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**CHICAGO DERMATOLOGICAL SOCIETY**
**RUSH UNIVERSITY MEDICAL CENTER**
**CHICAGO, ILLINOIS**
**MAY 18, 2005**

**CASE PRESENTED BY: Michael D. Tharp, M.D. Lady Dy, M.D., and Darrell W. Gonzales, M.D.**

**History**: This 2 year-old white female presented with a one year history of an expanding lesion on her left cheek. There was no history of preceding trauma. The review of systems was normal. Initially the lesion was thought to be a pyogenic granuloma and treated with two courses of pulse dye laser. After no response to treatment, a shave biopsy was performed. Because the histopathology was interpreted as an atypical melanocytic proliferation with Spitzoid features, a conservative, but complete excision with margins was performed. The pathology of this excision was interpreted as malignant melanoma measuring 4.0 mm in thickness. A sentinel lymph node biopsy was subsequently performed and demonstrated focal spindle cells within the subcapsular sinus of a left preauricular lymph node. Additional consultation by dermatopathologists and surgical oncologists from outside institutions felt the pathologic changes were consistent with a "malignant Spitz's nevus." After great deliberation by the family, a left total parotidectomy and modified radical neck dissection was performed. Because this tumor was felt to be a malignant Spitz nevus no adjuvant therapy was done.

**Past Medical History:** No significant past medical history

**Physical Findings:** On physical exam the patient's left cheek demonstrated a 0.5 X 0.3 cm erythematous papule with hemorrhagic crust. There was no evidence of cervical or supraclavicular lymphadenopathy.

**Laboratory Data:** A CT of the neck prior to total parotidectomy and modified radical neck dissection demonstrated reactive lymph nodes in the bilateral posterior triangles. No abnormal soft tissue densities or enhancing mass was seen.
A CT of the chest, abdomen, and pelvis performed at the same time was negative for evidence of metastatic disease. All other laboratory values were within normal limits.

**Biopsy Description:** Shave biopsy (S03-16991): A broad area of parakeratosis was identified overlying a partially necrotic epidermis with a lateral collarette surrounding a dermal infiltrate of nested cells. A lack of maturation was noted in the nests of cells at the deeper levels of the dermis and Kamino bodies were also identified. The nests of cells stained positively for S-100 protein supporting the melanocytic nature of the proliferation. These findings were felt to be supportive of a dermal Spitz nevus.

Excision (S03-19221): There is an asymmetrical and striking aggregation of nearly vertically oriented aggregations of cells with peculiar geometric outlines and several foci of sheet-like

confluence. There are also significant numbers of atypical mitotic figures both at the margins and within the tumor. Dsymaturation is notable with deeper cells larger than those superficially. The depth is measured at 4.0 mm and extends close to the margins.

**Diagnosis:** **Malignant Spitz's nevus**

**Present Course & Therapy:** Following modified radical neck dissection with left total parotidectomy, the patient continues to be well with no evidence of recurrence or metastasis.

**Discussion:** Spitz nevi are benign melanocytic neoplasms present in both men and women in all age groups, but are uncommon beyond the ages of 40 to 50 years. Most Spitz nevi present as solitary lesions, but variants including agminated and disseminated Spitz nevi have been reported. They are frequently well-circumscribed, dome-shaped papules or nodules varying in color from pink to tan to dark brown. Spitz nevi may involve any part of the body, but the head and neck are probably the most common sites.

Typically, Spitz Nevi display striking nests of large epitheliod cells, spindle cells or both, usually extending from the epidermis into the reticular dermis in an inverted-wedge configuration. Both mononuclear and multinucleate giant epitheloid cells are frequently observed. In general, there is orderly infiltration of the dermal collagen by these nests or cells with maturation. Although a nearly definite diagnosis can be made in most cases, the histological distinction between Spitz nevi and melanomas is equivocal in about 6 to 8% of cases.

Indeed, spindle and/or epithelioid melanocytic proliferations that display overlapping histopathologic features of Spitz nevus and Spitz-like melanoma are diagnostically difficult and controversial melanocytic tumors. Complicating this vexing issue are the infrequent, but well-known reports of metastatic spread of these lesions to regional lymph nodes with an even smaller subset having wide dissemination resulting in death. The controversial name "malignant Spitz nevus" refers to those with metastasis to regional lymph nodes, but still thought benign due to absence of dissemination and patients ultimately doing well. Proponents of this tumor believe that the presence of melanocytic nests within lymph nodes is not invariable evidence of malignancy. They cite that giant congenital nevus which may be accompanied by apparently benign nests of melanocytes within nodes.

The discordance between the histopathologic features and clinical course of these lesions has led some pathologists to define the borderline entities as designations such as "metastasizing Spitz's nevus," "atypical Spitzoid melanocytic neoplasm," and "problematic Spitzoid melanocytic lesion." Other dermatopathologists believe the efforts to distinguish atypical Spitz from melanoma to be "linguistic maneuvers" avoiding the "tentativeness" on the part of the histopathologist. Thus, a vocal subset of dermatopathologists feels that any nevus capable of metastasizing is a melanoma.

Ancillary diagnostic techniques that may better discriminate benign lesions from malignant melanocytic lesions have been proposed, but no single technique has been found that unequivocally discriminates among these borderline lesions.

Given the controversy surrounding an atypical nevus, it is no surprise then that the clinical management of such a lesion is equally difficult. Some believe that equivocal or atypical Spitz nevi should be removed by margins of 5 mm or more. Others take an even more conservative approach recommending sentinel lymph node biopsy as an aid to confirming

unrecognized melanoma and a means of identifying patients who may benefit from early therapeutic lymph node dissection and/or adjuvant therapy.

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**Case #2**

**CHICAGO DERMATOLOGICAL SOCIETY**
**RUSH UNIVERSITY MEDICAL CENTER**
**CHICAGO, ILLINOIS**
**MAY 18, 2005**

**CASE PRESENTED BY: Arthur R. Rhodes, M.D. and Michael K. O'Donoghue, M.D.**

**History**: This 34 year-old woman presented to our clinic in March of 2005. A very large lesion of her skin was present at birth and enlarged gradually with growth of the involved body sites. She denied changes of the lesion or appearance of new lesions in the past 10 years. During infancy and childhood, the patient underwent four surgeries on the face, upper arms and abdomen. She also reports a single nodule that was biopsied. All of the excised tissues, including the nodule, were examined histologically, and the patient reports that no evidence of melanoma was noted. Magnetic resonance imaging of the brain and spinal column in 1994 is said to have revealed no abnormalities. A complete review of systems was unremarkable.

**Past Medical History**: The patient has a history of asthma and had an appendectomy at age 10. There is no personal or family history of melanoma or giant congenital nevi.

**Physical Findings**: On the back and abdomen was a giant dark-brown plaque involving about 25% of the total body surface area, covered with coarse hair. There were more than 200 satellite lesions on the trunk, scalp, and all four extremities. There were no subcutaneous nodules, enlarged lymph nodes, or enlarged liver or spleen. There were no ulcerations or suspicious surface pigmentary changes.

**Diagnosis**: **Giant Congenital Nevocellular Nevus with Numerous Satellite Nevi**

**Present Course & Therapy**: Recommendations were made for close surveillance using total skin photography.

**Discussion**: Giant congenital nevocellular nevi (GCNN) are defined as nevomelanocytic proliferations present at birth, involving major portions of major anatomical areas. The prevalence of congenital nevi at least 9.9 cm in greatest diameter has been estimated to be 1 in 20,000 newborns, and GCNN about 1 in 500,000 newborns.

The lifetime risk of malignant degeneration associated with GCNN has been reported to be between 5% and 40%. The literature reveals that approximately 70% of the melanomas reported in patients with GCNN occurred before puberty. Only 1% of melanomas in general are diagnosed before puberty. The longest follow up study was reported from Denmark. There were 151 patients gathered from the records of a hospital and radiation center, registered from 1915 through 1975. Mean age at registration was 8.2 years, and the mean observation period was 23 years. There were 8 deaths among the 151 patients, with 3 attributed to metastatic melanoma. From these data, the lifetime risk of metastatic melanoma associated with GCNN has been estimated to be at least 6.3%. During the same time period, the estimated cumulative age-adjusted incidence rate for melanoma in Denmark was estimated to be 0.38% which includes metastatic and non-metastatic melanoma. Taking these results together, it was estimated that an individual with a GCNN has a minimum of 17-fold

increased lifetime risk of developing metastatic melanoma compared to the general population. In these studies, about 67% of patients had surgical excision of the GCNN in part or in toto. In up to two-thirds of patients with melanoma developing in association with GCNN, the melanoma will have a non-epidermal origin and present as a deep dermal nodule or metastatic disease.

Associations with GCNN include scoliosis, spina bifida, clubfoot, elephantiasis, cranial bone hypertrophy, and neurocutaneous melanocytosis. Neurocutaneous melanocytosis (NCM) is a rare congenital syndrome characterized by the presence of large and/or multiple congenital melanocytic nevi of the skin, and benign or malignant melanocytic or nevomelanocytic proliferation of the leptomeninges. Most patients present in the first two years of life with neurological manifestations of increased intracranial pressure, mass lesions, or spinal cord compression that may be attributable to increased cerebrospinal fluid pressure and hydrocephalus as a result of blockage of the cisternal pathways and obliteration of the arachnoid villi by the proliferating melanocytes or nevomelanocytes. DeDavid et al. reported the largest series of NCM in patients with GCNN. They found that 12% of patients (33/289) had developed manifest NCM. The most frequent neurological manifestations were hydocephalus, followed by seizures, papilledema, headaches, increase in head circumference, paresis, and mental retardation. The mean age at the time of the first neurological manifestation was 7.5 years. All of the patients with NCM had nevi involving the posterior axial location, i.e. Paraspinal area, head and neck. Satellite nevi were present in 78% of patients with GCNN in this series, and 94% (31/33) of patients with NCM. The mean age of death for patients with NCM in tis series was 11.4 years.

Management of patients with GCNN is centered on periodic surveillance for complications and palliative or curative treatment. Physical examination should be focused on changes in the main lesion or in new or changing satellite lesions, such as surface color changes, or the presence of nodules and ulceration. Several studies have found that lesions larger than 50 cm in greatest diameter and large numbers of satellite lesions are at a higher risk of malignant transformation. Excision of atypical lesions should extend to the muscle fascia, but there are reports of deeply situated (muscle and even bone) melanoma even after wide and deep excisions. Neurological examinations should focus on signs and symptoms of increased intracranial pressure, mass lesions, or spinal cord compression. The routine use of magnetic resonance imaging with gadolinium (MRI-Gd) and cerebrospinal fluid (CSF) analysis for asymptomatic patients is controversial. MRI-Gd has been found to be more sensitive that computed tomography (CT) and noncontrast MRI, but the sensitivity of the MRI-Gd has been shown to decrease with advancing patient age. Although MRI-Gd has been recommended for baseline studies and also to evaluate the spinal cord for possible tethering, the questions remain about what to do with an asymptomatic patient with significant abnormal findings on routine imaging. There is no effective therapy for leptomeningeal melanocytosis or CNS melanoma other than supportive/palliative care.

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**Case #3**

# CHICAGO DERMATOLOGICAL SOCIETY
# RUSH UNIVERSITY MEDICAL CENTER
# CHICAGO, ILLINOIS
# MAY 18, 2005

**CASE PRESENTED BY: Mark D. Hoffman, M.D. and Laura D. Hoffman, M.D.**

**History:** This 63 year old Eastern Indian male with a 10 year history of psoriasis presented for management of widespread papulosquamous and pustular disease. Treatment with acitretin followed by UVB phototherapy had resulted in near clearing of the skin lesions.

In August 2003 while on topical maintenance therapy he developed new onset pain and swelling of his left knee, ankle and shoulder; several toes on the left foot; and a finger on the right hand. There was also worsening of his skin disease. Consultation with a rheumatologist led to a diagnosis of psoriatic arthritis and methotrexate was begun, leading to improvement in both skin and joint disease.

In March 2004--approximately 6 months after initiating methotrexate and during dose escalation--the patient developed 4-5 firm SQ papules and nodules on the shaft of his penis. These lesions were asymptomatic.

**Medications:** Methotrexate 17.5 mg per week (15 mg/week 1 month prior to onset of nodules); folic acid; rofecoxib; omeprazole; metformin.

**Family History:** Negative for psoriasis.

**Physical Findings:** Firm skin-colored papulo-nodules ~5-10mm on the shaft of the penis. No finger or elbow nodules identified. Few psoriasiform papules on the shins.

**Laboratory Data:**
Rheumatoid factor: negative
ANA: negative
EKG: unremarkable

**Biopsy Description:** Palisading granulomatous infiltrate with central eosinophilic fibrinoid degeneration.

**Diagnosis:** **Penile Methotrexate Nodulosis**

**Present Course & Therapy:** Treatment with methotrexate was continued, as the skin lesions were asymptomatic. All of the nodules resolved without therapy within 6 months, and have not recurred. The patient has continued on methotrexate at 17.5 mg/week with good control of both skin and joint disease.

HLA-DR oligotyping was performed. The results were positive for the *HLA-DRB1*1001* and *DRB1*1501* alleles; *HLA-DRB1*0401* was not detected.

**Discussion:** Methotrexate nodulosis (a.k.a. methotrexate-induced accelerated rheumatoid nodulosis) refers to a phenomenon of rapid-onset nodular lesions precipitated by methotrexate, whose histology is typically indistinguishable from that of rheumatoid nodules. First described in 1986, there have now been more than 60 patients reported with this disorder.

Nearly all cases of methotrexate nodulosis have occurred in patients with rheumatoid arthritis (RA); 80% are also rheumatoid factor positive. The only exceptions that appear in the literature are single instances of its occurrence in the context of psoriasis (with arthritis) and dermatomyositis. It has been suggested that the development of methotrexate nodulosis in a patient with "psoriatic" arthritis should prompt reconsideration of the diagnosis in favor of RA.

