglobinemia of 20%. Dapsone was immediately discontinued and patient was given an infusion of methylene blue at 2 mg /kg over 10 minutes. Repeat methemoglobin level post transfusion was 7.8% and continued to drop over the course of his stay in the medical intensive care unit. He was discharged with topical tacrolimus ointment for the mouth and cyclosporine eyedrops. At follow up four weeks later, the patient complained of worsening oral and ocular lesions. After extensive discussion with the patient, etanercept 25 mg subcutaneous injections were initiated twice weekly with increase to 25 mg three times

weekly. The patient noted significant improvement and near resolution of disease after three weeks and has continued to remain in remission. At his most recent visit, his etanercept dose was decreased to 25 mg twice weekly with no flare in oral or mucosal lesions.

DISCUSSION

Mucous membrane pemphigoid (MMP), previously known as cicatricial pemphigoid, is a heterogenous group of immune-mediated, subepithelial blistering diseases. Any mucous membrane can be involved, but the most commonly involved sites include the oral mucosa (85%), conjunctiva (64%), skin (24%), pharynx (19%), external genitalia (17%), nasal mucosa (15%), larynx (8%), anus (4%), and esophagus (4%). Oral MMP most commonly presents as desquamative or erosive gingivitis, but severe disease can lead to ulcerations, fibrosis, and adhesions of the oral mucosa. Ocular MMP is characterized by conjunctival inflammation and, when chronic, leads to symblepharon, surface keratinization, neovascularization, and blindness. Involvement of other mucosal surfaces can also lead to severe sequelae, such as airway obstruction and stricture formation. For patients who present with isolated oral disease, the incidence rate for the development of ocular disease is 0.03 per person per year and a cumulative incidence of 15% by 5 years. MMP is most common in women in the 7^{th} to 9^{th} decades, but childhood cases have been reported.

Several autoantibodies against epithelial basement membrane antigens have been discovered in patients with MMP. These include bullous pemphigoid antigens 1 and 2, laminin 5 and 6, type 7 collagen, integrin beta 4 subunit, uncein, and a few unidentified antigens (45 kDa, 168 kDa, 120 kDa). In a study by Oyama et al. (Br J Dermatol 2006), examination of 124 patients with MMP revealed 85% of patients with ocular involvement had reactivity to beta 4 integrin. In addition, severe clinical features were associated with antibody reactivity to multiple antigens, as well as reactivity to multiple BP180 component antigens. A genetic predisposition to MMP has also been hypothesized, demonstrated by the association of human leukocyte antigen DQB1 and DRB1. This may have a role in T-lymphocyte recognition of antigens in the basement membrane zone.

The exact pathophysiology of MMP has not been elucidated, but recent evidence suggests a possible role of tumor necrosis factor alpha. A study by Lee at al. (Invest Ophtalmol 1993) revealed elevated TNF alpha levels in serum of patients with MMP compared with controls. More recent studies have confirmed the presence of TNF alpha in conjunctiva of patients with MMP. Coma et al. (Acta Ophthalmol 2007) revealed TNF alpha expression in both stroma and epithelia from conjunctiva in six of eight patients studied. All five controls were negative. TNF alpha has been shown to up-regulate endothelial cell activation, stimulate fibroblasts, and recruit inflammatory cells such as macrophages, neutrophils, eosinophils, lymphocytes, and mast cells. All of these factors in combination have led to tissue fibrosis and chronic inflammation.

The diagnosis of MMP is based on histology and immunoflourescence. Histologically, MMP is characterized by junctional separation at the level of the basement membrane with an inflammatory infiltrate consisting of eosinophils, lymphocytes, and neutrophils. Direct immunoflourescence (DIF) testing is both sensitive and specific for the diagnosis of MMP and is considered the gold standard. Immune deposits that reflect autoantibody deposition can be detected at the basement membrane zone in a linear pattern and often include IgG (97%) with C3 (78%). IgA (27%) and IgM (12%) may also be seen.

Mulyowa et al. (Int J Dermatol 1996) reported that IgG reactivity correlated with older age, whereas younger patients typically demonstrated IgA reactivity. Indirect immunoflourescence using salt-split skin can show antibasement membrane zone antibodies and can distinguish between antigens on the epithelial side of the split (B4 integrin and BPAg2) and those on the dermal side of the split (laminin 5). The lowest detection of circulating autoantibodies occurs in patients with ocular disease only (7%) and the highest in patients with both skin and mucosal involvement (81%). Electron microscopy has had limited usefulness in the diagnosis of MMP.

Treatment of MMP can be extremely difficult. Double-blind, controlled, multicenter studies comparing different systemic regimens have not been conducted. The choice of treatment relies upon the experience and comfort of individual clinicians. An international consensus meeting in 1999 suggested stratifying patients into high-risk and low-risk groups to determine appropriate therapy. Patients with high-risk disease include rapidly progressive disease or involvement of ocular, genital, nasopharyngeal, esophageal, and/or laryngeal mucosa. The consensus recommended initial treatment of these patients with prednisone and cyclophosphamide. Alternative therapy includes dapsone, azathioprine, or IVIG. Low risk patients include those with oral mucosal disease or oral mucosa plus skin disease. These patients can be treated more conservatively, with topicals, tetracycline and niacinamide, or systemic immunosuppressives.

More recently, the successful use of anti-TNF alpha agents (etanercept, infliximab) have been reported. These agents may have a lower side effect profile than other immunosuppressives, and have been shown to work in cases of MMP refractory to standard immunosuppressives. Canizares et al. (Ach Dermatol 2006) reported three patients with MMP who were treated with etanercept 25 mg subcutaneous injections twice weekly. All three patients had oral mucosal disease and one had severe ocular disease. Oral mucosal disease improved in all three patients and the ocular disease stabilized. Heffernan and Bently (Arch Dermatol 2006) described one patient with oral and ocular MMP refractory to multiple other systemic treatments, whose oral mucosal disease improved and ocular disease stabilized with infliximab infusions every eight weeks. Newer evidence suggests CD20 monoclonal antibodies (rituxumab) to be of benefit in severe, refractory cases of MMP.

A multidisciplinary approach to the management of MMP patients is encouraged. This often requires the involvement of ophthalmologists, dermatologists, dentists, oral surgeons, primary care physicians, gynecologists, otolaryngologists, and gastroenterologists. Patients with antiepiligrin (laminin 5) MMP have a higher incidence of solid organ malignancies than the rest of the population and cancer screening should be a priority.

REFERENCES

1. Canizares, MJ et al. Successful treatment of mucous membrane pemphigoid with etanercept in 3 patients. Arch Dermatol. 2006;142: 1457- 1461.

2. Coma, MC et al. Tumor necrosis factor alpha in conjunctiva affected by ocular cicatricial pemphigoid. Acta Ophthalmol. 2007; 85: 753-755.

3. Heffernan, MP et al. Successful treatment of mucous membrane pemphigoid with infliximab. Ach Dermatol. 2006; 142: 1268-1270.

4. Ricotti, C et al. Mucosal “peeling” biopsy technique for the immunopathologic evaluation of desquamative gingivitis-associated mucous membrane pemphigoid. Arch Dermatol. 2008; 144(11): 1538.
5. Scully, C and Muzio, L. Oral mucosal diseases: Mucous membrane pemphigoid. Br J Oral Max Surg. 2008; 46: 358-366.
6. Thorne, JE et al. Treatment of ocular mucous membrane pemphigoid with immunosuppressive drug therapy. Ophthalmology. 2008; 115(12): 2146-2152.
7. Thorne, Daniel E. Recent advances in mucous membrane pemphigoid. Curr Opinion Ophthalmology. 2008; 19(4): 292-297.

CHICAGO DERMATOLOGICAL SOCIETY **CASE # 5**

Presented by Kathryn Barlow MD, Kathleen Remlinger MD, James Swan MD, and David Eilers MD
Division of Dermatology, Hines Veterans Administration Hospital

HISTORY OF PRESENT ILLNESS

A 55-year old man with a history of chronic plaque psoriasis and psoriatic arthritis presented to the dermatology clinic for follow-up. He has previously been treated with PUVA, acitretin, topical triamcinolone ointment and calcipotriene cream with improvement, but was lost to follow-up for several years. His arthritis was previously treated by rheumatology with intermittent prednisone tapers, with the last dose taken in March, 2008. After discussing the risks, benefits and alternatives, treatment with adalimumab 40 mg every other week was initiated in March, 2008, with dramatic improvement over the next several months. On June 24, 2008, the patient presented to the emergency department with a six-day history of fever, progressive shortness of breath and cough. On exam, he was febrile (103.4F), had conversational dyspnea, and chest x-ray revealed dense consolidation of the left lobe. He was transferred to the MICU for further monitoring.

PAST MEDICAL HISTORY

Coronary artery disease
Hypertension
Dyslipidemia
Psoriasis and psoriatic arthritis

MEDICATIONS

Lisinopril
Simvastatin
Triamcinolone 0.1% ointment
Calcipotriene 0.005% cream
Adalimumab

ALLERGIES

No known drug allergies

FAMILY HISTORY

Non- contributory

SOCIAL HISTORY

Tobacco use: 30-pack year history, quit in 2007.
Occasional alcohol

PHYSICAL EXAM

The patient was examined in the MICU shortly after admission. He had resolving pink, thin plaques over the elbows, knees, and extremities. In addition, over the chest, abdomen and legs he had developed a morbilliform eruption of erythematous, non-scaling, blanchable macules coalescing into patches. Decreased breath sounds and expiratory wheezes were noted over the entire left lung.

LABORATORY RESULTS

The following tests were abnormal:
Urine Legionella antigen: positive
Sputum Legionella culture: positive
Creatinine: 4.5 (0.8-1.3)
Blood urea nitrogen: 60 (7-21)

RADIOLOGY

Chest X-ray: There was extensive pneumonic consolitation involving the left mid and lower lung fields, with a small left pleural effusion also noted.

DIAGNOSIS

Legionella pneumophila pneumonia associated with treatment of psoriasis with adalimumab

TREATMENT AND COURSE

Upon admission to the MICU, the patient was started on broad-spectrum antibiotic coverage with pipericillin/tazobactam and azithromycin, and the adalimumab was discontinued. Due to increasing respiratory distress, the patient required intubation shortly after admission. Once the urinary Legionella antigen was confirmed positive, antibiotic coverage was changed to azithromycin, with a 21-day course planned. Complications during the hospital course included evidence of acute renal failure requiring hemodialysis, thought to be due to dehydration and use of NSAIDS prior to admission. The macular eruption resolved after several days. His renal function eventually normalized, and pulmonary status gradually improved. After 12 days, the patient was successfully extubated, and eventually discharged home. His psoriasis began to flare off systemic therapy, and methotrexate15 mg weekly was initiated in the fall of 2008. Unfortunately, the patient failed to respond after 5 months of treatment, and in April 2009, the patient was started on acitretin 25 mg weekly, with PUVA added shortly thereafter.

DISCUSSION

Legionella pneumophila is a ubiquitous, opportunistic gram-negative intracellular pathogen. Transmission occurs from inhalation or aspiration of contaminated water, and person-person transmission has not been recorded. Besides pneumonia, neurologic and gastrointestinal manifestations may be present. There have been several reported cases of a morbilliform eruption associated with the infection. Although 64 different Legionella serogroups have been identified, 80-90% of adult cases of legionellosis are caused by serogroup 1. First line therapy is azithromycin or fluoroquinolones, with doxycycline and trimethoprim-sulfamethoxazole available as second line therapy.

It has long been known that tumor necrosis factor-α (TNF-α) antagonists are associated with an increased risk of infections. In particular, infections caused by intracellular microorganisms represent the highest risk, with active tuberculosis being the most common. TNF-α, a pro-inflammatory cytokine, plays an important role in host resistance against infections, especially those that multiply intracellularly. Specifically, TNF-α facilitates the recruitment of inflammatory cells to sites of infection, induces differentiation of monocytes and macrophages, and stimulates and maintains formation of granulomas.

A recent study in France reported the development of *Legionella pneumophila* pneumonia in 10 patients receiving anti-TNF-α therapy, including 6 patients on adalimumab, 2 patients on etanercept and 2 patients on infliximab over a one-year period. The patients were being treated for rheumatoid arthritis, psoriasis and pyoderma gangrenosum, and several were receiving concomitant methotrexate or corticosteroids. The calculated relative risk of legionellosis when receiving treatment with a TNF-α antagonist compared to the general population was between 16.5-21.0. Although rare, *Legionella pneumophila* pneumonia is a severe but curable infection that may complicate treatment with anti-TNF-α agents. It should be considered in the differential diagnosis and the initial antibiotic treatment should be effective against *L. pneumophila* in any patient on these therapies who develops a pneumonia.

REFERENCES

1. Tuback F, et al. Emergence of Legionella pneumophila Pneumonia in Patients Receiving Tumor Necrosis Factor-α Antagonists. *Clin Infect Dis*. 2006;43:95-100.

2. Rathore MH, Alvarez A. Legionella infection. eMedicine. Last updated February 5, 2009.

3. Mancini G, et al. Tuberculosis and *Legionella pneumophila* pneumonia in a patient receiving anti-tumour necrosis factor-α treatment. *Clin Microbiol Infect*. 2006;13:1036-1037.

4. Moiton MP, et al. Role of anti-tumour necrosis factor-α therapeutic agents in the emergence of infections. *Clin Microbiol Infect.* 2006;12:1151-53.

CHICAGO DERMATOLOGICAL SOCIETY **CASE # 6**

Presented by Tricia Hultgren MD, Stacy McClure MD, and Madhu Dahiya MD
Division of Dermatology, Loyola University Medical Center

HISTORY OF PRESENT ILLNESS

This 39-year old previously healthy Hispanic male was transferred from an outside hospital in September 2008 for further management of an acute bullous eruption. The patient reported a nine-day history of itchy pink papules on the neck and forearms that rapidly evolved into fluid-filled blisters that spread to the trunk, lower extremities and genitals. He denied ocular and oral involvement. He was hospitalized and treated empirically with levofloxacin and intravenous acyclovir for possible bacterial infection and disseminated herpes viral infection without improvement, and was transferred to our institution for further management. The only medication started prior to the eruption was escitalopram, which he began taking for depression 45 days prior to the onset of symptoms.

PAST MEDICAL HISTORY

Depression

MEDICATIONS

Escitalopram

ALLERGIES

No known drug allergies

FAMILY HISTORY

No family history of auto-immune bullous disorders

SOCIAL HISTORY

Patient denied tobacco and alcohol use, but admitted to daily marijuana use. He had history of cocaine use but quit 5 months prior to onset of symptoms.

REVIEW OF SYSTEMS

Negative for fever, chills, weight loss, nausea, vomiting, headache, arthralgias, myalgias, and preceeding illness. Positive for chronic diarrhea for the past five years.

PHYSICAL EXAM

On the upper chest, posterior upper arms, lateral neck>> abdomen, back and lower extremities there were numerous coalescing, erythematous, urticarial plaques with peripheral tense bullae and scattered erosions with hemorrhagic crust, some in an annular configuration. Erosions with hemorrhagic crust were present on the glans penis. The palms, soles, oral and ocular mucosa were spared.

