Chicago Dermatological Society

October 2011
Monthly Educational Conference

Program Information
Continuing Medical Education Certification
and
Case Presentations

Wednesday, October 12, 2011

David Fretzin Lecture

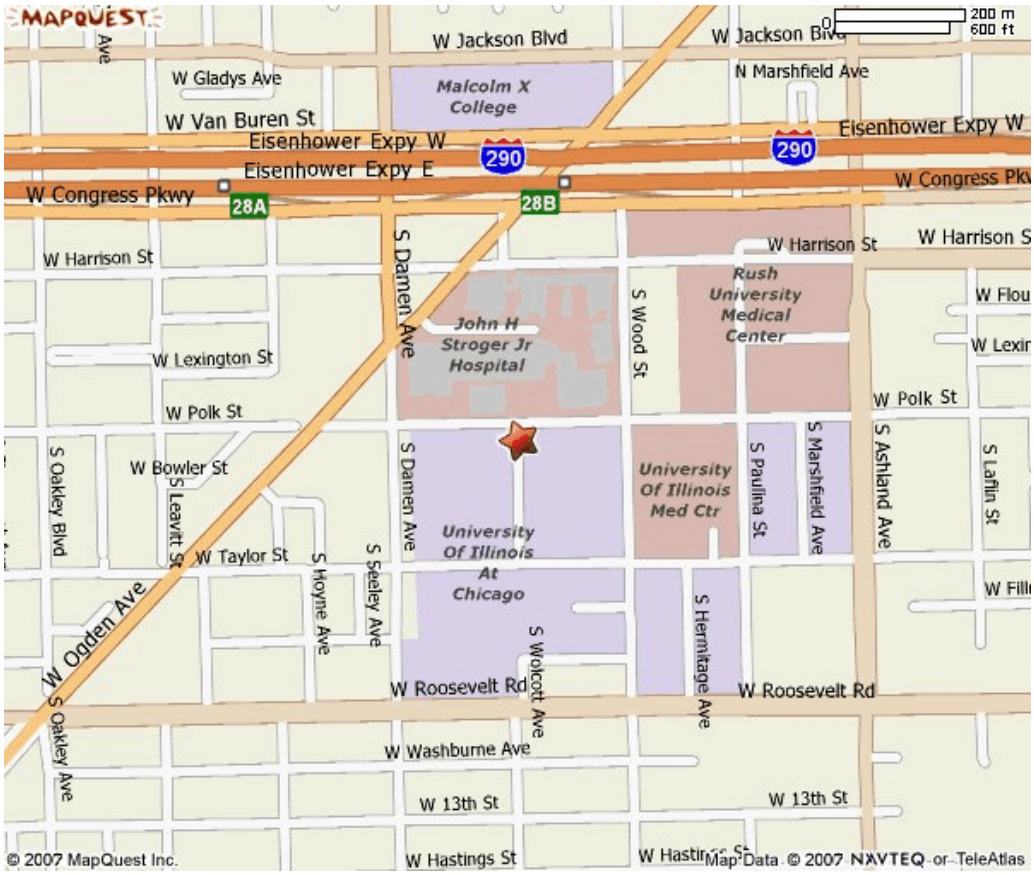
Conference Host:
Department of Dermatology
University of Illinois at Chicago
Chicago, Illinois

University of Illinois at Chicago

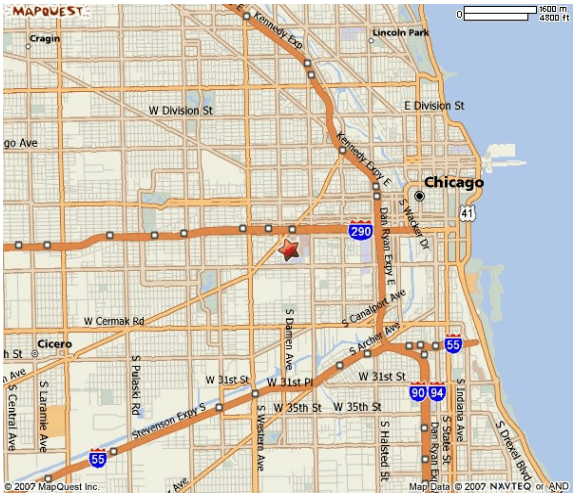
- UIC Student Center West (SCW) - 828 S. Wolcott Ave., 2nd Floor
  Registration, lectures, slide viewing, lunch and committee meetings
- UIC Outpatient Care Center, Dermatology Clinic - 1801 W. Taylor, Suite 3E
  Patient viewing only (no registration at this location! Protocol books will be available.)