The incidence of methotrexate nodulosis in methotrexate-treated individuals with RA has been estimated to be as high as 10%. In patients with RA, methotrexate nodulosis has been linked to the presence of the *HLA-DRB1*0401* allele. Only 2 patients have been reported with a DR2 allele (including *DRB1*1501*); ours represents the third. The *DRB1*1001* allele (which encodes a "rheumatoid epitope" amino acid sequence motif) has not been previously detected.

The lesions of methotrexate nodulosis differ from ordinary rheumatoid nodules by virtue of their sudden-onset and accelerated growth, as well as their peculiar distribution, which favors the hands, feet, and ears. The fingers are involved in 90% of cases while the elbows are affected in only 30%; the values for "genuine" rheumatoid nodules are 30% and 80% respectively. Methotrexate nodulosis has been reported to be confined to the penis, as in our patient, in a man with seronegative RA. Lesions may also occur in the heart, lungs, and meninges.

The onset of lesions averages nearly 3 years after starting methotrexate (range= 2-95 months), which has prompted speculation that lesions of "methotrexate nodulosis" may in actuality merely reflect the particular natural history of RA in these individuals, being entirely unrelated to the methotrexate therapy. In addition, only about 15% of reported cases can be rated as "probable" using the Naranjo scale, which rates medications according to their likelihood of truly causing purported drug reactions. The authenticity of the methotrexate nodulosis phenomenon, however, is supported by its unusual and characteristic presentation, the absence of similar reports prior to the advent and use of methotrexate, and instances in which lesions have disappeared with methotrexate cessation only to reappear with rechallenge.

Treatment of methotrexate nodulosis may include hydroxychloroquine, colchicine, sulfasalazine, or azathioprine. The development of nodulosis is not, however, necessarily an indication for stopping methotrexate in patients who are benefiting from this therapy, and nodules do occasionally disappear in spite of continuation of methotrexate.

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**Case #4**

# CHICAGO DERMATOLOGICAL SOCIETY
# RUSH UNIVERSITY MEDICAL CENTER
# CHICAGO, ILLINOIS
# MAY 18, 2005

## CASE PRESENTED BY: Mark D. Hoffman, M.D. and Laura D. Hoffman, M.D.

**History:** This 28 year old white woman presented for continued management of her "recurrent apthous stomatitis". She has experienced single to multiple (2-4) small and large (> 1 cm) painful oral ulcerations on both the attached and unattached mucosa (tongue; labial, gingival and buccal mucosae; palate; tonsillar fossae) since age 10. Flares occur every 2-4 weeks, typically associated with fatigue. She has also had several episodes of genital ulcerations, whose onset predated sexual activity. Herpes serology and mouth swabs for detection of HSV by PCR had been negative. Treatments had included oral amalgam replacement, nicotine gum, valacyclovir, and propranolol (no help); topical and systemic corticosteroids (very helpful); and most recently colchicine 0.6 mg BID (also very helpful).

Review of systems was notable for intermittent abdominal pain and diarrhea that predated the use of colchicine, and episodic knee pain. No fever, eye discomfort or visual changes.

**Past Medical History:**
Unexplained macrocytosis since 1998
ANA (+) since 2003
Fibromyalgia
Migraine headaches
Gilbert's syndrome

**Family History:** Mother and sister have both experience episodic and mild oral apthae.

**Physical Findings:** 2-5 mm shallow yellow to gray ulcerations involving the buccal mucosa and the labial sulcus.

**Laboratory Data:** RBC 3.3 (nl = 3.9-5.0); Hemoglobin 12.4 (nl = 12.0-15.5); Hematocrit 35.9 (nl = 34.9-44.5); MCV 108 (nl = 82-98); WBC 3.3 (nl = 3.5-10.5) with 34% neutrophils and 12% monocytes; Platelets 145 (nl = 150-450); total bilirubin 4.1 (nl = 0.2-1.3).

ANA > 1:1280 (centromere); C3 = 54 (nl = 77-179), C4 = 6 (nl = 13-49).

The following laboratory values were normal:
B12, folate, and iron studies; HIV; ds-DNA, RNP, Sm, SSA, SSB, Scl-70, ANCA, ESR, CRP, RF; remainder of blood chemistries.

**Studies:** The unexplained macrocytosis prompted consultation with hematology:

Peripheral-blood smear and flow cytometry: unremarkable.
Bone marrow aspirate and biopsy: slightly hypercellular marrow with mild erythroid dysplasia. Cytogenetic analysis demonstrated 47 chromosomes with trisomy 8 in all cells examined. These findings led to a diagnosis of myelodysplastic syndrome (MDS).
Peripheral blood lymphocytes: all cells studied contained 47 chromosomes with trisomy 8.
Skin fibroblasts: all cells showed a normal 46, XX karyotype.

**Diagnosis:** **Apthae associated with Trisomy 8-positive Myelodysplastic Syndrome**

**Present Course & Therapy:** An extensive multi-system workup was initiated. Gastrointestinal evaluation including EGD and colonoscopy was unremarkable except for non-erosive gastritis, likely related to NSAID use. An ophthalmology exam found no evidence for Behcet's, and a pathergy test performed while off colchicine was also negative. The patient has consulted with rheumatology: she was determined to be HLA-B51 positive, and has recently developed Raynaud's phenomenon; however, the consultant has felt that there is yet insufficient evidence to warrant a diagnostic assignment of scleroderma, lupus, or Behcet's. The oral ulcerations have been adequately controlled with colchicine. She will continue multidisciplinary follow-up with the hematology, rheumatology, gastroenterology, and dermatology services. She is also scheduled to receive genetic counseling.

**Present Course & Discussion:** Recurrent apthous stomatitis (RAS) is a common disorder estimated to affect 20% of the general population during their childhood or early adulthood years. RAS may be idiopathic or associated with a number of "correctable causes" or systemic disorders including hematinic deficiencies (B-vitamins, folate); GI diseases (celiac disease, IBD); SLE; HIV; or a variety of syndromes including cyclic neutropenia / hematopoesis, FAPA (fever, aphthosis, pharyngitis, adenitis) syndrome, MAGIC (mouth and genital ulcers, inflamed cartilage) syndrome, and Behcet's disease.

Although not described in indexed dermatology journals or reference texts, reports linking apthous stomatitis or Behcet's disease with macrocytosis or MDS have appeared in the hematologic, gastrointestinal, and medical genetics literatures. There have been more than 15 cases of the association of "Behcet's disease" with MDS, with trisomy 8 a feature in approximately 90% of them. Since trisomy 8 is ordinarily present in only 10% of MDS cases, this is a significant overrepresentation. Nearly all of these individuals with "Behcet's" and MDS have had oral ulcerations, with half of them experiencing genital lesions as well. Lesion distribution in this group of patients is also interesting and unusual in that 60% have had intestinal ulcers, while only 10% have had ocular lesions. Although these cases were designated "Behcet's disease", only half of them actually satisfied the diagnostic criteria of either O'Duffy or the International Study Group. Baidas and colleagues have reported a 32 year old woman with macrocytosis and intractable oral apthae since age 7 that was also found to have trisomy 8 in both the bone marrow and peripheral blood lymphocytes, but not in skin fibroblasts. This patient did not have MDS (or Behcet's) but otherwise bears resemblance to our patient.

The risk for transformation of the MDS into leukemia in these patients is not known. Our patient will also require careful monitoring for signs and symptoms of scleroderma. Autoimmune abnormalities--including classic connective tissue disorders--may complicate the disease course of up to 20% of MDS patients.

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**Case #5**

# CHICAGO DERMATOLOGICAL SOCIETY
# RUSH UNIVERSITY MEDICAL CENTER
# CHICAGO, ILLINOIS
# MAY 18, 2005

## CASE PRESENTED BY: Mark D. Hoffman, M.D. and Rachel Altman, M.D.

**History:** The patient is a 16-month-old Caucasian female who presented with a 6 month history of a perineal rash and a one month history of a periorificial and acral rash. In addition, the patient had an 8 month history of poor feeding with intermittent diarrhea. Oral food intake was very limited (juices, sauces) since formula weaning secondary to "oral food aversion". She was weaned from breast milk at 1 month of age and weaned from formula feedings at age 8 months.

**Past Medical History:** Anemia

**Medications:** 2.5% hydrocortisone cream bid & Aquaphor to diaper region

**Family History:** Non-contributory

**Social History:** Patient was reaching her appropriate developmental milestones and maintaining her appropriate height/weight until age 8 months when her oral intake drastically diminished.

**Physical Exam:** Patient was pale with slightly decreased hair density. Her extremities were edematous. Erythematous plaques with fissuring and scaling were noted on her perineum, extremities (accentuating flexural folds and wrists) and periorifically with mild angular cheilitis. Minimal periungual erythema or paronychia were noted.

**Laboratory Data:**

Albumin – 1.8 g/dL (nl: 2.9-5.5)
Total protein – 3.1 g/dL (nl: 5.6-8.5)
SGPT – 58 U/L (nl: 3-50)
SGOT – 41 U/L (nl: 5-55)
Alkaline phosphatase – 174 U/L (nl: 80-250)
LDH – 1020 U/L (nl: 200-650)
Serum zinc level – 40 ug/dL (nl: 70-150)
Hemoglobin – 10.4 g/dL (nl: 11-13)
Hematocrit – 32.6 % (nl: 33-39)
MCV – 77 fL (nl: 70-86)

The following have normal results:
Sweat chloride tests
Stool studies: guaiac, Clostridium difficile, Rotavirus, Giardia, ova & parasites, Antigliadin IgG
Blood lead level
Alpha 1-Antitrypsin; trypsin

Tissue transglutaminase IgA (Endomysial Ag)

**Studies:** Esophagogastroduodenoscopy; flexible sigmoidoscopy; upper GI and small bowel follow through - all normal

**Histo-pathology:** Skin (thigh):
Confluent parakeratosis with focal diminished granular layer, epidermal hyperplasia and mild superficial perivascular lymphocytic infiltrate. Pallor of the upper epidermis due to cellular edema was not appreciated.

**Diagnosis:** **Kwashiorkor secondary to food aversion**

**Course and Treatment:** The patient was admitted and underwent an extensive workup. She was noted to have anemia of chronic disease, low serum zinc levels, hyponatremia, hypoalbuminemia, hypocalcemia, and failure to thrive (minimal weight gain since age 8 months). The patient was diagnosed with nutritional deficiency secondary to poor feeding habits and improper solid food-intake teaching. Her parents underwent extensive dietary counseling. The patient was started on a soy milk and Isomil 30 kilocalories per ounce diet, and zinc acetate solution 10 mg orally daily was commenced. Rapid improvement in her cutaneous lesions was noted. Serum zinc levels normalized, and zinc supplementation was ultimately discontinued without a recurrence of cutaneous disease.

**Discussion:** Kwashiorkor is the edematous form of protein-energy malnutrition, distinguished from marasamus by the presence of edema, hypoalbuminemia and dermatosis. This condition is endemic in developing poor countries and is associated with protein deficient diets. However, several cases in developed countries have been reported in the contexts of chronic malabsorptive disorders (cystic fibrosis) as well as nutritional ignorance, food faddism, food allergies or food aversion. Food aversion comprises both psychological avoidance and psychological intolerance (an unpleasant bodily reaction induced by emotions associated with the food rather than the food itself). Although kwashiorkor occurs infrequently in the United States, it is the most common form of undernutrition affecting hospitalized patients in America. Treatment is directed to replace proteins, and complete recovery is usually achieved with adequate diet correction.

Clinical features include edema, muscle wasting, hypoalbuminemia, and mental changes such as irritability, apathy, and anorexia. Other findings may include diarrhea and hepatomegaly. Classically, skin findings include “flaking/peeling paint”: hyperpigmented hyperkeratotic plaques over points of pressure or friction eventually desquamating. However, other findings may include intertriginous fissuring, desquamation at the angles of the mouth and erosions of the mucous membranes. In addition, the nails may be dystrophic and the hair becomes hypopigmented, fine and friable. As the child recovers, the hair regrows and repigments leaving a band of depigmentation, referred to as the “flag sign”.

The distinctive histopathologic findings include a superficial perivascular infiltrate of lymphocytes, pallor of the keratinocytes in a band across the upper epidermis, and confluent parakeratosis. The most specific finding is this bandlike pallor, ballooning, and necrosis of keratinocytes and is considered to be pathognomonic for a dermatosis due to nutritional deficiency. However, alternative patterns have been described which lack this epidermal pallor and has only psoriasiform epidermal hyperplasia.

Zinc deficiency can complicate the rash of kwashiorkor and may be the cause of the dermatosis in some patients. It has been reported that zinc replacement alone can adequately treat the skin findings of kwashiorkor. However, some patients with both low serum zinc levels and kwashiorkor improve with adequate protein re-feeding without zinc supplementation.

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**Case #6**

**CHICAGO DERMATOLOGICAL SOCIETY**
**RUSH UNIVERSITY MEDICAL CENTER**
**CHICAGO, ILLINOIS**
**MAY 18, 2005**

**CASE PRESENTED BY: Lady Dy, M.D., Julie Ann Moore, M.D., Ashley Smith, M.D.**

**Diagnosis: "Unknown"**

**Case #7**

# CHICAGO DERMATOLOGICAL SOCIETY
# RUSH UNIVERSITY MEDICAL CENTER
# CHICAGO, ILLINOIS
# MAY 18, 2005

**CASE PRESENTED BY: Lady Dy, M.D., Michael Tharp, M.D., Rachel Altman, M.D.**

**History:** A 54 year old Hispanic female with a history of hypertension presented with an acute onset, sharp burning pain on her right lateral chest associated with immediate erythema. The pain progressed and began to radiate toward her anterior chest prompting her to visit the emergency room for further evaluation. She denied a history of arthropod bite, deep venous thrombosis, pulmonary emboli, use of anticoagulants, nausea/vomiting or myalgia.