HISTOPATHOLOGY

Histopathologic examination of a punch biopsy from the left forearm stained with hemotoxin and eosin revealed a dermal lympho-eosinophilic interstitial and perivascular infiltrate. Biopsy for frozen section showed a subepidermal vesicle. Direct immunoflourescence examination of perilesional skin from the left forearm demonstrated linear IgA deposition along the basement membrane.

LABORATORY RESULTS

The following tests were negative or normal:
Comprehensive metabolic panel
White blood cell count
Blood culture
Viral culture
HIV
TSH
ANA
Rheumatoid factor
SPEP
UPEP

The following tests were positive or abnormal:

Calcium 8.2 mg/dl	(8.9-10.3 mg/dl)
Glucose 148	(70-100 mg/dl)
Hemaglobin 12.9	(14-17 g/dl)
Hematocrit 37.3	(40-54 mg/dl)

DIAGNOSIS

Linear IgA bullous dermatosis

TREATMENT AND COURSE

During hospitalization, the patient's condition was managed by the burn team. He was placed on intravenous methylprednisolone and topical dressings were applied. Escitalopram was discontinued, and new blisters ceased to develop while on intravenous steroids. The patient was discharged on day seven without oral steroids and developed new lesions after three weeks, which subsequently resolved with 60mg prednisone daily. The patient was first seen in dermatology six weeks after discharge, and a slow prednisone taper was initiated. He was placed on calcium, vitamin D and received a baseline DEXA scan. He was seen by rheumatology and had no indication of connective tissue disease. A colonoscopy was obtained to further evaluate the patient's chronic diarrhea, which revealed nodularity of the terminal ileam. Biopsies showed no evidence of Crohn's disease. The patient's course was further compromised by vitamin B12 deficiency, perleche, and acute urticaria that resolved with antihistamines.

The patient remained blister-free until tapering to 2.5 mg prednisone every other day. He subsequently developed grouped erythematous papulovesicles on the left volar forearm, upper lip, and glans penis. Biopsy for H&E demonstrated a subepidermal vesicle with neutrophils and eosinophils, and repeat DIF showed linear IgA, IgG and C3 at the basement membrane zone. Recent laboratory tests revealed increased liver function tests, which is currently by evaluated by Gastroenterology. The patient is currently fairly well controlled on 5 mg of prednisone daily, and we will consider the addition of dapsone pending further work-up of his elevated liver enzymes.

Early in the patient's disease course, the etiology was debated (idiopathic vs. drug-induced secondary to escitalopram). After relapse and biopsy, the diagnosis of idiopathic linear IgA bullous dermatosis was confirmed.

DISCUSSION

Linear IgA bullous dermatosis (LABD) is an autoimmune subepidermal blistering disorder characterized by the deposition of linear IgA along the basement membrane zone (BMZ). Although most cases are idiopathic, LABD may be drug-induced, with vancomycin the most commonly implicated medication.

Clinical manifestations of LABD vary and are often indistinguishable from bullous pemphigoid and dermatitis herpetiformis. The eruption commonly presents with urticarial plaques and crops of tense bulllae. Lesions favor the trunk, groin, lower extremities and oral mucosa. Vesicles are often observed at the periphery of annular lesions, creating the "string of beads" sign. Cases of LABD mimicking erythema multiforme, toxic epidermal necrolysis and morbilliform drug eruption have also been reported.

Histologically, LABD demonstrates subepidermal blistering and a neutrophilic infiltrate. As lesions evolve, eosinophils become more frequent. The diagnosis is confirmed by direct immunoflourescence of perilesional skin, which demonstrates linear IgA along the BMZ, and rarely small amounts of C3 and IgG. Circulating IgA anti-BMZ antibodies are less frequent, detected in approximately 20% of drug-induced cases. Immune deposits resolve following remission in drug-induced LABD, whereas in idiopathic disease clearance of immunodeposits is less predictable.

Drug-induced LABD can often be deduced from a thorough medication history. In contrast to the idiopathic form, drug-induced LABD most often presents within 1-15 days of exposure to the offending medication and resolves within 2-7 weeks following drug withdrawal. Mucosal lesions occur less frequently in drug-induced LABD than in idiopathic LABD, but may be more common than initially suggested. Palmer *et al.* reported mucosal involvement in 13 of 29 drug-induced cases (45%).

A heterogeneous group of target antigens has been identified in idiopathic LABD, including the 97 kD extracellular domain of the 180 kD bullous pemphigoid antigen and type-VII collagen. Given the rarity of drug-induced LABD, fewer studies have been undertaken to delineate the target antigens. However, antibodies to BP230, the 97 kDa antigen, type VII collagen, and LAD 285 have been demonstrated.

Drug-induced LABD is most commonly associated with vancomycin and appears to be independent of dose and serum vanconycin levels (see table 1). To our knowledge, escitalopram has not been reported to cause LABD. The exact mechanism of drug-induced LABD is unknown. Theories of pathogenesis incude stimulation of disease by cross-reaction of target epitopes, conformational change of epitopes, or by unmasking previously unexposed antigens to the immune system. Idiopathic LABD has been linked to HLA antigens B8, DR3, and Cw 7. HLA sub-typing has not been studied in drug-induced disease.

LABD has been associated with malignancy, connective tissue disease, inflammatory bowel disease and infection. The significance of these findings is unknown, but a common mechanism involving stimulation of the IgA mucosal immune system has been postulated. Although rare, both hematologic and solid malignancies have been reported, including B-cell lymphoma, chronic lymphocytic leukemia, breast, thyroid, esophageal carcinoma and bladder cancer. Additionally, infectious agents have preceeded LABD in several cases. Wojnarowska et al. reported 26% of adults and 38% of children had an

infection prior to onset of disease. Infectious agents included viral upper respiratory illness, typhoid, brucellosis, tetanus, and streptococcal pharyngitis.

Autoimmune diseases reported with LABD include dermatomyositis, systemic lupus erythematosus, rheumatoid arthritis, hemolytic anemia and glomerulonephritis. Cases are rare and have not allowed for estimation of prevalence. Inflammatory bowel disease, including both Crohn's disease and Ulcerative Colitis, has also been reported in pts with LABD.

Dapsone remains first-line treatment for LABD, with clinical improvement usually seen within 48-72 hours. Prednisone is often added if symptoms are not controlled with dapsone. Occasionally, steroid-sparing agents such as azathioprine or mycophenolate mofetil may be required. Typically, idiopathic LABD takes a prolonged course marked by several years of active disease. Eventually, 10-50% of cases will spontaneously resolve. In contrast, drug-induced disease clears once the offending agent is withdrawn, usually within 2-7 weeks.

Table 1- Drugs associated with Linear IgA Bullous Dermatosis (1, 4, 7-9; additional references available upon request)

Medication	Number of reported cases
Vancomycin	32
Diclofenac	3
Phenytoin	3
Penicillin	2
Piroxicam	2
Trimethoprim-sulfamethoxazole Depot sulfonamide	2 1
Amiodarone	2
IL-2, gamma IFN	2
Vancomycin/rifampin	2
Vancomycin/tobramycin	1
Vancomycin/ampicillin	1
Vancomycin/ciprofloxacin	1
Vancomycin/cefazolin	1
Captopril	1
Captopril/trimethoprim-sulfamethoxazole	1
Somatostatin	1
Lithium	1
Cefamandole	1
Moxifloxacin	1
Rimantadine, zanamivir, and azithromycin	1
Vigabatrin	1
Cefamandole	1
IL-2	1
Iodine	1
Glibenclamide	1
Benazepril	1
Naproxyn	1
Gemcitabine	1
Ceftriaxone/metronidazole	1

Furosemide	1
Carbamazepine	1
Atorvastatin	1

REFERENCES

1. Kuechle MK, Stegemeir E, Maynard B et al. Drug-induced linear IgA bullous dermatosis: Report of six cases and review of the literature. J Am Acad Derm 1994;30:187-92.

2. Mobacken H, Kastrup K, Ljunghall H et al. Linear IgA dermatosis: a study of ten adult patients. Acta Dermatovener 1983;63:123-8.

3. Wojnarowska F, Marsden RA, Bhogal B et al. Chronic bullous disease of childhood, childhood cicatricial pemphigoid and linear IgA disease of adults. J Am Acad Derm 1988;19:792-805

4. Palmer RA, Ogg G, Allen J et al. Vancomycin-induced linear IgA disease with autoantibodies to BP180 and LAD285. Br J Derm 2001;145:816-820.

5. Zone JJ, Tayor TB, Meyer LJ, Petersen MJ. The 97 kDa linear IgA bullous disease is identical to a portion of the extracellular domain of the 180 kDa bullous pemphigoid antigen, BPAG2. J Invest Dermatol 1998;110:207-10.

6. Paul C, Wolkenstein P, Prost C et al. Drug-induced linear IgA disease: target antigens are heterogeneous. B J Derm 1997;136:406-411.

7. Wakelin SH, Allen J, Zhou S, Wojnarowska F. Drug-induced linear IgA disease with antibodies to collaged VII. B J Derm 1998;138:310-314.

8. Waldman MA, Black DR, Callen JP. Vancomycin-induced linear IgA bullous disease presenting as toxic epidermal necrolysis. Clin and exp dermatol 2004;29:633-36.

9. Nousari HC, Costarangos C, Anhalt GJ. Vancomycin-associated linear IgA bullous dermatosis. Ann Intern Med 1998;129:507-8.

10. Camilleri M and Pace J. Drug-induced linear immunoglobulin-A bullous dermatosis. Clin Dermatol 1998;16:389-91.

11. Godfrey K et al. Linear IgA disease of adults: associated with lymphoproliferative malignancy. Br J Derm 1997:123:447-52

12. Barrow-Wedel, Jordan RE, Arnett FC. Linear IgA disease associated with dermatomyositis. Arch Derm 1992:128;413-414.

13. Egan CA, Meadows KP, Zone J: Ulceratie colitits and immunobullous disease cured by colectomy. Arch Dermatol 1999; 135:214-215.

14. Sekula SA, Tschen JA, Bean SF, Wolf Jr JE:Linear IgA bullous disease in a patient with transitional cell carcinoma of the bladder. Cutis1986;38:354-356.362.

CHICAGO DERMATOLOGICAL SOCIETY **CASE # 7**

Presented by Jessica Kappelman MD, Anthony Peterson MD, Madhu Dahiya MD and Patricia Kammeyer
Division of Dermatology, Loyola University Medical Center

UNKNOWN

CHICAGO DERMATOLOGICAL SOCIETY **CASE # 8**

Presented by Aaron Pace MD, David Eilers MD, James Swan MD and Scott Wickless DO
Division of Dermatology, Hines Veterans Administration Hospital

HISTORY OF PRESENT ILLNESS

A 79-year old male with a history of a solitary lesion of Kaposi's sarcoma on the right posterior thigh, which was excised in June 2007 with clear margins, presented in August 2008 with new papules on the arms. The lesions had been present for four months and were growing in size. The papules were asymptomatic. The patient's review of systems was negative.

PAST MEDICAL HISTORY

Kaposi's sarcoma
Psoriasis
Hypertension
Status post CABG in 1997 with 1 unit of pooled platelets and 2 units packed erythrocytes
Hyperlipidemia
Neprolithiasis

MEDICATIONS

Calcipotriene cream
Clobetasol ointment
Fluocinolone solution
Clopidogrel
Gabapentin
Lisinopril
Metoprolol
Simvastatin

ALLERGIES

No known drug allergies

FAMILY HISTORY

No history of Kaposi's sarcoma.

SOCIAL HISTORY

The patient is of Irish descent having moved from Ireland as a child. He is heterosexual and lifetime monogamous having been married at 21. Has never traveled outside of Europe or the United States.

PHYSICAL EXAM

On exam the patient had four firm, non-compressible violaceous papules located on the right upper lateral arm, right forearm, left forearm, and left posterior upper arm and ranging in size from 4-6mm. On the right posterior thigh there was a well-healed scar without nodularity. No head and neck, axillary, or inguinal lymphadenopathy was present.

HISTOPATHOLOGY

Histopathologic examination of the biopsy from 3 lesions revealed a dermal proliferation of atypical spindle cells arranged in a perivascular and interstitial pattern. The surrounding stroma showed fibroplasia with cleft like spaces filled with erythrocytes. (Two of the sites revealed dilated vascular spaces with attenuated endothelium, consistent with the lymphangiomatous variant.) The dermis showed a variable mostly perivascular lymphohistiocytic infiltrate with some plasma cells. Immunohistochemistry revealed CD31, CD34, and HHV-8 positivity. There was a lack of eosinophilic hyaline granules.

LABORATORY RESULTS

The following were normal or negative: CBC, HIV, CD4 count, CMP, U/A

DIAGNOSIS

Kaposi's sarcoma

TREATMENT AND COURSE

The patient initially under went local excision with 0.5cm margins for the lesion on the right posterior thigh in June 2007. He first noticed his metastatic lesions in August of 2008 and they were definitively treated with intralesional vinblastine after biopsy. Initially one lesion was treated based on clinical appearance**.** He received intralesion viblastine at four sites all of which developed an indurated erythematous plaque consitent with an injection site reaction. One additional lesion was treated at a later point using this method and it also develped a reaction. The KS appears resolved at each site, however there was significant inflamation present. Given the patient's brisk response, and development of further new lesions of KS, it was decided to start a topical anti-angiogenic cocktail consisting of a topical steroid, calcipotriene cream, and tretinoin cream. It remains to be seen how the patient will respond this modality of treatment. The patient's disease remains limited to the upper extremities.

DISCUSSION

Kaposi's sarcoma (KS) was first described in five men in Hungary by Moritz Kaposi in 1872. KS has historically been considered a chronic, protracted disease primarily affecting elderly men, generally of Jewish or Mediterranean/Eastern European descent. It has also been reported in organ transplant patients and in its endemic form in Africa. KS was relatively rare, but gained notoriety when it became epidemic among men who have sex with men and was recognized as a sign of AIDS. Four types of Kaposi's sarcoma have been identified; classic KS (Mediterranean), endemic (African), iatrogenic (transplant and other immune suppression), and AIDS associated. The four types can appear similar clinically, although the African from is the only one that may occasionally demonstrate and infiltrative pattern. Typically the lesions are patches, plaques, or nodules, and thought to progress through the stages in that order.

In the mid 1990's human herpes virus 8 (HHV-8) was first associated with the disease. Although the pathogenesis has yet to be fully elucidated, HHV-8 is known to produce several important gene products that promote KS. HHV-8 has been intricately linked to the pathogenesis of the disease but it alone is unable cause KS. Cytokines, particularly oncostatin M and scatter factor, are necessary for the development of KS. In patients with AIDS, the HIV associated transactivating gene is of key importance as well.

Cytokines, HHV-8 and in certain cases, the HIV transactivating gene play overlapping roles in the development of the disease.

