CHICAGO DERMATOLOGICAL SOCIETY

Rush University Medical Center

Chicago, Illinois

Clinical Cases

May 17, 2006

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Case #1

CHICAGO DERMATOLOGICAL SOCIETY
RUSH UNIVERSITY MEDICAL CENTER
CHICAGO, ILLINOIS
MAY 17, 2006

CASE PRESENTED BY: Arthur Rhodes, MD, Laura Hoffman, MD

History: 81-year-old African American male presents with dramatically worsening dry skin over one year. The patient reports generalized excessive scale and skin shedding, with intermittent pruritus. Prior daily treatments with emollients and an unknown topical steroid offered no relief.

Past Medical History: Chronic Obstructive Pulmonary Disease, Asthma, Hypertension
Benign Prostatic Hyperplasia vs. Prostate Cancer (currently being evaluated)

Medications:
Hydrochlorothiazide
Atenolol
Ranitidine
Salmeterol/Albuterol Inhalers
Loratadine

Family History: No history of hereditary ichthyoses or atopy.

Review of Systems: Negative for recent fever, chills, night sweats, malaise or enlarged lymph nodes. Patient's appetite, weight, and energy level are stable. Patient denies neurologic, gastrointestinal, or urogenital symptoms.

Physical Examination: Generalized reticular scaling. No lymphadenopathy or hepatosplenomegaly.

Lab Data: PSA = 33.10 ng/ml (normal range 0.00-4.00)

Studies: 3/16/2006 – Retroperitoneal (Renal) Ultrasound: Suspected solid-appearing mass within the right kidney. Carcinoma cannot be excluded. Further assessment with MRI recommended. Bilateral renal cysts. Markedly enlarged prostate gland.

3/30/06 – Abdominal MRI Pre-Post Contrast: Several bilateral renal cysts. No definite MR evidence of malignant renal neoplasm. Prominent nodular prostate with mass effect on the urinary bladder.

Diagnosis: **Acquired Ichthyosis**

Course and Treatment: Patient was advised to soak in temperate tap water baths two times per day, followed by 20% urea cream under occlusion. An age appropriate malignancy evaluation is underway.

Discussion: Acquired ichthyosis is a non-inherited form of ichthyosis presenting for the first time during adulthood. It may be a marker for malignancy, infection, certain medications, metabolic abnormalities, or autoimmune disease.

Lymphoproliferative diseases are associated with acquired ichthyosis, most commonly Hodgkin's lymphoma, multiple myeloma, leukemia, B and T-cell lymphoma, and polycythemia rubra vera. Solid tumors associated with acquired ichthyosis include carcinoma of the breast, lung, ovary and cervix, hepatocellular carcinoma, and transitional cell carcinoma of the kidney.

Acquired ichthyosis has been reported in association with medications such as nicotinic acid, triparanol, butyropheonones, dixyrazine, cimetidine, and clofazimine. Other cases have been linked to infections (HIV, leprosy, tuberculosis), metabolic abnormalities (thyroid disease, hyperparathyroidism), and autoimmune disease (dermatomyositis and systemic lupus erythematosus).

The first step in the management of patients who have acquired ichthyosis is to determine the underlying cause. Skin manifestations usually follow the course of the underlying disease and should resolve with cure (if achievable). In the interim, management of the patient is focused on three key elements: hydration, humidification, and keratolysis.

The pathophysiologic mechanism of acquired ichthyosis is still not clear. One hypothesis considers the secretion of transforming growth factor (TGF-α) by tumor tissue. Another study suggested impaired lipogenesis.

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Case #2

CHICAGO DERMATOLOGICAL SOCIETY
RUSH UNIVERSITY MEDICAL CENTER
CHICAGO, ILLINOIS
MAY 17, 2006

CASE PRESENTED BY: Lady C. Dy M.D. and Michael O'Donoghue M.D.

History: Four-year-old Hispanic male who presents with a two-year history of dry, scaly lesions on the palms, soles, and lower legs. He was born by normal vaginal delivery after an uncomplicated pregnancy. Soon after birth, he was noted to have "dry" skin. Lesions first arose on the sole at age 2, and then spread to the palms and lower legs by age four. His skin lesions improve in the summer and worsen in the winter.

Past Medical History: Asthma at age two that has resolved.

Family History: Paternal Grandmother with Asthma
No family history of palmoplantar keratoderma.

Review of Systems: Negative

Physical Examination: Healthy Child. Palms and soles reveal orange-yellow hyperkeratotic plaques with linear fissures, no transgrediens, and no nail changes or alopecia. Legs show well-demarcated, slightly pink, shiny plaques. Back has scattered hypopigmented patches with slight scale. Scalp shows slight erythema with fine scale. Normal face, chest, teeth, genitalia, ocular, and ear examination. No evidence of musculoskeletal, neurological, visual, or auditory disturbance.

Histo-pathology: Punch Biopsy from the left anterior lower leg showed compact hyperparakeratosis with focal areas of parakeratosis overlying an acanthotic epidermis with broad rete ridges. The suprapapillary plates are thickened with a mild lymphocytic perivascular infiltrate.

Diagnosis: **Juvenile Pityriasis Rubra Pilaris**

Course and Treatment: The patient has been treated with LacHydrin, Carmol 40, and 2.5% hydrocortisone ointment with limited success. There is significant improvement with the use of petrolatum jelly after bathing.

Discussion: The classification of PRP which was proposed by Griffiths is based on age of onset, behavior, clinical appearance, and prognosis. The juvenile classical (type III) usually presents at the age of 1-2 years with lesions on the head, neck, or upper trunk. Skin lesions usually resolve by age three. This classic form is characterized by follicular hyperkeratotic papules that coalesce into large, scaly, erythematous plaques, palmoplantar keratoderma, diffuse furfuraceous scale of the scalp, and frequent progression to exfoliative erythroderma. Distinguishing features include "islands" of spared skin within generalized erythroderma, follicular keratotic plugs, and an orange hue to the involved skin.

The most common form of childhood PRP is type IV or juvenile circumscribed group. This is characterized by the formation of well-circumscribed, hyperkeratotic, erythematous plaques. Keratotic plugging is prominent with lesions largely confined to the elbows and knees. There may also be occasional erythematous scaly macules/papules over the trunk or scalp as well as mild to moderate palmoplantar keratoderma. The clinical course is marked by remissions and exacerbations.

Type V or the juvenile atypical group presents at birth or in the first few years of life and tends to run a chronic course. It is characterized by mild to severe erythema, follicular plugging, and keratoderma. There may also be some scleroderma-like changes on the hand and feet. Cases of familial PRP are usually of this type.

Gelmetti et al. found that the majority of their patients did not subscribe to the classification system proposed by Griffiths and proposed an alternate classification that categorized the disease into three types based solely on the duration: an acute form that resolves in 6 months, an acute form with a prolonged course resolving within a year, and a chronic form that persists for more than 1 year.

Piamphongsant and Akaraphant reported 168 cases of PRP from Thailand with many cases that possess clinical features that do not fit into any classification system. They proposed another classification that included both adults and children that is based on extent of disease beginning with type I that is only limited to palmoplantar keratoderma through type IV, that includes patients with extensive disease. The type II form involves palmoplantar keratoderma, circumscribed scaly erythematous patches on the elbows and knees, and follicular plugging in the patches.

Microscopically, the features of PRP are most impressive when taken from a very erythematous area. Histologic findings include irregular acanthosis, alternating orthokeratosis and parakeratosis in both vertical and horizontal directions, hypergranulosis, thick suprapapillary plates, short and thick rete

ridges, and a sparse to moderate lymphocytic perivascular infiltrate. Follicular papules reveal dilated infundibulum with keratotic plugging. Juvenile circumscribed PRP may reveal a dense lamellated hyperkeratosis, a normal or increased granular layer, and mild acanthosis.

The age of onset, behavior and clinical appearance give the patient a type IV classification according to Griffiths, a chronic form according to Gelmetti, and type II according to the classification by Piamphongsant and Akaraphant.

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Case #3

CHICAGO DERMATOLOGICAL SOCIETY
RUSH UNIVERSITY MEDICAL CENTER
CHICAGO, ILLINOIS
MAY 17, 2006

CASE PRESENTED BY: Michael Tharp, MD, Rachel Altman, MD

History: A 40-year-old African American female with a lifelong history of palmoplantar keratoderma presented to RUSH in October 2002. She noted a progressive thickening of the skin on her palms and soles which began at age three. At age nine, restrictive bands developed on her bilateral fifth toes which evolved into auto-amputation at age eleven. Similar constricting bands developed on additional fingers and toes requiring the use of a cane for ambulation. Of eight siblings, two sisters and one brother are also affected with a similar condition, in addition to her father. There is no history of hearing loss in the patient or her family members.

Past Medical History: Non-contributory

Physical Examination: Bilateral palms and soles revealed thickened, yellow keratotic plaques with transgriedens (involvement progressing to the dorsal aspect of the hands and feet). Constricting, firm bands on the third and fourth digits of both feet were present, while amputation of bilateral fifth toes were noted.

Diagnosis: **Vohwinkel's Syndrome (keratoderma hereditaria mutilans)**

Course and Treatment: Isotretinoin therapy was begun on January 2003 at a dose of 70 mg per day, however, it was lowered to 40 mg per day secondary to intolerable mucocutaneous side effects. The patient noted a significant reduction in pain allowing for ambulation without a cane. Neither progression of constricting bands nor additional constricting bands have developed since instituting this therapy.

Discussion: Vohwinkel's syndrome is a rare autosomal dominantly inherited dermatosis associated with several characteristic diagnostic features including (i) transgredient hyperkeratosis of the palms and soles, with a honeycomb appearance and hallmark parakeratosis; (ii) constricting bands encircling the digits of the hands and feet (pseudoainhum) which frequently lead to autoamputation of the fifth digits secondary to circulatory impairment and

deformity of the underlying bone; and (iii) dorsal warty papules and acral keratosis resembling "starfish" or knuckle pads. Other clinical findings noted with Vohwinkel's are either deafness or ichthyosis.

Genetic studies have revealed two different genetic defects in either connexin 26 (gap junction B2) or loricrin. Each of these genes is associated with different phenotypic findings. Ichthyosis is associated with a mutation in loricrin and deafness is associated with a mutation in connexin 26.

Connexin 26 is part of the gap junction. The connexin family in humans consists of approximately 20 distinct proteins, classified according to their molecular mass and grouped based on sequence similarities into GJA, GJB and GJG subtypes. These connexins are expressed in the epidermis, skin appendages, corneal epithelium and cochlear epithelium. Gap junctions are intercellular channels that mediate the exchange of metabolites, ions, and secondary messengers between cells. Each channel is formed by end-to-end connection of a connexon of one cell with a partner connexon of another neighboring cell. Connexin 26 defects are noted to be associated with sensorineural hearing loss in several genodermatoses including Vohwinkel's syndrome, Bart-Pumphrey syndrome, and Keratitis-Ichthyosis-Deafness syndrome (KID syndrome).

Loricrin, a small protein widely distributed in the superficial epidermis (granular layer and above), is the major structural component of the cornified cell envelope. The glutamine/lysine residues are believed to be necessary for cross-linking of the cornified envelope. Mutations in loricrin impair the formation of a mature and rigid cornified envelope including properly formed lipid envelopes thereby leading to a marked permeability defect and resultant ichthyosis. Loricrin defects are associated with two distinct genodermatoses: the ichthyotic variant of Vohwinkel's and with progressive symmetrical erythrokeratoderma (PSEK).

Synthetic retinoids, including etetrinate and isotretinoin, have been used successfully in several cases of patients with Vohwinkel's syndrome to both reverse the pseudoainhum and the keratoderma, however relapses occurred once these agents were discontinued. Doses have ranged from 0.5 mg/kg/day – 2 mg/kg/day with dramatic improvement noted within the first several weeks of therapy.