**Past Medical History:**
Hypertension
Asthma
Gastroesophageal reflux disease

**Medications:**
Diovan 80 mg po daily
Flagyl 250 mg po tid (day #4)
Albuterol MDI prn

**Allergies:** Intravenous contrast dye

**Family History:** Non-contributory

**Social History:** 10-20 "mixed alcoholic cocktails" per week.
Previous tobacco smoker 1 pack per day for 10 years, quit numerous years ago.
Denies illicit drug use.

**Review of Systems:** Five day history of diarrhea with intermittent bright red blood from rectum, currently treated with Flagyl 250 mg po tid x 4 days.

**Physical Examination:** Upon initial evaluation, her right lateral chest demonstrated a 9 cm by 6 cm ecchymotic plaque with a 13 cm by 9 cm surrounding halo of erythema. No crepitus or superimposed bullae were noted. The patient exhibited excruciating tenderness with minimal palpation of the affected area. She was afebrile with stable vital signs and demonstrated no signs of sepsis.

**Laboratory Data:**
Abnormal:
ESR – 54 mm/hr (0-27)
CRP – 89 ug/mL (0-5)
Stool Guaiac Positive
Anaerobic wound culture (10/12/04) - Peptostreptococcus
WBC/mcL (4,000-10,000): 9,950-12,200

Normal:
Complete metabolic panel
Creatinine kinase
Antithrombin III Antibodies, Factor V Leiden, Dilute Russell Viper Venom, Anticardiolipin Antibodies, Protein S & C free/total levels ANA <1:40
Stool: Negative Clostridium difficile toxin, Normal Culture, No Ova/Parasites, Aerobic wound culture, No wound Acid Fast Bacilli, No wound fungus, Blood cultures

**Studies:** CT chest, abdomen, pelvis (10/10/04): Subcutaneous fat stranding proximal to her right latissimus dorsi with a thickened right latissimus dorsi. No identifiable fluid or air collections were appreciated within the soft tissues.

CT chest, abdomen, pelvis (10/12/04): Subcutaneous inflammatory changes toward the right latissimus dorsi muscle have not significantly changed compared from 10/10/04. Interval development of subcutaneous edema, fat stranding and fascial thickening is identified along the right flank extending into the gluteal region. A degree of adjacent inflammatory changes of the flank musculature is suggested. No well-circumscribed drainable fluid collection identified.

CT chest, abdomen, pelvis (10/14/04): Subcutaneous inflammatory changes in the right latissimus dorsi have not significantly changed from 10/12/05. Subcutaneous edema, fat stranding, and fascial thickening along the right flank have not significantly changed. Interval increase in subcutaneous edema and fat stranding of the right lower gluteal region/hip region. No drainable fluid collection or air pockets were noted.

Esophagoscopy, gastroscopy, and duodenoscopy (11/10/04): Hiatal hernia

Colonoscopy (11/10/04): Sigmoid diverticulosis, Internal hemorrhoids

**Histo-pathology:** Skin from right lateral thorax (10/12/04):
Leukocytoclastic vascultits with fibrin thrombi.

Fascia and muscle from right breast (10/15/04):
Skeletal muscle and fascia without evidence of necrotizing fasciitis or other forms of sepsis.

Skin from right breast (10/15/04):
Small vessel vasculitis with extensive thrombi and associated ischemic necrosis of the epidermis. The vasculitis with associated thrombi extended into the deep dermis and also involved the vessels of the subcutaneous fat.

Right flank adipose (10/15/04):
Adipose tissue containing vessels with neutrophilic vasculitis and thrombi.

**Diagnosis:** **Gangrenous Cellulitis**

**Course and**

**Treatment:** The night after admission, the patient developed a new large focus of ecchymosis measuring 13 cm by 9 cm with a surrounding 15 cm by 15 cm halo of erythema on her right lower lateral torso. In addition, her original focus of involvement on her right chest began developing a large flaccid superimposed bulla. She remained afebrile with stable vital signs. Infectious disease service was consulted who started her on vancomycin and ertapenem. A skin biopsy revealed leukocytoclastic vasculitis with fibrin thrombi. The surgical team was consulted to rule out necrotizing fascitiis. On her fifth day of admission, she underwent a fascial biopsy. An anaerobic culture from her original right chest lesion grew Peptostreptococcus. Vancomycin was discontinued, ertapenem was continued and she was discharged home with a course of Augmentin. She subsequently underwent several debridements of the necrotic tissue and eventual split thickness skin graft and advancement flap reconstructions.

**Discussion:** Gangrenous cellulitis is a severe infection of the skin characterized by a widespread necrosis of subcutaneous tissues, which can include the fascia (fascitis). Necrotizing cellulitis is believed to be an obliterative endarteritis caused by the spread of micro-organisms. Necrotizing skin infections develop and progress rapidly and are characteristically accompanied by severe pain and tenderness with constitutional symptoms. Overlying skin changes can progress to bullae formation and frank necrosis because of vascular occlusion, ischemia and extensive tissue destruction.

Cellulitis in immunocompetent patients is usually caused by a compromise in the skin barrier, whereas the bloodborne route is more common in the immunocompromised. Factors that predispose patients to cellulitis include alcoholism, diabetes mellitus, malignancy, intravenous drug abuse, poor nutrition, and peripheral vascular disease. In cases of necrotizing cellulitis, the clinician should have a high clinical suspicion for malignancy, coagulation abnormalities, or underlying immunologic deficiency. In gangrenous cellulitis or infectious gangrene, the pathogen is usually Group A Streptococcus, and rarely groups C or G isolates, as well as a mixed infection with one or more anaerobes including *Peptostreptococcus* or *Bacteroides*. Anaerobic bacteria are common pathogens in skin and soft tissue infections. Most involve the cutaneous flora, especially *Peptostreptococcus*, or flora adjacent to mucosal surfaces. *Peptostreptococcus* also comprises normal intestinal and oral flora and is often involved in dental infections and peritonsillar abscesses.

Treatment of necrotizing cellulitis includes intravenous antibiotic therapy and surgical debridement of necrotic tissue. Recent studies suggest that clindamycin is superior to penicillin for treating Group A Streptococcal infections because it is not affected by inoculum size or stage of growth. Clindamycin suppresses toxin production, inhibits M-protein synthesis, and has an enduring post-antibiotic effect. Empiric antibiotics should cover both aerobic and anaerobic organisms, thus using ampicillin/clindamycin or metronidazole are good first choices. Gram negative coverage can be improved, especially if patients have been hospitalized previously, by substituting a third generation cephalosporin, carbapenem, fluorquinolone, or aminoglycoside for the ampicillin.

Recent case reports and retrospective studies suggest that nonsteroidal anti-inflammatory drugs relieve nonspecific symptoms and can theoretically delay diagnosis and treatment of necrotizing skin infections. However, prospective studies do not support a risk of developing Group A Streptococcus necrotizing skin infections, or a worsening of the established infection. To avoid a delayed diagnosis, clinicians must understand the early symptoms of necrotizing fasciitis infections including pain out of proportion to the clinical exam. A CT scan is the radiological choice in necrotizing skin infections to rule out involvement of the

fascia. CT is preferred for a suspected perforated neoplasm or underlying pathologic change in the fascia.

It is critical to accurately diagnose necrotizing cellulitis and to rule out accompanying fascial involvement. It is imperative to remember the polymicrobial nature of many infections in patients with underlying malignancies, immunodeficiency, and vascular disease and to treat accordingly with broad spectrum antibiotics and possible surgical intervention.

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**Case #8**

# CHICAGO DERMATOLOGICAL SOCIETY
# RUSH UNIVERSITY MEDICAL CENTER
# CHICAGO, ILLINOIS
# MAY 18, 2005

**CASE PRESENTED BY: Marianne O'Donoghue, Michael D. Tharp MD and Ashley A. Smith MD**

**History:** This 38-year-old African American female presented to the Rush Dermatology Clinic with a 22 year history of linear morphea. The patient's diagnosis was established by skin biopsy at Cook County Hospital at age 16. Her lesions began on her left arm and subsequently spread to her right thigh and face. Her arm and leg involvement have been stable without progression for many years. She believes her facial lesions are progressing. The lesions were occasionally pruritic. Past treatment included topical steroid without improvement. She denied any history of seizures. The patient presented for therapeutic options.

**Past Medical History:** The patient was in her usual state of good health. She reported occasional arthritis in her right shoulder and knee (joints not associated with overlying skin disease). She has two children. There was no family history of skin disease.

**Physical Findings:** On physical exam, she demonstrated a linear depression on her central forehead with right facial hemiatrophy and atrophic plaques on her right cheek. Her left extremity demonstrated a linear atrophic plaque extending from her upper arm to her fingers. Her right thigh had a large atrophic plaque. She had no tongue abnormalities. She was unable to elevate her right eyebrow.

**Laboratory Data:** ANA 1:320 homogenous (nl: <1-40)
Brain MRI: normal

**Biopsy Description:** Unavailable

**Diagnosis:** **Linear Morphea, en Coup de Sabre and Parry-Romberg Variant**

**Present Course & Therapy:** Her clinical exam and history were consistent with Linear Morphea. She was started on Dovonex Ointment treatment QD to facial plaques and BID to extremity lesions. This treatment was initiated since she felt the facial involvement was progressing. After a couple months of usage, she discontinued treatment secondary to poor response.

**Discussion:** Linear morphea is a variant of localized morphea. Morphea is a clinically distinct inflammatory disease which primarily affects the dermis and subcutaneous fat and ultimately leads to scar-like sclerosis. Linear morphea accounts for approximately 20% of cases of localized morphea. There is no gender predilection, in contrast to the other subtypes of morphea in which females predominate. In two-thirds of patients, linear morphea begins before age 18, and this is the subset of patients with the greatest likelihood of disability. Affected limbs may display stiff joints, joint contractures and permanent limb asymmetry.

Morphea en coup de sabre (sabre hit) is linear morphea of the forehead. Parry-Romberg or progressive facial hemiatrophy, is likely a severe variant of linear morphea. Morphea en coup de sabre and Parry-Romberg are often considered overlapping conditions. Hemiatrophy classically affects the maxillary region of the face but may extend to the chin and forehead.[1] It is characterized by progressive wasting of the skin, fat and muscles; bone and cartilage are rarely affected unless onset occurs before the second decade. Neurologic symptoms, including epilepsy, migraine and facial pain, and brain lesions on MRI and CT (focal atrophy and blurring of the gray-white matter interface under the skin lesions and skull thinning, respectively)[3,5], as well as eye (heterchromia, enophthalmos, uveitis), hair (depigmentation, alopecia), skin (hyperpigmentation, vitiligo), tongue, teeth and jaw complications have been described. Hemiatrophy may include ipsilateral, and rarely, contralateral arm, trunk and leg involvement.[1]

The pathophysiology of linear morphea appears to involve three major, closely connected components: vascular damage, activated T cells and altered connective tissue production by fibroblasts. A similar autoimmune mechanism is likely causative for both linear morphea and Parry-Romberg cases.[11] Although once thought to play a role in this disease, large studies have eliminated Borrelia burgdorferi as a cause for morphea.

The histology of morphea is dependent on the stage of disease (early inflammatory margin or central sclerosis) and the depth to which the disease extends. Inflammatory lesions show endothelial wall swelling and edema. Perivascular infiltrates consists predominantly of CD4+ T cells and sometimes eosinophils, plasma cells and mast cells. Later stages of disease show minimal epidermal changes with decreased number of blood vessels and increased collagen. Atrophic eccrine glands are present and the underlying subcutis is homogenized and hyalinized.

Linear morphea is frequently associated with an elevated ANA titer. Antihistone autoantibodies (AHAs) are higher in the generalized forms of scleroderma than in the less extensive forms. A recent study demonstrated that the AHAs correlate with the extent of disease and mirror disease activity[9].

Treatment modalities for linear morphea include hydroxychloroquine, methotrexate[10], calcipotriene, corticosteroids[5,10], phenytoin[12], PUVA and UVA. Surgical modalities are employed in more severe cases. Orthopedic bony procedures and release of joint and ligamentous contractures with excision of diseased skin and free soft tissue transfer for coverage have been successful.[8] A variety of plastic surgery techniques have been utilized for coup de sabre and Parry-Romberg repairs, including groin free flaps, rectus abdominis free flaps, latissimus dorsi free flaps, and pericranial-galeal padding flaps.[2,7] Fat injections, silicone injections, and bone implants are other treatment possibilities. More recently autologous tissue cocktail injection has been a useful method for the correction of depressed atrophy of linear scleroderma en coup de sabre.[6]

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**Case # 9**

# CHICAGO DERMATOLOGICAL SOCIETY
# RUSH UNIVERSITY MEDICAL CENTER
# CHICAGO, ILLINOIS
# MAY 18, 2005

**CASE PRESENTED BY: Kenneth Gordon, M.D. and Anthony Peterson, M.D.**

**History:** This 61-year-old gentleman was referred to our clinic for a three-month history of mildly painful, enlarging brown plaques on his lower extremities. A previous skin biopsy early in the course of the plaques was read as Erythema Elevatum Diutinum. His review of systems was significant for weight loss, generalized fatigue and malaise. He had recently suffered from right-sided facial pain and paralysis associated with a right parotid mass. A parotidectomy was performed for presumed malignant tumor and further work up had noted a large cavitating, necrotic lung mass and significant lymphadenopathy. Fine needle aspiration of the lung mass and histopathology of the parotid gland showed acute and chronic granulomatous inflammation and necrosis, with no evidence of malignancy.

**Past Medical History:** Generalized pustular Psoriasis, currently improved on Etanercept 25mg twice weekly.
Greater than 100 pack-year history of cigarette smoking.