HHV-8 has been identified in all forms of the disease and in 100% of lesions in most case series. The seroprevalence of HHV-8 is widely accepted to be significantly higher than the rate of KS. In the general population, HHV-8 rates have been shown to be as high as 15%. The virus is known to be transmitted by men who have sex with men as well as through heterosexual intercourse, organ transplant, intravenous drug use, blood transfusions, and insect bites.

HHV-8 is known to be transmitted by multiple routes. Solid organ transplant patients have demonstrated risks 100 times greater than the general population in endemic areas. North American blood products have shown an HHV-8 seroprevalence of 2.4-11%. Currently there is no screening method for HHV-8. This is due in part, to the fact that there is such a high prevalence of the virus in the population. Transfusion has been associated with a low transmission rate of HHV-8 of 0.082%. No reports of HHV-8 and KS attributable to blood or blood product transfusion were identified with a Medline search.

The histologic features of all forms of Kaposi's sarcoma do not vary significantly but there are slight variations depending on whether the lesions are in the patch, plaque, or nodular stage. Overall, KS tends to demonstrate increased spindle cells with vascular slits and vascular structures with a predominance of endothelial cells. Extravasated RBC's and hemosiderin-laden macrophages are often present. Patch stage lesions will have subtle histopathologic findings consisting of a proliferation of irregular jagged blood vessels around reticular dermal vessels and adnexal structures. Plaque stage disease expands to fill the entire dermis and has a significant spindle cell component. Nodular lesions have sheets of spindle shaped cells with slit-like vascular spaces and mitoses may be present. There is a lymphangiomatous variant which has more dilated vascular spaces, attenuated endothelium, and lacks the presence of RBC's within the spaces.

Treatments vary depending on the clinical presentation, stage, and immune status of the patient. Local treatments can be surgical, with radiation, topical, or intralesional (as our patient was treated). FDA approved treatments for KS include alitretinoin gel, interferon-α, paclitaxel, doxorubicin, and daunorubicin. For patients with proven advanced systemic disease and lacking underlying immune compromise, single agent vinblastine, combination chemotherapy with vinblastine and bleomycin, and the anthracyclines, daunorubicin and doxorubicin, are all considered acceptable treatment options. In AIDS patients, HAART is implemented and patients often require no further treatment. Protease inhibitors are particularly effective. Other systemic treatments include changing of immune suppressive regimens for transplant patients, immunotherapy, antiangiogenic therapy, retinoids, or antivirals.

Prognosis depends on clinical type; patients with classic and iatrogenic Kaposi's sarcoma generally die with the disease rather than from it. Of note Moritz Kaposi described a relatively severe prognosis more consistent with what is seen in untreated AIDS related KS. African type has a 3-year survival of 64%. AIDS related KS has a near negligible 3-year survival if untreated. Patients die either due to KS or infection. AIDS-KS patients do much better if treated with HAART.

REFERENCES

1. Surrida S et al. Classic Kaposi's sarcoma: a review of 90 cases. J of Dermatol. 1992;19:548-52.
2. Weissmann A et al. Epidemiological study of classic Kaposi's sarcoma: a retrospective review of 125 cases from Norther Israel. J Eur Acad of Dermatol and Vener 2000;14:91-5.
3. Ramirez J et al. Lymphangioma-like Kaposi's sarcoma. Cutan Pathol 2005;32:286–92.
4. Cohen A et al. Kaposi's sarcoma-associated herpesvirus: clinical, diagnostic, and epidemiological aspects. Critical Rev in Clin Lab Sci. 2005;42(2):101-53.
5. Swartz R et al. Kaposi sarcoma: A continuing conundrum. J Am Acad Dermatol. 2008;59(2):179-206.
6. Engels E et al. Risk of transfusion-associated transmission of human herpesvirus 8. J of the Nat Canc Inst. 1999;91(20):1773-5
7. Engels E et al. Risk factors for human herpesvirus 8 infection amoung adults in the United States and evidence for sexual transmission. J Invest Dermatol. 2007;196:199-207.
8. Bihl F et al. Transfusion transmitted infections. J of Translat Med. 2007;5(25):1-34.
9. Dodd R. Human herpesvirus-8: what (not) to do? Transfusion. 2005;45:463-5.
10. Kaposi M. Idiopathic multiple pigmented sarcoma of the skin. CA Cancer J Clin. 1982;32:342-7.

CHICAGO DERMATOLOGICAL SOCIETY **CASE # 9**

Presented by Linda Sheu MD, Elaine Kung MD, and Madhu Dahiya, MD
Division of Dermatology, Loyola University Medical Center

HISTORY OF PRESENT ILLNESS
This 30-year old male presented with a two month history of thickening and desquamating skin on the plantar feet. Concurrently, he had developed pruritic papules and plaques on the wrists, forearms, ankles, penis and peri-anal region.

PAST MEDICAL HISTORY
Generalized vitiligo with white forelock since the age of seven

MEDICATIONS
None

ALLERGIES
No known drug allergies

REVIEW OF SYSTEMS
He denied nausea, vomiting, diarrhea, fever, chills or unintended weight loss.

FAMILY HISTORY
Mother with thyroid disease
Brother with diabetes mellitus type I
Uncle with multiple sclerosis
Mother and sister with psoriasis

SOCIAL HISTORY
Non-contributory

PHYSICAL EXAM
On the wrists, dorsal hands, forearms, and ankles were multiple 1-5mm dome-shaped to flat-topped pink papules. The right plantar surface had an erosion with an underlying erythematous-to-violaceous base surrounded by a violaceous border and a collarette of scale. The left plantar surface had tender, hyperkeratotic, yellowish plaques. The buccal mucosa had bilateral white reticulate patches. The glans penis had a violaceous, flat topped plaque and perianal area had an erythematous patch. .
In addition, the patient had generalized depigmentation, blue eyes, and whitish-gray central forelock.

LAB DATA
The following were abnormal or positive:
ALT 82 [10-40 IU/L], AST 49 [15-45IU/L]

The following were normal or negative:
Complete blood count, basic metabolic panel, thyroid stimulating hormone, hepatitis B surface antigen, anti-hepatitis B core IgM antigen, anti-hepatitis A IgM, anti-hepatitis C.

HISTOPATHOLOGY
Histopathologic examination of biopsies from the left dorsal hand, left lateral foot, and right plantar surface revealed hypergranulosis, hyperkeratosis and saw-toothing of the rete ridges. A lichenoid interface lymphocytic infiltrate and civatte bodies were also seen.

DIAGNOSIS
Lichen planus with plantar involvement

TREATMENT AND COURSE
The patient was started on triamcinolone 0.1% ointment twice daily to the body, and tacrolimus 0.1% ointment twice daily to the penis. After one month, due to unsatisfactory response, he started applying clobetasol ointment in the morning and cyclosporine solution in the evening on plantar surfaces and clobetasol ointment as needed to papules on the arms and legs. He continued to apply tacrolimus 0.1% ointment as needed on the penis. He reported drastic improvement within the first week of applying clobetasol ointment and cyclosporine solution on his plantar surfaces and almost stopped treatment within one month of initiating therapy.

DISCUSSION
Lichen planus is an idiopathic, inflammatory dermatosis characterized by violaceous, pruritic, flat-topped papules favoring the wrists, ankles, forearms, genitalia and presacral region. It most commonly presents in the fifth or sixth decade of life. Clinical variants include ulcerative, bullous, hypertrophic, linear, annular and lichen planopilaris. Although its pathogenesis is not completely understood, it is hypothesized to have an autoimmune etiology due to its association with viral infections, autoimmune diseases, graft versus host disease, medications, vaccination and dental restorative materials.

Palmar plantar lichen planus is relatively uncommon. Due to its atypical clinical presentation, it is difficult to establish the diagnosis without other findings of lichen planus on physical examination. The histopathology of palmar plantar lichen planus is identical to classic presentations of lichen planus. Palmar plantar lichen planus may present as erythematous plaques, punctate keratosis, diffuse keratoderma, or ulcerative lesions.

In a recent study of 139 patients with lichen planus, approximately one quarter were found to have palmar plantar involvement. The findings also included a male predominance (2:1), a mean age of presentation of 42.6 years (range 13-71), a mean time to diagnosis of 7.2 months. The initial presentation was erythematous plantar papules in all but one patient. Lesions were bilateral and symmetric in approximately two thirds of cases. Erythematous scaly papules and plaques were more common than hyperkeratotic lesions. For plantar lichen planus, the internal arch of the foot was the most frequent location, whereas there was no particular area of predilection for palmar lichen planus. Of note, Wickham's striae were consistently absent. Biopsies demonstrated classic histopathology of lichen planus in all but one case.

In this study, treatment included a combination of topical steroids with or without oral steroids and anti-histamines. Average time of treatment response was 3.5 months for

clearance of palmar-plantar,and other affected areas. Mucous membrane lesions were chronic and slower to respond to therapy. Recurrence after treatment occurred in 29% of patients, with mean time to relapse being 5 months.

While palmar plantar lichen planus can be successfully treated with topical steroids, many cases are difficult to treat. For such cases, successful treatment has been reported with cyclosporine, acitretin in conjunction with topical and intralesional kenalog, and surgical excision with skin grafting. Fortunately, our patient was treated successfully with clobetasol ointment and topical cyclosporine solution. Having our patient paint cyclosporine solution on his plantar surface was a novel and low-risk approach to using this medication.

REFERENCES

1. Cheung-Lee MJ, Rao J: Violaceous papules on the palms and soles. J Cutan Med Surg 2009: 12 (1): 35-40

2. Cribier B, Frances C, Chosidow O: Treatment of Lichen Planus. Arch Dermatol 1998. 134:1521-1530.

3. Gunduz K, Inanir I, Turkdogan P, Saar H: Palmoplantar lichen planus presenting with vesicle-like papules. J Dermatol 2003; 30 (4): 337-40.

4 Moss AL, Harman RR: Surgical treatment of painful lichen planus of the hand and foot. Br J Plast Surg 1986. 39(3): 402-7

5. Sanchez-Perez J, Rios Buceta L, Fraga J, Garcia-Diez A: Lichen planus with lesions on the palms and/soles: prevalence and clinicopathological study of 36 patients. Br J Dermatol 2000. 142: 310-314.

CHICAGO DERMATOLOGICAL SOCIETY **CASE # 10**

Presented by Aaron Pace MD, Rama Vaitla MD, and Madhu Dahiya MD
Division of Dermatology, Loyola University Medical Center

HISTORY OF PRESENT ILLNESS

A 58-year old female with a history of adenocarcinoma of the ampulla of Vater 8 years ago presented to clinic for a lesion on left index finger that had been present for 3 months. It started as a small boil on her left index finger, which ruptured and progressed to involve the side and dorsal surface of her finger and eventually to the dorsal hand. She also reported associated pain that she rated as a 7/10. She believed it started after being traumatized with a sliver while doing laundry. She tried using animal acne cream, which seemed to improve the lesion slightly. Any greasy products make it worse.

PAST MEDICAL HISTORY

Diabetes
Hypertension
Hypercholesterolemia
Adenocarcinoma of the ampulla of Vater s/p Whipple procedure and adjuvant gemcitabine/5-fluoruracil/XRT.

PAST SURGICAL HISTORY

Whipple procedure

MEDICATIONS

Aspirin
Flonase
Glipizide
Pancrease
Simvastatin

ALLERGIES

Sulfa drugs

FAMILY HISTORY

Non-contributory

SOCIAL HISTORY

Works in an animal shelter and handles mammals as well as a fresh water aquarium. Only drinks alcohol on special occasion.

PHYSICAL EXAM

On the left proximal index finger and dorsal hand there was a 4.5x2cm erythematous verrucous plaque with raised borders.

HISTOPATHOLOGY

Histopathologic examination of a biopsy from the base of the left index finger revealed pseudoepitheliomatous hyperplasia with intraepidermal neutrophils and deeper lymphohistiocytic infiltrate. Special stains were negative. Direct immune fluorescence was also negative.

LABORATORY RESULTS

The following were abnormal:
Tissue culture grew methicillin susceptible Staphylococcus aureus.

The following were normal or negative: Tissue culture for fungus and atypical mycobacterium, HIV, CBC, CMP, bromide level, and chest radiograph.

DIAGNOSIS

Pyoderma vegetans (blastomycosis-like pyoderma)

TREATMENT AND COURSE

The patient was started on doxycycline 100mg po twice a day, which she took for 6 weeks with complete clinical improvement.

DISCUSSION

Pyoderma vegetans was first described in 1898 by Hallopeau, which he named pyodermite vegetante. In 1903 De Azua and Sada y Pons described the same condition, although they called it pseudoepitheliomas cutanes. Since then the disease entity has gone by many names. Currently the favored names in the literature are pyoderma vegetans and blastomycosis-like pyoderma. Clinically the lesions appear similar to blastomycosis, hence the name. Lesions usually present as verrucous plaques with raised borders, often with multiple pustules. Historically the area is often painful and begins as a smaller pustular lesion. Once treated, the lesions heal leaving cribiform scarring.

The differential diagnosis includes blastomycosis, deep fungal infection, atypical mycobacterial infection, cutaneous tuberculosis, halodermas, pyoderma gangrenosum, pemphigus vegetans, and squamous cell carcinoma. Su, Scott, and Perry proposed six diagnostic criteria to help confirm the diagnosis.

1. Verrucous plaques with pustules and elevated border
2. Pseudoepitheliomatous hyperplasia with epidermal and subepidermal abscesses on histopathology
3. Growth of at least one pathogenic bacterium from tissue culture
4. Negative culture for deep fungi, atypical mycobacteria, and *M. tuberculosis*
5. Negative fungal serology test result
6. Normal bromide and iodide levels in the blood.

Tissue culture is important because treatment failure has been reported when treating only swabbed bacteria.

The pathogenesis is related to ubiquitous skin pathogens. Implicated organisms include, Staphylococcus aureus (most common), β-hemolytic streptococci, Pseudomonas aeruginosa, Proteus mirabilis, Escherichia coli, Prevotella, Corynebacterium, and Candida albicans. Multiple organisms may be isolated. Nutritional deficiency, particularly when related to alcoholism, contributes to the development of the condition by impairing host defenses. Other causes of this impaired state may include; leukemia, immunosuppressive therapy, diabetes, malnutrition, AIDS, and obesity. Even local skin conditions known to alter immune function in the skin such as radiation for underlying malignancy and actinic damage are known to predispose. This patient had a Whipple resection and is thus missing a significant portion of her intestinal tract including her pancreas. She may be in a chronic nutritionally deficient state related to this. In these

immune compromised circumstances, a minor insult, such as trauma, foreign body, or tattoo, results in bacterial overgrowth followed by hypertrophic tissue response. Our patients "trauma" may have been the sliver she had while doing laundry. Interestingly, the condition has also been associated with inflammatory bowel disease, particularly ulcerative colitis. This association was first noticed because as patients were treated for their pyoderma vegetans their ulcerative colitis improved as well. In one case, flaring of the patient's ulcerative colitis 3 months after complete remission of her pyoderma vegetans corresponded to a relapse of her skin disease.