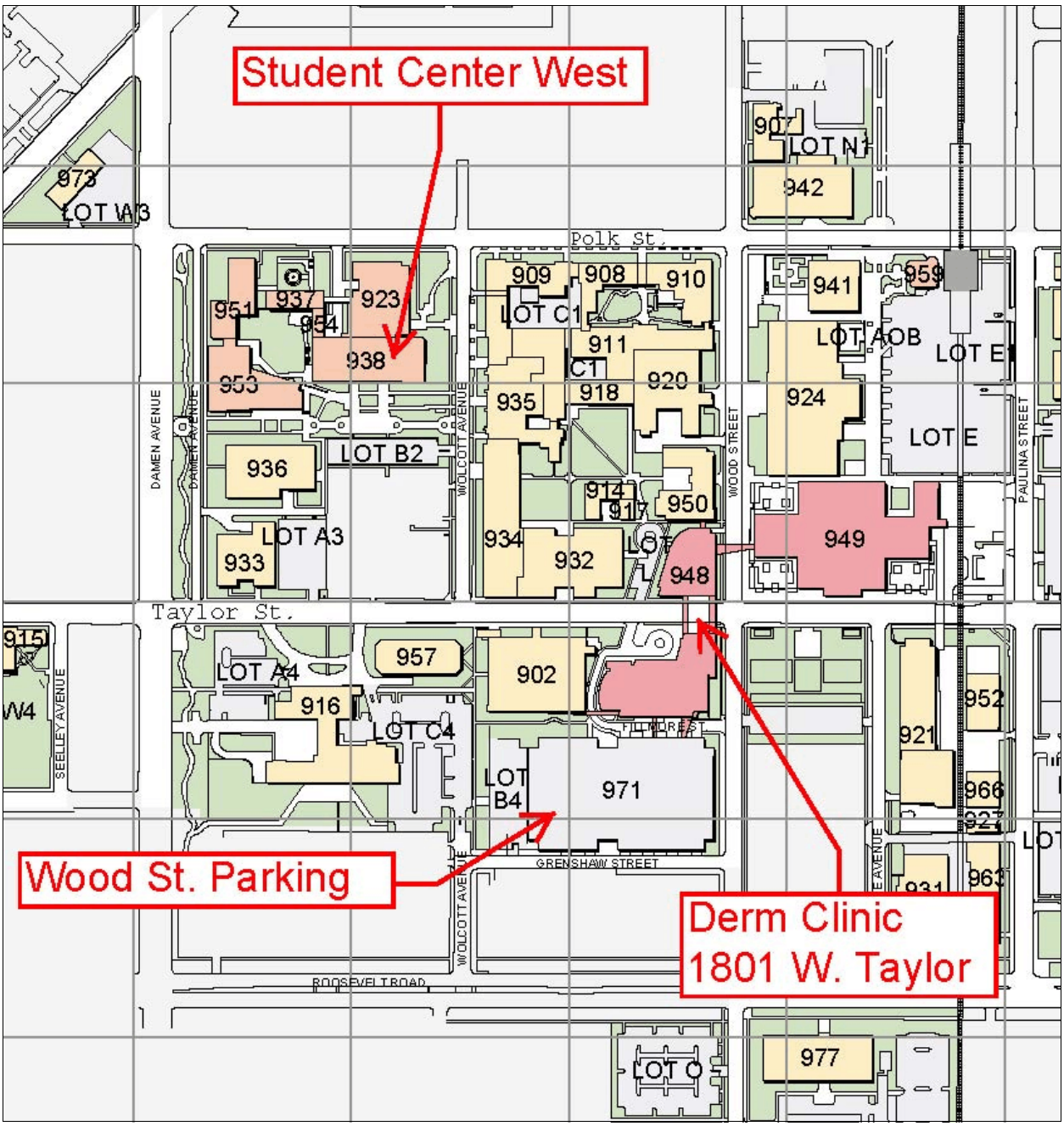
UIC parking – Use the Wood Street Parking Structure, 1100 S. Wood at the intersection of (Wood & Grenshaw, just south of the UIC Outpatient Care Center)

See reverse side for detailed campus map



From the Eisenhower Expressway, exit at Ashland/Paulina. Proceed south on Ashland to Taylor. Turn west on Taylor approximately two blocks to Wood St. Turn south on Wood for the entrance to the parking lot.

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Program

Conference Locations

Student Center West (SCW) – 828 S. Wolcott, 2nd Floor
Dermatology Clinic, 1801 W. Taylor St., Suite 3E

8:00 a.m.	**Registration Opens** *Student Center West, 2nd floor Foyer*
9:00 a.m. - 10:00 a.m.	**Resident Lecture** – *SCW Chicago Room A-C* "Spectrum of CD30+ Lymphoproliferative Diseases" *Samuel Hwang, MD, PhD*
9:30 a.m. - 10:45 a.m.	**Clinical Rounds** Patient & Poster Viewing *Dermatology Clinic, Suite 3E* Slide Viewing *Student Center West, Room 213 A/B*
11:00 a.m. - 12:15 p.m.	**General Session** - *SCW Chicago Room A-C* FRETZIN LECTURE: "An Update on Th17 Cells in Psoriasis" *Samuel Hwang, MD, PhD*
12:15 p.m. - 12:45 p.m.	**Box Lunches & visit with exhibitors** *SCW - 2nd Floor Foyer*
12:45 p.m. - 1:00 p.m.	**CDS Business meeting** – *SCW Chicago Room A-C*
1:00 p.m. - 2:30 p.m.	**Case Discussions** – *SCW Chicago Room A-C*
2:30 p.m.	**Meeting adjourns**

Mark the Date!

Next CDS monthly meeting – ***Saturday***, November 19, 2011 at the University of Chicago; Martin Weinstock, MD, PhD from Brown Medical School, Providence, Rhode Island

Watch for details on the CDS website: www.ChicagoDerm.org
Save time and money – consider registering online!

Guest Speaker

SAMUEL T. HWANG, MD, PHD

Chairman & Professor
Department of Dermatology
Medical College of Wisconsin
Milwaukee, WI

Delivering the David Fretzin Lecture

Dr. Hwang is a nationally recognized cancer researcher and physician. He earned his PhD from the University of Basle in Switzerland (1989) and received his Doctor of Medicine from Harvard Medical School (1991). After completing an internship at Brigham and Women's Hospital, Boston, he finished his dermatology residency at the University of California-San Fernando (1995).

Dr. Hwang previously has been a senior investigator at the National Cancer Institute. His interests are in skin cancers, including melanoma and cutaneous T-Cell lymphomas.