**Physical Findings:** The patient exhibited two 10 x 6 cm, slightly painful, brown, friable, vegetative plaques with surrounding erythema on the pre-tibial areas of the lower extremities. A centrally located ulceration with a necrotic base was noted overlying the left plaque. Cervical lymphadenopathy was also noted on exam. Scattered, well-demarcated, erythematous plaques with overlying silvery scale were also noted on the patient's trunk and extremities.

**Laboratory Data:** The following were normal or negative:

- Urinary Histoplasma Antigen
- Complete Blood Count
- Hemoglobin
- AFB, Fungal, Gram Stain of parotid tumor
- PPD
- PSA

The following were abnormal or positive:

- Leukocyte Count: 14.4 k/uL (4.0 – 10.0 k/uL)
- Platelets: 549 k/uL (150 – 400 k/uL)
- CT Chest: Right upper lobe cavitating mass with lymphadenopathy
- C – ANCA: 1: 20 dilution (positive)
- Anti-Proteinase 3: >100 U (Greater than 5.0 U positive)
- Anti-Myeloperoxidase: 1.0 U (Greater than 15.0 U positive)

**Biopsy Description:** The 4mm punch biopsy of the right lower extremity plaque sent for PAS-D, Fite, Steiner, and Gram stain was negative for an infectious process. An additional 4mm punch biopsy shows a superficial and deep perivascular and periadnexal inflammatory infiltrate of neutrophils,

lymphocytes, plasma cells and eosinophils. Additionally there was small and medium-sized vessel vasculitis without granulomas.

**Diagnosis:** **Wegner's Granulomatosis**

**Present Course and Therapy:** The patient was referred to Thoracic Surgery for open lung biopsy, which confirmed the diagnosis of Wegner's Granulomatosis. Etanercept was stopped. Rheumatology initiated treatment utilizing Cyclophosphamide 2mg/kg per day orally, along with Prednisone 1mg/kg per day. His lung and cutaneous findings of Wegner's improved. Unfortunately the patient suffered a severe stroke, attributed to Wegner's involvement of the central nervous system. He is currently hospitalized for myocardial infarction, a gastrointestinal bleed attributed to Prednisone therapy and most recently necrotizing pancreatitis. The Cyclophosphamide and Prednisone have since been discontinued.

**Discussion:** Classic Wegner's Granulomatosis is an uncommon disease characterized by chronic necrotizing, granulomatous vasculitis of the upper and lower respiratory tracts along with glomerulonephritis. The vasculitis involves both the small and medium-sized arteries and veins with variable degrees of dissemination. Any organ system can be affected, including the central nervous system, musculoskeletal, pulmonary and renal systems. Skin, eye and ear involvement is also commonly seen. It is felt that Wegner's represents an aberrant cell-mediated immune response to an exogenous or endogenous antigen.

Wegner's Granulomatosis equally affects males and females with prevalence of 3 per 100,000 persons. It is extremely rare in African-Americans. The mean onset of disease is approximately 40 years of age and it is felt that chronic nasal carriage of Staphylococcus Aureus may be an associated or predisposing factor.

The disease usually presents with non-specific ear, nose and throat symptoms including chronic cough, sinusitis, and otitis media. Pulmonary infiltrates, nodules and arthralgias are also common presenting findings. Upper airway involvement occurs in 95% of patients and usually manifests as purulent nasal drainage, sinus pain or epistaxis. Pulmonary involvement includes cough, hemoptysis dyspena and chest discomfort. Imaging of the chest often suggests cavitating, necrotic nodules or masses.

Musculoskeletal involvement occurs in over half of patients, usually as arthritis or arthralgias, however unlike other rheumatic joint diseases, rarely manifests with joint destruction or erosions.

Renal involvement is rare early in the course of disease, but usually dominates the clinical course and accounts for most of the mortality of Wegner's. Hematuria and protienuria usually are the first manifestations. The glomerulonephritis of Wegner's is indistinguishable from idiopathic rapidly progressive, cresentic glomerulonephritis. Once kidney involvement is noted, rapidly progressive renal failure usually occurs.

Cutaneous involvement is usually seen in roughly 50% of patients and varies clinically from palpable purpura to pyoderma-like ulcerations. Inflammatory papules, plaques, ulcers and subcutaneous nodules have also been noted. Histologically, there are no pathognomonic findings for Wegner's Granulomatosis. Leukocytoclastic angiitis is common, however not sufficient to make a diagnosis. Granulomas may or may not be found.

Pulmonary tissue by way of open lung biopsy offers the highest diagnostic yield, almost always revealing granulomatous vasculitis. Several supporting diagnostic tests such as C-ANCA, Myeloperoxidase and Anti-proteinase 3 can also be utilized, however positive results should not substitute for tissue diagnosis and clinical suspicion.

Concurrent oral Cyclophosphamide 2mg/kg daily and Prednisone 1mg/kg daily has been the mainstay of treatment. Usually given for one month with a slow taper off Prednisone over a six-month period. Improvement is seen in 90% of cases and remissions achieved in 75% of patients. Remission and relapses are based solely on objective evidence of disease activity and not on C-ANCA titers. Relapse is common. Azithioprine or Methotrexate may be considered in place of Cyclophosphamide after induction of remission, to reduce toxicity associated with chronic Cyclophosphamide therapy. Renal transplant has been performed in patients who developed irreversible renal failure but achieved remission. Despite the promise of Etanercept as maintainence therapy after achieving remission, recent studies have shown that it does not significantly prolong remissions with respect to controls.

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**Case #10**

# CHICAGO DERMATOLOGICAL SOCIETY
# RUSH UNIVERSITY MEDICAL CENTER
# CHICAGO, ILLINOIS
# MAY 18, 2005

**CASE PRESENTED BY: Arthur Rhodes M.D., Michael D. Tharp M.D. and Ashley A. Smith M.D.**

**History:** This 14-year-old Hispanic male presented to the Rush Dermatology Clinic with a 2 year history of multiple scaly, red, discrete patches on his chest, abdomen, buttocks and bilateral upper arms. The lesions were stable, and he denied pruritus. His treatment at presentation included an uncertain prescription cream which helped, and Vaseline. Two 4 mm punch biopsies were obtained.

**Past Medical History:** The patient was in his usual state of good health. He was hospitalized at age 2 months for pneumonia. There is no family history of skin disease.

**Physical Findings:** On physical examination, he demonstrated scattered scaly, red discrete patches on chest, abdomen, superior buttock, and proximal upper arms, involving approximately 3% total body surface area. Lesions were 5-50 mm in greatest dimension. There was no lymphadenopathy or organomegaly.

**Laboratory Data:**

| | |
|---|---|
| Complete Metabolic Panel normal except LDH 663 | (nl: 200-650) |
| CBC normal | |
| ESR 28 | (nl: 0-17) |
| Urinalysis normal | |

CT with contrast of chest, abdomen and pelvis: 1. Normal appearance of the chest, abdomen and pelvis, without evidence of enlarged lymph nodes. 2. Incidental bilateral symmetric gynecomastia.

T Cell Receptor Gene Rearrangement by PCR and heteroduplex analysis:
12/23/04- Specimen did not yield amplifiable DNA
4/11/05- Indeterminate for T cell receptor gamma gene rearrangement

**Biopsy Description:** Mildly acanthotic epidermis with superficial perivascular lymphocytic infiltrate, distributed in a lichenoid, bandlike pattern. Basal epidermotropism is evident, along with exocytosis of lymphocytes into the upper spinous layer, forming Pautrier's microabscesses.

**Diagnosis: Cutaneous T Cell Lymphoma, Patch Stage, in a 14-year-old**

**Present Course & Therapy:** The working diagnosis is patch stage cutaneous T cell lymphoma. Given his total body surface area involvement of 3% and negative CT scans, he is classified as clinical stage IA.

Triamcinolone ointment 0.1% BID was begun, with subtle improvement of his lesions. The patient admits to infrequently using his steroid ointment. Twice weekly Narrow Band UVB was added (initial dose 200mj/cm2), with incremental increase of 10-15% at each visit as tolerated. He improved.

**Discussion:** Mycosis Fungoides (MF) is the most common subtype of Cutaneous T Cell Lymphoma (CTCL), representing about 50% of all primary cutaneous lymphomas. It is a rare entity, with a reported incidence of about 0.3 per 100,000 persons per year.[1] Only 0.5 to 5% of all MF cases begin during childhood and adolescence,[5] with approximately 75% of patients diagnosed after age 50 years.[1] Several recent reviews and case reports document the development of MF in pediatric patients. Seven series (consisting of more than 5 cases per series, for a total of 83 patients) of early-onset MF in the literature have been published since 1990.[3,5,6,10,12,13]

The most common manifestation in children is patch-stage disease i.e. presenting as a "chronic dermatitis". Tumors or disseminated visceral involvement occur. Biopsy in these young patients is typically delayed, often for several years.

The largest study and review to date of pediatric CTCL included 34 patients with MF, with symptoms developing before 16 years of age.[9] This study showed a marked predominance of male patients (71%), similar to adult-onset disease. About half of these patients were diagnosed before 16 years of age, with a median delay of diagnosis of 15.5 years (range, 3-62 years) and median follow up period after diagnosis of 6 years (range, 1-45 years).

The hypopigmented variant of MF is overrepresented in children.[6,12] In three recent series, the percentage of patients with hypopigmented lesions was about 20%.[3,6,9] Additionally, two recent series report an overrepresentation of poikilodermatous MF in children.[9,10]

Typically, neoplastic cells in MF have a mature CD3+, CD4+, CD45RO+, CD8- memory T-cell phenotype and rarely, a CD8+ variant. However, in the childhood population, there appears to be an increased incidence of cytotoxic immunophenotype. In 3 recent series, 13-50% of pediatric cases were CD8+, as compared to the reported rate of less than 5% of adult cases.[5,9,10] Hypopigmented and poikilodermatous variants may be more likely to exhibit a cytotoxic phenotype.

There is marked variation in the literature regarding prognosis for juvenile-onset MF. Four series[3,6,9,10], comprising 71 patients, reported no disease progression beyond Stage IB disease, whereas 4 other series[5,9,12,13] documented 10 of 51 patients progressing (including 3 deaths from disease). It appears that disease specific survival at 5 and 10 years in pediatric patients with Stage IA disease is similar to adult patients. The hypopigmented and poikilodermatous variants portend a better prognosis than other variants.[9]

Juvenile-onset MF has a prognosis no worse than that of adult-onset disease. [9,13] However, long-term survival of younger patients with MF is significantly decreased when compared with a race-, age-, and sex-matched control population.[8]

Treatments require care in this young population, given the possible long term sequelae of phototherapy and radiotherapy. Treatment modalities utilized in the pediatric population have included topical steroids,[3] total skin electron beam radiation,[8,12] topical nitrogen mustard,[5,8] oral PUVA,[3,11,12] topical PUVA,[2] UVB,[3] anthralin and salicylic acid, carmustine,[11]

tar,[11] orthovoltage radiation therapy, and PUVA with interferon-alpha2a[7]. To our knowledge, there are no reports of NB-UVB treatment for pediatric CTCL.

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**Case #11**

# CHICAGO DERMATOLOGICAL SOCIETY
# RUSH UNIVERSITY MEDICAL CENTER
# CHICAGO, ILLINOIS
# MAY 18, 2005

## CASE PRESENTED BY: Lady Dy, M.D., Rachel Altman, M.D.

**History:** A 14-year-old healthy African American male presents with a one-year duration of asymptomatic, progressively lightening of the skin.

**Past Medical History:** None

**Medications:** None

**Physical Examination:** The patient has diffusely scattered hypopigmented slightly scaling patches affecting his torso and all extremities.

**Laboratory Data:** CD4/CD8 ratios:
% T cells – 71 (nl: 56-84)
% CD4 – 44 (nl: 32-60)
% CD8 – 22 (nl: 21-39)

**Studies:** CT scan of chest, abdomen, pelvis (2/5/05):
No mediastinal, axillary, retroperitoneal, pelvic or inguinal lymphadenopathy. No intrapulmonary lesions or mass. No abnormalities demonstrated in the kidneys, bladder, liver, spleen, pancreas or adrenals.

**Histo-pathology:** 10/1/04 - Right buttock:
Acanthotic epidermis with focal areas of spongiosis and few scattered lymphocytes in the upper epidermis. Papillary dermis with mild perivascular lymphocytic infiltrate.

10/1/04 – Left arm:
Superficial perivascular lymphocytic infiltrate with exocytosis of mildly atypical lymphocytes into the epidermis.

12/10/04 – Left buttock x 2:
Acanthotic epidermis with exocytosis of lymphocytes and superficial lymphohistiocytic perivascular infiltrate.

**T Cell Receptor Gene Rearrangement PCR:**
3/11/05 – Indeterminate for T cell receptor gamma gene rearrangement

**Diagnosis:** **Hypopigmented Mycosis Fungoides**

**Treatment & Course:** The patient has undergone several months of therapy with triamcinolone 0.1% ointment twice daily with no clinical resolution of his cutaneous lesions. He recently has commenced narrowband UVB treatment 2 times weekly with some clinical improvement noted.

**Discussion:** Mycosis fungoides is the most common type of primary cutaneous T-cell lymphoma. Several unusual variants have been observed, including pustular, bullous, hyperpigmented, purpuric, follicular, verrucous, and hypopigmented forms. Hypopigmented mycosis fungoides is a variant of mycosis fungoides characterized by the presence of hypopigmented patches as the sole manifestation of the disease or may be associated with erythematous patches, plaques or tumors. Scattered hypopigmented patches on the trunk or extremities comprise the usual presentation. The first described case of hypopigmented mycosis fungoides was in a 14 year old West Indian male and was published in 1978 by Smith and Samman. This variant has been described predominantly in young African American or dark-skinned patients with an age of onset much earlier than in patients with classical disease. However, several Caucasian patients have been reported. Until July 2003, 106 patients with hypopigmented mycosis fungoides have been reported. The incidence of mycosis fungoides in persons younger than 40 years old is approximately 0.5 in 100,000 with 0.5% -5% of all mycosis fungoides cases beginning during childhood/adolescence. A benign course has been suggested based on long term (30-year) survival rate of patients with stage IA mycosis fungoides similar to the expected survival rates of control populations. The differential diagnosis includes pityriasis alba, vitiligo, atopic dermatitis, post-inflammatory hypopigmentation, sarcoidosis, leprosy, pityriasis lichenoides chronica, and tinea versicolor.