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Case #4

CHICAGO DERMATOLOGICAL SOCIETY
RUSH UNIVERSITY MEDICAL CENTER
CHICAGO, ILLINOIS
MAY 17, 2006

CASE PRESENTED BY: Arthur Rhodes, MD, Sarah Kasprowicz, MD

History: This 23-year-old African American male presented with diffuse, generalized ichthyosis since very early infancy. He notes mild pruritus and scaling. The patient was delivered at term by Cesarean section because labor failed to progress. No history of a collodion membrane was noted at delivery. There is no history of deafness, photosensitivity, or blindness. Patient requires glasses for astigmatism. He has a seizure disorder for which he takes Lamictal. He is said to have "cerebral palsy."

Physical Exam: Height 4' 8". Present on chest, back, torso, legs, arms, and dorsal feet is profuse icthyosiform scaling with flexural sparing. There are large, brown-plate like scales with associated fine scale. Palate is normal. Limbs are spastic. Axillary and pubic hair is present. Testicles are borderline small. No beard hair is evident. Head is small in proportion to body with abnormal head shape.

Laboratory Results: The following were within normal limits: cholesterol, triglycerides, chylomicrons and serum elecrophoresis. Chest X-ray: within normal limits. Scrotal Ultrasound: unremarkable, normal testicles.

Histo-pathology: Biopsy date: 1/6/06, 4 mm punch/abdomen. Acanthotic epidermis with overlying compact orthokeratosis, suggestive of lamellar ichthyosis.

Diagnosis: **Ichthyosis, associated with short stature, dysmorphic facies, seizure disorder and spasticity.**

Treatment and Course: Various over-the-counter and prescription medicines with little or no relief. Currently, he uses LacHydrin cream to the skin and Ketoconazole 2% shampoo to the scalp once a day. Aquaphor is also used after bathing.

Discussion: In 1927, Einar Rud, a Danish physician, described a 22-year-old male with ichthyosis, hypogonadism, short stature, epilepsy, anemia, and polyneuritis. Over the next 60 years, an additional 35 published reports described "Rud syndrome," with varying inclusion criteria. Rud syndrome, once considered a rare recessive

disorder, is now classified as an ichthyosis subset, a neuro-ichthyosis with cutaneous findings similar to those found in x-linked recessive ichthyosis. Ichthyosis and hypogonadism are the predominant features, but the neurologic deficits are variable. The pathophysiology of Rud syndrome is not known. However, defects in steroid sulfatase (located on the X chromosome) have been identified.

Clinical manifestations of Rud syndrome are said to appear at birth or shortly thereafter. The prevalence of Rud syndrome is unknown but thought to be extremely rare. There is no known predilection for any specific ethnic group and no gender predilection for Rud syndrome has been identified. However, some investigators report steroid sulfatase deficiency in Rud syndrome linked primarily to male patients. Cases of Rud Syndrome suggestive of an autosomal recessive inheritance pattern have also been reported.

This patient's cutaneous findings, short stature, and neurological associations are consistent with Rud's Syndrome. The term Rud's syndrome has been discontinued by some authorities, and it remains a controversial diagnosis. Further evaluation of our patient is in progress, including steroid sulfatase deficiency analysis through Fluorescent in situ Hybridization (FISH). FISH is the application of fluorescently labeled DNA molecules to metaphase chromosomes and interphase nuclei for the detection of chromosome abnormalities and mutations. FISH analysis is performed on metaphase chromosomes using a probe specific for this locus.

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Case #5

CHICAGO DERMATOLOGICAL SOCIETY
RUSH UNIVERSITY MEDICAL CENTER
CHICAGO, ILLINOIS
MAY 17, 2006

CASE PRESENTED BY: James Swan, MD, Brian Bonish, MD/PhD

History: This 48-year-old gentleman was referred to our clinic by his primary care physician for severely dry skin. Upon questioning, the patient complained of severely dry, cracked skin since childhood, which worsened in the winter and seemed to improve during warmer months. He had not previously seen a dermatologist nor sought any medical advice regarding his skin condition. He noted having a brother and a nephew with a similar skin problem.

Past Medical History: None pertinent

Medications: None

Allergies: None

Family History: One brother and one nephew (sister's son) with similar skin disorder

Social History: Non-contributory

Review of Systems: Negative

Physical Examination: The patient exhibited large, prominent, dirty brown scales overlying mild erythema on the anterior and lateral neck, trunk, and extensor surfaces of all four extremities. The patient's scalp, face, anticubital and popliteal fossae, as well as palms and soles were spared. A slit-lamp examination was not performed.

Laboratory Data: None

Histo-pathology: Left leg 4mm punch biopsy:
-Skin with benign keratosis, mild spongiosis and minimal perivascular chronic inflammation
-negative for PAS-D special stain

Diagnosis: **X-linked Ichthyosis**

Course and Treatment: Education was provided to the patient regarding his skin condition, including diagnosis, inheritance pattern, and proper care of his skin. The use of gentle skin cleansers and frequent applications of emollients were recommended. He continues to do well.

Discussion: X-linked ichthyosis (XLI) is a relatively common disease of defective desquamation, which manifests itself as large polygonal sheets of adherent brown scale. XLI is caused by a loss of activity of the microsomal enzyme steroid sulfatase (STS). This loss leads to impaired cholesteryl sulfate hydrolysis and cholesterol 3 sulfate (CSO_4) accumulation in the skin and other organs. In the skin, STS is normally present in lamellar bodies and is secreted with other lipid hydrolases in the stratum corneum. Normally, STS slowly breaks down the CSO_4, an inhibitor of serine proteases, which allows for normal comeodesmosin breakdown and desquamation.

XLI overwhelmingly affects males and occurs in the population at a prevalence of 1:6000. Female carriers are asymptomatic. Ninety percent of cases are caused by a deletion of all or a portion of the STS gene from the distal tip of the short arm of the X chromosome at Xp22.32. The remaining cases are caused by other inactivating mutations in the STS gene.

XLI skin changes appear soon after birth as mild erythroderma and generalized peeling of large translucent scale. Later the typical adherent sheets of polygonal brown scale ("dirty neck") develop and persist for life. The neck and preauricular areas are almost invariably involved while the palms, soles and face are spared. This pattern is considered almost pathognomonic for XLI. Unlike other ichthyosis, the symptoms do not improve with age.

The histopathology of XLI shows hyperkeratosis or parakeratosis overlying a normal or slightly thickened granular layer. While the epidermis is slightly thickened but the proliferation is normal. In the stratum corneum, desmosomes are retained and there are an increased number of melanosomes.

Diagnosis is based on clinical findings, loss of STS activity or deletion of the STS gene from Xp22.32. Loss of STS activity can be detected by measuring the level of CSO_4 from scale or from serum by performing serum lipoprotein electrophoresis. Loss of Xp22.32 can be detected in carriers by fluoresence in situ hybridization (FISH) or by PCR in males.

In addition to changes in the epidermis, the loss of STS activity has several extradermal effects. Loss of STS activity impairs DHEAS deconjugation, leading to decreased estrogen production in the placenta. This results in a failure of labor induction that is relatively oxytocin insensitive, and there is a failure of cervical dilation. These pregnancies usually require Cesarean section delivery. An affected pregnancy can be detected through decreased estrogen as well as increased non-hydrolyzed sulfated sterols in the urine of the mother. XLI patients are also at a 20-fold increased risk of cryptorchidism. Regardless of testicular descent, these patients are also at increased risk of testicular cancer and hypogonadism. Finally, affected males and female carriers can have

asymptomatic corneal opacities. One study of Italian XLI patients found 26.6% of affected males had these opacities.

Treatment for XLI is conservative with topical emolients, keratolytics and retinoids. In these patients vitamin D analogues are irritating. As the symptoms of XLI are usually mild, systemic retinoids are rarely needed.

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Case #6

CHICAGO DERMATOLOGICAL SOCIETY
RUSH UNIVERSITY MEDICAL CENTER
CHICAGO, ILLINOIS
MAY 17, 2006

CASE PRESENTED BY: Anthony Peterson, MD

CASE: ***"UNKNOWN"***

Case #7

CHICAGO DERMATOLOGICAL SOCIETY
RUSH UNIVERSITY MEDICAL CENTER
CHICAGO, ILLINOIS
MAY 17, 2006

CASE PRESENTED BY: James Swan, MD, Toral Patel, MD

History: This 74-year-old Caucasian male presented in August 2005 with a two month history of diffuse, nonpruritic skin redness and scaling. The symptoms began on the patient's scalp and then spread caudally. He had been treated with topical steroids only prior to his initial visit. The patient suspected that the rash may have been related to pesticide exposure two weeks prior to the onset.

Past Medical History: Recently treated with azithromycin for sinusitis.

Medications: None

Allergies: None

Family History: Non-contributory

Social History: Social alcohol use.
No tobacco use.
Denies illicit drug use.

Review of Systems: Positive for chills, rhinorrhea. The patient denied any nausea, vomiting, fever, night sweats, weight loss, diarrhea, adenopathy, arthralgias or myalgias.

Physical Examination: The patient is an older well-developed white male who is visibly shivering and appears uncomfortable.
There are large nearly confluent orange-red erythematous scaly plaques on the scalp, face, back, chest, abdomen and all four extremities, with islands of sparing.
There are numerous scattered brown stuck-on one to two centimeter plaques on the chest and abdomen.
The palms and soles have a waxy keratoderma with orange-red erythema.
There is yellowing and dystrophy of all 20 nails.
There is 2+ pitting lower extremity edema.

Laboratory Data: The following were within normal limits:
Complete blood count, complete metabolic panel, lipid profile

Histo-pathology:

8/05	Left upper arm & left lateral back: Subacute spongiotic dermatitis
10/05	Right upper back: Spongiotic dermatitis with eosinophils and dermal acute and chronic inflammation
10/05	Right lower back: Subacute spongiotic dermatitis, excoriated
2/06	Forearm: Psoriasiform dermatitis with few eosinophils
2/06:	Knee: Psoriasiform dermatitis consistent with psoriasis
3/06	Left upper flank: Psoriasiform and spongiotic dermatitis with eosinophils; immunofluorescence negative
4/06	Left thigh: pending

Diagnosis: **Erythrodermic psoriasis with secondary allergic contact dermatitis to topical agents. Sign of Leser-Trelat in erythroderma.**

Course and Treatment: The patient was initially diagnosed with erythroderma, likely secondary to psoriasis; salmon colored erythema with islands of sparing and palmoplantar waxy keratoderma were present. Follicular lesions, however, were not present. He was started on acitretin 25mg daily, as well as topical steroids under occlusion. The patient was on acitretin only briefly as it was discontinued due to peeling of the hands. He was then started on cyclosporine 200mg twice daily, with no response after one month.

The patient subsequently developed features very suggestive of pityriasis rubra pilaris. Acitretin was then restarted at the same dose of 25mg daily, which resulted in initial mild improvement but subsequent worsening of his erythema and scaling as well as worsening symptoms. The acitretin dose was tapered to 25mg every other day, and narrow band UVB (NB-UVB) treatments three times weekly were added. No improvement was seen with this regimen. Acitretin and NB-UVB were both discontinued at this point and the patient was started on etanercept, 50mg twice weekly. The patient showed no improvement on etanercept alone, so methotrexate was added. While still on low dose methotrexate, the patient complained of worsening severity of symptoms and was given a two week prednisone taper. This produced fairly striking improvement, with a reduction of erythema and scaling. However, subsequently, the patient's erythema and scaling worsened considerably and he showed an acute eczematous dermatitis, especially on his back. He also noticed that he had a flare of dermatitis on the scalp upon using Lidex solution. He was admitted to the hospital for treatment of erythroderma and superimposed allergic contact dermatitis with wet dressings over desoximetasone ointment which resulted in a marked improvement of scaling, edema and symptoms. Etanercept was discontinued due to lack of clinical improvement and the patient's concern about long-term side effects, and the patient was continued on methotrexate alone. His dose of methotrexate was titrated to his current level of 20 mg per week with continued improvement of his condition. At the same time, his topical applications were limited to desoximetasone ointment, petrolatum and allergen restricted cleansers. He noted localized worsening of dermatitis if he used other topicals. Multiple topical therapies were tried throughout the patient's treatment

course which produced little improvement, including triamcinolone 0.1% ointment, Aquaphor, Eucerin and Atopiclair.