The histopathology reveals pseudoepitheliomatous hyperplasia with intra and subepidermal micro abscesses composed of neutrophils. In the dermis a dense inflammatory infiltrate is often present. Focal areas of granuloma formation may be seen. Direct immune fluorescence will be negative and differentiates this from pemphigus vegetans, which may have similar histopathologic features.

Treatment is centered on appropriate systemic antibiotics for the cultured organism. Even with antibiotics focused to the organism's particular sensitivities, a prolonged course may be necessary. Other treatments reported effective include; intralesional corticosteroids, curettage and electrodessication, cryosurgery, excision, carbon dioxide laser, etanercept, and low dose acitretin (10mg daily for 3-4 months). Our patient responded well to a 6-week course of doxycycline.

REFERENCES

1. Sawalka SS, Phiske MM, Jerajani HR. Blastomycosis-like pyoderma. Indian J Dermatol Venereol Leprol. 2007;73:117-9.
2. Su WP, Duncan SC, Perry HO. Blastomycosis like pyoderma. Arch Dermatol 1979;115:170-3.
3. Su O, Demirkesen C, Onsun N. Localized blastomycosis-like pyoderma with good response to cotrimoxazol and cryotherapy. Internatlonal Journal of Dermatology 2004;43:388-90.
4. Nguyen T, Beardmore G. Blastomycosis-like pyoderma: Successful treatment with low-dose acitretin. Australasian Journal of Dermatology 2005;46:97-100.
5. Harish K et al. Pyoderma vegetans and ulcerative colitis. J Postgrad Med 2006;52:302-3.
6. Bianchi L et al. Pyoderma vegetans and ulcerative colitis. British J of Dermatol. 2001;144:1224-7.
7. Carrera C et al. Pyoderma vegetans associated with severe psoriatic arthritis: good response to etanercept. Dermatology 2007;214:77–81.

CHICAGO DERMATOLOGICAL SOCIETY **CASE # 11**

Presented by Joshua Mandrell MD, and Anthony Peterson MD
Division of Dermatology, Loyola University Medical Center

HISTORY OF PRESENT ILLNESS

This 39-year old male patient presented with complaints of multiple nevi and a family history of melanoma. He denied a personal history of melanoma or any lesions that were new, changing, or symptomatic. During the clinic visit, chest and nipple asymmetry was noted. Upon questioning, the patient stated it had been present since birth, was asymptomatic and did not limit his activity.

PAST MEDICAL HISTORY

Non-contributory

MEDICATIONS

Multivitamins
Fish oil

ALLERGIES

No known drug allergies

FAMILY HISTORY

Melanoma in brother

SOCIAL HISTORY

Married
No tobacco, tanning, or illicit drug use
Social alcohol use

PHYSICAL EXAM

The patient had decreased terminal hair growth over the left chest and left axilla and an elevated and hypoplastic left nipple. The patient's left arm, hand, and fingers were normal in appearance.

DIAGNOSIS

Poland's syndrome

TREATMENT AND COURSE

No treatment was indicated for this incidental finding. Imaging studies are being pursued.

DISCUSSION

Poland's syndrome (PS) is a congenital anomaly first described by Alfred Poland in 1841. The condition has also been called hand and ipsilateral thorax syndrome, limb/body-wall defect, fissure thoracis lateralis, acro-pectoral-renal field defect, subclavian artery supply disruption sequence, pectoral-aplasia-dysdactylia syndrome, and unilateral chest-hand deformity. Poland's syndrome classically consists of unilateral

aplasia of the sternocostal head of the major pectoralis muscle with an ipsilateral hypoplastic hand and simple syndactyly with short fingers (brachysyndactyly). Aplasia or hypoplasia of thoracic muscles occurs in 1 in 3000 to 1 in 10,000 children. In 10% of these cases, it is associated with other features of Poland's syndrome (PS) with a total incidence of 1 in 7,000 to 1 in 100,000 newborns. Other common features of PS include hypoplasia of the breast and nipple, minimal subcutaneous tissue, absence of pectoralis minor muscle, aplasia or deformity of the costal cartilages of ribs II to IV or III to V, and alopecia of axillary and mammary regions. Absence of the pectoralis major muscle and breast hypoplasia are diagnostic of the syndrome. Less common features include hypoplasia of the latissimus dorsi, serratus anterior (which can lead to Sprengel's deformity or winged scapula), external oblique, deltoid, infraspinus, supraspinus, and intercostal muscles, as well as axillary webs, soft tissue syndactyly, lung herniation (in 8% of patients), scoliosis, rib cage depression, and a contralateral pectus carinatum.

The etiology is thought to be from a vascular disruption in the subclavian arteries or a "subclavian artery supply disruption sequence" in the 6th week of gestation. Data indicates a decreased size of the subclavian artery and low flow velocity in utero in some patients. The site and degree of impairment determines the degree and extent of the abnormal features. Hypoplasia of the internal thoracic artery could be the cause of the absence of the sternocostal portion of pectoralis major muscle and hypoplasia of brachial artery may lead to hand anomalies. Other possible causative mechanisms include early damage or disruption of the lateral embryonic plate mesoderm at day 16-28 after fertilization. Other hypotheses include autosomal dominant inheritance, single gene defects, viral infections, trauma, intrauterine insults from attempted abortion, and the teratogenic effects of the environment (including medications given to mother) have all been proposed. Smoking in the mother may also be a factor.

In sporadic cases, it is more common in males (2:1 to 3:1) and on the right side of body (60 to 75% of patients). In familial cases, the incidence is equal on both sides of body and among females and males. The risk of recurrence within the same family is less than 1%. It is thought that the paradominance concept of the delayed mutation of a gene is responsible for some familial occurrences.

Poland's syndrome has variable expressivity. Most commonly, patients lack hand involvement and have "partial Poland sequence". Overall, hand anomalies have been reported in 13.5% to 56% of patients. Ten percent of patients with syndactyly have Poland syndrome. Hypoplasia or aplasia of the middle phalanges is not necessarily confined to the digits that are in the syndactyly. A system of classification of hand anomalies has been developed which ranges from type 1 (normal) to type 7 (most severe, phocomelia-like deficiency) to further classify the degree of hand involvement.

There is a well-known association with Möbius syndrome (bilateral congenital facial nerve palsy with paralysis of the abductors of the eye). Fifteen percent of patients with Möbius syndrome have thoracic and hand abnormalities and apparent Poland-Möbius syndrome. Other associations include Klippel-Feil syndrome (shortness of the neck), Adams-Oliver syndrome, facio-auriculo-vertebral dysplasia (Goldenhar syndrome), hemifacial microsomia, atrial septal defect, dextrocardia (1 in 30,000 births with usual shift to unaffected side), eye abnormalities, and renal malformations (unilateral renal agenesis or duplication of the urinary collecting system) defined as an acro-pectoral-renal field defect which can lead to renal hypertension. Malignancies such as leukemia, non-Hodgkin lymphoma, Wilms' tumor, neuroblastoma, lung carcinoma, cervical

carcinoma, leiosarcoma, and breast carcinoma (especially in the hypoplastic breast) have also been described in association with PS. It is thought that this may be due to abnormal homeobox and tumor suppressor genes.

The differential diagnosis includes anterior thoracic hyoplasia. This entity, which has previously been misdiagnosed as Poland's syndrome, is characterized by hypoplasia of the ipsilateral breast, superior location of the nipple-areola complex compared to contralateral side, and normal pectoralis muscles.

REFERENCES

1. Freitas RdaS, o Tolazzi AR, Martins VD, Knop BA, Graf RM, Cruz GA. Poland's syndrome: different clinical presentations and surgical reconstructions in 18 cases. Aesthetic Plast Surg. 2007; 31(2): 140-6.

2. Fokin AA, Robicsek F. Poland's syndrome revisited. Ann Thorac Surg. 2002; 74(6): 2218-25.

3. Mentzel HJ, Seidel J, Sauner D, Vogt S, Fitzek C, Zintl F, Kaiser WA. Radiological aspects of the Poland syndrome and implications for treatment: a case study and review. Eur J Pediatr. 2002; 161(8): 455-9.

4. Al-Qattan MM, Al Thunayan A. The middle phalanx in Poland syndrome. Ann Plast Surgery. 2005; 54(2): 160-4.

5. Rosa RF, Travi GM, Valiatti F, Zen PR, Pinto LL, Kiss A, Graziadio C, Paskulin GA. Poland syndrome associated with an aberrant subclavian artery and vascular abnormalities of the retina in a child exposed to misoprostol during pregnancy. Birth Defects Res A Clin Mol Teratol. 2007; 79(6): 507-11.

6. Al-Qattan MM. Classification of hand anomalies in Poland's syndrome. British Journal of Plastic Surgery. 2001; 54(2): 132-36.

7. Katz SC, Hazen A, Colen SR, Roses DF. Poland's syndrome and carcinoma of the breast: a case report. The Breast Journal. 2001; 7(1): 56-59.

8. Tamiolakis D, Venizelos D, Antoniou C, Tsiminikakis N, Alifieris E, Papadopoulos N. Breast cancer development in a female with Poland's syndrome. Onkologie. 2004; 27(6): 569-71.

9. Spear SL, Pelletiere CV, Lee ES, Grotting JC. Anterior thoracic hypoplasia: a separate entity from Poland syndrome. Plas Reconstr Surgery. 2004; 113(1): 69-77.

CHICAGO DERMATOLOGICAL SOCIETY **CASE # 12**

Presented by Aaron Pace MD, Anthony Peterson MD, and Madhu Dahiya MD
Division of Dermatology, Loyola University Medical Center

HISTORY OF PRESENT ILLNESS

A 64-year-old male patient with a history of invasive squamous cell carcinoma (SCC) of the mandible, and multiple cutaneous non-melanoma skin cancers, presented to our clinic with large non-healing ulcerative wounds on the scalp, face and bilateral thighs. He had undergone extensive surgical resection of his mandible and left face followed by radiation to the affected area for his invasive SCC in 2002. His post-operative course was complicated by: osteomyelitis, chronic non-healing ulcerations, and an orocutaneous fistula. He has received hyperbaric oxygen therapy, debridement, several split thickness skin grafts (STSG), wound vacuum therapy, as well as immunosuppression with low dose prednisone and mycophenolate mofetil. Despite extensive therapy he continued to have graft failure and non-healing ulcerative wounds on his scalp and face. Additionally, his healed donor sites began to ulcerate as well.

This patient's full history and timeline is complicated but is presented as follows:

2002 - The patient had an SCC of left mandible, underwent excision and local radiation, and subsequently developed an orocutaneous fistula.
2003 - He developed a cutaneous SCC of the left cheek and temple.
- He underwent hyperbaric oxygen therapy in preparation for free flap from the back and excision of his cutaneous SCC.
2005 - Free flap from the back was applied to the face over the old radiation bed and new defects.
- The graft failed.
2006 - In February, the wound vac and STSG were performed from the right thigh.
- The graft failed and the donor site ulcerated
- In August, another free flap from the back was performed and failed within 2 months.
2007 - Early in the year, mycophenolate mofetil and prednisone were begun
- The wound vac was placed again.
- Topical tacrolimus application began, and resulted in slight improvement.
- In June, the patient developed a recurrent SCC of the left brow and underwent Mohs surgery, which required grafting. He also had a basal cell carcinoma of the nose and underwent a forehead flap which healed well.
2008 - In February, the patient was thought to be well controlled and underwent STSG from the left thigh to cover the left forehead and temple.
- Tacrolimus was continued topically as well as oral prednisone and mycophenolate mofetil orally.
- The graft and left thigh donor site began to breakdown.
- In early spring of 2008 the patient presents to dermatology.

PAST MEDICAL HISTORY

Depression

Anxiety
Spinal stenosis
Squamous cell carcinoma of the skin
Kidney stone

MEDICATIONS
Minocycline 100mg daily
Dapsone 100mg daily
Metronidazole gel daily
Tacrolimus topically daily
Dilute vinegar washes bid
Clobetasol cream bid
Paroxetine
Trazodone
Tobramycin/dexamethasone eye drops
Zolpidem

ALLERGIES
No known drug allergies

FAMILY HISTORY
Father died of prostate cancer at age 90.

SOCIAL HISTORY
The patient smoked 1.5 packs per day for 30 years and quit in 2002. He has drunk alcohol heavily in the past but not currently.

PHYSICAL EXAM
There are erythematous plaques on both anterior thighs. The left half of the scalp, forehead, temple, and cheek have scarring and atrophy. There are no open ulcerations, but there are large clumps of crusted material, some with greenish tint but the debris is not foul smelling.

HISTOPATHOLOGY
Histopathologic examination of a biopsy from the left thigh in 2008 revealed epidermal ulceration, dermal fibrosis with neutrophilic infiltrate. Special stains GMS, PAS, AFB, and gram stain were negative. No acanthosis or dermal eosinophils were seen.

Histopathologic examination of a biopsy from the facial lesions in 2006 and 2008 revealed ulceration with granulation tissue, with acute and chronic inflammation. Gram stains and special stains GMS, PAS, and AFB have been negative.

LABORATORY RESULTS
The following were abnormal:
Aerobic swabs have yielded Staphylococcus aureus, Proteus mirabilis, and Pseudomonas aeruginosa.
Tissue culture yielded methicillin sensitive Staphylococcus aureus.
CBC consistently reveals a slight anemia with a hemoglobin of around 12.5 gm/dl.
LFT's revealed a slightly elevated alkaline phosphatase.
ANA was positive with an atypical speckled pattern.

C ANCA was positive.
CRP and ESR were both elevated at 1.6 and 93 respectively.

The following were normal or negative:
Viral, fungal, and AFB culture were negative.
Herpes DFA was negative.
BMP
Hepatitis C virus negative.
Anti-myeloperoxidase and proteinase-3 were negative.
Urinalysis was within normal limits.

DIAGNOSIS
Pyoderma gangrenosum

TREATMENT AND COURSE
The patient presented to the dermatology clinic and the diagnosis of pyoderma gangrenosum was suspected due to the clinical appearance and persistent nature. Sevaral biopsies from representative sites were taken from the face and leg for both histology as well as pan culture. Given his immunosuppression with mycophenolate mofetil and prednisone as well as his extensive history of squamous cell carcinoma, acitretin was started for skin cancer prophylaxis. In October 2008 the patient grew methicillin susceptible staph aureus and proteus in the non-healed areas. Due to the lack of efficacy, mycophenolate mofetil and prednisone were stopped after approximately 1 year of therapy. Acitretin was also discontinued. The treatment regimen was switched to minocycline and dapsone orally, followed by topical metronidazole and tacrolimus, which resulted in moderate improvement of both the face and the thigh lesions. Later, the patient was also started on clobetasol cream and white vinegar rinses twice daily to the affected areas, which provided further improvement.

DISCUSSION
Pyoderma gangrenosum (PG) is an uncommon chronic ulcerative cutaneous condition of uncertain etiology. It is associated with systemic diseases in at least 50% of affected patients. These diseases include inflammatory bowel disease, arthritis, and hematologic abnormalities. Ulcerations of PG may occur after trauma or injury to the skin in 30% of patients, this is known as pathergy.