The mechanism for the hypopigmentation is still unknown, however two explanations have been postulated:
a) disordered melanogenesis with a decreased transfer of melanosomes to surrounding keratinocytes
b) degenerative changes in the melanocytes secondary to cytotoxic effects of suppressor T cells on melanocytes.
Electron microscopy has demonstrated decreased numbers of melanosomes within epidermal keratinocytes.

Immunologic analysis tends to give varying results. Unlike classic mycosis fungoides which demonstrates a predominance of helper T cells (CD4), many cases of the hypopigmented variant display a predominance of suppressor T cells (CD8) or a normal helper/suppressor T cell ratio. This may be explained by the fact that these clinical variants seem to correspond to the early stages of mycosis fungoides, which may not show typical immunophenotypic changes and may be indistinguishable from reactive lymphocytic infiltrates. The T-suppressor lymphocytes may play an immunoregulatory and suppressive role in the disease process before the onset of more aggressive disease. This suppression may explain the long history of disease in many cases before diagnosis.

Histopathologic findings for hypopigmented mycosis fungoides are the same as for classical patch stage mycosis fungoides. Patch stage MF findings include a relatively sparse papillary dermal lymphocytic infiltrate. Lymphocytes are typically confined to the epidermal basal layer either as single cells in a ‘string of pearls’ configuration or as small groups of cells. These cells are often surrounded by a clear halo. Pautrier microabscesses are uncommon in the patch stage. In addition, fibrosis of the papillary dermis is found with haphazardly arranged wiry bundles of collagen.

Proposed successful treatments have included topical corticosteroids, topical nitrogen mustard (mechlormethamine), and topical carmustine (BCNU), sunlight, UVB, and PUVA. One proposed mechanism of action for topical nitrogen mustard is that it may reverse the defect in the transfer of melanosomes and activate the melanocytes to repigment the hypopigmented areas. Remission periods following treatments have been described ranging from 2 months – 3 years with common clinical relapses upon discontinuation of therapy.

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**Case #12**

# CHICAGO DERMATOLOGICAL SOCIETY
# RUSH UNIVERSITY MEDICAL CENTER
# CHICAGO, ILLINOIS
# MAY 18, 2005

## CASE PRESENTED BY: Arthur Rhodes M.D. and Ashley A. Smith M.D.

**History:** This 49-year-old white male presented to the Rush Dermatology Clinic for skin cancer screening. He was diagnosed one year ago with Fabry's disease. His diagnosis was made subsequent to his nephew's similar diagnosis. The patient has characteristic lesions on his torso and oral mucosa. The patient reports burning of his hands and feet as a child, diagnosed as arthritis at a children's hospital. He has daily headaches and occasionally abdominal pain. He endorses symptoms consistent with Raynaud's phenomenon. He states that the mottled pigmentation of his legs is chronic and stable. He developed blindness in his right eye in 2000. He has atrial fribrillation. The patient was referred to Rush Medical Center for initiation of enzyme replacement therapy for his Fabry's disease.

**Past Medical History:** Cerebral atrophy, cerebral microvascular disease, atrial fibrillation, right eye blindness, right sided hearing impairment, frequent urinary tract infections, tonsillectomy, appendectomy

**Physical Findings:** The patient demonstrated dozens of discrete purple-red papules on his torso. He had similar lesions on his buccal mucosa. His thighs and legs had mottled, lividoid purplish pigmentation. His great toes demonstrated violaceous discoloration. He had dense freckling of the shoulders and a benign nevus pattern.

**Laboratory Data:** CBC normal
Complete metabolic panel normal, except BUN 24, Cr 1.5, CO2 32
Lipids normal
Urinalysis: positive for protein and trace blood
PSA 1.40
PT (INR) 2.62 (patient is on Coumadin)

Ultrasound of Retroperitoneum: Area of cortical prominence in the mid right renal pole. This cannot be proven to be normal and correlated imaging such as CT may be helpful. Otherwise, few upper pole peripelvic cysts on the right and inferior pole peripelvic cysts on the left are noted.

Brain MR with and without contrast: There is more than age appropriate cerebral atrophy. Ill-defined and multiple areas of T2 signal change are seen in the periventricular white matter and the centrum semiovale consistent with chronic microvascular disease which is known to occur inpatients with Fabry's disease. Old lacunar infarcts are noted in the right basal ganglia and the external capsule.

**Biopsy:** None performed

**Diagnosis:** **Fabry Disease (Angiokeratoma Corporis Diffusum)**

**Present Course & Therapy:** Patient is currently receiving intravenous recombinant alpha-galactosidase A enzyme therapy every two weeks at Rush Hospital.

**Discussion:** Fabry's disease, an inborn error of glycosphingolipid metabolism, results from defective activity of the lysosomal enzyme, alpha-galactosidase A. In 1898, Fabry, in Germany, and Anderson, in England, independently described the entity known as angiokeratoma corporis diffusum or Fabry's disease. The frequency of Fabry's disease has not yet been determined but it is very rare and estimated to occur once in every 117,000 live births.[1] Traditionally, the disease has been thought to be an X-linked recessive disease with complete penetrance and variable clinical expressivity in affected males and occasional mild penetrance in heterozygous females. However, a couple recent studies demonstrated significant disease in females carriers, therefore Fabry's disease could be considered a storage disease transmitted as an X-linked dominant disease.[2,3,4,5]

The alpha-galactosidase defect leads to progressive deposition of predominantly globotriaosylceramide in most visceral tissues and fluids of the body. The birefringent glycosphingolipids are primarily in the lysosomes of the vascular endothelium, in muscle cells of the cardiovascular-renal system, and to a lesser extent in reticuloendothelial, myocardial and connective tissue cells of the cornea and kidney, and in the cells of the autonomic nervous system.

Onset of the disease usually occurs during childhood or adolescence with periodic crises of severe pain in the extremities (acroparasthesias), the appearance of vascular cutaneous lesions (angiokeratomas), hypohydrosis, and the characteristic corneal and lenticular opacities. With advancing age, the progressive accumulation leads to early demise secondary to renal, cardiac or cerebrovascular involvement.

The single most debilitating symptom is the acroparasthesias, characterized by episodic crises of agonizing, burning pain with parasthesias, initially in the palms and soles. They are usually triggered by exercise, fatigue, emotional stress, or rapid climatic change.[1] The pain is usually associated with a low grade fever and an elevated erythrocyte sedimentation rate, which has led to the clinical misdiagnosis of arthritis, rheumatic fever or eythromelalgia. Of older patients with Fabry's disease, 10-20% deny any history of these acroparasthesias.

There is a progressive increase in the number and size of the angiokeratomas with age. The lesions are dark red to blue angiectases that are flat or slightly raised and do not blanch with pressure. They are most densely located between the umbilicus and the knees, with a tendency toward symmetry. Involvement of the oral mucosa and conjunctiva is common. Angiokeratoma similar to or indistinguishable from the cutaneous lesions in Fabry's disease have been described in patients with other lysosomal storage diseases, including fucosidosis, sialidosis, beta-galactosidase deficiency, aspartylglucosaminuria, alpha-N-acetylgalactosaminidase deficiency and beta-mannosidase deficiency.[6]
Cardiac disease occurs in most hemizygotes, including anginal chest pain, myocardial infarction, ischemia, congestive heart failure and cardiac enlargement. There is a subtype of

individuals with residual activity of their alpha-galactosidase A enzyme compatible with their milder phenotypes. These "cardiac variants" have cardiomegaly and electrocardiographic abnormalities consistent with cardiomyopathy.[7] Patients are asymptomatic most of their lives and do not experience the early classic manifestations of the disease.

Progressive glycosphingolipid deposition in the kidney results in proteinuria with gradual deterioration of renal function and development of azotemia in middle age. Birefringent lipid globules with characteristic "maltese crosses" can be observed free in the urine or in the urine sediment with polarization.

Ocular involvement is most prominent in the cornea and lens. A characteristic corneal opacity, observed by slit-lamp microscopy, is found in all males with the disease and in most heterozygous females. The opacities appear as "whorl-like opacities". There is also an unusual opacity of the lens termed the "Fabry cataract". Vision is not impaired by these defects.

Other clinical feature include chronic bronchitis with airway obstruction, lymphedema of the legs, episodic diarrhea with vomiting and flank pain, and anemia due to decreased red blood cell survival.

The clinical course of the heterozygous female differs significantly from the affected males. Approximately 30% have a few isolated skin lesions, fewer than 10% have acroparasthesias, and 70% have whorl-like corneal opacities.[2] Severe renal and cardiac disease rarely occurs.

The pathology of the skin lesions is described as telangiectases or small superficial angiomas. Ultrastructurally, there is a typical pattern of concentric or lamellar lipid inclusions with alternating light and dark staining bands.[1]

A presumptive diagnosis can be made by careful ophthalmologic examination and by skin biopsy. Biochemical confirmation is demonstrated by deficient alpha-galactosidase A activity in plasma, tears, or biopsied tissues, and by increased concentration of ceramides from plasma or urine sediment. Prenatal diagnosis can also be accomplished.

Until recently, the treatment of patients with Fabry's disease was symptomatic and included hydantoin and carbamazepine for acroparasthesias, and long-term hemodialysis for renal failure. Affected males died by average age 41.[7] Recombinant alpha-galactosidase A enzyme, Fabrazyme by Genzyme, has recently become available and was shown to safely and effectively clear the deposits of globotriaosylceramide in the capillary endothelium of the kidneys, heart and skin of patients with Fabry's disease.[8] The infusion is given every other week for a total of six months to a year. There has been a reported significant reduction in the pain associated with acroparasthesias. [12] Fabry's disease now joins Gaucher's disease, which is due to a deficiency of beta-glucosidase, as a lysosomal storage disease that is treatable using enzyme replacement.[7]

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**Case # 13**

# CHICAGO DERMATOLOGICAL SOCIETY
# RUSH UNIVERSITY MEDICAL CENTER
# CHICAGO, ILLINOIS
# MAY 18, 2005

**CASE PRESENTED BY: Michael Tharp, M.D., Lady Dy, M.D., and Darrell W. Gonzales, M.D.**

**History:** This 44 year-old white female presented with a 20 year history of progressive alopecia. It initially began as a focal patch of hair loss that gradually expanded over the last 15 years. The patient has reported intermittent foul smelling, purulent drainage along with pain. During the last 20 years she has been treated with countless courses of antibiotics for both gram positive and negative coverage including tetracycline, cephalexin, azithromycin, levofloxacin, ciprofloxacin, and trimethoprim/sulfamethoxazole with little to no improvement. She has also received systemic antifungals including terbinafine, griseofulvin, and itraconazoles. Dapsone was given, but complicated by peripheral neuritis. The patient has also been treated with azathioprine, cyclophosphamide, isotretetinoin, and thalidomide with no improvement. Finally, topical, intralesional, and systemic steroids have also failed to demonstrate benefit.

**Past Medical History:** No significant past medical history
Vitamin supplements

**Physical Findings:** On physical exam the patient demonstrated along the crown and vertex of her scalp a well defined tethered and atrophic palm sized area of marked hair loss with a pink hue and scattered yellow crusts. In addition, at the edge of this atrophic patch were well defined tufts of hair with perifollicular erythema and yellow crust.

**Laboratory Data:** Normal CBC and complete metabolic profile
ANA negative
RPR non-reactive
Erythrocyte sedimentation rate and C reactive protein normal
Bacterial cultures: rare growth of staphylococcus aureus (coagulase negative) resistant to penicillin, but susceptible to all other antibiotics.
Fungal cultures and acid fast bacilli cultures and smears were negative.

**Biopsy Description:** 12/26/94: A punch biopsy of the scalp demonstrated an atrophic epidermis with extensive fibroplasias and sparse perivascular lymphoplasmacytic infiltrates.

06/28/96: A punch biopsy demonstrated superficial scarring of the dermis with an interstitial and perivascular lymphohistiocytic infiltrate with focal prominent plasma cells. Distortion of the hair follicles was noted as they traversed through the inflammatory process. Numerous hair follicles were present without prominent scarring or fibrous track replacement.

02/22/1999: Punch biopsy for direct immunofluorescence examination: Negative for IgG, IgA, IgM, and C3.

02-22-1999 (slide available): A punch biopsy with vertical and horizontal sections demonstrated a moderate perifollicular inflammatory infiltrate of lympyhocytes, histiocytes, and plasma cells. A moderate degree of fibrosis was present around these follicles.

09/16/2004 (Slide available): A punch biopsy demonstrated a superficial and deep dermal infiltrate consisting of lymphocytes, neutrophils, eosinophils, and plasma cells. Numerous normal appearing hair follicles were present with some dermal fibrosis.

**Diagnosis:** **Cicatricial alopecia, unclassified**

**Present Course & Therapy:** Despite multiple courses of antifungals, antibiotics, and systemic immunosuppressants the patient continues to demonstrate erythema and scaling. She is currently on no therapy.

**Discussion:** Scarring or cicatricial alopecia leads to patches of irreversible hair loss. It is characterized clinically by the loss of hairs and their follicular ostia and histopathologically by the loss of pilosebaceous follicles. Following the exclusion of physical or chemical injury or an acute infectious aetiology, such as inflammatory tinea, the primary scarring and infiltrative alopecias need to be differentiated. Cicatricial alopecia may be the terminal event of several interrelated clinical conditions, recognized through their explicit idiopathic or known etiology. Nonetheless, the conditions responsible for cicatricial alopecia may prove to be elusive.