At his most recent clinic visit, the patient's erythema and scaling were noted to have improved considerably on his current regimen of methotrexate 20mg weekly. A new dermatitis was noted on his upper thighs, consisting of dense clusters of follicular papules consistent with pityriasis rubra pilaris or follicular psoriasis. Pathology is pending.

Discussion: Erythroderma, or exfoliative dermatitis is defined clinically by the presence of erythema and scaling involving more than 90% of the skin surface. It may be the clinical presentation of a number of systemic and cutaneous diseases. Establishing the underlying diagnosis can be difficult; 9%-47% of cases of erythroderma are classified as idiopathic.

Erythroderma is more common in males; the average age of onset is 41-61 years. It is frequently due to the exacerbation of a preexisting dermatosis. The most common underlying diagnoses are psoriasis, spongiotic dermatitis, drug eruptions and cutaneous T cell lymphoma. Commonly implicated medications are allopurinol, sulfa drugs, anticonvulsants, isoniazid, cisplatin, dapsone and minocycline. Other diseases that may present with erythroderma are pityriasis rubra pilaris, immunobullous disorders such as pemphigus vulgaris and bullous pemphigoid, dermatomyositis, chronic actinic dermatitis, sarcoidosis and crusted scabies. Sezary syndrome is defined as erythroderma, lymphadenopathy, hepatosplenomegaly and circulating Sezary cells.

Erythrodermic psoriasis is generally preceded by typical psoriatic plaques. Its onset is most often due to the withdrawal of topical or systemic steroids or methotrexate. Other potential triggers include topical irritants, phototherapy, burns, infections, pregnancy, and systemic illness.

Pityriasis rubra pilaris often begins as a seborrheic dermatitis-like eruption on the scalp, with erythema and fine scaling. It quickly evolves to develop follicular papules on an erythematous base, which coalesce to form salmon-colored plaques with small, discrete islands of sparing. Perifollicular keratotic papules are seen on the knees, elbows and dorsal hands. The palms and soles frequently show an orange-red waxy keratoderma. Erythroderma in atopic dermatitis is most often seen in patients with moderate to severe disease. Lichenification and skin atrophy may be seen.

Other clinical findings associated with erythroderma include palmoplantar keratoderma, lymphadenopathy, lower extremity pitting edema, nail dystrophy, ectropion, conjunctivitis, alopecia and hepatosplenomegaly. Pruritus is a common complaint in erythroderma; in particular, the pruritus in Sezary syndrome is typically severe. Constitutional symptoms include malaise, chills and fatigue. There have been case reports of transient, eruptive seborrheic keratoses (the sign of Leser-Trelat) in erythrodermic patients.

Treatment of erythroderma is tailored towards both identification and control of the underlying disease, as well as management of acute complications. The

erythrodermic patient is at high risk for secondary infections, cardiovascular compromise, fluid imbalance, and thermoregulatory disturbance. All of these issues should be promptly addressed, in an inpatient setting if necessary.

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Case # 8

CHICAGO DERMATOLOGICAL SOCIETY
RUSH UNIVERSITY MEDICAL CENTER
CHICAGO, ILLINOIS
MAY 17, 2006

CASE PRESENTED BY: David Eilers, MD, Anthony Peterson, MD

History: This 56-year-old male Vietnam veteran with a history of renal transplantation on cyclosporine, presented to our clinic with multiple enlarging asymptomatic papules on his face as well as numerous, soft, subcutaneous masses on his trunk and extremities. Upon questioning, he denied a history of teenage acne or known exposure to Agent Orange, however noted the onset of a few scattered inflammatory cysts during his tour of duty in Vietnam, which continued after his discharge from the military. After his renal transplant in 1996 however, his condition rapidly worsened, with the development of multiple new subcutaneous nodules that often become inflamed and express foul smelling material. Over the course of his disease process, he has received multiple courses of antibiotics as well as undergone elective excision of several of his subcutaneous masses.

Past Medical History:
Hypertension
Hyperparathyroidism and parathyroidectomy
Renal Transplant 1996
Anemia
Squamous Cell Carcinoma of the Skin 2004
Hepatitis C
L4-L5 Fusion

Medications:
Prednisone 3mg PO daily
Cyclosporine 100mg PO twice daily
Mycophenolate Mofetil 1000mg PO twice daily
Diltiazem 300mg PO daily
Labetalol 200mg PO twice daily
Calcitriol 0.25mg PO daily
Ferrous Sulfate 324mg PO three times daily

Allergies: None

Family History: No history of colon cancer, cutaneous cysts or significant acne

Social History: Current tobacco use, greater than 50 pack-year history
Remote history of alcohol use
No illicits
Vietnam Veteran, former iron worker, now retired

Review of Systems: Positive for malaise, fatigue and low back pain

Physical Examination: The patient exhibited numerous, 2 to 7mm yellowish, dome-shaped, asymptomatic umbilicated papules on the forehead, cheeks and nose. Additionally, multiple, non-tender 1.0 to 12cm polypoid, soft mobile, subcutaneous nodules and masses were located on the trunk, extremities and genitalia. Most were discrete, however several larger masses were confluent, most notably on the lower back, flanks and buttocks. The majority of the lesions were free of inflammation and non-tender, all were freely mobile. The skin overlying the trunk was scattered with occasional keratotic plugs and superficial, non-inflamed sinus tracts.

Laboratory Data:

Abnormal or Positive:
HCV (+)
Creatinine – 3.6 (0.8 – 1.3)
AST – 5 (10 – 37)
ALT – 26 (10 – 65)
Hemoglobin – 11 (13 – 17)
MCV – 77 (83 – 99)

Normal or Negative:
WBC
RPR
Bilirubin
Alk Phos
INR / PT
B12 / Folate
TSH
Calcium

Studies: Colonoscopy (2005): Normal

Magnetic resonance imaging (2006): multiple fluid collections in the subcutaneous tissue of the lower back bilaterally, the largest measuring 8.4cm by 6.6cm.

Histo-pathology: Simple excision of a subcutaneous nodule on the left upper extremity shows a cystic cavity filled with laminated keratin and keratin fragments, lined by a stratified squamous epithelium, including a granular layer.

Diagnosis: **Multiple Epidermoid Cysts**

Course and Treatment: A negative family history, normal colonoscopy, and absence of jaw osteomas, make the diagnosis of Gardner's syndrome less likely. Unfortunately, the patient is continuing to progress with present cysts increasing in size and new cysts continuing to form. Consultation with the patient's transplant physician regarding substitution of cyclosporine for sirolimus (Rapamune) is currently underway. Additionally, the patient is undergoing serial local excisions of his most symptomatic cysts.

Discussion: Epidermoid cysts, also known as epidermal inclusion cysts or infundibular cysts, are the most common cutaneous cyst and generally occur in young or middle-aged adults. Although usually localized on the upper trunk and face, they can occur anywhere on the body. Histologically, they are differentiated from other types of cutaneous cyst by laminated keratin contents, presence of a granular layer and absence of pilosebaceous structures or keratinocyte atypia. The exact pathogenesis is unknown, however damage to the pilosebaceous unit is thought to be the underlying mechanism. Once formed, trauma or acute inflammation from bacteria often can result in cyst wall rupture and foreign body reaction, due to spillage of keratin into the surrounding dermis. Treatment includes simple excision or incision and drainage.

Multiple, large epidermoid cysts are sometimes seen as a complication of cyclosporine therapy in transplant recipients. The association is considered to be dose and duration dependent. Additionally, multiple cysts may also suggest the possibility of Gardner's syndrome. A retrospective study, of 67 cyclosporine-treated renal transplant recipients, noted epidermoid cysts in roughly 28% of its patients. However, in a separate retrospective study of 200 patients not receiving cyclosporine, the prevelence was zero. It is thought that cyclosporine induces increased keratinization, resulting in the occlusion of hair follicles and subsequent development of cysts. Several case reports in Japan have shown an association with HPV 60 infection and epidermoid cysts developing on the palms and soles. This has prompted more recent retrospective studies of non-palmoplantar epidermoid cysts, looking for HPV 60 antigen within the cyst wall. In one study of 59 non-palmoplantar cysts, 14% were found to be positive for HPV 60 by PCR. This evidence suggests that perhaps human papillomavirus may play a role in pathogenesis of some epidermoid cysts.

Sebaceous gland hyperplasia is a documented, well-known complication of cyclosporine-treated, male transplant recipients, with an estimated prevelence of 10 – 16%. The pathogenesis is thought to be the result of a direct and casual effect of cyclosporine on the sebaceous gland, although the exact mechanism is unknown. Histological evaluation of cyclosporine-induced sebaceous gland hyperplasia, shows hyperplasia of undifferentiated sebocytes and inhibition of differentiation, leading to multi-layered basal cells and only a few islands of differentiated sebocytes. Whereas in senile sebaceous gland hyperplasia, a

reduced cell turnover occurs, leading to low numbers of differentiated, lipid-producing cells. Other factors must also be present for cyclosporine-induced sebaceous hyperplasia to develop, as the condition does not occur in transplanted children receiving cyclosporine. This suggests a potential role of hormonal influence on the sebaceous gland in developing hyperplasia.

Although this patient states a history of epidermoid cysts prior to cyclosporine administration, perhaps a mechanism of action similar to cyclosporine's effect on the sebaceous gland is responsible for the progression and development of multiple epidermal cysts. However, since this patient is a Vietnam veteran, potential exposure to dioxin is an unfortunate confounding variable. Exposure to dioxin has been shown to cause chloracne in humans, and in murine models to induce keratinocyte differentiation in vivo and vitro. It is unknown how much, if any of this patient's current condition, is due to dioxin exposure.

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Case #9

CHICAGO DERMATOLOGICAL SOCIETY
RUSH UNIVERSITY MEDICAL CENTER
CHICAGO, ILLINOIS
MAY 17, 2006

CASE PRESENTED BY: Michael Tharp MD, Ashley Smith MD

History: Patient is a 15-year-old Caucasian male adolescent with recalcitrant urticaria since April 2005. He developed daily urticarial outbreaks, predominantly affecting his hands, feet and distal legs. A skin biopsy was performed which demonstrated a superficial perivascular dermatitis with mild papillary edema, consistent with urticaria. Eventually his entire body became involved and his pruritus escalated. He was unresponsive to combined H1 blockers (Allegra 360 mg daily and Zyrtec 10 mg TID). Prednisone was introduced due to break throughs on combined antihistamines, colchicine and dapsone. He suffered from occasional fevers, headaches, photophobia, sore throats, earaches, and stomach aches. His appetite was poor and he had severe fatigue; subsequently he became unable to attend school. These mononucleosis-like symptoms were evaluated with a monospot test which was negative. The patient was subsequently felt to have a possible dapsone hypersensitivity reaction. Further evaluation ultimately demonstrated common variable immunodeficiency syndrome (CVID).