There are four main clinical variants of pyoderma gangrenosum including ulcerative, pustular, bullous, and vegetative. Ulcerative PG is characterized by a deep ulceration with a violaceous border that overhangs the ulcer bed. These lesions of pyoderma gangrenosum most commonly occur on the legs. Pustular PG lesions are smaller and most frequently on the extremities. In the bullous type, patients develop painful bullae most frequently on the arms and face. Bullous PG is frequently associated with myeloproliferative disorders. Vegetative PG occurs most frequently on the trunk and lacks the violaceous border, pustular base, and undermined periphery. This form typically has no associated systemic disease and is the type that most close resembles our patient's disease process. Peristomal PG occurs when ulcerations appear in a peristomal location. This is most frequently associated with Crohn's, but can also occur in ulcerative colitis or in those with stomas for other reasons. (A more broad classification scheme has also been proposed which defines classic, atypical, and peristomal variants.)

Pathergy has been associated with the development of pyoderma gangrenosum. Trauma has been identified as the causative event in as many as 40% of cases. The atypical appearance is most frequently demonstrated when pathergy is involved. It has been noted after burns, C-section, hip replacement, cosmetic surgery (particularly breast), blunt trauma, insect bite, canine bite, and at graft donor sites. Grafting of the defect must be performed carefully, not only because the donor site may develop disease, but also because the debridement necessary at the recipient site may worsen the disease.

The diagnosis of pyoderma gangrenosum is made by excluding other causes of similar appearing cutaneous ulcerations, including infection, malignancy, vasculitis, collagen vascular diseases, diabetes, and trauma. The histopathology in pyoderma gangrenosum is nonspecific, however the biopsy can be suggestive. Typical lesions demonstrate neutrophilic infiltrates, often with leukocytoclasia, particularly in untreated lesions. Full-blown vasculitis is usually not present. Other features include hemorrhage and necrosis of the overlying epidermis.

Treatment of pyoderma gangrenosum is mainly medical, however there is a role for surgical treatment options. Systemic treatment is frequently required; prednisone at 1-2 mg/kg/day usually results in rapid response over days and cyclosporine with response seen over weeks are first line for significant disease without underlying systemic disease or in which the systemic disease has been adequately treated. Infliximab should be considered first line therapy for patients with Crohn's and PG. It frequently results in rapid remission of both conditions. Thalidomide, mycophenolate mofetil, tacrolimus, IVIG, cyclophosphamide, dapsone, and azathioprine have all been shown to be effective. Successful surgical therapy of affected areas includes grafting with split thickness skin grafts and muscle flaps, debridement, wound vac assisted closure, and hyperbaric oxygen in combination with these modalities. If grafting or debridement is attempted it must be done after disease progression has been halted with systemic medical therapy.

REFERENCES

1. Powell F et al. Pyoderma gangrenosum: classification and management. J of Amer Acad Dermatol. 1996;34(3):395-409.
2. Su W et al. Pyoderma gangrenosum: clinicopathologic correlation and proposed diagnostic criteria. 2004;43:790-800.
3. Callen J et al. Pyoderma gangrenosum: an update. Rheu Dis Clin N Am 2007;33:787-802.
4. Reichrath J et al. Treatment recommendations for pyoderma gangrenosum: an evidence-based review of the literature based on more than 350 patients. J Am Acad Dermatol. 2005;53(2):273-83.
5. Cliff S et al. Split thickness skin grafts in the treatment of pyoderma gangrenosum a report of four cases. Dermatol Surg. 1999;25:299-302.

CHICAGO DERMATOLOGICAL SOCIETY **CASE #13**

Presented by Kathryn Barlow MD, James Swan MD, David Eilers MD, and Scott Wickless DO
Division of Dermatology, Hines Veterans Administration Hospital

HISTORY OF PRESENT ILLNESS

An otherwise healthy 47-year old male presented to the dermatology clinic with a 10-15 year history of asymptomatic small papules on his face and neck. The number of papules had increased slowly over time. He denied any family history of similar lesions, but stated a brother had “pockmarks” on his face as well.

PAST MEDICAL HISTORY

Reflex sympathetic dystrophy of the leg
Intravertebral disk displacement

MEDICATIONS

Methadone
Ibuprofen
Cyclobenzaprine
Topiramate
Omeprazole
Albuterol inhaler

ALLERGIES

No known drug allergies

FAMILY HISTORY

No family history of renal cancer or pneumothorax.

SOCIAL HISTORY

Smokes one-half pack per day for the past 11 years.

PHYSICAL EXAM

Over the bilateral cheeks, posterior auricular areas and neck were multiple, 1-4mm firm white to flesh colored, monomorphous, dome-shaped papules. On the chest were scattered, fine flesh colored 1mm papules. One pedunculated flesh-colored papule was present in the left axilla.

HISTOPATHOLOGY

Histopathologic examination of a biopsy from the left neck revealed dense, fibrocollagenous tissue with an encapsulated, elliptical, loosely woven admixture of collagen and mucinous material surrounding a distorted follicular unit. Focal hyalinization and multiple thin-walled blood vessels were also noted. These findings were consistent with a trichodiscoma.

Histopathologic examination of the right preauricular cheek revealed concentric layers of collagen producing an “onion skin” effect around hair follicles. There were scattered foci of artifactual clefts separating the fibroma from the adjacent connective tissue and rare

areas of mucinous material surrounding the hair follicles. These findings were consistent with a perifollicular fibroma.

LABORATORY RESULTS

The following tests were within normal limits:
Urinalysis.

The following tests were abnormal:
Pulmonary function tests (PFTs) with arterial blood gas: Mild restrictive pattern in the flow-volume loop consistent with smoking. Normal acid/base status and normal oxygenation.
Folliculin gene mutation (FISH): positive for a heterozygous G to T nucleotide substitution at the –1 position of intron 5.

RADIOLOGY

Computed tomography (CT) abdomen/pelvis: Normal.
Chest X-ray: Normal.

DIAGNOSIS

Birt-Hogg-Dube Syndrome

TREATMENT AND COURSE

Once confirmation of the diagnosis was made via skin biopsy and positive genetic testing for the folliculin gene, the patient was referred to nephrology for consultation. A CT scan of the abdomen and pelvis was normal without evidence of renal masses, and it was recommended for the patient to have a CT or an ultrasound of the kidneys every 1-2 years. After consulting with the pulmonary service, a chest x-ray and PFTs were ordered and found to be normal. The patient was encouraged to pursue smoking cessation and continues to do well. He will continue to follow-up with the recommended screening.

DISCUSSION

Birt-Hogg-Dube syndrome (BHDS) is an autosomal dominantly inherited genodermatosis first described in 1977. The syndrome is characterized by cutaneous fibrofolliculomas, trichodiscomas and achrocordons arising in the second to third decade of life, as well as renal tumors, pulmonary cysts, and spontaneous pneumothorax. The incidence of BHDS is unknown, but is thought to be underdiagnosied.

In 1975, Hornstein and Krickenberg described an inherited syndrome in 2 patients with multiple perifollicular fibromas and intestinal polyps. However, BHDS and Hornstein-Krickenberg syndrome are now considered to be the same syndrome. Larger epidemiologic studies performed since the original descriptions of these syndromes have not indicated an increased risk of intestinal polyps or colonic adenocarcinoma in patients with BHDS.

BHDS has recently been found to be caused by heterozygous loss-of-function mutations in the BHD tumor suppressor gene located on chromosome 17p11.2. The mutation results in a truncated form of the protein folliculin. The exact function of this gene in tumorgenesis is not known, but expression of BHD mRNA has been identified in skin

and skin appendages, in cells within the nephron of the kidney and in pneumocytes of the lung.

There have been numerous reports of multiple tumors in patients with BHDS since its initial description. Renal cell cancer is the most common, and patients with BHDS are 9.3 times more likely to develop a renal tumor, and 32.2 times more likely to develop a pneumothorax than unaffected persons. 15-30% of patients with BDHS will develop renal cancer, and older age and male gender further increase this risk. The risk of spontaneous pneumothorax is thought to be inversely related to age. Other reported tumors include neurothekeomas, meningiomas, lipomas, parathyroid adenomas, and parotid oncocytoma, although no definitive association with these tumors has been proven.

There are no strictly defined guidelines for management and screening of these patients. It is recommended that abdominal CT and/or ultrasound are performed at the time of diagnosis and interval screening should be performed every 3-5 years. Patients should be counseled to quit smoking, and cautioned about the increased risk of pneumothorax with scuba diving and air travel. Siblings should also be screened for cutaneous findings starting at the age of 20. The risk of colon polyps and colon adenocarcinoma is not increased in BHDS, but routine screening should be followed for all patients over the age of 50.

REFERENCES

1. Adley BP, et al. Birt-Hogg Dube Syndrome: Clinicopathologic Findings and Genetic Alterations. *Arch Pathol Lab Med*. 2006;130:1865-1870.

2. Kim EH, et al. A Case of Birt-Hogg-Dube Syndrome. *J Korean Med Sci*. 2008;23:332-335.

3. Toro JR, et al. Lung Cysts, Spontaneous Pneumothorax and Genetic Associations in 89 Families with Birt-Hogg-Dube Syndrome. *Am J Respir Crit Care Med*. 2007;175:1044-1053.

CHICAGO DERMATOLOGICAL SOCIETY **CASE # 14**

Presented by Linda Sheu MD, Elaine Kung MD, and Madhu Dahiya MD
Division of Dermatology, Loyola University Medical Center

HISTORY OF PRESENT ILLNESS

This 47-year old female presented to our clinic in January 2009 with worsening of her skin lesions around the nose because she did not have insurance for the last few years. She has had pulmonary sarcoidosis limited to hilar lymphadenopathy since the early 1990s and cutaneous sarcoidosis since 2001. She had an anterior orbitotomy with debulking of sarcoidosis of the right eyelid in 2004. Past medical treatments included multiple short courses of low dose prednisone and 2 months of methotrexate. She did not notice improvement with these short courses of systemic therapy. She has had partial response of her nasal lesions with topical and intralesional steroids.

PAST MEDICAL HISTORY

Pulmonary sarcoidosis (early 1990s)
Cutaneous sarcoidosis (2001)
Goiter

MEDICATIONS

None

ALLERGIES

No known drug allergies

REVIEW OF SYSTEMS

Patient reported coughing and difficulty breathing. Review of systems was otherwise non-contributory.

FAMILY HISTORY

Non-contributory

SOCIAL HISTORY

Non-contributory

PHYSICAL EXAM

Multiple red purple to red brown nodules and plaques were present on the cheeks, medial canthi, as well as, nasal tip and rim resulting in nasal enlargement. On the chest, arms and right thigh were 2-8cm red purple to red brown indurated plaques with hypopigmented halo at their periphery.

LAB DATA

The following were abnormal:
WBC 3.3 [4.0-10 K/UL]; CBC otherwise within normal limits
Albumin 3.5 [3.6-5.0 GM/DL]; CMP otherwise within normal limits
CXR: bilateral hilar adenopathy

The following were normal:
EKG: normal sinus rhythm, no heart block

CT sinus: no nasal septum perforation
Angiotensin Converting Enzyme
TSH/free T4

HISTOPATHOLOGY
1/2009: Histologic evaluation of a punch biopsy from the left arm plaque near the antecubital fossa revealed non-caseating granulomas in the dermis. Special stains for microorganisms were unremarkable.

DIAGNOSIS
Cutaneous sarcoidosis with lupus pernio

TREATMENT AND COURSE
The patient was started on tacrolimus 0.1% ointment twice daily to the face, clobetasol 0.05% ointment twice daily to the trunk and extremities, hydroxychloroquine 200mg daily, and doxycycline 100mg twice daily. At follow-up one month later, she noted improvement of cutaneous lesions and also improvement of her breathing. Doxycycline was discontinued due to nausea and she was started on methotrexate 7.5mg weekly. The methotrexate dose could not be increased successfully because of gradual decline of white blood cell count. After 2 months, methotrexate was discontinued and was replaced with minocycline 100mg twice daily.

In addition, split-lesion therapy was instituted on left arm plaques with pulsed dye laser (PDL) therapy at settings of 7mm, 10ms, 7 J/cm^2 on the right-half of lesions and intralesional kenalog (ILK) 10mg/cc on the left-half of lesions. The plaque on her right arm and nasal lesions were treated with a combination of PDL and ILK.

After 1 session of PDL and ILK detailed above, she reported significant improvement of all areas treated. She estimated improvement to be 75% with PDL and ILK on right arm plaque and 50% for left arm plaques treated with either PDL or ILK compared to untreated plaques on her right thigh. She also reported that the erythema of her nasal lesions improved with combination of PDL and ILK.

DISCUSSION
Treatment of cutaneous sarcoidosis is determined by the extent, progression, degree of disfigurement and function impairment of patient's disease. Limited cutaneous involvement may be treated with an ultra-potent topical fluorinated steroid. More severe cutaneous involvement may be treated with intralesional triamcinolone at concentrations of 3 to 20 mg/ml. Systemic corticosteroid therapy at doses of 40 to 80 mg per day tapered over weeks to months is usually reserved for widespread, disfiguring, or destructive lesions.

Antimalarials such as chloroquine and hydroxychloroquine have anti-inflammatory properties which have long been used in the treatment of cutaneous sarcoidosis. An initial step in granuloma formation is antigen presentation by antigen presenting cells to CD4 T-cells. Antimalarials increase the pH within lysosomes, impairing the processing of major histocompatibiliity complex-peptide complexes and their transportation to the cell surface. Therapy is associated with high relapse rates after discontinuation, and is understood to be suppressive rather than curative.

Methotrexate is considered second-line therapy for cutaneous sarcoidosis. It is a folate analogue that inhibits dihydrofolate reductase. At high doses, it has anti-proliferative properties used in the treatment of neoplastic conditions. At low doses, it has anti-inflammatory and granuloma-suppressing properties. It has a delayed onset of action prior to clinical efficacy.

Newer therapies for cutaneous sarcoidosis including pentoxyfylline, isotretinoin, leflunomide, thalidomide, infliximab and laser surgery have all demonstrated efficacy in case reports and small studies. PDL has been reported effective in cutaneous sarcoidosis. Two cases of lupus pernio were recently reported to be effectively treated by flashlamp PDL. However, erythema and telangiectasia recurred after six months in one of the two patients. Another case report of lupus pernio treated with PDL showed significant clinical improvement. However, a post-treatment biopsy demonstrated persistent granulomas suggesting an improvement in cosmesis rather than in underlying disease activity.

In our patient's case, PDL with or without ILK was an effective addition to her systemic regimen since the lesions treated with the adjuvant therapy improved more than those that were not. PDL with ILK was more effective than PDL or ILK alone. In addition, PDL was as effective as ILK when we performed split-plaque comparisons between the two adjuvant therapies.