The criteria used to classify the various forms of cicatricial alopecia are relatively imprecise and so classification is controversial and in a state of evolution. There are five distinctive forms of cicatricial alopecia: chronic cutaneous lupus erythematosus, lichen planopilaris, dissecting cellulitis (perifolliculitis abscedens et suffodiens), acne keloidalis, and central centrifugal scarring alopecia. Not all patients with cicatricial alopecia can be confidently assigned to one of these five entities, and "cicatricial alopecia, unclassified" would be an appropriate label for such cases.

Chronic cutaneous lupus erythematosus may have typical "discoid" lesions, but often the clinical findings mimic other forms of scarring alopecia. Histologic findings may demonstrate vacuolar degeneration of the basal cell layer of the follicular epithelium and/or epidermis. Perivascular and perieccrine chronic inflammation helps to differentiate lupus erythematosus from lichen planopilaris. Direct immunofluorescence may demonstrate deposition of immunoreactants at the dermoepidermal junction, but it is often negative even in clear cut cases of chronic cutaneous lupus erythematosus.

Central centrifugal scarring alopecia is a diagnostic category that features hair loss centered on the crown or vertex of the scalp as a chronic disease with progressive symmetrical expansion and eventual "burnout." Folliculitis decalvans, follicular degeneration syndrome, and pseudopelade are grouped together as variants within this category. Folliculitis decalvans is characterized by pustule formation at the expanding margin. Histopathology demonstrates epithelial atrophy with concentric lamellar fibroplasia and chronic inflammatory cells (including plasma cells and lymphocytes). Eventual migration of the hair shaft into the

dermis with ensuing massive inflammation and epithelial destruction with follicular scars is typically noted.

Assessment of hair loss must be a systematic process beginning with a thorough history to determine speed and onset, family history, grooming practices, and chemical insults. Scalp examination may immediately suggest the underlying aetiology. Features including pattern and distribution of hair loss, pustules, presence and location of erythema, assessment of induration, and follicular keratosis may all aid in the diagnosis. A 4 mm punch biopsy at the active edge for both horizontal and vertical sections is often necessary to determine the underlying cause of scarring alopecia. Direct immunofluorescence of scalp biopsies may help in distinguishing lichen planopilaris and discoid LE. Even after a thorough evaluation the histologic and clinical overlap between the forms of cicatricial alopecia may prove to make a definitive diagnosis difficult to render.

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**Case #14**

# CHICAGO DERMATOLOGICAL SOCIETY
# RUSH UNIVERSITY MEDICAL CENTER
# CHICAGO, ILLINOIS
# MAY 18, 2005

## CASE PRESENTED BY: John Kalis, M.D. and Laura D. Hoffman, M.D.

**History:** A 9 month old white female presented with a changing "birthmark" on the left posterior shoulder. Her mother reported that the lesion appeared within the first few months of life and had slowly enlarged. It was pruritic.

**Past Medical History:** Full term uncomplicated pregnancy. The child is healthy and reaching all developmental milestones.

**Physical Findings:** A solitary 11 x 11 mm yellow-orange oval plaque was present on the left posterior shoulder. Darier's sign was positive.

**Diagnosis:** **Solitary Cutaneous Mastocytoma**
**(Type Ia – Indolent mastocytosis without systemic disease)**

**Present Course & Therapy:** A therapeutic trial with tacrolimus ointment 0.1% was initiated without effect. Treatment was changed to cetirizine 2.5 mg PO QD, along with topical clobetasol ointment delivered under occlusion BID. Although excision was considered, it became unnecessary as the lesion resolved with this therapy.

**Discussion:** Mastocytosis encompasses a range of diseases characterized by a pathological increase in mast cells in a variety of tissues. Most commonly seen in the skin, mast-cell disease can involve the skeletal, GI, and central nervous systems. A number of different clinical patterns may be seen, with associated signs/symptoms dependent upon the particular organs that are affected and the effects of secreted mast cell mediators, i.e.: histamine, eicosanoids, and cytokines.

The current classification scheme organizes mastocytosis into sub-types I-IV. Most patients, especially children, fall under type Ia--indolent mastocytosis without systemic disease--and have only cutaneous lesions associated with local pruritis; extra-lesional symptoms such as flushing, GI complaints, and headaches are infrequent. C-kit activating mutations—although generally linked with adult-onset mastocytosis—may at times be detected in children with this disorder.

Solitary cutaneous mastocytomas are usually found in pediatric patients, and most appear within the first 3 months of life. They have a variety of clinical presentations, ranging from macular to nodular, yellowish red to brown, round to oval, and can measure several centimeters. A positive Darier's sign (an erythematous, whealing response provoked by firm stroking of the lesion) supports the diagnosis. In children, solitary cutaneous mastocytomas rarely harbinger systemic disease and, to date, have not been reported to show malignant transformation. Most lesions are self-limited and will spontaneously involute before

adolescence. Treatments available to expedite resolution include topical corticosteroids with occlusion, serial intralesional corticosteroid injections, or excision.

Although the spontaneous regression of solitary cutaneous mastocytomas is a familiar feature, its mechanism is poorly understood. One Japanese report (2002) suggests that the mast cells' proliferative potential becomes exhausted. Using serial biopsies from a pediatric patient, investigators performed immunohistochemical analyses during the proliferative and regressive stages of a single lesion. Labelling for proliferative cell nuclear antigen expression, 1.7% of mast cells were positive in the proliferative versus 0% in the regressive stage. Interestingly, this study also found comparatively increased levels of stem cell factor (SCF)--an anti-apoptotic growth factor--in the regressive stage mast cells. This may account for the extended survival of those mastocytomas that involute slowly or not at all.

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**Case #15**

# CHICAGO DERMATOLOGICAL SOCIETY
# RUSH UNIVERSITY MEDICAL CENTER
# CHICAGO, ILLINOIS
# MAY 18, 2005

## CASE PRESENTED BY: Lady C. Dy, M.D. and Laura D. Hoffman, M.D.

**History:** This 50 year-old African-American woman presented for the evaluation of lesions on her left neck. The lesions first appeared approximately fifteen years ago and had gradually increased in number. They were usually asymptomatic, although she reported a sensation of occasional "pinching."

**Past Medical History:** Hysterectomy secondary to fibroids at age 30
Negative for renal cancer or disease

**Family History:** Daughter status post myomectomy at age 24
Negative for renal cancer or disease

**Physical Findings:** The left lateral neck demonstrates approximately a dozen firm, red-brown papules ranging from 4 to 9 mm. No similar lesions identified elsewhere on the body.

**Laboratory Data:** N/A

**Biopsy Description:** There is a dermal infiltrate consisting of fasicles of spindle shaped cells that are blunt ended. A Masson Trichome stain was performed and revealed densely staining red infiltrate within the dermis representing muscle tissue. A Neuron Specific Enolase, smooth muscle actin, and muscle specific actin immunohistochemical protein marker stains were performed revealing positive staining of the infiltrate. A S100 immunohistochemical protein marker stain was negative.

**Diagnosis:** **Cutaneous Piloleiomyomas**

**Present Course & Therapy:** All lesions have remained stable, and the patient has not requested treatment. Genetic sequence analysis to detect a mutation in the fumarate hydratase gene is being explored.

**Discussion:** Cutaneous leiomyomata are benign smooth muscle tumors that arise from the arrector pili muscles, the muscles surrounding the dermal blood vessels, or the dartoic, vulvar, or mammary smooth muscles. Most cutaneous leiomyomata are spontaneous, but familial cases have also been reported. A familial, autosomal dominant syndrome characterized by multiple cutaneous as well as early uterine leiomyomata has been recognized and named the "multiple cutaneous and uterine leiomyomata syndrome" (MCL). MCL may overlap with a related syndrome designated the "hereditary leiomyomatosis and papillary renal cell cancer syndrome" (HLRCC.) The gene defect for both syndromes has been localized to chromosome 1q42.3-43 where the gene for fumarate hydratase is positioned and mutated.

Studies of patients with leiomyomas not associated with familial uterine/cutaneous leiomyomas reveal no such mutations.

Fumarate hydratase (fumarase or FH) is the enzyme that converts fumarate into malate in the Krebs cycle. It is also thought to act as a tumor suppressor gene, based on the loss of the wild-type allele and diminished fumarase enzymatic activity in MCL and HLRCC patient's skin, uterus, and kidney tumor biopsy specimens. The actual mechanism by which fumarase deficiency results in tumorigenesis remains inconclusive and is an area for future studies.

HLRCC (previously known as Reed's syndrome) was first described in a handful of kindred in Europe and Israel. However, a recent report evaluated 35 families in North America with features suggestive of HLRCC, and DNA sequence analysis revealed relevant fumarase germline mutations in 90% of them. Cutaneous leiomyomas were exhibited by 80% of the members of these families. The women in these families showed a higher prevalence (98%) and earlier mean age of diagnosis (30 years) of uterine fibroids then did women in the general population (44% and 42 years respectively), and most required hysterectomy before the age of 30. Importantly, 13 members from 5 of these families were affected with renal cell carcinoma; 7 of these were papillary carcinoma associated with an aggressive disease course.

The overall likelihood of a patient with cutaneous and uterine leiomyomata having syndromic (MCL or HLRCC) disease appears to be low. However, it may be prudent to screen for renal malignancy in those patients with a family history of renal cancer. An additional concern for women who are found to be members of pedigrees in which MCL or HLRCC is operative relates to establishing early diagnosis of uterine leiomyomas. Women carrying the mutant allele who intend to have children should be advised to consider conceiving at an earlier age to avoid the potential complication of infertility caused by uterine leiomyomata. When confronted with any patient with multiple leiomyomas, it is vital to inquire about a family history of cutaneous leiomyomas, uterine fibroids, and renal cancer, so that appropriate DNA screening and genetic counseling and can be initiated if warranted.

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**RUSH UNIVERSITY MEDICAL CENTER**
**CHICAGO, ILLINOIS**
**MAY 18, 2005**

**CASE PRESENTED BY: Marianne O'Donoghue, M.D., Clarence Brown, M.D., and Darrell W. Gonzales, M.D.**

**History:** This 49 year-old African American female presented with a 3 month history of a lesion on her right anterior thigh. The lesion began as a raised dark bump that progressively enlarged. She denied any history of preceding trauma to the affected area. The patient reported only intermittent pruritus. Topical application of Neosporin made no improvement in the size of the lesion.

**Past Medical History:** No significant past medical history.

**Physical Findings:** On physical exam the patient's right anterior thigh demonstrated a 14 X 13 mm well defined circular plaque with a verrucous pink surface. There were no other suspicious lesions either on the head, oral mucosa, trunk, or extremities.

**Laboratory Data:** All laboratory values were normal including bacterial and fungal cultures and smears.

**Biopsy Description:** A shave biopsy of the lesion demonstrated broad fascicles of polygonal cells arranged in sheets among the collagen bundles of the dermis. Within the cells were notable eosinophilic fibrolysozomal granules filling the cytoplasm. The nuclei of these cells were small to oval and centrally located.

**Diagnosis: Granular Cell Tumor**

**Present Course & Therapy:** Following the shave biopsy the patient underwent an excision of the granular cell tumor. To date, she has had no recurrence of the lesion on her right thigh and no new lesions have developed elsewhere including the oral mucosa.

**Discussion:** In 1854, Weber was the first to describe a case of granular cell tumor. In 1926, Abrikossoff named this type of tumor granular cell myoblastoma believing it to be muscular in origin. Granular cell tumors are rare lesions most often found from the second to sixth decade of life. They are more common in African Americans and women with a 3:1 female to male ratio.

Although cutaneous granular cell tumors may develop in any location, half of them occur in the head-and-neck region. One third of these tumors develop on the tongue, one third on the skin, and one third in internal organs. Granular cell tumors can be found in almost all internal organs including the esophagus, stomach, appendix, larynx, bronchi, pituitary gland, uvea, and skeletal muscle. Because 25% of granular cell tumors occur as multiple lesions, especially in African-American patients, the diagnosis of one requires a careful physical examination for the presence of others.

The clinical morphology of granular cell tumors is variable. Frequently these tumors present as subcutaneous nodules with either normal, hyperpigmented, or tufts of hair on the overlying skin. Verrucous changes or ulcerated nodules are also common. Although many of these lesions are asymptomatic, they have also occasionally been reported as tender or prurituc. Interestingly, the cut surface of these tumors is often white to yellowish, similar to the color of nerve bundles.

In the biopsy specimen, broad fascicles of tumor cells infiltrate the dermis among collagen bundles arranged in nests or sheets. Pseudoepitheliomtous hyperplasia often overlies the tumor cells, which are round to polygonal and have distinct membranes. Small, uniform, eosinophilic fibrolysozomal granules fill the cytoplasm. Scattered, laminated cytoplasmic globules have peripheral halos (residual bodies). Nuclei are small, round to oval, and centrally located. Neurotropic spread along peripheral nerves does occur occasionally.

The histogenesis of granular cell tumor has been a source of controversy since its recognition. Early suggestions that granular cell tumor may have a myoblastic origin have been discounted and use of the term granular cell myoblastoma is now discouraged. Most investigators currently favor a Schwann cell derivation based on immunohistochemical and electron microscopic findings. Immunostain is positive for S-100 protein, peripheral nerve myelin proteins, and neuron-specific enolase. The lysozymes in the granular cell cytoplasm stain positively for CD68. Under electron microscope, degenerated myelinated axons are seen in the cytoplasm of these tumor cells.

Approximately 1% to 2% of granular cell tumors are malignant. The diagnosis of malignancy usually is based on the clinical behavior of the tumor, as there is no set diagnostic histologic criteria for malignancy. Features suggestive of malignancy include size greater than 4 cm, necrosis, metastases to lymph nodes, aggressive clinical behavior, nuclear pleomorphism, and ulceration.