University of Illinois at Chicago
Department of Dermatology

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Amanda Cooper, MD
Eliana Krulig, MD
Adrienne Schupbach, MD
Karl Vance, MD

First Year

Juliana Choi, MD, PhD
Patricia Dymek, MD
Steven Kahn, MD
Amanda Silverio, MD
David Smart, MD

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Case # 1

Case Presented by Juliana Choi, MD, PhD, Renuka Bhatt, MD
Iris Aronson, MD, and Lawrence Chan, MD

Patient A

History of Present Illness:
This 58 year old male presented in April 2011 with a three month history of a painful ulceration on the right buttock. The lesion began as a "boil" and within a few days ulcerated and continued to rapidly enlarge. Prior treatments included two debridements and multiple antibiotics, both oral and intravenous, including ciprofloxacin, clindamycin, levofloxacin, piperacillin/tazobactam, trimethoprim/sulfamethoxazole, and vancomycin. He had a similar eruption in 2007 on the right chest which was eventually treated with a skin graft and healed.

Past Medical and Surgical History:
Skin graft in 2007 and two debridements

Medications:
None

Allergies:
No known drug allergies

Family History:
Father with non-melanoma skin cancer and psoriasis; grandmother with history of breast cancer

Review of Systems:
The patient denies fevers, chills, weight loss, oral erosions, shortness of breath, arthralgias, or fatigue.

Physical Examination:
A solitary 13 cm x 13 cm, red, tender ulceration with rolled borders, surmounted by yellow discharge is noted over the right lateral buttock. Extending from the medial border is a violaceous 4 cm x 4 cm non-ulcerated plaque.

Laboratory Data:
The following were positive or abnormal:
Serum protein electrophoresis detected an M-spike in the gamma region. The monoclonal protein peak accounts for 0.87 g/dL of the total 1.40 g/dL of protein in the gamma region. Serum immunofixation pattern shows an IgG type kappa monoclonal protein with an additional faint band in IgA. Urine protein electrophoresis detected monoclonal free kappa light chains. Urine immunofixation pattern shows faint bands in IgG and IgA.

The following were negative or within normal limits:
Anaerobic culture of right buttock, complete blood count with differential, complete metabolic panel, cryoglobulins, desmoglein 1 and 3 antibodies, antiphospholipid antibody panel, anticardiolipin antibodies, proteinase-3 antibody, and myeloperoxidase antibody.

Diagnostic Procedures and Tests:
Bone marrow aspirate (05/24/11): There is slightly hypocellular marrow with orderly trilineage hematopoiesis, and a focal, slight increase of plasma cells (5-9% on core biopsy by CD138 immunohistochemical study).

Bone survey (05/18/11): No osteolytic lesions.

Histopathology/Immunopathology:
Border of ulcer on right buttock, skin: Sections show a diffuse dermal infiltrate predominantly of neutrophils, with a small number of eosinophils and lymphocytes. This is associated with superficial dermal edema and dilated small blood vessels. Some of the endothelial cells are swollen. The overlying epidermis is hyperplastic with spongiosis and exocytosis of neutrophils.

Direct immunofluorescence, right buttock, peri-lesional skin: Sections revealed IgA and IgG positive cytoid bodies at the lower epidermis and upper dermis. There is no staining to indicate an immunobullous disorder.

Diagnosis:
Pyoderma gangrenosum with monoclonal gammopathy of undetermined significance

Treatment and Course:
Treatment began with prednisone 20mg daily and doxycycline 100mg twice daily. He immediately noticed significant pain reduction upon initiation of therapy and also noted a mild reduction in size. Dapsone 25mg daily was added as a steroid sparing agent and he was also started on tacrolimus 0.1% ointment twice daily. The lesion on his right buttock continued to improve, but he then developed a new similar periumbilical lesion. Dapsone was increased to 50mg daily and prednisone to 40mg daily. Both lesions are now healing well and prednisone is being tapered. Hematology/oncology work-up demonstrated monoclonal gammapathy of undetermined significance and continued monitoring without treatment was recommended.

Patient B

History of Present Illness:
This 54 year old male presented with an 8 year history of bumps on his face, ears, neck, arms, and legs. The lesions on his arms and legs began while he was in Iraq in 2003 and were pruritic. They progressed to involve his neck and in 2008 he developed numerous bumps on his face and ears. He has undergone 8 laser treatments to treat his face in the past with minimal improvement.

Past Medical and Surgical History:
Diabetes mellitus, hypertension, gastroesophageal reflux, diverticulitis, cataracts, bilateral carpal tunnel syndrome in 2008, right biceps tendon rupture and right rotator cuff tear in 2010, chronic knee pain from previous bilateral anterior cruciate ligament tears, bilateral meniscal degeneration, and previous left meniscal tear in 1988, degenerative disc disease with disc bulges at C3-4 and C4-5, and central stenosis at C3-4 and C4-5

Medications:
Amlodipine, bisacodyl, docusate, hydrochlorothiazide/triamterene, metformin, aspirin, fluticasone nasal spray, and cetirizine

Allergies:
Lisinopril – develops angioedema; sulfa – develops tongue and lip swelling

Review of Systems:
The patient reports numbness over the pre-auricular skin, ear swelling, headache, chronic knee and back pain, and chronic hand numbness and tingling after an injury in 2010. He denies fevers, chills, weight loss, vision changes, dysphagia, dyspnea on exertion, chest pain, muscle weakness, strokes, or seizures.

Physical Examination:
There are multiple flesh-colored to slightly pink papules over the nasal bridge clustered into a plaque over the nasal root and innumerable 1-3 mm similar flesh-colored papules on the forehead. The posterior scalp has few flesh-colored papules. The ears have diffuse thickening with a hint of nodularity over the helices

and ear lobules, and there are clusters of flesh-colored papules in bilateral posterior auricular regions. Bilateral arms have innumerable 1-2 mm folliculocentric flesh-colored papules. The upper back has few scattered similar flesh-colored papules. The chest and abdomen are clear. Bilateral legs have multiple 1-2 mm folliculocentric flesh-colored to slightly hyperpigmented papules.