REFERENCES

1. Baughman R, Elyse E. Evidence-based therapy for cutaneous sarcoidosis. Clin Dermatol 2007;25:334-40.

2. Cl S, Felix R, Singh L, Harland C. The successful treatment of lupus pernio with the flashlamp pulsed dye laser. Journal of Cutaneous Laser Therapy 1999; 4: 49-52

3. Goodman MM, Alpern K. Treatment of lupus pernio with the flashlamp pulsed laser. Lasers Surg Med 1992; 12 (5): 549-51

4. O'Donoghue NB, Barlow RJ. Laser remodeling of nodular nasal lupus pernio. Clin Exp Dermatol 2006; 31 (1): 27-9.

5. Stagaki E, Mountford WK, Lackland DT, Judson MA. The treatment of lupus pernio: results of 116 treatment courses in 54 patients. Chest 2009; 135(2): 468-76

6. Young HS, Chalmers RJ, Griffiths CE, August PJ. CO2 Clinics in Dermatology. 2007; 25: 334-340. Laser vaporization for disfigurig lupus pernio. J Cosmet Laser Ther 2002; 4:87-90

CHICAGO DERMATOLOGICAL SOCIETY **CASE # 15**

Presented by Joshua Mandrell MD, and Kathleen Remlinger, MD
Division of Dermatology, Loyola University Medical Center

HISTORY OF PRESENT ILLNESS

This 17-year-old male Iraqi refugee presented with complaints of brown spots on his entire body. The patient stated that largest spot on his back was mildly itchy and limited his sleep at night. He had been kept out of school and was not able to keep jobs due to fear of a contagious component. He denied a history of headaches, parasthesias, or muscle weakness. The patient had undergone surgery shortly after birth in an attempt to partially remove the largest lesion on his back.

PAST MEDICAL HISTORY

None

MEDICATIONS

None

ALLERGIES

No known drug allergies

FAMILY HISTORY

No family history of similar lesions

SOCIAL HISTORY

Lives with parents
No history of alcohol use, tobacco use, illicit drug use, or tanning.

PHYSICAL EXAM

There was a 47 x 66 cm dark brown plaque involving the entire back from flank to flank. Within this plaque, there was a hypopigmented linear scar on the mid-back and a 1.5 x 1.2 cm dark brown nodule on the left mid-back. At least 300 satellite brown papules, macules, plaques, and patches were prominent on the face, extremities, and trunk, many with hypertrichosis. The largest satellite lesions included a 3.0 x 3.2 cm brown plaque on the right upper lateral thigh and a 6.0 x 3.0 cm brown plaque on the right posterior thigh. Mild xerosis was present including areas overlying the nevi.

DIAGNOSIS

Giant congenital melanocytic nevus

TREATMENT AND COURSE

For pruritus and xerosis, the patient was treated with Sarna sensitive skin, Vaseline, and doxepin 10 mg at night. At the last visit, the patient had stopped doxepin due to dizziness and reported no improvement in pruritus with Sarna or Vaseline. Dry skin care was again reviewed and hydrocerin moisturizer was prescribed. Also at his follow-up visit, the patient's father had noted subjective change in the 1.5 x 1.2 cm dark brown

nodule on the left mid-back. All other lesions were stable. The patient deferred biopsy. The patient continues to have a negative neurological review of systems.

DISCUSSION

Congenital melanocytic nevi (CMN) are present at birth and are found in approximately 1% of newborns. Because of the phenomenon of the "kissing nevus" or divided nevus of the upper and lower eyelid, it is thought that the congenital nevus appears when the eyelids are fused between the 9th and 20th week of gestation. Giant congenital melanocytic nevi (GCMN), however, are rare and are seen in approximately 1 per 20,000 neonates. Synonyms for GCMN include bathing trunk nevus, giant hairy nevus, garment nevus, giant pigmented nevus, and nevus pigmentosus and pilosus. Some studies have shown CMN being more common in females. However, they are more likely to be associated with complications in males including melanoma and death. Although the data showing giant CMN to have an increased melanoma risk is clear, whether smaller CMN have an increased risk is still controversial. With a median age of melanoma diagnosis of 7 years, studies have shown the melanoma risk to vary from 0.7% to 2.6% in all congenital nevi. It is also clear that the risk of melanoma and fatality increases as the diameter of the CMN increases. Varying criteria have been used to define large CMN including the absolute size, percent body surface area covered, size of CMN relative to the patient's palm, body site involved, and whether the CMN can be surgically excised with primary closure. While Kopf *et al*, in 1979, proposed classifying large CMN as those greater than 20 cm, the more recent classification uses the largest projected adulthood diameter to divide CMN as small (less than 1.5 cm), medium (1.5 to 10 cm), large (11 to 20 cm), and giant (greater than 20 cm). Giant CMN are further subdivided into G1 (21 to 30 cm), G2 (31 to 40 cm), and G3 (greater than 40 cm). Patients with GCMN and more than 50 satellite lesions can be classified in one class above their corresponding size classification. According to published nonograms, an infant's CMN of 12 cm on the head or 7 cm on the torso correlates with an adult diameter of 20 cm. Reported developmental abnormalities associated with giant CMN include scoliosis, spina bifida, atrophy, asymmetry, clubfoot, elephantiasis, and cranial bone hypertrophy.

Giant CMN are also associated with increased risks of cutaneous melanoma and leptomeningeal melanoma. Although most believe the melanoma risk in these patients to be near 6%, varying studies have estimated the lifetime risk from 5-40% and the 5-year risk from 2.3-5.7%. (Most studies do not follow patients long enough to accurately predict lifetime risk.) There is a higher risk of melanoma in patients with increased CMN diameters, especially in lesions over 40 cm. There also appears to be a higher risk of melanoma in patients with an increased number of satellite lesions, which parallels the increased risk of melanoma in adults with increased numbers of acquired melanocytic nevi. Seventy percent of melanomas in patients with giant CMN develop before puberty with most of these occurring before the age of 3. In contrast, less than 1% of all melanomas in the general population occur before puberty. Although some studies have contradicted the finding, others have found increased rates (nearly 90%) of CMN leading to melanoma being found in an axial or truncal location with 1/3 of these being fatal.

The principle complication of giant congenital melanocytic nevi is neurocutaneous melanocytosis (NCM) or neuromelanosis, which is seen in 2.5% to 33% of patients. The importance of NCM cannot be overstated as some studies have shown the risk for death in these patients either from benign or malignant NCM being higher than development of fatal non-CNS melanoma. NCM is defined by a benign or malignant proliferation of

melanocytes in the leptomeninges in conjunction with a large CMN or three or more small CMN. It is thought that NCM occurs as an error of morphogenesis in the neural ectoderm of the embryo and abnormal expression of the hepatocyte growth factor/scatter factor (HGF/SF) may be involved. The highest risk of NCM occurs in patients with nevi in axial locations on the head, posterior neck, or paravertebral areas. There is also a higher risk of NCM in patients with increased giant CMN diameters and numbers of satellite lesions. An increased risk of NCM in patients with giant CMN in axial locations, with many satellite lesions, and in those with larger diameters can be secondary to selection bias as these patients receive more frequent imaging. A recent study reports an association between CMN in males and neurological complications. The clinical signs and symptoms of headaches, seizures, and an abnormal neurological exam are due to increased intracranial pressure as a result of a blockage of the cisternal pathways and obliteration of arachnoid villi by the proliferating melanocytes. The Dandy-Walker complex has also been associated. Although 53% of patients have symptoms, in many patients NCM is asymptomatic and only detectable by radiological imaging. The most common finding on MRI is T_1 shortening in the cerebellum, temporal lobes, pons, and medulla. Most cases of NCM occur in early childhood with 88% of patients presenting before the age of four. Approximately 40-65% of patients with NCM develop CNS melanomas. Manifest NCM has a poor prognosis with greater than 90% of patients dying regardless of whether or not malignant melanocytes are present. Most patients die within 3 years of their initial neurological symptoms with 70% dying before the age of 10 years.

In addition to increased rates of melanoma being associated with an increased size of congenital melanocytic nevi, increased rates of death have also been associated with CMN size. For example, the death rate in patients with CMN greater than 40 cm was 6.5% in one study. For this reason, work-up of all patients is important. Most recommend regular careful neurological and developmental assessment along with an MRI with gadolinium contrast enhancement of all infants with a CMN greater than 2 cm in diameter found on the head or in an axial location. Some recommend MRI for all patients with giant CMN, those with satellite lesions, or those with abnormal neurodevelopment. Myelination during the first 2 years of life may obscure radiological signs of melanosis. Frequent examinations are more important early in life when the risk for NCM, melanoma, and other complications is highest.

Perhaps the most difficult and controversial issue in the management of patients with congenital melanocytic nevi is the issue of prophylactic surgical excision. Because 1/3 of melanomas will develop outside the CMN lesion, prophylactic excision does not guarantee protection against melanoma. In addition, giant CMN, which are at greatest risk for malignancy, are many times too large to excise completely and the morbidity of the procedure can be severe and many times not discussed in literature. Because nevus cells can infiltrate muscle or the lining of the CNS, incomplete or superficial excision could theoretically mask the appearance of a melanoma arising in the primary lesion. However, when it is possible, excision certainly does reduce the risk although a quantitative analysis is difficult to attain. Each case should be evaluated on its individual merits as the presence or absence of NCM in infants may affect the decision regarding excision. Regarding giant CMN, some have proposed that the following patients should be offered prophylactic surgery: patients with facial CMNs or large facial satellites for cosmetic reasons, physically troublesome lesions, areas suspected for malignancy, and those with parents who feel strongly that the lesion should be removed. Routine sampling of the CMN has not been shown to be advantageous.

The literature also lists other treatment options including staged excisions with grafting, dermabrasion, curettage, Q-switched ruby laser (which does not eliminate the risk for malignant transformation), and close observation. Possibly more controversial is the management of small and medium-sized congenital melanoctyic nevi, which is beyond the scope of this discussion.

REFERENCES

1. Hamming N. Anatomy and embryology of the eyelids: a review with special reference to the development of divided nevi. Pediatr Dermatol 1983;1:51-8.
2. Hale EK, Stein J, Ben-Porat L, Panageas KS, Eichenbaum MS, Marghoob AA, Osman I, Kopf AW, Polsky D. Association of melanoma and neurocutaneous melanocytosis with large congenital melanocytic naevi – results from the NYU-LCMN registry. British Journal of Dermatology. 2005; 152: 512-17.
3. Castilla EE, da Graca Dutra M, Orioli-Parreiras IM. Epidemiology of congenital pigmented naevi: 1. Incidence rates and relative frequencies. British Journal of Dermatology 1981, 104: 307-15.
4. Tannous ZS, Mihm MC, Sober AJ, Duncan LM. Congenital melanocytic nevi: Clinical and histopathologic features, risk of melanoma, and clinical management. J Am Acad Dermatol. 2005; 52: 197-203.
5. Kinsler VA, Chong WK, Aylett SE, Atherton DJ. Complications of congenital melanocytic naevi in children: analysis of 16 years' experience and clinical practice. British Journal of Dermatology. 2008; 159: 907-14.
6. Marghoob AA, Schoenbach SP, Kopf AW, Orlow SJ, Nossa R, Bart RS. Large Congenital Melanocytic Nevi and the Risk for the Development of Malignant Melanoma: A Prospective Study. Archives of Dermatology. 1996; 132(2): 170-75.
7. Bittencourt FV, Marghoob AA, Koft AW, Koenig KL, Bart RS. Large Congenital Melanocytic Nevi and the Risk for Development of Malignant Melanoma and Neurocutaneous Melanocyosis. Pediatrics. 2000; 106(4): 736-41.
8. Rhodes AR, Albert LS, Weinstock MA. Congenital nevomelanocytic nevi: proportionate area expansion during infancy and early childhood. J Am Acad Dermatol 1996;34:51-62.
9. Elder DE. The blind men and the elephant. Different views of small congenital nevi. Arch Dermatol 1985;121:1263-5.
10. Krengel S, Hauschild A, Schafer T. Melanoma risk in congenital melanocytic naevi: a systemic review. British Journal of Dermatology. 2006; 155: 1-8.
11. Bett BJ. Large or multiple congenital melanocytic nevi: occurrence of cutaneous melanoma in 1008 persons. J Am Acad Dermatol 2005; 52: 793-7.
12. Rhodes AR, Melski JW. Small congenital nevocellular nevi and the risk of cutaneous melanoma. J Pediatr 1982;100: 219-24.
13. DeDavid M, Orlow SJ, Provost N, et al. A study of large congenital melanocytic nevi and associated malignant melanomas: review of cases in the New York University Registry and the world literature. J Am Academy Dermatology. 1997; 36: 409-416.
14. Ruiz-Maldonado R. Measuring congenital melanocytic nevi. Pediatr Dermatol 2004; 21: 178-9.

15. Rhodes AR. Benign neoplasias and hyperplasias of melanocytes. In: Fitzpatrick TB, editor. Dermatology in general medicine. 5th ed. New York: McGraw-Hill; 1999. p. 1026-37.
16. Pack GT, Davis J. Nevus giganticus pigmentosus with malignant. Surgery 1961;49:347-54.
17. Reed WB, Becker SW Sr, Becker SW Jr, Nickel WR. Giant pigmented nevi, melanoma, and leptomeningeal melanocytosis. Arch Dermatol 1965;91:100-18.
18. Solomon LM. The management of congenital melanocytic nevi. Arch Dermatol 1980;116:1017.
19. Sober AJ, Burstein JM. Precursors to skin cancer. Cancer 1995; 75:645-50.
20. Kaplan EN. The risk of malignancy in large congenital nevi. Plast Reconstr Surg 1974;53:421-8.
21. Kang S, Milton GW, Sober AJ. Childhood melanoma. In: Balch CM, Houghton AN, Milton GW, editors. Cutaneous melanoma. Philadelphia: JB Lippincott; 1992. p. 312.

CHICAGO DERMATOLOGICAL SOCIETY **CASE # 16**

Presented by Tricia Hultgren MD, Anthony Peterson MD, and Madhu Dahiya MD
Division of Dermatology, Loyola University Medical Center

HISTORY OF PRESENT ILLNESS

This 60-year old female with history of neurosarcoidosis and secondary panhypopituitarism treated with chronic steroids, presented to our clinic with a warm, tender, violaceous plaque on the left anterior thigh. The lesion had been present for one month, was growing steadily and occasionally bled. She denied proceeding trauma to the site. She denied fever, weight loss and vomiting but reported recent chills and nausea.

PAST MEDICAL HISTORY

Neurosarcoidosis
Panhypopituitarism
Hyperlipidemia
Hypertension
Depression
Anxiety
Fibromyalgia
History of CVA

MEDICATIONS

Desmopressin spray
Hydrocortisone, po and IM daily
Lorazepam
Metoprolol
Norvasc
Sertraline
Levothyroxine
Calcium + vitamin D

ALLERGIES

Sulfa, intravenous contrast

FAMILY HISTORY

No history of skin cancer or connective tissue disorders

SOCIAL HISTORY

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

PHYSICAL EXAM

On the left anterior thigh there was a well-circumscribed 6.0 cm x 2.0 cm violaceous non-ulcerated plaque with overlying scale. Proximal to this was a 1cm violaceous nodule.