Although granular cell tumors rarely grow back after simple excision, wide local excision usually is recommended. Recurrence is possible. Moh's micrographic surgery with S-100 staining may be beneficial. Evidence of successful treatment with either systemic chemotherapy or radiation is lacking. Due to the potential for recurrence, metastasis, and multiple lesions patients with biopsy confirmed granular cell tumors require regular follow-up with complete physical examinations.

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**CASE PRESENTED BY: Arthur Rhodes, M.D., Darrell W. Gonzales, M.D.**

**History:** This 37 year old African-American female presented with an 8 month history of lesions on her face and back. The lesions were reported to be increasing in size and number with pain and ulceration. Systemic antibiotics from her primary care physician did not improve her course. She denied history of recent travel abroad. She denied fevers, chills, or weight loss. She reported recent headaches and several weeks of intermittent cough, with no response to several trials of systemic antibiotics. The remainder of her review of systems was unremarkable.

**Past Medical History:** The patient's past medical history was significant for non-insulin dependant diabetes mellitus.

**Physical Findings:** Physical examination revealed a well-appearing and well nourished woman who was afebrile. On her left cheek, right oral commisure, and left mid back were well-defined pink verrucous plaques with significant induration and some focal points of erosion. On 10X magnification, there appeared to be small pustules studded throughout the surface. There was submental lymph node enlargement with no evidence of cervical or supraclavicular lymphadenopathy. Her pulmonary examination was unremarkable. There was no enlargement of liver or spleen.

**Laboratory Data**: CBC: normal except for WBC 11.400, with a normal differential.
Erythrocyte sedimentation rate: of 98 mm/hr.
Chest X-ray and CT of the chest demonstrated a left apical posterior nodule measuring 1.2 x 1.6cm, with a left-sided pleural effusion. There was also radiographic evidence of left axillary, mediastinal, left hilar, and perihilar adenopathy.
A bronchoschopy with broncho alveolar lavage was normal, with negative aerobic and anaerobic bacterial and fungal cultures. Sputum gram stain and AFB stains were also negative.
An MRI brain scan without and with contrast demonstrated a peripherally enhancing lesion in the inferior posterior left cerebellar hemisphere with surrounding vasogenic edema.
All other laboratory values were normal.

**Biopsy Description:** A 3.0 mm punch biopsy from the lesion on her right chin demonstrated pseudoepitheliomatous hyperplasia of the epidermis with overlying serum crust and abundant lobular collections of neutrophils. Extending from the papillary dermis into the dermal subcutaneous junction were numerous lobular collections of neutrophils along with a granulomatous infiltrate. Both PAS and Methenamine Silver stains confirmed the presence of rare budding yeast forms, consistent with blastomycosis.

**Diagnosis: Disseminated Blastomycosis**

**Present Course & Therapy:** The patient was initially begun on intravenous Amphotericin B, resulting in diminution in the size of her cutaneous lesions after two weeks. Her course, was complicated by acute tubular necrosis secondary to Amphotericin B nephrotoxicity. After being changed to intravenous

Ambisone, the patient developed cellulitis at the site of her PICC line. Because the patient was reluctant to continue with IV antifungals, she was started on oral Voriconazole 200 mg b.i.d. with the intention of elimination of her disease. She will continue on Voriconazole for a two year course. A repeat MRI of the brain two months into the course of her therapy demonstrated a significant decrease in the size of the peripherally enhancing lesion seen in the left cerebellar hemisphere.

**Discussion:** North American blastomycosis, also known as Gilchrist's or Chicago disease, is an uncommon, highly variable infection caused by the dimorphic fungus *Blastomyces dermatitidis*. It was first described in 1894 by Dr. Gilchrist, a pathologist at Johns Hopkins. An endemic mycosis, most cases of blastomycosis occur in the states surrounding the Mississippi and Ohio rivers, primarily Kentucky, Arkansas, Mississippi, North Carolina, Tennessee, Louisiana, Illinois, and Wisconsin.

Soil from endemic areas is the presumed source of infection, but only a few investigators have successfully recovered the organism from the soil. A review of reported outbreaks indicates no sex, age, race, occupation or seasonal predilection for blastomycosis. Exposure to soil, whether related to work or recreation, appears to be the common factor associated with both endemic and epidemic forms. The incubation period is three weeks to three months after exposure.

The major acquired host defense against *B. dermatitidis* is cellular immunity, which is mediated by antigen-specific T lymphocytes and lymphokine-activated macrophages. In contrast to cellular immunity, specific antibodies against *B. dermatitidis* does not appear to confer resistance to or hasten recovery from clinical infection.

The clinical disease can be classified into types characterized by primary pulmonary, chronic cutaneous, single organ system, and generalized disseminated involvement. Virtually all cases of blastomycosis are thought to begin from a pulmonary portal of entry via inhalation of conidia, with the exception of a few reported cases of direct cutaneous inoculation. If the organism is not cleared by bronchopulmonary macrophages after inhalation, it will multiply in the yeast phase in the lung parenchyma. The acute primary pulmonic infection may be asymptomatic or resemble an atypical pneumonia. Chronic pulmonary involvement includes cavitation, pleural fibrosis, and hilar adenopathy, which may simulate tuberculosis. Pulmonary blastomycosis in asymptomatic patients may be detected by routine radiographs.

Extrapulmonary disease secondary to lymphohematogenous spread has been described in as many as two-thirds of patients with chronic blastomycosis. The most common extrapulmonary sites of infection are skin, bone, and genitourinary tract. CNS involvement is rare, except in immunocompromised patients.

About 80% of patients show skin lesions at some time during the course of disease. Frequently, patients with cutaneous blastomycosis do not have clinically active pulmonary disease. Sites of predilection include the face, mucous membranes, and areas not covered by clothing. Characteristic skin lesions have an advancing verrucous border, often laden with pustules, and an atrophic center.

The diagnosis of blastomycosis is typically made by histopathologic findings and culture. At room temperature, the organism grows rapidly in mycelial phase producing a white and fluffy colony when cultured on Sabaroud's glucose agar. Cultures at body temperature reveal a slow-growing brown and wrinkled yeast colony. On histopathologic examination, the

cutaneous blastomycosis lesion reveals pseudoepitheliomatous hyperplasia with epidermal microabscesses containing giant epithelioid cells, plasma cells, and lymphocytes. A dermal polymorphonuclear infiltrate is present. The cells of Blastomyces dermatitidis may be found lying freely in the tissue or within giant cells. These round yeast forms have characteristic broad-based budding and thick, double-countoured walls. Special staining with periodic acid-Schiff stain or methenamine sliver enhances the visual detection of organisms.

Before antifungal therapy was available, blastomycosis was thought to have a chronic progressive course with eventual dissemination and associated mortality rates of up to 90 percent. Recent studies have reported cure rates of greater than 85 percent and mortality rates less than 10 percent in conjunction with appropriate treatment. When severe or progressive disease occurs, including CNS involvement and/or diffuse pulmonary infiltration, blastomycosis requires systemic treatment with amphotericin B (cumulative doses > 1g). In less severe or limited disease, the azole antifungals, namely itraconazole and ketoconazole, may be of benefit. Itraconazole has been demonstrated to be effective in some advanced cases. The role of fluconazole in the treatment of blastomycosis is limited, with only a few successful outcomes reported to date.

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**Case #18**

**CHICAGO DERMATOLOGICAL SOCIETY**
**RUSH UNIVERSITY MEDICAL CENTER**
**CHICAGO, ILLINOIS**
**MAY 18, 2005**

**CASE PRESENTED BY: Marianne O'Donoghue, M.D., Rachel Altman, M.D.**

**History:** This 8 month-old Asian male presented at 6 weeks of age for evaluation of a rash present on his face and head for 2 weeks.

**Past Medical History:** The patient was born at term via normal spontaneous vaginal delivery to a mother with a history of subacute cutaneous lupus erythematosus diagnosed in April 1997, quiescent at the time of birth.

**Family History:** Mother – history of Subacute Cutaneous Lupus Erythematosus

**Social History:** Patient has achieved developmental milestones

**Physical Examination:** The patient had approximately 10 dime sized erythematous slightly scaling plaques on his forehead, frontal scalp, and periorbitally.

**Laboratory Data:**

Patient:
SSA – 4.91 (nl:0.00-0.89)
SSB – 10.48 (nl: 0.00-0.89)
ANA >= 1:1280 Speckled (nl: <1:40)

Mother:
SSA – 3.72 (nl:0.00-0.89)
SSB – 10.75 (nl:0.00-0.89)
ANA >= 1:1280 Speckled (nl: <1:40)
Intrauterine serial ultrasounds – normal developing four chamber heart with normal pulse
RF – 79 IU/ml (nl: <28)
Anti-DS DNA – 15 IU (nl: 0-22)
Antiscleroderma 70 Ab – 17 U/ml (nl: 0-99)
Anti –RNP Ab/ Anti-Smith Ab - 0.06 (nl:0.00-0.89)
Anti-Smith Ab – 0.09 (nl:0.00-0.89)
C4 – 17 mg/dl (nl: 13-49)
C3 – 109 mg/dl (nl: 77-179)

**Diagnosis:** **Neonatal Lupus Erythematosus**

**Treatment**

**& Course:** One percent hydrocortisone ointment was prescribed however, never administered. The lesions spontaneously began resolving at age 8 weeks and have subsequently completely resolved without sequelae. A pediatric cardiologist was consulted to rule out congenital heart block. Strict sun avoidance was recommended.

**Discussion:** Neonatal lupus erythematosus (NLE) is an autoimmune disease characterized primarily by subacute cutaneous lupus erythematosus lesions and/or cardiac, hepatic and hematologic manifestations. NLE affects approximately 1 in 12,500 live births, in 1-2% of children born to women with SLE, and 15-20% in children born to women with both SLE and anti-Ro antibodies. The majority of these infants are females born of anti-Ro (52kDa and 60kDa SSA) antibody and/or anti-La (48 kDa SS-B) positive mothers, and occasionally anti-nRNP (U1 RNP) positive mothers. Half of the cases manifest skin disease and half have congenital heart block, while ten percent have both findings. The laboratory hallmark of the disease is the presence of autoantibodies directed against the Ro ribonuclear protein. Maternal autoantibodies of the Ro/SSA and La/SSB family are essentially ubiquitous, however only approximately 1-2% of mothers with these autoantibodies will deliver a baby with neonatal lupus. The consistent presence of maternal autoantibodies and the transient nature of the disease implicate maternal autoantibodies as the cause of the disease. Fetal/neonatal injury are presumed to result from the transplacental passage of IgG autoantibodies from the mother (who may have systemic lupus erythematosus, Sjogren's syndrome, or other connective tissue diseases, or may be entirely asymptomatic) into the fetal circulation. The diagnosis rests on compatible cutaneous findings with maternal autoantibodies to Ro and/or La or rarely, to U1 ribonuclear protein.

Cutaneous lesions may be present at birth but more often develop within the first few weeks of life. The cutaneous manifestations are similar to those in subacute cutaneous lupus erythematosus. These lesions are most often localized to the face and scalp with a predilection for the periorbital regions giving an "owl-like" appearance. At the time of the disappearance of the maternal IgG antibodies from the infant's serum, the lesions resolve usually without scarring.

The most common cardiac manifestation is complete heart block, which typically develops in utero during the second or third trimester. Anti-Ro/SSA antibodies are linked to the development of complete congenital heart block. Isolated congenital heart block occurs in 1 in 15,000 to 20,000 live births. The incidence is 15-30% of affected infants. NLE accounts for 80% of all cases of congenital heart block. In some cases, cardiomyopathy may occur simultaneously. Rare cases of endocardial fibroelastosis have occurred in the absence of heart block. Because subsequent post-natal progression of less-advanced degrees of heart block can occur, electocardiography should be obtained on all infants born to mothers with anti-SSA/Ro-SSB/La antibodies. The signature lesion of congenital heart block is fibrosis of the AV node. Studies have suggested that that the congenital heart block occurs as a consequence of unresolved scarring of the AV node secondary to the transdifferentiation of cardiac fibroblasts to unchecked proliferating myofibroblasts which is initiated by maternal autoantibodies. Once established, the complete heart block is irreversible with a 15-30% mortality with two thirds of those affected possibly requiring a cardiac pacemaker.

Several other manifestations include hepatobiliary disease and hematologic cytopenias, both of which are generally self-limited and affect 10% of cases. Three clinical variants of hepatobiliary disease have been observed including:
1) severe liver failure occurring in utero or during the neonatal period
2) infantile transient conjugated hyperbilirubinemia with mild or no elevations of transaminases

3) transient transaminase elevations occurring at 2-3 months of life.
Hematologic manifestations may include thrombocytopenia, neutropenia, or anemia.

The clinical approach to management of a pregnancy in a mother with anti-SSA/Ro antibodies requires serial echocardiographic monitoring in anticipation of a cardiac block that may be developing in utero. The measurement of the mechanical PR interval of the fetal heart has been suggested to be the earliest reliable noninvasive echocardiographic marker of AV nodal dysfunction (first-degree AV block) and/or myocardial injury.

Treatment of the cutaneous lesions is usually with mild topical corticosteroids or topical immunomodulators. Due to the transient nature of the lesions, aggressive treatment is not warranted. Ultraviolet light should be avoided. Approximately half of mothers are asymptomatic at the time of delivery, however some of these women eventually develop symptoms of autoimmune diseases. Monitoring of future pregnancies is necessary because if a anti-Ro (SS-A) positive mother has one child with NLE the recurrence rate of NLE is 25%. If an anti-Ro (SSA) positive pregnant woman is detected by echocardiogram to have a fetus with a conduction defect, long-term oral dexamethasone may be given to deter the inflammatory infiltrate in the neonate's heart. Dexamethasone, unlike prednisone, crosses the placenta. For infants born with isolated congenital heart block, pacemaker implantation and revision is frequently required.