Laboratory Data:
The following were positive or abnormal:
Serum protein electrophoresis detected a 0.78 g/dL monoclonal protein peak in the gamma region. Serum immunofixation pattern shows an IgG type kappa monoclonal protein.

The following were negative or within normal limits:
Complete blood count with differential, complete metabolic panel, thyroid stimulating hormone

Diagnostic Procedures and Tests:
Bone marrow aspirate (01/24/11): Not indicated as the monoclonal protein peak is less than 1.5 g/dL.

Bone survey (06/21/11): No osteolytic lesions.

Histopathology:
Left glabella and right posterior ear lobe, skin: Sections of both biopsies show similar changes. There is proliferation of plump fibroblasts in the upper dermis, associated with increased dermal mucin, and mild perivascular infiltrate of lymphocytes and a few plasma cells. The increased mucin is highlighted by colloidal iron stain.

Diagnosis:
Scleromyxedema

Treatment and Course:
Multiple treatment options including acitretin, isotretinoin, systemic corticosteroids, intravenous immunoglobulin, mycophenolate mofetil, cyclophosphamide, and methotrexate were considered. Treatment with acitretin 10mg daily for one month then increased to a goal of 25mg daily was discussed with the patient. He will research the medication and return to clinic to initiate treatment. Hematology/oncology work-up demonstrated monoclonal gammapathy of undetermined significance and continued monitoring without treatment was recommended.

Discussion:
Monoclonal gammopathies are characterized by a clonal proliferation of plasma cells that produce a homogenous or monoclonal immunoglobulin protein. These disorders include monoclonal gammopathy of undetermined significance (MGUS), multiple myeloma, Waldenstrom macroglobulinemia, heavy chain diseases, plasmacytoma, and primary amyloidosis. MGUS accounts for greater than 60% of monoclonal gammopathies.

MGUS is found in approximately 3% of patients older than 70 years of age. It is associated with a monoclonal paraprotein band less than 3g/dL, bone marrow aspirate with less than 10% plasma cells, absence of or a small amount of M protein in the urine, and without radiographic evidence of lytic lesions, and without laboratory evidence of anemia, hypercalcemia or renal insufficiency. MGUS does not require treatment but is closely monitored as there is a risk of progression to multiple myeloma. IgG gammopathy is the most common type overall, however, some skin disorders associated with monoclonal gammopathies have demonstrated an increased incidence of IgA gammopathy.

Multiple skin disorders have been associated with monoclonal gammopathies. They are divided into 4 groups: [1] skin disorders that are infiltrative and result from either extension and proliferation of malignant plasma cells in the skin (e.g. Waldenstrom macroglobulinemia cutis, primary cutaneous plasmacytoma, osteosclerotic myeloma/polyneuropathy, organomegaly, endocrinopathy, monoclonal

gammopathy, and *s*kin changes [POEMS]) or deposition of protein related to the primary M protein (e.g. primary AL amyloidosis, type I cryoglobulinemia); [2] skin disorders that are not due to malignant cell infiltration or deposition but have a strong association with monoclonal gammopathy (e.g. scleromyxedema, scleredema, necrobiotic xanthogranuloma, plane xanthoma, Schnitzler syndrome, pyoderma gangrenosum, Sweet syndrome, leukocytoclastic vasculitis, neurophilic dermatosis, erythema elevatum diutinum, subcorneal pustular dermatosis); [3] skin disorders anecdotally associated with monoclonal gammopathy; and [4] skin disorders related to M proteins but not specific for the diagnosis of monoclonal gammopathy.

Pyoderma gangrenosum (PG) is a rare ulcerative disorder of the skin classified into classic (or ulcerative), bullous, pustular, or vegetative types. Clinically, PG is characterized by rapidly enlarging pustular papules and plaques that ulcerate with violaceous borders and a necrotic base. Diagnosis can oftentimes be difficult as there are no pathognomonic findings on pathology. A combination of biopsy to rule-out other causes of cutaneous ulcers, negative cultures, and clinical exam can help with diagnosis. PG is idiopathic in 25-50% of patients, however, it has been associated with a variety of diseases most commonly monoclonal gammopathy, inflammatory bowel disease, and rheumatoid arthritis. There is no gold standard of treatment but a variety of treatment modalities have been successfully implemented. Classic ulcerative PG is oftentimes treated with high-dose oral corticosteroids. For lesions that do not fully resolve or are unresponsive, corticosteroid-sparing agents may be added such as dapsone, cyclosporine, methotrexate, and thalidomide. Intravenous immunoglobulin and biologic agents have also been used successfully.

Scleromyxedema, also known as papular mucinosis or generalized lichen myxedematosus, is a rare disorder characterized by a widespread, grouped, flesh-to-cream-colored or erythematous, firm, waxy mucinous papules and plaques and diffuse thickening of the skin. Small papules of 2-3mm in size often erupt in clusters with symmetric distribution on the face, neck, upper trunk, forearms, and hands. Histologically, there is diffuse mucin deposition in the papillary and reticular dermis, stellate fibroblasts, and a perivascular inflammatory infiltrate. In addition to the cutaneous and histologic findings, scleromyxedema is characterized by a monoclonal gammopathy and the absence of thyroid disease. Scleromyxedema is a chronic and progressive disease and is frequently associated with extracutaneous manifestations including gastrointestinal, neurologic, muscular, and pulmonary complications. A variety of treatment modalities have been tried but treatment is difficult. Melphalan, systemic corticosteroids, plasmapheresis, isotretinoin, etretinate, topical corticosteroids, intralesional corticosteroids, and others have been tried with variable success.

Essential Lessons:

- A wide spectrum of skin disorders, including pyoderma gangrenosum and scleromyxedema, have been associated with monoclonal gammopathies.
- Skin manifestations may be the initial presentation of an underlying monoclonal gammopathy.