HISTOPATHOLOGY

Initial punch biopsy from the left anterior thigh demonstrated suppurative and granulomatous inflammation. Special stains including gram, GMS, PAS, AFB and AFB-fite were negative for microorganisms.

Repeat punch biopsy from the left anterior thigh one month later revealed irregular acanthosis with prominent suppurative and granulomatous inflammation. PAS revealed round structures with internal structures suggestive of endosporulation or fungal infection, associated with multinucleated giant cells. GMS, mucicarmine, gram, AFB, and Fontana-Masson stains were negative.

Final excisional biopsy of the left anterior thigh showed septal panniculitis with mixed acute and chronic inflammation. No microorganisms were seen with PAS and GMS stains. Tissue culture from this excisional biopsy grew a few colonies of *Mycobacterium Chelonae*.

DIAGNOSIS

Cutaneous *Mycobacterium chelonae* infection in an immunocompromised patient mimicking cutaneous sarcoidosis

TREATMENT AND COURSE

The infectious disease service was consulted. It was unclear as to if the atypical mycobacterium represented contaminant versus a true pathogen. However, given the histopathologic findings and the patient's immunocompromised state, it was decided to treat the lesions as a true infection. The patient was started on clarithromycin 500 mg twice daily and levofloxacin 750 mg once daily. She subsequently developed a new nodule on the right thigh, and both lesions were excised to accelerate treatment response and to minimize the risk of dissemination. Histopathology from the excisions again showed suppurative and granulomatous inflammation and repeat special stains were negative. She has had no recurrences at the excision sites, but recently developed one additional lesion on the right anterior thigh that was subsequently excised.

DISCUSSION

Mycobacterium chelonae is non-tuberculous, rapidly growing mycobacterium implicated in a variety of infections including skin and soft tissue, bone, pulmonary, ocular and disseminated disease. Atypical mycobacteria are grouped according to their growth rate and pigment production following UV exposure, a system known as the Runyon Classification, established in 1959. Runyon group IV consists of rapidly growing, non-pigment producing mycobacteria and includes *M. chelonae, M. fortuitum, M. abscessus, M. smegmatis, M. immunogenum, M. goodii, M. wolinskyi*, and *M. cosmeticum*.

M. chelonae is an ubiquitous pathogen found in water, soil and dust. Tap water is a recognized reservoir for the pathogen and may contribute to surgical-related inoculation. Infection with *M. chelonae* often occurs with trauma and has reported following acupuncture, liposuction, face lift, mesotherapy, breast augmentation, intravenous catheter placement, pacemaker implantation, pedicure, subcutaneous injection, and dermatologic surgery. More recently the organism has been associated with intracanalicular plug placement and hospital washing equipment and bronchoscopes,

increasing the iatrogenic nature of *M. chelonae* infection. Disseminated disease usually affects immunosuppressed patients and may not have a known site of entry.

Cutaneous findings most commonly manifest as violaceous, fluctuant or firm subcutaneous nodules. Lesions are often multiple and may ulcerate or form sinus tracts. Diagnosis is often delayed, as cultures and biopsies from wounds are frequently negative. A recent retrospective chart review by Uslan *et al*. reported a median duration of symptoms of 86 days prior to diagnosis of rapidly growing mycobacteria in 63 patients. Our case mirrors these findings, with numerous biopsies and tissue cultures performed prior to diagnosis.

Immunosuppression is a clear risk factor for atypical mycobaterial infection. Our patient was taking high dose corticosteroids secondary to neurosarcoidosis, which predisposed her to infection. A recent review of *M. chelonae* infection showed that 92% of those with disseminated disease and 62% of all infected patients were taking corticosteroids.

Approximately 20-30% of patients with systemic sarcoidosis will experience cutaneous manifestations,and our patient's medical history placed cutaneous sarcoidosis high on the differential diagnosis. Although the clinic presentation could be consistent with cutaneous sardoidosis, biopsy failed to show typical well-formed pauci-inflammatory granulomas characteristic of sarcoidosis; alternatively it demonstrated suppurative granulomas, commonly seen with infectious etiologies. Although acid-fast stains were negative, tissue culture confirmed the diagnosis. Infection with atypical mycobacteria has previously been misdiagnosed as systemic disease. *M. chelonae* infection clinically mimicking cutaneous vasculitis was described in two patients with systemic lupus erythematosus and idiopathic multifocal uveitis on immunosuppressive therapy.

Treatment of cutaneous *M. chelonae* consists of both surgical excision and antibiotic treatment. Excision should be viewed as a mechanism to reduce organism burden and not as curative. *M. chelonae* is rarely susceptible to traditional tuberculosis antibiotics and has high minimum inhibitory concentrations (MIC) for older drugs like doxycycline, erythromycin and sulfamethoxazole. Recent studies have shown clarithromycin to have a low MIC and high bacteriacidal activity against *M. chelonae*, now making it the standard of care as part of multi-drug therapy. Additional studies have demonstrated combinations of clarithromycin with gentamicin, fluoroquinolones, rifampicin, linezolid, other aminoglycosides, doxycyline and carbapenems to be effective treatment regimens. There is no general consensus as to which additional antimicrobial is most effective, and susceptibility testing is recommended for each case. Upon diagnosis, our patient was started on clarithromycin 500mg twice daily and levofloxaxin 75 mg daily, which she will continue for a total of one year.

We present this case for clinical interest and to demonstrate the ability of *M. chelonae* to mimic cutaneous sarcoidosis. A high degree of suspicion is necessary when diagnosing immunocompromised patients with cutaneous granulomatous disease. Multiple biopsies and often large excisional biopsies are needed to definitively diagnose atypical mycobacterial infections.

REFERENCES

1. Griffith, D.E., Aksamit, T. Brown-Elliott, B.A., Catanzaro, A. Daley, C., Gordin, F., Holland, S.M., Horsburgh, R., Huitt, G., Iademarco, M.F., Iseman, M., Olivier, K., Ruoss, S., von Reyn, C.F., Wallace, R.J. Jr., Winthrop, K. ATS Mycobacterial

Diseases Subcommittee. American Thoracic Society. Infectious Disease Society of America. An official ATS/IDSA statement: diagnosis, treatment, and prevention of nontuberculous mycobacterial diseases. American Journal of Respiratory and Critical Care Medicine 2007;175:367-416.

2. Bartralot, R., Garcia-Patos, D. Rodriguez-Cano, L., Mollet, J., Martin-Casabona, N., Coll, P., Castells, A., Pujol, R.M. Clinical patterns of cutaneous nontuberculous mycobacterial infections. British Journal of Dermatology 2005;152:727-734.

3. Sanudo,A., Vallejo, F., Sierra, M., Hoyos, J.G., Yepes, S., Wolff, J.C., Correa, L.A., Montealegre, C., Navarro, P., Bedoya, E., Sanclemente, G. Nontuberculous mycobacteria infection after mesotherapy: preliminary report of 15 cases. International Journal of Dermatology 2007;46:649-53.
4. Dessy, L.A., Mazzocchi, M., Fioramonti, P., Scuderi, N. Conservative management of local Mycobacterium chelonae infection after combined liposuction and lipofilling. Aesthetic Plastic Surgery 2006;30:717-722.

5. Saha, M., Azadian, B.S., Ion, L., Bunker, C.B. Mycobacterium chelonae infection complicating cosmetic facial surgery. British Journal of Dermatology 2006;155(5):1097-1098.

6. Fowler, A.M., Dutton, J.J., Fowler, W.C., Gilligan, P. Mycobacterium chelonae canaliculitis associated with SmartPlug use. Ophthalmic Plastic & Reconstructive Surgery 2008;24:241-243.

7. Fraser, V. J., Jones, M., Murray, P.R., Medoff, G., Zhang, Y, Wallace, R.J. Jr. Contamination of flexible fiberoptic bronchoscopes with Mycobacterium chelonae linked to an automated bronchoscope disinfection American Review of Respiratory Disease 1992;145:853–855.

8. Samtson, AV. Cutaneous sarcoidosis. International Journal of Dermatology 1992; 31: 385-391.

9. Gordon, M.M., Wilson, H.E., Duthie, F.R., Jones, B., Field, M. When typical is atypical: mycobacterial infection mimicking cutaneous vasculitis. Rheumatology 2002;41:685-690.

10. Cremades, R., Santos, A., Rodriguez, J.C., Garcia-Pachon, E., Ruiz, M., Royo G. In vitro bactericidal activity of antibiotic combinations against clinical isolates of Mycobacterium chelonae. Journal of Chemotherapy 2008;20:43-47.

11. Vemulapalli, R.K., Cantey, J.R., Steed, L.L., Knapp, T.L., Thielman, N.M. Emergence of resistance to clarithromycin during treatment of disseminated cutaneous Mycobacterium chelonae infection: case report and literature review. Journal of Infection 2001;43:163-168.

12. Uslan, DZ et al. Skin and soft tissue infections due to rapidly growing mycobacteria. Arch Dermatol. 2006;142:1287-1292

CHICAGO DERMATOLOGICAL SOCIETY **CASE # 17**

Presented by Aaron Pace MD, and James Swan MD
Division of Dermatology, Hines Veterans Administration Hospital

HISTORY OF PRESENT ILLNESS

A 46-year old male presented to our clinic with a 5-year history of alopecia. Symptoms occurred shortly after he received the hepatitis B vaccine series 5 years ago. He reported limited hair loss on the temporal scalp after the initial dose, followed by near complete hair loss involving all other hair bearing areas after the second and third doses. He denied pruritus, erythema, and scaling of the areas.

PAST MEDICAL HISTORY

Depression
Hypertension

MEDICATIONS

Mirtazapine

ALLERGIES

No know drug allergies

FAMILY HISTORY

No history of hair loss in children, siblings, or parents.

SOCIAL HISTORY

Non-smoker

PHYSICAL EXAM

There is diffuse alopecia involving the scalp, face, trunk and extremities. There are only a small number of thin hairs on the central chest and sparse eye lashes. Underlying skin is normal without erythema or follicular scarring.

LABORATORY RESULTS

The following were normal or negative:
TSH is 0.61 (normal range 0.59-1.61)

DIAGNOSIS

Alopecia universalis, likely triggered by hepatitis B vaccine.

TREATMENT AND COURSE

The patient has deferred treatment for his condition and has noted only slight re-growth on the chest and eye lashes.

DISCUSSION

Alopecia areata (AA) is a non-scarring autoimmune hair loss, which is frequently recurrent and resistant to treatment. Although its pathophysiology remains unknown, it is postulated that CD4+ and CD8+ T cells reactive to hair bulb auto antigens induce the inflammatory process leading to hair loss. In this respect, AA is frequently associated

with other autoimmune diseases such as insulin-dependent diabetes, rheumatoid arthritis, vitiligo or Hashimoto's disease.

Alopecia areata is often multifocal, with the incidence of progression to alopecia totalis or universalis ranging from 7 to 40%. In alopecia universalis and totalis patients, the onset is typically younger with a mean age of 18.5 years. Patients with alopecia totalis or universalis are more likely to have associated autoimmune disease, atopic disease, and to have a family history of these conditions.

Hair loss is reported very rarely following immunizations. Under reporting is a problem with the passive surveillance system used to gather data about alopecia and vaccines. That being said, only 60 cases were reported during a 10-year period in which approximately 1 billion vaccine doses were given. This implies alopecia is a rare complication of vaccination. Post-vaccination hair loss, when it develops, was found to occur within the first month in 84% of patients. Alopecia occurring after vaccination is often mild and self-limited. Of the 60 identified patients with alopecia due to vaccines, 46 had received the hepatitis B vaccination. About 40% of respondents experienced severe hair loss. Approximately 20% reported persistent hair loss consistent with alopecia areata although specific diagnosis was not sought. In patients who re-grew their hair the loss was attributed either to telogen effluvium or alopecia areata that went into remission. In the AA type cases, it was hypothesized that the vaccination may share epitopes with the hair follicle

Randomized controlled trials of treatment options are scarce. Current treatments include: topical, intralesional, or systemic corticosteroids; oral or topical cyclosporine; topical immunotherapy; anthralin; or minoxidil. The only treatments that have been proven effective and stand up to the mandates of evidence-based medicine in randomized control trials are the topical contact sensitizers diphenylcyclopropenone and squaric acid dibutylester (2 older RCTs showed efficacy of topical steroids, but more recent studies do not support the findings). Response rates range from 29-78% with topical contact sensitizers. Topical steroids are frequently used although their efficacy is poor due to their lack of penetration, even when used under occlusion. A recent study of AA totalis and universalis clobetasol under occlusion resulted in terminal hair re-growth in 8 of 28 patients, 3 of these then relapsed and all three failed repeat treatment. The time to hair re-growth ranged from 6-14 weeks when using clobetasol under occlusion. Novel liposomal vehicles are being developed that may deliver medications much deeper into the dermis. Tacrolimus also may become effective in the future as new vehicles are developed that will allow deeper penetration.

Alopecia totalis and universalis will likely remain a difficult treatment conundrum for some time. Theoretically there is always a potential for hair re-growth because the follicle is still intact, but practical clinical experience reveals that alopecia totalis and universalis patients rarely are able to re-grow hair. With treatment patients will often have some hair return although the long-term course of the disease remains unchanged even with aggressive intervention. Less than 10% of patients with AA universalis re-grow their hair and even those who report significant hair growth often still wear a wig.

REFERENCES

1. Freyschmidt-Paul P et al. Alopecia areata: treatment of today and tomorrow. J Invest Dermatol 2003;8(1):12-7

2. Tosti A et al. Alopecia areata: a long term follow-up study of 191 patients. J Am Acad Dermatol. 2006;55(3):438-41.

3. Goh C et al. Profile of 513 patients with alopecia areata: associations of disease subtypes with atopy, autoimmune disease and positive family history. J of the Eur Acad of Dermatol and Vener. 2006;20:1055-60.

4. Wise R et al. The bald truth. Amer J Gastroenterology. 1999;94(4):1104.

5. Tosti A et al. Clobetasol propionate 0.05% under occlusion in the treatment of alopecia totalis/universalis. J Am Acad Dermatol. 2003;49(1): 96-98.

6. Wise R et al. Hair loss after routine immunizations. J of the Amer Med Assoc. 1997;278:1176-78.

CHICAGO DERMATOLOGICAL SOCIETY **CASE # 18**

Presented by Kathryn Barlow MD, and Anthony Peterson, MD
Division of Dermatology, Loyola University Medical Center

HISTORY OF PRESENT ILLNESS

An otherwise healthy 49-year old female presented with a six-month history of increasing pain and nail discoloration of the right fourth fingernail. After injuring the finger in a car door 6 months prior, she noted some discoloration at the tip of the nail. Sometime later, she noted dark discoloration near the cuticle with erythema and swelling of the distal digit. The pain in the area was intermittently severe with pressure and throbbing. She reported chills and fatigue, but no fever. Of note, she wears artificial nails and visits the nail salon frequently.