Past Medical History: Seizure at age two, Ocular Migraine

Medications: Colchicine 0.6 mg PO BID (11 days), Dapsone 50mg PO QD (7 days) Prednisone 20-40mg PO QD (3 weeks), Allegra 180 mg PO BID, Zyrtec 10 mg PO TID, Singulair 10mg PO QD

Allergies: Ceclor, Dilantin

Physical Examination: Healthy appearing white male with red, urticarial plaques over arms, chest, and legs. Total body surface area affected: 18%

Laboratory Data:

Normal	***Abnormal***
BMP, LFT, Hgb, Hct, platelets, TSH, T4, ANA, G6PD, Monospot, EBV IgM and IgG, C3, C4, RF, CRP, ESR	WBC: 12 (normal 4.2-11.0), neutrophils 79% (normal 33-63%), lymphocytes 16% (normal 27-47%)
Anti-microsomal Ab, Anti-thyroglobulin	Measles IgM and IgG antibody negative
IgE 2 (normal 0-125 IU/ml)	**IgG** 255 (normal 596-1584 mg/dl), **IgA** 38 (normal 71-350 mg/dl), **IgM** 32 (normal 35-213 mg/dl)
CSF: glucose 58 (normal 45-70) CSF cultures (viral, bacterial, fungal)	CSF: WBC 55 (normal 1-10), protein 56 (normal 15-45 mg/dl)

While on Dapsone: total bilirubin 3.1 (normal 0.1-2.0 mg/dl), reticulocyte count 5.6% (normal 0.5-2.5)

Studies: MRI brain: Normal

Histo-pathology: Punch biopsy, right thigh: Superficial perivascular dermatitis and mild papillary dermal edema; the infiltrate consists of occasional neutrophils, lymphocytes and many eosinophils (consistent with urticaria).

Diagnosis: **Chronic Urticaria as presentation of Common Variable Immunodeficiency**

Course and Treatment: The pediatric immunologist started monthly IVIG treatments in January of 2006. He remains on monthly IVIG treatments, with nearly complete clearing of his urticaria.

Discussion: Chronic idiopathic urticaria (CIU) is the designation assigned to 80-90% of patients with persistent urticaria and is defined has having nearly daily hives for greater than 6 weeks. This diagnosis is made when no specific physical, history or laboratory abnormalities can be identified as the cause of urticaria. CIU can be subdivided into autoimmune or unknown cases. Approximately 30-40% of CIU patients have evidence of autoantibodies to thyroid tissue or have other autoimmune diseases (e.g. diabetes mellitus, rheumatoid arthritis).

Our patient has CIU and common variable immunodeficiency (CVID). His diagnosis of CVID was established during his evaluation of chronic disabling urticaria, fatigue and mononucleosis-like symptoms. The first cases of CIU with CVID (outside of the context of HIV), were described by Altscheul and Cunningham-Rundles[1] in 2002. In their review of 256 patients with CVID, they presented six patients who also had CIU. Each of these six patients was diagnosed with CVID after an initial presentation with CIU. All patients had substantially reduced levels of IgG and IgA; four also had reduced IgM (a characteristic of CVID). All of the patients who were known to have received IVIG treatment (four of six patients) had complete resolution of CIU. The average patient age was 33 years (range 20-51 years), and males and females were equally represented. Only two of the six patients had a history of recurrent infections, making clinical suspicion even more difficult. Given the response to IVIG, it is likely the urticaria is related CVID.

CVID or hypogammaglobulinemia is a heterogeneous primary immunodeficiency disease in which B cells produce little or no antibody. It is the most prevalent of the primary immunodeficiencies, and is characterized by low IgG and IgA, and sometimes IgM. About half of the patients have T cell dysfunction and recurrent bacterial illnesses are common. Due to its protean manifestations, diagnosis is often delayed until the second or third decade, often with resultant irreversible organ damage (namely, bronchiectasis). There is some evidence for genetic susceptibility, with 20% of patients having a dominantly inherited disorder with variable expression. The majority of patients present with recurrent sinopulmonary infections, however it is a multisystem disorder and thus dermatologists must be aware of it. Within the dermatology literature, cases of furunculosis[4], alopecia universalis[6] and pityriasis lichenoides[7] have been described in relationship to CVID.

It has been proposed that CIU, in the setting of CVID, might be a symptom of infection-induced complement activation resulting from inadequate humoral immunity. Alternatively, patients with CVID are prone to the development of autoimmune conditions and it is possible that a subset of these patients might have IgG autoantibodies to the alpha-chain of the high-affinity IgE receptor. Such antibodies could directly cross-link adjacent receptors, triggering basophil or mast cell activation, and thus urticaria.

IVIG is a complex therapeutic which not only restores antibody function, yet also has an anti-inflammatory potential which might control autoantibody-mediated inflammation. Due to its immunomodulatory role, recent studies have evaluated the use of IVIG for patients with severe unremitting CIU. The first study reported 10 patients with CIU treated with IVIG 0.4 g/kg per day for 5 days.[8] Clinical benefit was reported in 90% of the patients. A subsequent report of 3 similar patients did not support the previously reported favorable outcome.[9] The author suggested that most of the effect of IVIG on CIU was associated with an anti-idiotype effect rather than other immunomodulatory activities.

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Case #10

CHICAGO DERMATOLOGICAL SOCIETY
RUSH UNIVERSITY MEDICAL CENTER
CHICAGO, ILLINOIS
MAY 17, 2006

CASE PRESENTED BY: Marianne O'Donoghue, MD, Melanie Palm, MD

History: A 39-year-old Caucasian man with a history of systemic lupus erythematosus and hypercoaguable state presented with a progressive eruption over the face, neck, upper chest, and back. Flesh-to yellow-colored papules first appeared over the central forehead, then spread caudally to involve the cheeks, lower face, lateral neck, post-auricular area, and central chest. This distribution was identical to the pattern of skin injury incurred by an episode of Stevens-Johnson syndrome in 1996. The lesions were non-pruritic and non-painful, but enlarged over time. Minor trauma led to occasional bleeding and surrounding erythema of individual lesions.

Past Medical History:
Systemic Lupus Erythematosus, diagnosed in 1996
Hypercoaguable State
Deep Vein Thrombosis
Grand Mal seizures secondary to lupus cerebritis
Stevens-Johnson Syndrome secondary to Phenobarbital, phenytoin, or antibiotic

Medications:
Valproic acid 750 mg po Qam, 1125mg po Qhs
Gabapentin 900mg po Qam, 1500mg po Qhs
Azathioprine 100mg po BID
Prednisone 10 mg po Qhs
Warfarin 4mg po Qhs

Allergies:
Penicillin (rash)
Phenytoin (hypersensitivity reaction)

Social History: Works as salesman, lives with wife
Non-smoker, occasional alcohol consumption, no illicit drug use

Physical Examination: Diffuse yellow papules, 1-5mm in diameter, some with a central dell distributed most densely over face and neck, with additional lesions over shoulders, chest and upper back. No surrounding erythema. Lesions non-painful to palpation.

Laboratory Data:

Lupus serology:			Normal or negative lab values:
C3	84 mg/dL	[64-166]	Complete blood count
C4	11 mg/dL	[15-45]	Comprehensive metabolic panel
ANA	<1:20	[<1:160]	Urinalysis
anti-DNA Ab	<10 IU/ml	[<50]	Dihydrotestosterone
C-reactive protein	<0.5 mg/dL	[0-0.9]	
Cardiolipin IgG Ab	>120GPL-U/ml	[<12]	
β-2 glycoprotein I IgG Ab	132 U/mL	[<14.5]	

Histo-pathology: Punch biopsy, left chest (7/29/05):
clusters of hypertrophic sebaceous glands within the dermis

Diagnosis: **Diffuse sebaceous hyperplasia**

Course and Treatment: The patient was started on finasteride, 1 mg po QD in September 2005. This was at the suggestion of Dr. Warren Piette during Grand Rounds discussion. The patient completed a 60-day trial and noted reduction in size and height of sebaceous hyperplasia. Per patient history, appearance of new lesions ceased. In November 2005, the patient developed right lower extremity ulcers during a lupus flare and discontinued finasteride. The patient was placed on Prednisone, tapering from 30mg to 10mg po QD from September 2005 to March 2006. While on the steroid taper and off finasteride, the diffuse sebaceous hyperplasia returned with new and enlarging lesions over the forehead, cheeks, and chest.

Discussion: Sebaceous hyperplasia is a common, benign enlargement and proliferation of sebaceous lobules, and glands, respectively. Sebaceous glands develop between the 13th and 16th week of fetal life from the most superficial bulge of the follicular unit. Sebaceous glands are found on all hair-bearing areas of the skin, but the greatest density of sebaceous glands is located on the face and scalp. Diagnosis is usually evident clinically, but biopsy is performed to rule out basal cell carcinoma.

Sebaceous gland hyperplasia is more common among the elderly, individuals with significant ultraviolet radiation exposure, hemodialysis patients, and organ transplant recipients. Approximately 10-16% of immunosuppressed organ transplant recipients develop sebaceous hyperplasia. Furthermore, a subgroup of renal transplant recipients on long-term cyclosporin A in combination with steroids are particularly prone to developing glandular hyperplasia. It is unclear whether the appearance of sebaceous gland hyperplasia is dose-dependent, but sebaceous hyperplasia has not occurred in cyclosporin A patients completing less than four years of immunosuppressive therapy. Premature or diffuse sebaceous gland hyperplasia has also been reported in familial and sporadic cases.

Sebaceous hyperplasia is most often treated for cosmesis. Treatment options for sebaceous hyperplasia include cryotherapy, cauterization, electrodessication, bi- or trichloracetic acid, isotretinoin, laser (pulse dye laser, 1450nm diode laser, argon laser, CO2 laser), or excision. As increased sebaceous gland activity is

linked to acne and seborrheic dermatitis, treatment modalities for the latter including anti-androgens and isotretinoin have been intensely investigated. Dihydrotestosterone (DHT) is an important androgen stimulant for sebocytes and thus, acne. DHT is converted from testosterone by the enzyme 5-alpha reductase, which exists as two isozymes. Isozyme 1 is found predominately within sebaceous glands, where as isozyme 2 localizes to the prostate, terminal hair follicle, the sebaceous duct, and weakly to the sebaceous gland basal layer. 5-alpha reductase inhibitor (e.g. finasteride) exerts an anti-androgen effect by inhibiting isozyme type 2 and is used in the treatment of benign prostatic hypertrophy. However, finasteride may play an additional role in the skin by inhibiting sebaceous duct and possibly sebaceous gland activity. Disappointingly, no decrease in sebum production of men treated with finasteride 5mg po QD was demonstrated in one study. On the other hand, type 1 5-alpha reductase inhibitors may represent a future class of agents for use in acne and sebocytic-related disorders.

Diffuse sebaceous gland hyperplasia has not been reported as a long-term complication of Stevens-Johnson Syndrome (SJS). Reported long-term sequelae of SJS can result in significant morbidity to mucocutaneous tissues. Resultant sequelae of SJS include ocular complications (canalicular and nasolacrimal duct obstruction, corneal scarring, keratoconjunctivitis sicca syndrome, dacryocystocele formation, en-and ectropion, and trichiasis), esophageal and vaginal strictures, bronchiolitis obliterans, and skin pigmentary changes.

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Case # 11

CHICAGO DERMATOLOGICAL SOCIETY
RUSH UNIVERSITY MEDICAL CENTER
CHICAGO, ILLINOIS
MAY 17, 2006

CASE PRESENTED BY: Lady Dy MD, Arthur Rhodes MD, Ashley Smith MD

History: Patient is a 65-year-old white man with a three year history of "eruptive" vascular lesions, distributed initially over his chest, then his face, neck and arms. He continues to develop new lesions. The lesions are occasional pruritic but otherwise without symptoms. Subcutaneous "nodules" have recently appeared on his arms. He denies epistaxis, hematuria, or hematochezia.

Past Medical History: Hypertension, Gastroesophageal reflux, Angina pectoris, Hypothyroidism, Hernia, Hemorrhoids

Medications: Diovan, Hyoscyamine, Ranitidine

Allergies: Statins

Family History: Non-contributory

Review of Systems: Appetite, energy, and weight are stable. No fevers, chills, night sweats, headaches, epistaxis, cough, hemoptysis, nausea, diarrhea, hematuria, or hematochezia. There are no neurological signs or symptoms.