References:

1. Daoud MS, et al. Monoclonal gammopathies and associated skin disorders. *J Am Acad Dermatol.* 1999; 40(4): 507-535.
2. Rongioletti F, et al. The histological and pathogenetic spectrum of cutaneous disease in monoclonal gammopathies. *J Cutan Pathol*. 2008; 35(8): 705-721.
3. Decaux O, et al. Systemic manifestations of monoclonal gammopathy. Eur J Intern Med. 2009; 20(5):457-461.
4. Miller J, et al. Pyoderma gangrenosum: a review and update on new therapies. J Am Acad Dermatol. 2010; 62(4):646-654.
5. Ruocco E, et al. Pyoderma gangrenosum: an updated review. J Eur Acad Dermatol Venereol. 2009; 23(9):1008-1017.
6. Pomann JJ, Rudner EJ. Scleromyxedema revisited. Int J Dermatol. 2003; 42(1):31-35.
7. Cokonis Georgakis CD, et al. Scleromyxedema. Clin Dermatol. 2006; 24(6):493-497.

Case # 2

Case Presented by Brendan Thomas, MD, Michelle Bain, MD and Aaron Dworin, MD

History of Present Illness:
This 7 year old male presented with an approximately four month history of worsening skin firmness over the entirety of the body. The skin changes occurred gradually, and without other associated symptoms. Several weeks prior to onset the patient had traveled to Mexico with his family, at which time his long standing eczema was noted to have worsened, characterized by several opens sores with overlying crusts located on the arms. His mother also stated the patient had been treated with oral antibiotics three months prior for a streptococcal pharyngitis.

Past Medical and Surgical History:
Atopic dermatitis, allergic rhinitis

Medications:
Fluticasone propionate 0.005% ointment and urea 40% lotion

Allergies:
No known drug allergies

Family History:
Diabetes mellitus

Social History:
The patient is adopted and has normal development.

Review of Systems:
The patient denies changes in vision, palpations, muscle or joint pain, limitation of eye, mouth, or other body movements, or difficulties swallowing or breathing.

Physical Examination:
The skin on the head, neck, trunk, and extremities was indurated. The induration was most prominent over the face, upper torso and arms, with the lower legs noted to be less indurated by comparison. The antecubital fossa and wrists where characterized by hyperpigmented, lichenified plaques. Folliculocentric, monomorphic, hyperkeratotic papules were noted on the bilateral posterolateral upper arms and central chest. He had no difficulty opening the mouth or protruding the tongue, and all joints had full range of motion.

Laboratory Data:
The following were positive or abnormal:
Eosinophil percentage 10% (0-7), absolute eosinophil count 0.8 thousand/mm3, erythrocyte sedimentation rate 16mm/hr (0-15)

The following were negative or within normal limits:
Basic metabolic panel, total serum protein, serum immunofixation electrophoresis, glucose, calcium, liver function tests, creatine phosphokinase, antinuclear antibody assay, thyroid function tests, urinalysis

Histopathology:
Left dorsal forearm, skin: Multiple sections show markedly thickened dermis with collagen extending into the subcutis. The collagen fibers are separated from one another. The Alcian blue stain highlights increased dermal mucin between collagen fibers.

Diagnosis:
Scleredema Type 1

Treatment and Course:
Aside from skin induration the patient was asymptomatic; therefore, given that no reliably helpful treatments are known, the patient and family were counseled regarding the generally self-limited nature of type 1 scleredema, and encouraged to observe the skin for gradual resolution over the next six to twenty-four months.

Discussion:
Scleredema is an idiopathic condition characterized by thickening of the dermis from increased deposition of mucin. Depending on the clinical presentation, this condition may be divided into three types: (1) following an acute febrile illness, (2) occurring without preceding illness and associated with a monoclonal gammopathy, and (3) associated with preexisting diabetes mellitus. With regard to type 1, most cases develop within ten weeks of the antecedent acute febrile illness — conditions often infectious in etiology, with streptococcal pharyngitis and pyoderma being two more common causes. Cases of scleredema type 1 may be benign and self-limited; however, the course can be complicated by several sequelae resulting from the tight skin, including dysphagia and impaired range of motion. Numerous other associations have also been reported with this type, including myositis, pericardial effusions, and hyperparathyroidism. In less straightforward cases the differential diagnosis includes disabling pansclerotic morphea of childhood, and other disorders characterized by increased mucin deposition like papular mucinosis, lupus erythematosis, and dermatomyositis. No reliably helpful treatments are known, but resolution of type 1 cases often occurs within six to twenty-four months after presentation.

Essential Lessons:
- Scleredema is an idiopathic condition of increased dermal mucin deposition.
- Type 1 cases follow an acute febrile illness and usually resolve within 6 to 24 months.

References:

1. Rongioletti F, Rebora A. Mucinoses in Dermatology. Second Edition. Bolognia JL editor in chief. Spain: Elsevier Limited, 2008:616.
2. Cron RQ, Swetter SM. Scleredema revisited. A poststreptococcal complication. *Clin Pediatr*. 1994;33(10): 606-610.
3. O'Connell TX, et al. Understanding and interpreting serum protein electrophoresis. *Fam Physician*. 2005;71(1): 105-112.
4. Paller AS, Mancini AJ. Hurwitz Clinical Pediatric Dermatology. Fourth Edition. Saunders, 2011. Pg 518.
5. Parmar RC, et al. Scleredema adultorum. *J Postgrad Med*. 2000;46(2): 91-3.