PAST MEDICAL HISTORY

Pituitary microadenoma
Migraine headaches

MEDICATIONS

Topiramate
Naratriptan
Cabergoline
Microgestin

ALLERGIES

No known drug allergies

FAMILY HISTORY

Non-contributory

SOCIAL HISTORY

No smoking or alcohol.

PHYSICAL EXAM

On the right fourth digit was a dark blue-black area of discoloration present at the proximal nail plate and proximal nailfold with surrounding erythema, swelling, and significant tenderness with palpation. Distal onycholysis was noted extending from the lesion. The remaining nails were covered with artificial nails.

LABORATORY RESULTS

The following tests were normal or within normal limits:
Erythrocyte sedimentation rate, complete metabolic panel.
The following tests were abnormal:
Complete blood count: 12.1 (4-10 K/UL)
Culture from biopsy of the nail bed and nail plate: *Aspergillus flavus* and *Rhizomucor* species

DIAGNOSIS

Rhizomucormycosis and aspergillosis of the nail.

TREATMENT AND COURSE

A partial nail avulsion of the proximal nail was performed, with the nail plate and tissue biopsy of the nail bed sent for fungal, and bacterial cultures. The cultures returned as *Aspergillus flavus* and *Rhizomucor* species. The patient was referred to infectious disease and posaconazole 400 mg twice daily was initiated. She returned one month later for complete removal of the nail, and culture of the distal portion of the nail plate revealed *Aspergillus flavus*. Patient has tolerated posaconazole therapy well, and a 6-month course is anticipated.

DISCUSSION

Rhizomucor spp belong to the order Mucorales and are ubiquitous in soil and decaying organic matter. It is one of several species responsible for causing mucormycosis. After candidiasis and aspergillosis, it is the third most common invasive fungal infection. Mucormycosis typically presents as an angioinvasive infection in immunocompromised patients, however there have been rare reports of invasive mucormycosis in immunocompetent healthy adults. Five major forms of infection exist including rhino-orbito-cerebral, pulmonary, disseminated, cutaneous and gastrointestinal.

Cutaneous mucormycosis can develop after trauma, burns, surgery, intravenous lines or intramuscular injections. There have also been reports of outbreaks of cutaneous infection linked to contaminated Elastoplast tape. The cutaneous variant of mucormycosis is the form of infection least likely to be associated with an underlying disease or immunocompromised state. It can present as a superficial or deep infection, and can appear clinically as pustules, vesicles, nodules, ulcerations, or cellulitic plaques. Cutaneous mucormycosis has a better prognosis compared to other forms of mucormycosis. It has the lowest mortality (16%), compared to 67% for rhinocerebral, 85% for pulmonary and 100% for disseminated or gastrointestinal mucormycosis.

Skin biopsy for histopathologic confirmation is the gold standard for diagnosis of mucormycosis; however, our patient did have a positive culture from a biopsy of the nail bed that ultimately grew both *Aspergillus* and *Rhizomucor*. While *Aspergillus* is a well-known nail pathogen, to our knowledge, *Rhizomucor* spp has not been previously described as a fungal nail pathogen. The possibility that the *Rhizomucor* isolated is a contaminant cannot be completely ruled out, however, after consulting with infectious disease, it was ultimately decided to treat both isolated pathogens as potential causative agents of the patient's infection. Posaconazole was chosen due to its activity against both *Aspergillus* and *Rhizomucor* and its availability as an oral agent.

Special thanks to Patricia L. Kammeyer, Department of Microbiology.

REFERENCES

1. Prabhu RM, Patel R. Mucormycosis and entomophthoramycosis: a review of the clinical manifestations, diagnosis and treatment. *Clin Microbiol Infect.* 2004;10(Suppl.1):31-47.
2. Ribes JA, et al. Zygomycetes in human disease. *Clin Microbiol Rev*. 2000;13(2):236-301.
3. Sun QN, et al. In vivo activity of posaconazole against *Mucor* spp in an immunosuppressed mouse model. *Antimicrob Agents Chemother*. 2002;46(7):2310-2312.

4. Solano T, et al. Disseminated Mucormycosis due to *Saksenaea vasiformis* in an immunocompetent adult. *Clin Infect Dis*. 2000;30:942-943.

CHICAGO DERMATOLOGICAL SOCIETY **CASE # 19**

Presented by Linda Sheu MD, David Eilers MD, and James Swan, MD
Division of Dermatology, Hines Veterans Administration Hospital

HISTORY OF PRESENT ILLNESS

This 58-year old Caucasian male presented with hyperkeratotic plaques on the hands and feet since childhood. In his adult years, the hyperkeratosis had considerably worsened on his hands, resulting in mild restriction of movement. He also had cracking of the skin resulting in pain. He used emollients in the past, including petrolatum ointment multiple times daily with minimal relief.

PAST MEDICAL HISTORY

Squamous cell carcinoma treated with chemotherapy and radiation therapy in 2005
Hypothyroidism secondary to radiation therapy
Gastroesophageal reflux disease
Hypertension
Chronic obstructive pulmonary disease

MEDICATIONS

Atenolol
Levothyroxine
Omeprazole

ALLERGIES

No known drug allergies

FAMILY HISTORY

Mother and maternal grandfather with hyperkeratosis of the palms and soles
Parents are non-consanguineous

SOCIAL HISTORY

Non-contributory

PHYSICAL EXAM

There was diffuse hyperkeratosis of the palmar hands and plantar feet, with prominent plantar furrows and few fissures.

DIAGNOSIS

Unna Thost disease

TREATMENT AND COURSE

The patient was started on urea cream 40% applied twice daily with improvement.

DISCUSSION

The inherited palmoplantar keratodermas (PPK) consist of a complex, heterogeneous group of genodermatoses characterized by hyperkeratosis of the palms and soles. These can be clinically classified as diffuse, focal or punctate. Unna Thost disease (non-epidermolytic palmoplantar keratoderma), is among the diffuse pattern palmoplantar keratodermas, which also includes Vorner's disase (epidermolytic

hypereratosis), erythrokeratoderma variablis, Mal de Meleda, Vohwinkel's syndrome, Papillon-Lefevre syndrome, and Clouston's syndrome.

Unna-Thost disease is the most common form of inherited palmar plantar keratoderma. It may be inherited as an autosomal dominant disease or present as a spontaneous mutation. Genetic analysis of familial Unna-Thost has established linkage to the type II keratin locus on band 12q11-13, corresponding to the keratin 1 gene.

The condition most often presents within the first few months of life and signs are usually well developed by age 3-4 years. It is characterized by waxy, diffuse, symmetric hyperkeratosis of the palms and soles, often with an erythematous rim of demarcation at the periphery. Palmoplantar hyperhidrosis may or may not be present. Without hyperhidrosis, deep grooves and fissures result. Involvement of other locations, especially over knuckles, finger joints, elbows, and knees may occur. Nails may also be thickened.

There is no racial predilection, and males are more frequently affected then females. The condition has a tendency to worsen during the winter months. Complications include infection (fungal or bacterial), malodor, inflammation and pain.

While clinically identical to Vorner's disease the histopathology of Unna Thost disease typically lacks epidermolysis, differentiating it from Vorner's epidermolytic palmoplantar keratoderma. Histologic findings include orthokeratotic hyperkeratosis with hyper- or hypogranulosis, and moderate acanthosis.

Treatment includes topical keratolytics, such as salicylic acid, 50% propylene glycol in water under occlusion, lactic acid and urea cream. Mechanical debridement with a blade is often useful. For severe and diffuse forms, systemic retinoids such as etretinate and acitretin have been reported with success.

REFERENCES

1. Itin PH, Fistarol SK. Palmoplantar keratoderms. Clin Dermatol. 2005; 23 (1) 15-22.

2. Kansky A, Stanimirovic A, Basta-Juzbasic A. Isolated cases of palmoplantar keratoderma, Unna-Thost type. Cutis. 1992; 29 (6):406-8

3. Kimyai-Asadi A, Kotcher LB, Jih MH. The molecular basis of hereditary palmoplantar keratodermas. J Am Acad Dermatol. 2002; 47 (3): 327-43

CHICAGO DERMATOLOGICAL SOCIETY **CASE # 20**

Presented by Tricia Hultgren MD, David Eilers MD, James Swan MD, Scott Wickless DO and Madhu Dahiya, MD
Division of Dermatology, Hines Veterans Administration Hospital
Division of Dermatology, Loyola University Medical Center

Patient A

HISTORY OF PRESENT ILLNESS
This 74-year old male with history of multiple non-melanoma skin cancers presented to the VA dermatology clinic for routine follow-up. He reported a rapidly growing lesion on the left temple that was tender to palpation. He also noted a smaller growth on the left cheek that occasionally bled with shaving. Both lesions had been present for 3-4 weeks. He noted recent fatigue, chills and nausea, but denied fever and weight loss.

PAST MEDICAL HISTORY
Hypertension
Hepatitis C
Coronary artery disease
Peripheral vascular disease
History of squamous cell lung cancer- status post right lobectomy 2001
Porphyria cutanea tarda
History of multiple non-melanoma skin cancers

MEDICATIONS
Aspirin
Clopidogrel
Docusate
Finasteride
Hydrochlorothiazide
Lisinopril
Metoprolol
Simvastatin
Trazadone
Hydrocodone/acetaminophen

ALLERGIES
No Known Drug Allergies

FAMILY HISTORY
Noncontributory

SOCIAL HISTORY
Patient was retired and quit smoking 18 years ago. He denied alcohol and illicit drug use.

PHYSICAL EXAM
On the left temple there is a 1.2 cm x 1.0 cm pink, firm shiny nodule with telangectasia. A similar 8 mm x 7 mm pink infiltrative, eroded papule is present on the left lateral cheek.

HISTOPATHOLOGY
Histopathologic examination from a biopsy of the left cheek and left temple revealed squamous cell carcinoma with focal glandular features. Focal angiolymphatic invasion by tumor cells was identified. The tumor extended to the deep margin of both specimens.

Tumor cells were positive for high molecular weight cytokeratin, CK 7 and p63 and were negative for CK 20, TTF1 and S100. Mucin stain was focally positive in the tumor cells. Immunoperoxidase stain for CD 34 was positive. The above findings were consistent with adenosquamous cell carcinoma, most likely metastasis from a lung primary.

DIAGNOSIS
Lung adenosquamous cell carcinoma with cutaneous metastasis

TREATMENT AND COURSE
The patient developed left arm pain while skin biopsies were still pending and work up revealed a pathologic fracture of the humerus. Further imaging showed a 4.3 cm spiculated left upper lobe lung mass, confirming the diagnosis of a second primary lung cancer with cutaneous and bone metastasis. Unfortunately, the patient passed away six weeks later due to metastatic disease.

Patient B

HISTORY OF PRESENT ILLNESS
A 66-year old male was seen on the inpatient dermatology consultation service for evaluation of multiple subcutaneous nodules. The patient reported two growths on the back and one on the left chest that had been present for three months. The lesions were non-tender, non-pruritic and did not bleed. The patient had been admitted for pneumonia and underwent CT scan of the chest/abdomen/pelvis that revealed a large right hilar and mediastinal mass and multiple metastatic lesions of the liver, spleen and adrenal glands. Brain imaging revealed multiple metastatic lesions. He denied fever, chills, weight loss, night sweats and cough but noted chronic abdominal pain.

PAST MEDICAL HISTORY
Metastatic carcinoma, unknown primary
Peptic ulcer disease
Diverticulosis

MEDICATIONS
Pantoprazole
Docusate sodium
Fentanyl patch
Hydromorphone

ALLERGIES
No Known Drug Allergies

FAMILY HISTORY
Noncontributory

SOCIAL HISTORY
Patient had a 15-year pack history; quit smoking in July 2007. He denied alcohol and illicit drug use.

PHYSICAL EXAM
On the central upper back and left upper back were two approximately 4.0 cm firm, slightly mobile, non-tender subcutaneous nodules without surface change. A 3.0 cm similar lesion was present on the left lateral chest.

HISTOPATHOLOGY
Initial histopathologic examination from a punch biopsy of the left chest was unremarkable.

Follow-up excisional biopsies of all three lesions revealed multiple dermal tumor nests composed of small blue cells with salt and pepper nuclear chromatin and nuclear molding. Areas of crush artifact were present within the tumor.

Immunohistochemical studies demonstrated positive staining for CK 7, TTF-1, CD56 and NSE. CK 20 was negative.

DIAGNOSIS
Small cell carcinoma of the lung with cutaneous metastasis

TREATMENT AND COURSE
The patient was seen by radiation oncology and medical oncology. He was started on dexamethasone for brain metastasis and initiated chemotherapy with etoposide and cisplantin. He also received brain and abdominal radiation therapy. The patient underwent therapy for six weeks before succumbing to metastatic disease.

DISCUSSION
Cutaneous involvement of internal malignancies is relatively uncommon, occurring in 0.7% to 9% of all cancer patients. Mechanisms responsible for cutaneous metastasis include hematogenous, lymphatic and contiguous spread. Iatrogenic implantation may also occur. Previous studies in Caucasian populations suggest that breast cancer has the highest rate of skin metastasis (18.6%-26.5%), followed by cancer of the oral mucosa (4.6%-17.3%), then lung cancer (0.6%-5.9%). A recent retrospective study from Taiwan demonstrated a low overall rate of cutaneous metastasis of 1%, and a drastically decreased rate of metastasis of breast cancer of only 2.4%, suggesting racial differences in the biologic characteristics of cancer cells.

Skin involvement may be the initial presentation of malignancy. In a series of patients with cutaneous metastasis, skin findings were the presenting sign in 37% of men and 6% of women. The gender difference is likely due to the higher frequency of lung and

renal cancer in men; both tend to be relatively quiescent but metastasize early in the disease course.

Both of our patients developed cutaneous metastasis from lung cancer prior to the diagnosis of underlying malignancy. A recent retrospective study from Japan revealed the rate of cutaneous metastasis from lung cancer to be 2.8% among 579 cases. In the same study, 7% of patients had evidence of skin metastasis prior to diagnosis of lung cancer. The most common clinical findings of cutaneous metastasis from lung cancer are multiple erythematous nodules with intact overlying epidermis. The back, abdomen and anterior chest.are the most frequent sites of involvement. Adenocarcinoma is the most likely histologic subtype to metastasize, followed by squamous cell and small cell carcinoma. Bronchioalveolar and large cell carcinoma rarely spread to the skin.

Cutaneous metastasis portends a poor prognosis as multiple organ systems are often involved. Mean survival time after skin metastasis ranges from 3 to 5 months.

REFERENCES

1. Schwartz RA. Cutaneous metastatic disease. J Am Acad Derm. 1995;33:161-82.

2. Hidaka T, Ishi I Y, Kitamura S. Clinical features of skin metastasis from lung cancer. Int Med. 1996;35:459-62.

3. Terashima T, Kanazawa M. Lung cancer with skin metastasis. Chest. 1994;106:1448-50

4. Hu S, Gwo-Shing C, Ching-Shuang W et al. Rates of cutaneous metastasis from different internal malignancies: Experience from a Taiwanese medical center. J Am Acad Derm.. 2008;60:379-87.

NOTES

NOTES