Physical Examination: On his face, chest, back and arms are dozens of scattered blue papules ranging in size from 1mm to 8mm in diameter. There are at least 6 soft subcutaneous masses on his forearms, ranging in size from 1-3 cm in diameter.

Laboratory Data: Normal: basic metabolic panel, protein, albumin, bilirubin, cholesterol, free T4, Hepatitis A Ab IgM, Hepatitis B surface Ag, Hepatitis B Core Ab, Hepatitis C, SPEP

Abnormal: AST 46 (normal 10-42), ALT 77 (normal 10-40), Hgb A1c 6.8 (normal 4.6-6.2), TSH 5.62 (normal 0.34-5.6)

Studies: Chest X-Ray: The heart size is at the upper limits of normal. The lungs are clear. The pulmonary vasculature is normal. There are degenerative changes of the thoracic spine.
Esophogastroduodenoscopy: normal
Colonoscopy: no vascular abnormalities; few benign appearing polyps

Histo-pathology: 10/2005 left neck (Beth Ruben, UCSF): "Hemangioma, with some features of sinusoidal hemangioma"

11/2005 left shoulder: Consistent with cavernous hemangioma. The epidermis is unremarkable with the dermis showing multiple blood vessel proliferations that are lined with thin endothelial cells. There is a solitary dilated blood vessel found in the deeper dermis. Dr. Daniel Santa Cruz interpreted these histologic findings as cavernous hemangioma. Dr. Omar Sangueza interpreted histologic results as venous lake.

12/2005 left forearm: Mildly increased dermal vascular proliferation, confirmed by anti-CD31 and anti-CD34 antibody immunohistochemical protein marker stains. Dr. Daniel Santa Cruz interpreted these histologic findings as cavernous hemangioma.

4/2006 left forearm x 2: Cavernous hemangioma. Fairly well-circumscribed subcutaneous nodule composed of well formed dilated vascular spaces filled with blood. The vascular spaces are separated by thin fibrous septae and are lined by flattened endothelial cells with no significant pleomorphism. Connections between the vascular channels or pseudopapillae characteristic of the sinusoidal variant of cavernous hemangioma are not prominent.

Diagnosis: **Eruptive "Cavernous Hemangiomas"**

Course and Treatment: No treatment to date.

Discussion: Our patient's histopathological specimens were consistent with "cavernous hemangiomas". Indeed, the term "cavernous hemangioma" is a misnomer, since the lesion is a vascular (venous) malformation and not a vascular tumor. By definition, venous malformations are hemodynamically inactive, slow-flowing structural anomalies of the veins that are present at birth and slowly worsen throughout the patient's lifetime. Malformations differ from hemangiomas on the basis of their normal endothelial cell turnover and lack of excessive endothelial proliferation. Studies have identified markers of proliferation, such as proliferating cell nuclear antigen, type IV collagenase, vascular endothelial growth factor (VEGF) and basic fibroblast growth factor (bFGF) which characterize hemangiomas, but not vascular malformations.[5] In venous malformations, some of the apparently localized and superficial venous lesions tend to coexist with venous ectasias and deep vein anomalies.

Cutaneous venous malformations may be a component of several complex syndromes, including blue rubber bleb nevus syndrome, Maffucci's syndrome,

Klippel-Trenaunay syndrome, Gorham's syndrome, Bannayan-Riley-Ruvalcaba syndrome, and other rare miscellaneous syndromes.[1]

To our knowledge, there are no reports of eruptive cavernous venous malformations in the literature. Eruptive vascular lesions have been reported in POEMS (polyneuropathy, organomegaly, endocrinopathy, M protein, and skin changes) syndrome. In POEMS syndrome, the specific histopathologic finding is a glomeruloid hemangioma. However, tumors have been variously described as showing features of cherry angioma, capillary hemangioma, cavernous hemangioma, lobular hemangioma and targetoid hemangioma.[2] Our patient did not manifest polyneuropathy, organomegaly or have an M protein spike in his serum protein electrophoresis. He was found to have hypothyroidism. Our patient appears to have isolated cutaneous involvement with eruptive venous malformations.

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Case #12

CHICAGO DERMATOLOGICAL SOCIETY
RUSH UNIVERSITY MEDICAL CENTER
CHICAGO, ILLINOIS
MAY 17, 2006

CASE PRESENTED BY: Michael Tharp, MD, Sarah Kasprowicz, MD

History: Patient is a 42-year-old white female who presented with a one year history of pruritic, erythematous, hypertrophic plaques with adherent scare on the bilateral dorsal forearms and face. The plaques had developed slowly over the course of the previous six months and had been treated by an outside physician with Aldara for what was thought to be "skin cancer." A biopsy was not performed at that time of presentation to our clinic due to the patient's financial restrictions. She had presented to the outside physician a year previous to us with an acute red, pruritic eruption on bilateral arms and malar erythema immediately following an acute episode of sun exposure.

Past Medical History: Non-contributory and no other medications

Social History: 1.5 ppd smoker, no ETOH

Family History: Non-contributory

Physical Exam: Erythematous, hypertrophic, indurated plaques with serpiginous borders and diffuse adherent white scale on bilateral dorsal forearms and face. Her scalp, chest and upper back were normal.

Laboratory Results: ANA titer: >= 1:1280 (speckled)

Histo-pathology: Left forearm (2/7/06)-Hypertrophic Lupus Erythematosus: A Periodic Acid-Schiff stain reveals thickened basement membrane at focal area. Although the epidermis reveals areas of hypergranulosis, the collagen within the dermis is widely spaced apart. Colloidal iron stain confirms the presence of dermal mucin.
Right forearm (2/7/06)-Hypertrophic Lupus Erythematosus: A Periodic Acid-Schiff stain reveals slightly thickened basement membrane. A colloidal iron stain reveals increased dermal mucin deposit. These histologic findings are consistent with lupus erythematosus.

Diagnosis: **Hypertrophic Lupus Erythematosus**

Treatment and Course: Patient was treated with Plaquenil (400 mg once a day) for 6 weeks, Clobetasol ointment to affected areas of skin was used and diligent use of sunscreen and sun protection was advised. Lesions were completely cleared after 6 weeks of treatment.

Discussion: Hypertrophic lupus erythematosus (HLE) is rare subset of discoid lupus erythematosus, also known as verrucous lupus erythematosus or keratotic lupus erythematosus. HLE is seen in 2% of chronic lupus erythematosus cases. HLE manifests as dull, red, indurated verrucous-topped lesions that occur on the face, scalp, upper extremities and occasionally the back. HLE may occur with pre-existing or co-existing DLE and SLE lesions.

Diagnostic criteria for HLE include the following: a) dull red, indurated lesions covered by multi-layered scales; b) frequent association with typical discoid lupus erythematosus lesions; and c) characteristic histologic alterations (marked acanthosis, hyperkeratosis and hypergranulosis).

Hypertrophic lupus erythematosus histopathologically shows marked acanthosis, hyperkeratosis and hypergranulosis with a pronounced mononuclear infiltrate. HLE may also show pseudocarcinomatous hyperplasia and the diagnosis of squamous cell carcinoma must be considered. Immunopathologically, HLE is similar to DLE where you see IgG and IgM deposition in the dermal-epidermal junction. It is unlikely that HLE patients will have positive serological markers.

Hypertrophic lupus erythematosus is typically less responsive to conventional treatments. Cyrotherapy, Isotretinoin, Acitretin, intralesional tramcinolone and systemic antimalarials have all been utilized. Systemic isotretinoin (1mg/kg/day for 11 wks) has been shown to effectively clear lesions.

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Case #13

CHICAGO DERMATOLOGICAL SOCIETY
RUSH UNIVERSITY MEDICAL CENTER
CHICAGO, ILLINOIS
MAY 17, 2006

CASE PRESENTED BY: James Swan MD, Brian Bonish MD/PhD

History: The patient is a 76-year-old man who presented to clinic one year ago with a four year history of pain and scaling of the fingertips and dystrophic nails of his left hand. He had been treated with various topical steroids and methotrexate in the past and was using calcipotriene twice a day at presentation.

Past Medical History: Benign prostatic hypertrophy

Medications: Hytrin

Family History: None pertinent

Social History: Non-smoker, occasional alcohol

Physical Examination: Left hand 2nd, 4^{th} and 5^{th} distal digits with erythema, scaling, pustules, dystrophic nails and pitting of other nails

Laboratory Data: CBC, CMP and Lipids within normal limits
except glucose 117 mg/dl (nl <100) and LDL 132 mg/dl (nl<100)

Histo-pathology: Fifth digit of left hand 3mm punch biopsy: Psoriasiform dermatitis consistent with psoriasis. Sections from the fifth digit show skin with hyperkeratosis, parakeratosis with many neutrophils, epidermal hyperplasia, and uniform club-shaped elongation of the rete ridges. The dermis shows a perivascluar lymphocytic infiltrate. PAS-D and gram stains do not stain for micro-organisms.

Diagnosis: **Acrodermatitis Continua of Hallopeau**

Course and Treatment: The patient was started on acitretin 25mg po daily and desoximetasone ointment with minimal response. Hand PUVA soaks three times a week were added again with minimal improvement. Acitretin was discontinued and etanercept 50mg biweekly begun with continued desoximetasone ointment. Within one month the patient noticed improvement and has had continued to improve with etanercept.

Discussion: Acrodermatitis continua of Hallopeau is a considered to be a rare subtype of psoriasis. It is often resistant to treatment and has a high level of morbidity. Clinically, one or more nails of the hand are involved or rarely of the toes. Involvement of other sites is rare, although there are case reports of progression to generalized pustular psoriasis. Continued pustules of the nail lead to onychodystrophy and in more severe cases to erosion of the bone of the distal phalanx. The course is chronic and frequently relapses with cessation of therapy. In one study of the course of 46 patients, only one half responded to treatment and only two these patients achieved long term remission. None of these patients progressed to more generalized disease. Of this cohort the majority only had involvement of a single nail and only 7 had involvement of more proximal components of the nail bed. None had involvement of the palms or soles.

The histopathology of the nail bed of acute lesions of acrodermatitis of Hallopeau shows neutrophils, dilated vessels, slight epidermal hyperplasia and spongiform neutrophilic pustules. In chronic lesions there may be a mixed superficial infiltrate, dilated vessels and a psoriasaform hyperplasia. Biopsy and cultures may be needed to rule out bacterial paronychia, viral paronychia, or onychomycosis due to non-dermatophyte mold infection.

Numerous therapies have been published as case studies in the literature but there remains no consistent therapy for this disease. Treatment with topical and intralesional steroids, tacrolimus under occlusion, calcipotriene, PUVA, and systemic therapy with methotrexate, cyclosporine, retinoids have all been successful in individual patients. More recently case studies have been reported using biologics alone and in combination with retinoids to be successful. Our patient failed to respond to topical therapy, PUVA and acitretin but did finally respond well to etanercept.

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Case #14

CHICAGO DERMATOLOGICAL SOCIETY
RUSH UNIVERSITY MEDICAL CENTER
CHICAGO, ILLINOIS
MAY 17, 2006

CASE PRESENTED BY: Edward J. Keuer, MD, Toral Patel, MD

History: This six-year-old Hispanic male presents with a history of hypopigmented lesions on the trunk of unknown duration, as well as a larger palpable lesion on his left lower back. The lesions are asymptomatic. The patient was recently evaluated for a seizure disorder that initially presented six to nine months prior to his visit.

Past Medical History: Complex partial seizures, developmental delay, learning difficulties in school, status post tonsillectomy/adenoidectomy & bilateral myringotomy with tube placement.

Prenatal history: mother had gestational diabetes; patient was delivered by Cesarean section without complications.