Case # 3

Case Presented by Eliana Krulig, MD
and Aleksandar Krunic, MD, PhD

History of Present Illness:
This 58 year old male was referred to our clinic for evaluation of a nasal growth. Two months prior to presentation, he noted a small pimple on the left side of his nose that had been rapidly enlarging. The lesion occasionally bled. He denied any trauma to the area. Patient reported traveling to St. Louis, Indiana and Kentucky within the prior six months.

Past Medical and Surgical History:
Diabetes, dyslipidemia, cholecystectomy

Medications:
Lisinopril, metformin, metoprolol, and colesevelam

Allergies:
Penicillin – develops hives; Intravenous contrast media – develops hives

Family History:
No history of skin cancer

Social History:
The patient works as a teacher in Chicago. He reports occasional alcohol intake, but denies tobacco use.

Review of Systems:
The patient reports an intentional weight loss of 20 pounds over the prior year. He denies fever, chills, weakness, shortness of breath, cough, hemoptysis, skin rash, nausea, vomiting, diarrhea or headache.

Physical Examination:
Over the left nasal wall extending to the nasal tip there is a 4x4 cm well-defined, exophytic, verrucous plaque surrounded by a rim of erythema, with an area of central ulceration and purulent drainage. There are no palpable cervical, post-auricular, occipital, submental or axillary lymph nodes.

Laboratory Data and Diagnostic Procedures:
The following were positive or abnormal:
Chest computed tomography revealed patchy bandlike infiltrates within the left mid lung, possibly representing inflammatory process. No evidence of lymphadenopathy or pleural effusions.
Brain MRI with and without contrast showed abnormal signaling in the paranasal sinuses greatest in the maxillary and sphenoid regions. No acute intracranial process was identified.

The following were negative or within normal limits:
Complete blood count with differential, complete metabolic panel, HIV, lipid panel, chest X-ray

Histopathology:
Left nasal wall, skin: Multiple sections show marked pseudoepitheliomatous hyperplasia associated with predominantly suppurative and focally granulomatous inflammation. Multiple thick-walled fungal spores measuring 10 to 12 microns are identified. Single broad-based budding is present focally. The fungal elements are highlighted by Periodic Acid-Schiff (PAS) and Gomori Methenamine Silver (GMS) stains.

Diagnosis:
Cutaneous Blastomycosis

Treatment and Course:
Oral itraconazole was started at a dose of 200 mg twice daily, and he experienced a rapid improvement in the size and appearance of the nasal lesion. After ten weeks of treatment, the patient self-discontinued the

medication. When seen in clinic for follow up, a new 3 mm erythematous papule was noted superior to the right lateral eyebrow, and biopsy of this lesion returned consistent with blastomycosis. Itraconazole was restarted and progressive improvement of the skin lesions was noted, though a residual pink, scarred patch remained, causing notching deformity of the left alar rim. The patient completed 6 months of continuous therapy.

Discussion:

Blastomycosis is a granulomatous and suppurative fungal infection caused by the dimorphic fungus *Blastomyces dermatitidis*, a condition first described by Gilchrist in 1894. In North America, most cases are seen in individuals living in endemic areas including the midwestern, southeastern and south central United States.

Primary cutaneous disease is extremely rare, but may occur after direct skin inoculation. Secondary cutaneous blastomycosis, which is more common, occurs after lymphohematogenous spread from a primary pulmonary infection, and may occur in the absence of overt pulmonary disease. Skin is the most frequent site of dissemination, followed by bone, genitourinary tract, and central nervous system.

Differential diagnosis is wide, including other granulomatous inflammatory conditions, infections and neoplastic processes. Histopathologic examination of affected tissues can reveal spores which are better visualized with special stains such as GMS or PAS stains. The organism appears as a round to oval, multinucleated yeast cell, 8 to 15 microns in diameter, with a single broad-based bud. Thick, refractile cell walls are easily recognized. Other histologic features include pseudoepitehliomatous hyperplasia, suppurative and granulomatous inflammation, and intraepidermal microabcesses. Fungal cultures require a two to four week incubation period and should be considered when microscopy is inconclusive or negative. Serological tests are not routinely used given their low sensitivity and specificity.

The most recent clinical guidelines recommend treatment with oral itraconazole as the drug of choice, 200 to 400 mg daily given for 6 to 12 months.

Essential Lessons:

- Differentiation between primary and secondary cutaneous disease can represent a diagnostic challenge, as the primary pulmonary infection is frequently subclinical once the skin lesions manifest.
- Cutaneous blastomycosis should be treated with oral itraconazole for 6-12 months, in order to avoid recurrence.

References:

1. Bonifaz A, et al. Endemic systemic mycoses: coccidioidomycosis, histoplasmosis, paracoccidioidomycosis and blastomycosis. *J Dtsch Dermatol Ges* 2011; 9(9):705-15
2. Chapman SW, et al. Clinical practice guidelines for the management of blastomycosis: 2008 update by the Infectious Diseases Society of America. *Clin Infect Dis* 2008; 46(12):1801-12
3. Emer JJ and Spear JB. Primary Cutaneous Blastomycosis as a Cause of Acute Respiratory Distress Syndrome. Case report and literature review. *J Clin Aesthet Dermatol* 2009; 2(3): 22–30
4. Mason AR, et al. Cutaneous blastomycosis: a diagnostic challenge. *Int J Dermatol* 2008; 47(8):824-30
5. Osmond GW, Walters RW, Puri PK. Cutaneous alternariosis microscopically mimicking blastomycosis. *J Cutan Pathol* 2011; Epub ahead of print
6. Rodríguez-Mena A, et al. Blastomycosis: report of an imported case in Mexico, with only cutaneous lesions. *Rev Iberoam Micol* 2010; 27(4):210-2
7. Saccente M and Woods GL. Clinical and laboratory update on blastomycosis. *Clin Microbiol Rev* 2010; 23(2):367-81
8. Smith JA and Kauffman CA. Blastomycosis. *Proc Am Thorac Soc* 2010; 7(3):173-80

Case # 4

Case Presented by Amanda Cooper, MD
and Iris Aronson, MD

History of Present Illness:
This 59 year old male presented with a 20 year history of ocular dryness and irritation as well as problems with his eyelashes. He awoke one day in early November 2010 with severe pain, photophobia and reduced vision in the right eye. Ophthalmology exam showed a corneal ulcer, prompting placement of a corneal patch graft and a conjunctival biopsy for immunofluorescence. Additionally, the patient reported a long history of dyspnea on exertion due to upper airway narrowing. He denied any oral, nasal or genital ulcerations, dysphagia or any cutaneous lesions.