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**Case #19**

**CHICAGO DERMATOLOGICAL SOCIETY**
**RUSH UNIVERSITY MEDICAL CENTER**
**CHICAGO, ILLINOIS**
**MAY 18, 2005**

**CASE PRESENTED BY: Arthur R. Rhodes, M.D., Clarence W. Brown, M.D. and Michael K. O'Donoghue, M.D.**

**History**: This 46 year-old white male presented in March 2005, with multiple asymptomatic soft masses on his arms, legs and torso. The first mass appeared at age 14 on his forearm, and additional masses appeared on his upper arms, back, abdomen, and thighs. A biopsy of a lesion on his back was interpreted as a lipoma. The patient denied a family history of lipomas.

**Past Medical History**: Systemic lupus erythematosus was diagnosed 13 years prior, currently treated with prednisone. He has had lower leg ulcers, deep vein thrombosis and mild depression. He denies diabetes, neuropathy, hypercholesterolemia or alcoholism.

**Physical Findings**: On the forearms, upper arms, lower back, abdomen and thighs are numerous non-tender, moderately firm, mobile masses without surface change. The shoulders, neck and scalp are free of lesions. Neurological and musculoskeletal examinations are normal.

**Biopsy Description:** Left forearm: unremarkable epidermis with a dermal mass of sebaceous lobular proliferation consisting of mature adipocytes separated by fibrous septae.

**Diagnosis**: **Multiple Lipomas**

**Present Course & Therapy**: The patient will return for annual examination, or sooner for symptomatic lesions.

**Discussion**: Lipomas are the most common type of soft tissue tumor, with a prevalence of 2.1 per 1000 people. Predisposing factors include obesity, diabetes mellitus, and elevated serum cholesterol. Multiple lipomas may be seen in patients with one of the lipomatoses, or in the setting of a multi-system syndrome. Conditions that are characterized by multiple abnormalities along with lipomas include Proteus syndrome, Bannayan-Riley-Ruvalcaba Syndrome, Multiple Endrocrine Neoplasia Type I, Frohlich's Syndrome, and Gardner's Syndrome.

Multiple symmetrical lipomatosis (MSL), or Madelung's disease, is characterized by the formation of multiple non-encapsulated, non-tender lipomas with a symmetrical distribution around the neck, shoulders and upper arms, with sparing of distal arms and legs. The onset is usually in the fourth or fifth decades of life with a male predominance, and a high prevalence of individuals of Mediterranean descent. Other significant findings include alcoholism, dyslipidemia, hyperuricemia, impaired glucose tolerance, and somatic or autonomic neuropathy.

Familial multiple lipomatosis is a dominantly inherited syndrome characterized by discrete, mobile, encapsulated, asymptomatic lipomas of the forearms and thighs, with sparing of the shoulders and neck. There is a male predominance, with lesions developing in the third decade of life.

Angiolipomas are clinically similar to lipomas, but they usually measure less than 2.0 cm in diameter and are commonly painful. Two-thirds of lesions are found on the forearms, and less common sites include the trunk and upper arms. Histologic sections show mature adipose tissue with variable number of small vessels that are occasionally occluded with fibrin thrombi. Patients with angiolipomas are typically young adults in their late teens or early twenties.

Our patient is interesting since his clinical presentation does not conform to any of the above noted disorders. His early age of onset, lipoma distribution, and pathology are most compatible with familial multiple lipomatosis; however there is no positive family history, and we have been unable to find literature documentation of spontaneous mutations. The clinical presentation and pathology clearly do not support the diagnosis of MSL or angiolipomas, and presently, there are no other signs or symptoms for Proteus syndrome, Bannayan-Riley-Ruvalcaba Syndrome, Multiple Endrocrine Neoplasia Type I, Frohlich's Syndrome, or Gardner's Syndrome. We present this patient for interest and diagnosis.

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**Case #20**

# CHICAGO DERMATOLOGICAL SOCIETY
# RUSH UNIVERSITY MEDICAL CENTER
# CHICAGO, ILLINOIS
# MAY 18, 2005

**CASE PRESENTED BY: David Eilers, M.D. and Anthony Peterson, M.D.**

**History:** This 53-year-old gentleman of Mediterranean heritage was referred to our clinic for a one-year history of mildly painful, violaceous, purpuric plaques and patches on the feet. Prior attempts at treatment, including topical Terbinafine and oral Ciprofloxacin had failed. His course had been complicated by periods of superficial ulcerations and mild drainage. He was begun on vinegar soaks and chlorhexidine washes twice daily, along with Keflex 500mg qid after a swab grew out Acinetobacter Baumannii. After failure to improve, Peripheral Vascular Surgery was consulted for evaluation of arterial and venous insufficiency and two 4mm punch biopsies were performed on the left medial ankle and sent for culture and H&E. Tissue culture returned showing multiple bacterial organisms. Histology returned showing changes consistent with severe stasis dermatitis. Later, a repeat biopsy was performed on the left 3rd submetatarsal head and sent for histology and stains for CD34 due to concern for Kaposi's Sarcoma.

**Past Medical History:**
Quadriplegic and Anarthric since 1972 secondary to a basilar artery thrombosis
Communicates through the use of a keyboard and voice speaker
Prior multi-drug resistant urinary tract infections

**Physical Findings:** The patient exhibited mildly tender, violaceous macules and patches with surrounding petechiae and exudates at the bilateral bases of the third submetatarsal heads. Similar violaceous patches were seen on the lateral and medial malleoli. Scattered areas of petechiae were also noted on the dorsum of the feet. Mild edema and strong dorsalis pedis pulses were palpable bilaterally.

**Laboratory Data:** The following were normal or negative:
Complete Metabolic Panel
Complete Blood Count
Urinalysis
Hepatitis C Screen
Cryoglobulins
Erythrocyte Sedimentation Rate
Fibrinogen
Ankle Brachial Index
Arterial Dopplers
AFB, Fite and Fungal stains on tissue biopsy

The following were abnormal or positive:

C-Reactive Protein: 2.0 mg/dL (0.0 – 0.5 mg/dL)

Wound Swabs and Tissue Cultures grew:

Staph Aureus
Acinetobacter Baumannii
Pseudomonas Aeruginosa
Klebsiella Pneumoniae
Beta Hemolytic Streptococcus
Enterococcus Faecalis

**Biopsy Description:** A shave biopsy of the skin from the 3rd left submetatarsal head shows proliferation of small, regular, vascular spaces and narrow vascular channels in the superficial dermis. Vascular channels are lined with spindle cells lacking atypical nuclei. Extravasated red blood cells and hemosiderin deposition is noted. Staining with CD34 highlights endothelial cells but not the surrounding perivascular cells.

**Diagnosis:** **Acroangiodermatitis of Mali**

**Present Course & Therapy:** The patient has continued to improve on vinegar and water soaks twice daily, elevation and topical antibiotic therapy with Clindamycin . However, he recently developed a suppurative infection of the left 3rd digit, which resulted in swelling and pain. A repeat culture again grew out multiple organisms and he was placed on oral Gatifloxacin 400mg daily with slow improvement.

**Discussion:** Acroangiodermatitis is a rare, benign process involving the feet, first described in 1965 by Mali in 18 male patients, aged 30 to 60 years, with chronic venous insufficiency. Originally described as peculiar purple "eggplant-colored" macules and plaques on the extensor side of the digits of the foot, Acroangiodermatitis usually occurs in areas without direct pressure. Mali also noted reticular pigmentation of the ankles centered under the malleoli, preservation of arterial pulses, elevated venous pressures and edema of the ankle or foot.

Since it's initial description, several other authors (Stewart, Bluefarb and Adams) have noted similar lesions in patients with congenital arteriovenous malformations of the lower extremity, later termed Stewart-Bluefarb syndrome. Several other cases have been described in Klippel-Trenaunay Syndrome and poorly fitting suction- type prostheses in patients with lower extremity amputations. Cases of upper extremity Acroangiodermatitis have been found in patients with iatrogenic arteriovenous shunts for hemodialysis. Chronic leg dependency and paralysis have also been show to predispose to Acroangiodermatitis

Although the etiology of Acroangiodermatitis is unknown, it is felt that chronic edema, venous stasis and tissue hypoxia may result in fibroblast proliferation and neovascularization.

It is felt by some to be a severe form of stasis dermatitis. Several case reports have shown association with homozygous activated protein C resistance.

Histologically, Acroangiodermatitis closely resembles and may be mistakenly diagnosed as Kaposi's Sarcoma (KS). Several authors use the term Pseudo-Kaposi's Sarcoma interchangeably. Acroangiodermatitis differs from KS by the regularity of the proliferating vessels and lack of jagged and irregular spaces. Additionally, there is absence of splitting of collagen bundles by vessels, absence of the tendency of proliferating vessels to surround pre-existing blood vessels, commonly seen in KS. Absence of atypical nuclei, more prominent edema and hemosiderin deposition also help distinguish Acroangiodermatitis from KS. Most recently the use of CD34 staining has been used to help differentiate the two diseases, with only the endothelial cells in Acroangiodermatitis staining positively for CD34, while KS stains not only the endothelial cells, but the surrounding perivascular cells as well. Some authors also advocate staining for HHV-8.

Treatment includes elevation and compression to reduce venous pressures, along with meticulous foot care. Surgical ligation and embolization of feeding vessels have shown some improvement in extreme cases, but recurrences are frequent. Several case reports of improvement with oral Erythromycin have been seen in patients with Acroangiodermatitis involving the upper extremities in iatrogenic shunts.

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**Case # 21**

# CHICAGO DERMATOLOGICAL SOCIETY
# RUSH UNIVERSITY MEDICAL CENTER
# CHICAGO, ILLINOIS
# MAY 18, 2005

## CASE PRESENTED BY: Arthur R. Rhodes, M.D. and Michael K. O'Donoghue, M.D.

**History:** The patient is a 55 year-old African American male who presented with a 23 year history of a lesion on the scalp. The lesion was first noted by the patient's wife on his return from Vietnam in 1970. Initially, the lesion was described as a "small, black, pin head sized spot" which gradually enlarged on the back of his head. There were no associated symptoms except for occasional bleeding with minimal trauma. The patient had been treated at a veteran's hospital with various topical ointments and creams without resolution of the lesion.

**Physical Findings:** Dark brown hyperpigmented, vegetative, non-tender, 27x32x2 mm exophytic plaque on the occipital scalp. No lymphadenopathy was noted, and there were no other suspicious lesions found on total mucocutaneous examination.

**Biopsy Description:** Basal cell cancer of mixed type with nodular and micronodular pattern with cystic changes. Melanin pigment is found primarily within the basaloid tumor islands. The basaloid proliferation is embedded in a collagineous stroma that is myxoid and fibrotic, with scattered melanophages.

**Diagnosis:** **Pigmented Basal Cell Carcinoma**

**Present Course & Therapy:** The patient underwent a Mohs procedure with an O to T rotation flap repair. There has been no recurrence of the tumor after 24 months of follow-up.

**Discussion:** Nonmelanoma skin cancer is the most common malignancy in the United States, with an estimated incidence of over one million cases per year. In the white population, the incidence is 233 cases per 100,000 per year, while in the black population, the annual age-adjusted incidence is 3.4 cases per 100,000. In Africa, the incidence of basal cell carcinoma has been found to comprise 2.5 to 8% of all cutaneous cancers. Basal cell carcinoma is the most common form of nonmelanoma skin cancer in the white population, and basal cell carcinoma is second to only squamous cell carcinoma in the black population.

In two large studies at primarily African-American hospitals (Howard University and Charity Hospitals) in the United States, a retrospective review of skin cancer in the African-American community over three decades found a total of 68 basal cell carcinomas. Lesions were found in most patients between the $5^{th}$ and $7^{th}$ decades of life, with both sexes equally affected. The lesions were usually solitary, and metastatic disease was found in only one case. Of these cases, over 88% were found on the head and neck. These findings are similar to those in the white population, in which there is a greater proportion of basal cell carcinoma on the head and neck corresponding with increased age at diagnosis. The clinical features of basal cell carcinoma in African-American blacks are essentially identical to those found in other ethnic groups. Classically, there is a pearly rolled boarder with central ulceration and telangiectasias, but the lesion can appear as a papule, nodule, plaque, or an indurated or pedunculated mass.

The pigmented basal cell carcinoma may be mistaken for other pigmented tumors, including melanoma.

The frequency of pigmented basal cell carcinoma in the white population is about 6-7% of all basal cell carcinomas. In contrast, pigmented basal cell carcinoma accounts for 67% of all basal cell carcinomas occurring in African-American blacks. In both groups, the most common histological patterns of pigmented basal cell carcinoma is the nodular/micronodular variant, with characteristic nests or cords of small, dark staining epithelial cells, with palisading of peripheral cells. There are varying degrees of pigment, but the majority of pigment is found within melanophages, with a small amount found free in the dermis. This pigment is melanin. In the pigmented areas, melanocytes are found along the basement membrane and interspersed among tumor cells in the central parts of the tumor nests. These melanocytes tend to be twice the size of those found in nonpigmented areas and possess hypertrophic dendritic processes in the majority of cases. Other common findings in pigmented basal cell carcinoma are lymphocytic infiltration in the dermis, ulceration, and rare or absent mitotic figures.

Skin type may have a significant role in finding melanin in basal cell carcinomas. The Howard University study found that of the patients with pigmented basal cell carcinoma, almost 67% of the patients had fair or olive skin, as compared to 10% of randomly chosen individuals without history of basal cell cancer. Pigmented basal cell carcinoma is also found with increased frequency in the Hispanic population. One prospective study demonstrated the presence of pigment in 66% of all basal cell cancer in that population. It was also found that in the non-Hispanic population, patients who did have pigmented basal cell carcinoma tended to have darker skin, with skin types III and IV predominating. The mechanisms of melanocyte activation and melanin production in pigmented basal cell carcinoma are unknown.

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