Medications: Lamotrigine

Family History: The patient has three older siblings: two brothers and one sister. He lives at home with his mother and siblings. His parents are nonconsanguinous.

The patient has an older brother with learning disability, and maternal cousins with developmental delay.

Social History: Non-contributory.

Review of Systems: Positive for seizures.

Physical Examination: There are multiple hypopigmented macules on the trunk. There is a large, raised flesh-colored patch on the left lower back, consistent with a shagreen patch.

Laboratory Data: TSC 1 & 2 DNA analysis pending

Imaging Studies: Head CT at outside hospital: subependymal calcifications MRI of the brain & brainstem: multiple cortical, subcortical, white matter and periventricular lesions, consistent with tuberous sclerosis. A small enhancing lesion adjacent to the frontal horn of the left lateral ventricle may be a subependymal nodule, but a

small giant cell astrocytoma at this site cannot be excluded. Findings are seen also consistent with bilateral ethmoid and bilateral maxillary sinusitis.

Diagnosis: **Tuberous Sclerosis**

Course and Treatment: The patient was started on lamotrigine for control of his seizure disorder. He continues to have seizures, but they are less frequent. An eye exam was unremarkable and negative for findings of tuberous sclerosis. A renal ultrasound is pending. His family was referred for genetic counseling; studies are pending.

Discussion: Tuberous sclerosis (TS) is an autosomal dominant, multisystem disease with an incidence of approximately 1 in 10,000 births. It is characterized by seizures, mental retardation and multiple cutaneous findings. Two genes have been identified as being associated with TS. TSC 1, on chromosome 9q34, encodes a protein known as hamartin; TSC 2, on chromosome 16p13, encodes a protein known as tuberin. Many cases also arise from spontaneous mutations. It is a hamartomatous disorder, with abnormalities in cellular proliferation, migration and differentiation. The classic clinical triad is adenoma sebaceum, seizures and mental retardation; however, less than a third of patients display all of these features.

Cutaneous findings in TS include hypomelanotic macules, facial angiofibromas, ungual fibromas, and the shagreen patch. Hypomelanotic macules are seen in over 90% of TS patients and are usually present at birth. The "ash leaf" spot is characteristic of tuberous sclerosis, although these hypomelanotic macules can have varying configurations. Facial angiofibromas are found in 75% of all patients with TS. They are found primarily on the nasolabial folds, cheeks and chin and present as pink papules. Ungual fibromas (Koenen tumors) are present in 25% of affected patients; they develop later in childhood or adulthood. The shagreen patch is a connective tissue nevus found most commonly in the lumbosacral region; it appears as a skin-colored plaque with an uneven texture, giving the skin an "orange peel" appearance.

Hamartomas in the cortex of the central nervous system give rise to architectural disorder and abnormal cells, with features suggestive of incomplete neuronal differentiation. Subependymal nodules may calcify and some may grow as giant cell astrocytomas. Multiple cortical tubers can be detected by MRI in most patients.

In addition to the central nervous system and skin, many other organs may be affected in TS. Cardiac rhabdomyomas are found in over 80% of infants with TS and are present at birth; they tend to resolve over time. Renal involvement usually manifests as multiple bilateral angiomyolipomas; these lesions are usually asymptomatic unless they grow in size over 4cm. Some individuals also develop renal cysts. Renal cell carcinoma does occasionally develop in TS patients. Retinal lesions are seen in approximately 50% of individuals with TS; these hamartomas do not usually impair vision. Pulmonary and gastrointestinal involvement has also been reported in TS.

The diagnosis of tuberous sclerosis is based on diagnostic criteria consisting of major and minor features. The major features are facial angiofibromas, ungual fibromas, hypomelanotic macules (three or more), shagreen patch, multiple retinal nodular hamartomas, cortical tubers, subependymal nodules, subependymal giant cell astrocytoma, cardiac rhabdomyoma, lymphangioleiomyomatosis and renal angiomyolipoma. The minor features are dental enamel pits, hamartomatous rectal polyps, bone cysts, cerebral white matter radial migration lines, gingival fibromas, non-renal hamartoma, retinal achromic patch, confetti skin lesions, and multiple renal cysts.

A definitive diagnosis may be difficult, due to the subtle manifestations exhibited by many patients. However, the presence of either two major features, or one major plus two minor features, can help to establish the diagnosis of tuberous sclerosis with certainty.

Treatment of TS is tailored to the organ systems involved. Medication is required to control seizures. All newly diagnosed individuals should have a thorough dermatologic exam. Subsequent yearly skin examinations are recommended, as well as careful education of parents, so that new lesions can be anticipated and addressed in a timely manner. These patients should also undergo regular neuroimaging (with either CT or MRI), at baseline to look for confirmatory evidence of disease, and every few years to assess for enlarging giant cell astrocytomas. Individuals should also have a renal ultrasound and ophthalmologic exam at the time of diagnosis. Age-appropriate neurodevelopmental and psychiatric evaluation should be performed.

Parents should be referred for genetic counseling; when one parent is known to carry the TSC1 or TSC2 gene, the risk of having an affected child is 50% with each subsequent pregnancy. It may be appropriate to evaluate family members of the affected individual should with a Wood's lamp examination, to better delineate hypomelanotic macules.

A multidisciplinary approach to tuberous sclerosis, with an emphasis on patient and family support, is crucial in the management of these patients. The Tuberous Sclerosis Alliance (www.tsalliance.org) and the Tuberous Sclerosis Association (www.tuberous-sclerosis.org) are two organizations that can provide valuable assistance and information to patients and their families.

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Case #15

CHICAGO DERMATOLOGICAL SOCIETY
RUSH UNIVERSITY MEDICAL CENTER
CHICAGO, ILLINOIS
MAY 17, 2006

CASE PRESENTED BY: Michael Tharp, MD, Rachel Altman, MD

History: A 51-year-old African American female presented to the hospital in September 27, 2004 with increasing shortness of breath, drainage from her left plural catheter, and lower extremity edema with pain. She was diagnosed with right breast adenocarcinoma in 1987 and subsequently treated with a right breast lumpectomy, axillary lymph node dissection and radiation therapy. A repeat left axillary lymph node dissection in March 2002 and an MRI of her left breast revealed recurrence of her metastatic adenocarcinoma for which she underwent four cycles of chemotherapy with Adriamycin, Cytoxan, and Taxol. Metastases were subsequently noted in her lumbar vertebrae in April 2003 and thoracic cavity, left lung, left lateral/anterior chest wall in August 2003. She developed ataxia and dizziness prompting a brain MRI which revealed multiple brain metastases requiring a right frontal lobectomy (March 2004) and 10 cycles of radiation with high-dose steroids. In April 2004, cutaneous lesions developed on her right chest and back. A left malignant pleural effusion developed in June 2004 requiring placement of a pleural catheter. She developed a pulmonary embolism on September 1, 2004 and was treated with coumadin.

Past Medical History: Hypertension
Hypercholesterolemia

Family History: Maternal aunt – breast cancer

Physical Examination: An expansive, infiltrative, fungating, erythematous, edematous, firm nodular plaque was noted on her right chest, abdomen and back with focal erosions, ulcerations and active bleeding. Of note, chronic left upper extremity edema was noted as well as bilateral lower extremity pitting edema to her knees.

Histology: 3/12/02: Left axillary lymph node – metastatic carcinoma with necrosis (Estrogen/ Progesterone Receptor and Her2-neu negative, Mib-1 intermediate proliferative index 10%)

7/31/02: Left axillary lymph node – metastatic adenocarcinoma with papillary features and focal necrosis (cytokeratin AE1/AE3, 7 positive, CEA positive, cytokeratin 20/vimentin positive, thyroglobulin/TTF-1 negative, ER/PR negative)

3/29/04: Right frontal brain – metastatic carcinoma (ER/PR negative, Mib-1 unfavorable >20%, Her2-neu negative, EGFR negative)

7/15/04: Left pleural fluid – adenocarcinoma (cytokeratin 7 positive, ER/PR negative, Her2-neu negative, TTF negative, E-cadherin positive)

9/29/04: Left shoulder skin – metastatic poorly differentiated carcinoma consistent with patient's known breast primary carcinoma

Diagnosis: **Metastatic Breast Cancer**

Course and Treatment: Bilateral lower extremity duplex venous ultrasound revealed deep venous thromboses of the distal right femoral and popliteal veins in addition to thrombosis of the left common, femoral and popliteal veins. The cutaneous lesions on her right torso were biopsied and revealed metastatic poorly differentiated carcinoma consistent with her primary breast carcinoma. After therapeutic levels of Lovenox and Coumadin were achieved, she was discharged to hospice for subsequent end-of-life care.

Discussion: Breast cancer is the most commonly diagnosed cancer in women and the second leading cause of death among women in the United States. After melanoma, breast cancer is the most common cancer to metastasize to the skin. Nearly half of all observed cutaneous metastases in patients with cancer are secondary to progression of breast cancer. Most commonly, breast cancer metastases to the skin occurs via direct extension or through vascular or lymphatic channels. Cutaneous metastases of breast cancer are generally found on the chest, abdomen and scalp.

There are four presentations of breast carcinoma with cutaneous involvement including inflammatory, telangiectatic, nodular and carcinoma en cuirasse. Carcinoma en cuirasse is a sclerodermatous change of the chest wall comprised of an indurated, leathery plaque invading cutaneous lymphatics. This is either a presentation of primary untreated breast carcinoma with extensive cutaneous involvement or more commonly as a local chest wall recurrence following treatment for a known breast carcinoma. Carcinoma en cuirasse has an early stage of swelling with pitting erythema followed by an advanced stage of thickening with brawny stiffness of the skin.

Cutaneous metastatic breast cancer often presents simultaneously with distant metastases and is considered to be marker for distant metastatic disease, therefore

necessitating a full restaging to rule out other metastases before definitive treatment. Computerized tomographic scans of the chest, abdomen, pelvis, and brain as well as a bone scan, serum chemistry panel, and tumor markers should be assessed before deciding on treatment options. These lesions can be evaluated either via punch biopsy or fine needle aspiration biopsy (FNAB); however, FNAB may not provide adequate tissue to evaluate for hormone receptor (estrogen and progesterone) or Her2-neu status. Her2-neu status rarely changes from that reported at the initial diagnosis but up to twenty percent of estrogen receptor content between primary and metastatic lesions may change.

Three different treatment modalities exist for metastatic breast cancer: endocrine therapy, chemotherapy, and biologic targeted therapy. For hormone-sensitive (positive estrogen and/or progesterone receptor positivity) non-life-threatening cancer, endocrine therapy should be considered. If the patient is *post-menopausal* options include; (i) aromatase inhibitors, either non-steroidal (letrozole, anatrozole, vorozole) or steroidal (exemetane) or (ii) pure antiestrogens (fulvestrant). For *pre-menopausal* patients with hormone-sensitive (positive estrogen and/or progesterone receptor positivity) non-life-threatening disease, the available options are ovarian ablation (through surgery, radiation therapy, or leutenizing hormone releasing hormone analogues), tamoxifen, or a combination of both. For women with estrogen receptor and Her2-negative endocrine-resistant disease, chemotherapy may be the only therapeutic option. New treatment modalities include biological therapies such as the following: trastuzumab (monoclonal Ab against Her2 receptor), bevacizumab (monoclonal Ab against vascular endothelial growth factor), gefinitib or erlotinib (inhibits epidermal growth factor receptor tyrosine kinase).

On average, survival from the diagnosis of breast metastases to death is 18-30 months. The change in disease status from potentially curable to incurable necessitates the patient, friends and family to accept the prognosis and address end-of-life concerns.

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Case #16

CHICAGO DERMATOLOGICAL SOCIETY
RUSH UNIVERSITY MEDICAL CENTER
CHICAGO, ILLINOIS
MAY 17, 2006

CASE PRESENTED BY: Mark Hoffman, M.D., Michael O'Donoghue M.D.