Past Medical and Surgical History:
Four parotid gland resections 2002-2006 for recurrent ductal occlusion, blepharoplasty 2005, stenosis of trachea and left main stem bronchus requiring stenting 2007 with many subsequent airway dilations and changing of stents, Nissen fundoplication 2010 with complete resolution of reflux symptoms

Medications:
Prednisone 60mg daily, albuterol inhaler, and ocular drops (prednisolone, gatifloxacin, besifloxacin, brimonidine, latanoprost and atropine)

Family History:
Mother with lung cancer; three sisters and one brother with diabetes mellitus

Social History:
The patient denies current or previous smoking, alcohol, or illicit drug use.

Physical Examination:
The patient has a hoarse voice and edematous, erythematous upper and lower eyelids bilaterally and symblepharon over the medial and lateral sclera bilaterally with neovascularization. Oral and nasal mucosal examination as well as total body skin exam reveal no abnormalities.

Immunodermatology:
ELISA: desmoglein 1 and 3 antibodies negative, IgG bullous pemphigoid (BP) antigen 180 antibody 24.64 units/mL (positive >9), IgG BP antigen 230 antibody 7.21 units/mL (positive >9)
Indirect immunofluorescence on salt split skin showed no staining with IgG or IgA

Diagnostic Procedures and Tests:
Numerous bronchoscopies showed narrowing of the trachea and left main stem bronchus. Numerous computed tomography (CT) scans of the neck and chest also illustrated this stenosis, with narrowing of the subglottic trachea and left mainstem bronchus down to 4mm and 1mm in diameter, respectively.

Immunopathology:
Direct immunofluorescence, right conjunctiva: IgG highly positive linear basement membrane zone, C3 granular and linear band basement membrane zone

Diagnosis:
Cicatricial pemphigoid with advanced ocular and tracheal involvement

Treatment and Course:
The patient was continued on prednisone 60mg daily after the initial visit. Additionally, he was started on cyclophosphamide. His initial corneal patch graft failed and another patch graft was placed in February

2011. This also failed, and an amniotic corneal graft was placed in May 2011. Intravenous immunoglobulin (IVIg) was started in May 2011 and course was repeated in June 2011. His ocular symptoms as well as his vision and his breathing have now improved. His most recent corneal graft remains in place at this time. His cardiothoracic surgeon reports the lining of the trachea is much less inflamed, but mucous production continues to be problematic. He is continued on cyclophosphamide and prednisone has been tapered.

Discussion:

Cicatricial pemphigoid (CP) is a rare autoimmune disease caused by antibodies that target the basement membrane zone. This disease most commonly affects the oral and ocular mucosa but may also involve anogenital mucosa and cutaneous skin. Rarely, CP can also involve the upper aerodigestive tract, which can be life-threatening. Prednisone remains a mainstay in treatment, with the goal to taper after the addition of steroid-sparing agents such as mycophenolate mofetil, azathioprine, tetracycline/nicotinamide, cyclosporine or dapsone.

More advanced disease that threatens vision or airway compromise requires more aggressive treatment. Cyclophosphamide at 1-2milligrams/kilogram/day has been used in these cases because of its rapid efficacy. IVIg, typically given at a dose of 2 grams/kilogram divided over three days, has also been used for its more rapid onset of action. IVIg is generally well tolerated and lacks the immunosuppressive effects that are seen in other therapies. More recently, rituximab, an anti-CD20 antibody that specifically targets the antibody-producing B cells, has been used for treatment of aggressive CP. This has been used alone or in combination with IVIg or other immunosuppresants. Rituximab has been reported to have a high success in clearing or improving lesions; however, relapses appear to occur frequently and fatal infections have been reported.

Essential Lessons:

- Disease activity in cicatricial pemphigoid varies from mild mucosal disease to aggressive forms that may lead to blindness or respiratory compromise.
- Cyclophosphamide, rituximab and IVIg have been used to treat the more aggressive forms of cicatricial pemphigoid.

References:

1. Foster CS, et al. Combination of rituximab and IVIG for recalcitrant ocular cicatricial pemphigoid: preliminary report. *Ophthalmology* 2010;117(5):861-9.
2. Gürcan HM, et al. Intravenous immunoglobulin treatment in laryngeal pemphigoid. *Clin Exp Dermatol* 2009;34(8):884-6.
3. Higgins TS, et al. Laryngeal mucous membrane pemphigoid: a systematic review and pooled-data analysis. *Laryngoscope* 2010;120(3):529-36.
4. Kasperkiewicz M, et al. Rituximab for treatment-refractory pemphigus and pemphigoid: A case series of 17 patients. *J Am Acad Dermatol* 2011;65(3):552-8.
5. Knudson RM, et al. The management of mucous membrane pemphigoid and pemphigus. *Derm Therapy* 2010;23:268-280.
6. Le Roux-Ville C, et al. Rituximab for patients with refractory mucous membrane pemphigoid. *Arch Dermatol* 2011;147(7);843-9.
7. Parker S and MacKelfresh J. Autoimmune blistering diseases in the elderly. *Clin Derm* 2011;29:69-79.
8. Thorne JE, et al. Treatment of Ocular Mucous Membrane Pemphigoid with Immunosuppressive Drug Therapy. *Ophthalmology* 2008;(115): 2146-52.