History: 28-year-old gravida 3, para 2-0-1-2 African American woman who presented with a one day history of an eruption that began on her abdomen and progressed to her thighs and later involved the lower legs, axillae, and soles. There was associated pruritus that was minimally controlled with diphenhydramine. The patient denied any history of skin disease during or after her previous pregnancies. Three days prior to the onset of the rash, the patient had delivered a healthy male infant. The infant was of normal birth weight and did not possess any skin lesions.

Past Medical History: First trimester spontaneous abortion in 1994; full term Cesarean section secondary to failed dilation and preeclampsia in 1995

Physical Examination: Annular erythematous papules and plaques with a pink juicy rim becoming confluent over the mid-abdomen and thighs. There were some discrete lesions on the legs and flanks and a few tiny papules on the soles. There were no lesions on the back, palms or on any mucosal surfaces.

Laboratory Data: ANA, antithyroid antibodies, TSH, and free T3/T4 within normal limits

Histo-pathology: H&E Right Thigh Lesion: Spongiotic dermatitis with eosinophils
Immunofluorescence Right Thigh Perilesional: 3+ linear staining of the basement membrane zone for C3 and 2+ staining for IgG

Diagnosis: **Gestational Pemphigoid**

Course and Treatment: The patient was given hydroxyzine and betamethasone dipropionate ointment to the lesions twice a day. The lesions cleared in 2-3 months with residual hyperpigmentation without any evidence of recurrence.

Discussion: Gestational Pemphigoid is a rare autoimmune disease that has an incidence of about 1 in 50,000 deliveries. Patients present with a sudden onset of intensely pruritic, urticarial papules and plaques that are followed by the development of blisters in a few days to weeks localized to the areas of the urticarial erythema. In about 90% of cases, the eruption begins in the peri-umbilical area and spreads to involve the abdomen, thighs, palms, and soles. The disease manifests itself most

commonly during the second and third trimester although the initial onset in the immediate postpartum period occurs in approximately 20% of cases. The disease runs a variable course; but a flare at the time of delivery is a typical feature, seen in 75% of cases. About half of the cases first occur in primiparous and the other half in multiparous patients. Recurrence in subsequent pregnancies is common and in 5-8% of patients there may be an uninvolved or "skip" pregnancy following a previously affected pregnancy. Neonatal skin lesions have been found in 2-5% of cases and follow a limited and benign course. There is no increase in fetal mortality, but various studies have revealed an increased risk of prematurity and a tendency for small-for-gestational age neonates.

The most common histopathological features of gestational pemphigoid include a subepidermal vesicle, a spongiotic epidermis, papillary dermal edema, and a mild perivascular infiltrate of lymphocytes, histiocytes, and many eosinophils. Direct Immunofluorescence of perilesional skin shows linear C3 +/- IgG along the basement membrane zone. Indirect Immunofluorescence demonstrates a circulating IgG1 autoantibody directed against the noncollagenous domain (NC16A) of the 180 kDa hemidesmosome glycoprotein BP180.

Immunogenetic studies in gestational pemphigoid indicate a significant increase in HLA antigens DR3 and DR4 and nearly 50% of cases have simultaneous presence of both. The presence of the HLA-DR3 antigen is associated with Grave's disease. In the largest study of gestational pemphigoid patients in which HLA testing was completed on all patients, the incidence of Grave's disease was found to be 10.3% (9/87), while the prevalence of females with Grave's disease in the general female population is 0.4%. The majority of the patients were diagnosed with Grave's disease prior to the diagnosis of gestational pemphigoid.

Treatment of gestational pemphigoid largely involves the use of systemic steroids. Mild disease may require only topical steroids, but in the largest study to date over 80% required prednisolone at a dose of 0.5 mg/kg. Other adjuvant therapies shown to be of benefit include cyclosporine, plasma exchange, and IVIG. The treatment of pruritus includes the first generation antihistamines diphenhydramine, chlorpheniramine, and hydroxyzine.

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Case #17

CHICAGO DERMATOLOGICAL SOCIETY
RUSH UNIVERSITY MEDICAL CENTER
CHICAGO, ILLINOIS
MAY 17, 2006

CASE PRESENTED BY: Mark Hoffman, MD, Arthur Rhodes, MD, Melanie Palm, MD

PATIENT A

History: A 29-year-old Caucasian woman presented with an erythematous "rash" over her left cheek, left side of nose, and left upper lip. Lesions first appeared in the left infraorbital region at age 18, coincident with the initiation of oral contraceptive pill (OCP) use for menometrorrhagia. During the past 10 years, lesions have increased in number and size, forming a V2 distribution. The patient has continued her OCP use since the onset of facial lesions.

Medications: Norgestimate/ethinyl estradiol
mometasone furoate monohydrate nasal spray

Family History: No history of similar skin lesions

Social History: Works as a dentist, lives with husband
Non-smoker, no alcohol consumption, no illicit drug use

Review of Systems: No history of hepatic disease

Physical Examination: Numerous wiry and "spider" telangiectasias were present over the left cheek, left nasal dorsum and sidewall, and left upper lip. Lesions blanched with pressure and were non-painful. No oral or ocular lesions were noted.

Diagnosis: Unilateral Nevoid Telangiectasia

Course and Treatment: The patient was counseled on findings at time of visit; no treatment was initiated.

PATIENT B

History: A 34-year-old gravida 1, para 1 woman presented for full skin examination and was noted incidentally to have asymptomatic, erythematous, wiry macules over her left medial eyebrow, left side of nose, and left upper lip. The patient first noted the appearance of these lesions around her 20th week of pregnancy (approximately November 2003). The lesions became more erythematous as her

pregnancy progressed, then faded by approximately nine months post-partum. The patient had been on OCP therapy for seven years prior to pregnancy without development of skin lesions.

Past Medical History: History of ovarian cyst

Medications: None

Family History: No history of similar skin lesions

Social History: Works as director of business operations; lives with husband and son; No alcohol or tobacco use.

Review of Systems: No history of hepatic disease

Physical Examination: Fine, linear, blanchable telangiectasias were noted over the left medial eyebrow, left nose and left upper lip. No ocular or oral lesions.

Laboratory Data:

The following were normal or negative:
Complete blood count, comprehensive metabolic panel, thyroid stimulating hormone

Diagnosis: **Unilateral Nevoid Telangiectasia**

Course and Treatment: The patient was counseled on findings at time of visit; no treatment was initiated.

Discussion: Unilateral Nevoid Telangiectasia (UNT) is a rarely reported disorder, with fewer than 100 cases in the literature. It was first described by Blaschko in 1899, but Selmanowitz proposed the name UNT in 1970. UNT occurs in a segmental pattern. Lesions most often follow a distribution within the C3 to T3 dermatomes, corresponding to linear lesions on the neck, shoulder or upper thorax. Areas of predilection also include the face. However, lower thoracic segments have been documented. Although acquired cases of UNT predominate, congenital occurrences have been reported. UNT is not considered to have a familial inheritance.

While the pathogenesis is unknown, the most widely accepted cause of UNT is elevated estrogen receptors in a segmental distribution, the result of somatic mosaicism. Upon a physiologic or pathological stimulus of estrogen excess, the affected skin develops telangiectasias. Oftentimes, the telangiectasias recede after the estrogen stimulus (pregnancy, exogenous hormone use) is removed. While Uhlin et al supported this theory, demonstrating an increase in both estrogen and progesterone receptors in UNT-involved skin, these results have not been duplicated by subsequent studies.

UNT has been classified into congenital and acquired cases. Acquired cases of UNT are further sub-classified into physiologic estrogen-increase related cases (e.g. puberty in women, pregnancy, oral contraceptive use) and pathologic cases due to alcoholism or hepatic disease. One UNT case has been reported with carcinoid syndrome. Most cases occur in women during puberty or pregnancy and are located on the upper body, while alcoholic cirrhosis is the most common association in men.

Although the diagnosis of UNT is largely made on clinical grounds, a punch biopsy of both lesional and perilesional skin may be performed for comparison. On histological examination, affected skin demonstrates dilated capillaries in the mid to superficial dermis. Screening for other systemic abnormalities has not been recommended.

Treatment of UNT is largely elective. For acquired UNT, observation and evaluating possible sources of estrogen excess is recommended. To electively improve cosmesis, UNT lesions may be camouflaged with cosmetics or treated with vascular lasers (Pulse dye laser or Pulsed KTP).

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Case #18

CHICAGO DERMATOLOGICAL SOCIETY
RUSH UNIVERSITY MEDICAL CENTER
CHICAGO, ILLINOIS
MAY 17, 2006

CASE PRESENTED BY: Kelle Berggren MD, Julie Moore MD, Ashley Smith MD

History: A 56-year-old African American woman presented to the dermatology clinic for "peri-lesional" nodules, five months after surgical excision of a benign parotid tumor. She reported that her surgical wound initially healed well, but approximately three months after the operation, the inferior portion of the scar became red and pruritic. Subsequently, she developed several small tender nodules, which drained sero-sanguinous fluid. She denied any antecedent trauma, swimming, fish tank contact or wound contamination. She returned to her ENT physician who prescribed triamcinolone cream for one week and a course of Keflex, both without improvement. She used topical "retinol oil" for a few weeks, with slight improvement, prior to presentation to dermatology.

Past Medical History:
Pleomorphic adenoma (benign mixed tumor) of left parotid gland (excised and repaired with a sternocleidomastoid muscle rotational flap and AlloDerm graft)
Pulmonary Sarcoid
Hypertension
Asthma
Cervical cancer and hysterectomy
Umbilical hernia repair

Medications:
Triamterene/Hydrochlorthiazide
Albuterol MDI
Pulmocort inhaler

Review of Systems: She reported no fever, chills or night sweats. She did have a ten pound weight loss following surgery (she reported decreased appetite secondary to anxiety related to her persistent wound). The patient otherwise felt well with no contributory symptoms.

Physical Examination: On the patient's left lateral cheek and neck, anteriorly and inferiorly to her tragus, she had a well healed surgical scar. At the inferior-most portion of her scar, she had a 5 mm area where the wound edges were no longer approximated. There was no exudate or warmth. She had four red-violaceous, peri-lesional soft nodules, all 5-10 mm from the initial surgical scar, which were tender to palpation.

Laboratory Data:

Abnormal: Acid fast bacilli (AFB) culture with Smear: No AFB with fluorochrome stain. Positive growth of AFB ("Mycobacterium other than tuberculosis"-MOTT) after 9 days. Final identification (DNA sequencing): *Mycobacterium Fortuitum.*
CBC (10/05): MCV 72.2 (normal 82-103), otherwise normal

Normal: Aerobic/Anaerobic Culture and Gram stain: non-contributory
Complete Metabolic Panel (11/05): normal

Studies: CT of neck 1/06: There is abnormal soft tissue with stranding of the subcutaneous fat in the left supraclavicular region. This may be due to enlarged left supraclavicular lymph nodes. No discrete fluid collection/abscess is seen.

Histo-pathology: Dermal granulomatous inflammation. The dermal infiltrate consists of a few multinucleated giant cells, lymphocytes, abundant plasma cells, neutrophils and occasional eosinophils. Special stains for bacterial, atypical and fungal organisms (Gram stain, Periodic Acid-Schiff stain, Gamori Methenamine Silver stains, Fite stain) all negative.

Diagnosis: **Post-Operative Cutaneous Mycobacterium Fortuitum Infection**

Course and Treatment: Once her culture demonstrated light growth of AFB, she was initiated on Minocycline 50mg orally twice daily and was referred to the Infectious Disease (ID) department. Tissue biopsy cultures identified M. fortuitum and ID commenced a six month course of Tequin (gatifloxacin) 400 mg orally daily and Minocycline 100 mg orally twice daily. The patient developed vulvar candidiasis; therefore her Minocycline dose was decreased to 50mg orally daily. Since treatment with oral antibiotics (9/05), she has not developed any new nodules but has had very slow improvement of her nodules.

Discussion:

Mycobacterium Fortuitum (M. Fortuitum) is one of three organisms classified as rapidly growing mycobacteria (RGM). The other two organisms are M. chelonae and M. abscessus. Of these three pathogens, M. fortuitum is encountered in clinical practice and the clinical microbiology laboratory most frequently. The RGM are distinct in that they usually grow in culture within only one week.

All of the RGM are hardy, environmental organisms with a worldwide distribution. They have been isolated from soil, dust, water, terrestrial and aquatic animals, hospital environments, and contaminated reagents and pharmaceuticals.

M. fortuitum causes human infection primarily via direct inoculation, including primary skin and soft tissue infections, surgical wound infections and catheter related sepsis. Surgical site infections with RGM have occurred after heart surgery, LASIK, cosmetic surgery procedures, face-lifting, laser resurfacing, Mohs surgery, soft-tissue augmentation, liposuction, and punch biopsies.[3,4] Non-sterile water and ice are most commonly implicated as the etiologic source.

Skin and soft tissue infections present with nodules (often with purple discoloration), recurrent abscesses, or chronic discharging sinuses.

Mycobacterial infections should be considered in post-operative wounds that show delayed healing and do not respond to antibiotics. Often wounds heal initially after surgery (as in our patient), then later become red and break down, producing a non-healing superficial wound with discharging sinuses.[1] Most infections occur 3 weeks to 12 months after injury, with an average interval of 4-6 weeks, and the disease tends to follow a chronic and indolent course.[2] Often tissue cultures are required for diagnosis, as staining with Ziehl-Neelsen and Fite are less sensitive.[1]

In general, M. fortuitum is typically susceptible to amikacin, ciprofloxacin and ofloxacin, sulfonamides, and imipenem. For soft tissue and skin infections, dual agent oral antibiotics are favored (in order to prevent acquired resistance and treatment failures). Treatment regimens should be continued for a minimum of four months. The RGM are resistant to antituberculous agents. The RGM do not require public health tracking.

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Case #19

CHICAGO DERMATOLOGICAL SOCIETY
RUSH UNIVERSITY MEDICAL CENTER
CHICAGO, ILLINOIS
MAY 17, 2006

CASE PRESENTED BY: Mark Hoffman, MD, Laura Hoffman, MD

History: A 66-year-old African American woman presents with a draining lesion on the left chin for two years. A prior surgical excision had revealed granulation and scar tissue with signs of acute and chronic inflammation, findings deemed consistent with a ruptured cyst. Patient states that the area never completely healed after surgery and will occasionally discharge purulent material or bleed. Patient denies tenderness.

Past Medical History:

Hypertension	Diabetes Mellitus, type 2
Hypothyroidism	Cerebral Vascular Accident
Depression	

Medications:

Amlodipine	Bupropion
Carvedilol	Insulin
Loradipine	Valsartan
Warfarin	

Review of Systems: Patient reports a loose upper left tooth, but denies oral pain, fever, or chills.

Physical Examination: Along the left mandibular jawline was a 12 x 9 mm erythematous, crusted plaque with central dimpling. Dental consultation noted extensive and advanced periodontal disease with multiple carious and abscessed teeth.

Diagnosis: **Cutaneous Odontogenic Sinus**

Course and Treatment: Patient had a full-mouth tooth extraction performed. She reported complete lesion resolution when contacted eight weeks later.

Discussion: Cutaneous sinus tracts of dental origin have been well documented in the dermatologic and non-dermatologic literature. The presentation is typically that of a recurrent lesion that has undergone several trials of antibiotics, biopsies, and/or surgical excisions. Periapical dental abscesses secondary to a carious tooth are the major cause of cutaneous odontogenic sinus formation. Other etiologic factors include pulpal degeneration due to trauma or periodontal infection. A chronic dental infection can eventually penetrate alveolar bone and

then spread along the path of least resistance into the soft tissues. The site of drainage will depend upon which tooth is involved. Approximately 80% of reported cases have involved the madibular teeth: half were anterior teeth, leading to sinus tracts in submental and chin regions, while diseased molars usually exit the mandibular, submandibular, and neck areas. Other extra-oral sites of drainage include the cheek, canine space, nasolabial fold, nose, upper lip, and even the medial canthus of the eye.

Evaluation of a suspected odontogenic cutaneous sinus should begin with a thorough history with close questioning of the patient about any current oral symptoms such as tooth pain. However, it is important to note that because the tract allows drainage of the abscess and release of any soft tissue pressure, patients are commonly asymptomatic. The cutaneous physical exam findings may include the presence of a soft, depressed nodule fixed to underlying structures. Palpation may reveal a cord-like tract that should express purulent material upon manipulation. Oral exam may reveal one or more severely decayed teeth. A dental consultation with pulpal and periradicular diagnostic testing should be performed. The differential diagnosis may include deep fungal or bacterial infections, trauma, or neoplasm.

Appropriate therapy for the dental disease, (usually via root canal or devitalized tooth extraction,) leads to resolution of the skin lesion. The abscesses are regarded to be localized so systemic antibiotics have generally been considered unnecessary. Because the cutaneous lesion will likely heal following corrective dental work, its surgical removal is also usually unnecessary. However, because some residual fibrotic changes or dimpling of the skin usually remains, surgical revision for reasons of cosmesis may be warranted.

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Case # 20

CHICAGO DERMATOLOGICAL SOCIETY
RUSH UNIVERSITY MEDICAL CENTER
CHICAGO, ILLINOIS
MAY 17, 2006

CASE PRESENTED BY: James Swan, MD, Anthony Peterson, MD

History: This 48-year-old male patient with a diagnosis of Klippel-Trenaunay syndrome presented to our clinic for an unrelated dermatological condition. Upon questioning, he stated he was born with hypertrophy of his left thorax, abdomen, lower extremity and bilateral feet. Additionally he also noted two, large congenital "birth-marks" on his abdomen, initially flat, however with increasing age had become rough to the touch. At 10 years of age, he underwent a left ankle disarticulation (amputation) secondary to painful hypertrophy of the foot, followed two years later by a right ankle disarticulation. A percutaneous left tonsillectomy was performed at the age of 11 years, due to capillary venous malformation of the left tonsil, which nearly resulted in airway obstruction. On several occasions, he has been diagnosed with pulmonary emboli and treated with Coumadin. A previous hypercoagulable work-up returned negative results. He also notes several occurrences of sharp, stabbing pain in the area of abdominal hypertrophy.

Past Medical History:
Bilateral ankle disarticulations (left 1968, right 1970)
Multiple Pulmonary Emboli
Rotary Scoliosis
Left orchiectomy for sertoli cell tumor
Tonsillectomy
Spinal fusion surgery

Medications: Previously on Coumadin (discontinued in 1997)

Allergies: None

Family History: None pertinent

Social History: No tobacco, alcohol or illicits

Review of Systems: Chronic back pain, occasional intermittent abdominal pain

Physical Examination: The patient exhibited kyphoscoliosis with marked hypertrophy of his left hemi-thorax, abdomen and left lower extremity. On closer inspection, large tortuous varicosities were visible below the skin surface. On the left posteriolateral flank and left abdomen were two large violaceous, geographic plaques with vascular ectasias. Additionally, the left helix and left lower extremity showed soft tissue hypertrophy without overlying vascular abnormalities. There were bilateral amputations at the level of the ankle.

Laboratory Data:

Abnormal:
Hemoglobin – 12.9 (14 – 17)

Normal:
Complete Metabolic Profile
WBC, Platelets

Studies: Computed tomography of the abdomen and pelvis shows extensive soft tissue abnormality extending from the left posterior chest, over the lateral left abdomen and the left anterior pelvis. Additionally, the abnormality extends from the level of the sub-cutaneous tissue to the level of the transversalis. There are scattered phleboliths. No focal lesions seen in the liver, spleen, pancreas, adrenal glands or kidneys. Post-surgical changes and surgical hardware are seen in the spine.

Normal Echocardiogram

Histo-pathology: None

Diagnosis: **Klippel -Trenaunay Syndrome**

Course and Treatment: The patient's course remains stable and non-progressive. He continues to have chronic back pain, which is disabling. He has had no new pulmonary emboli and remains off of coumadin. In the last few years he has undergone an evaluation by general surgery for potential resection of his abdominal vascular malformation, however due to significant size, general surgery is reluctant to proceed with surgical intervention.

Discussion: Klippel-Trenaunay syndrome is a rare, sporadic, congenital disorder, first described in 1900 by Maurice Klippel and Paul Trenaunay. They characterized

the disorder by limb hypertrophy, overlying capillary nevus and varicose veins. Shortly thereafter F. Parkes Weber, a London physician, identified the triad above, with associated arterio-venous malformations. Although the terms Klippel-Trenaunay syndrome (KTS) and Klippel-Trenaunay-Weber syndrome are often used interchangeably, most prefer the term Parkes-Weber syndrome to describe KTS in association with significant hemodynamic arteriovenous malformations. Klippel-Trenaunay is currently defined as a triad of slow-flow capillary venous malformation (with or without lymphatic-venous malformation), soft-tissue or bony hypertrophy, and venous varicosities. Although much overlap is often seen with Proteus syndrome, the lack of palmar or plantar cribriform hyperplasia and epidermal nevi help to distinguish the two. KTS occurs in an estimated 1 in 20,000 to 40, 000 live births and has no sex or racial predilection.

The pathogenesis of KTS is not well known. Several theories have evolved over the years including a primary obstruction of the venous system, venous hypertension and subsequent tissue overgrowth, as well as failure of regression of a lateral limb bud. Lastly, an alteration in the tight balance between angiogenesis and vasculogenesis has been postulated. This last theory has been supported by the recent identification of two gene defects associated with VG5Q, in several KTS patients. VG5Q acts as a potent angiogenic factor in promoting angiogenesis. The first mutation is a chromosomal translocation (5,11), which increases VG5Q transcription, thus promoting angiogenesis. The second is mutation E133K, which enhances the angiogenic effect of VG5Q. Although rare reports of familial cases exist, a recent case report of identical monozygotic twins, discordant for KTS, supports a possible paradominant inheritance pattern, allowing the mutation to be transmitted unperceived through many generations.

A range of complications is seen in patients with KTS including stasis dermatitis, cellulitis, thrombophlebitis and pain (associated with chronic venous insufficiency, intraosseous vascular malformations or calcification of vascular malformations). More serious complications include congestive heart failure, bleeding from abnormal vessels in the pulmonary, gastrointestinal and genitourinary systems, as well as deep venous thrombosis and pulmonary embolism. Involvement of the peripheral nerves due to epineurial and endoneurial vascular coils has lead to peripheral neuropathy.

Management is individualized and generally conservative, including psychological counseling and symptomatic treatment of venous insufficiency with compression. In patients with extensive involvement or significant arteriovenous malformations, radiographic imaging, including computed tomography and magnetic resonance imaging are helpful to access the extent of visceral and soft-tissue involvement. Laboratory studies to evaluate for a hypercoagulable state, and monitoring for heart failure should be considered. Appropriate anticoagulation with low molecular weight heparin or coumadin should also be considered for patients diagnosed with, or considered high-risk for, DVT or pulmonary embolism. Life-threatening bleeding is treated with transfusions and direct surgical intervention. Treatment modalities of skin capillary venous malformations need to address both the superficial and deep vascular component of the malformation. Several case reports show the successful use of sclerosant foam to treat venous angiomata in KTS. Additional

case reports note improvement of the superficial portion of the capillary venous malformation with a 585 pulsed-dye as well as a 595 long-pulsed-dye laser.

The Klippel-Trenaunay support group website is: www.k-t.org.

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