Case # 5

Case Presented by Carmen Schwartz, MD
and Iris Aronson, MD

UNKNOWN CASE

This 67 year old male presented with a rash on his hands.

Case # 6

Case Presented by Patricia Dymek, MD, Aashish Taneja, MD and Iris Anderson, MD

History of Present Illness:
This 49 year old female presented with a 2 year history of recurring pruritic urticarial lesions on the trunk and extremities and ocular erythema. Each of the skin lesions resolved within weeks. Treatment used by multiple physicians for chronic urticaria and lupus (after direct immunofluorescence showed findings consistent with lupus erythematosus) included prednisone, hydroxychloroquine, desloratidine, ranitidine, and topical steroids, which were all ineffective. Prior to the urticarial lesions, she was diagnosed with sarcoidosis based on skin biopsy, elevated angiotensin converting enzyme levels, and chest CT showing bilateral hilar lymphadenopathy.

Past Medical History:
Myocardial infarction (1995), stroke (1994), sarcoidosis, fibromyalgia, hypertension, hyperlipidemia, osteopenia, obstructive sleep apnea, degenerative disc disease

Medications:
Warfarin, metoprolol, amlodipine, duloxetine, potassium chloride, morphine sulfate, ezetimibe, rosuvastatin, pantoprazole, hydrocodone/acetaminophen, alendronate, and vitamin B12 injections

Allergies:
Penicillin – develops rash

Family History:
No history of skin cancer, skin conditions, or autoimmune disease

Social History:
The patient had a 57 pack-year smoking history and continued tobacco use.

Review of Systems:
The patient denies fevers, chills, joint swelling, shortness of breath, cough, fatigue, abdominal pain, nausea, vomiting, diarrhea, or dry eyes.

Physical Exam:
Over the upper chest, back, flanks, forearms, and legs were many scattered 1-5 cm ovoid erythematous, edematous papules and scattered superficial erosions. Additionally, she had an erythematous left sclera, enlarged left olecranon bursa, and 2+ lower extremity pitting edema.

Laboratory Data:
The following were positive or abnormal:
Complement C3: 52 mg/dl (79-152), complement C4: < 6 mg/dl (16-38), complement CH50: 0 (60-144), complement component C1q undetected (109-242 μg/ml), anticardiolipin IgM 29 mpl (0-12), factor V Leiden - heterozygous mutation, alpha 1 antitrypsin - MZ genotype

The following were negative or within normal limits:
Complete metabolic panel, complete blood count with differential, erythrocyte sedimentation rate, complement C2, antinuclear antibody, rheumatoid factor, anticardiolipin IgA and IgG, anti-SSA IgG, anti-SSB IgG, QuantiFERON®-TB Gold test, alpha 1 antitrypsin

Histopathology/Immunopathology:
Right upper arm, skin: Multiple sections show perivascular and interstitial infiltrate of numerous neutrophils and eosinophils. Many small blood vessels show reactive changes with plump endothelial cells. Fibrinoid necrosis of the vessel wall is identified focally.

Direct immunofluorescence, right upper arm, lesional skin: There are multiple speckles of IgG, IgM, IgA, and C3 in the upper dermis. IgG is deposited in a granular band at the basement membrane zone.

Diagnosis:
Hypocomplementemic urticarial vasculitis

Treatment and Course:
Patient has been referred to rheumatology, pulmonology, and ophthalmology for further work-up. The plan is initiate treatment with dapsone.

Discussion:
Urticarial vasculitis (UV), a small vessel immune-complex mediated vasculitis, is more common among women with a peak incidence in the fourth decade of life. Approximately 5% to 10% of patients diagnosed with chronic urticaria have UV. UV is divided into two groups based on classical pathway complement levels: normocomplementemic urticarial vasculitis (NUV) and hypocomplementemic urticarial vasculitis (HUV). Most cases are idiopathic, but some are associated with other diseases including connective tissue diseases, hepatitis B and C, or malignancies.

Urticarial lesions with UV last more than 24 hours presenting with burning or painful sensations rather than pruritus and may resolve with residual purpura or hyperpigmentation. Systemic involvement is more common in patients with HUV than with NUV. Hypocomplementemic urticarial vasculitis syndrome (HUVS) is diagnosed by the presence of urticaria for more than six months and hypocomplementemia along with two of the following minor criteria: dermal venulitis on biopsy, arthralgias or arthritis, uveitis or episcleritis, mild glomerulonephritis, recurrent abdominal pain, or decreased C1q levels. Anti-C1q antibodies are present in 95% to 100% of patients with HUVS; however, they are non-specific. Histologically UV presents with features of leukocytoclastic vasculitis. Direct immunofluorescence may show immunoglobulin and complement deposition in a granular pattern around the blood vessels of the upper dermis and the basement membrane.

Antihistamines are used for the relief of pruritus. Corticosteroids are the mainstay of treatment and can be combined with steroid-sparring agents. Dapsone has been associated with sustained remissions. Other treatments used with some success include colchicine, hydroxychloroquine, mycophenolate mofetil, methotrexate, cyclosporine, azathioprine, cyclophosphamide with pulse dexamethasone, rituximab, intravenous immunoglobulins, anakinra, and plasmapheresis.

Essential Lessons:
- Five to ten percent of patients with a diagnosis of chronic urticaria have urticarial vasculitis (UV).
- Evaluation for systemic involvement and underlying causes are crucial after a diagnosis of UV is made.

References:

1. Davis MD, Brewer JD. Urticarial vasculitis and hypocomplementemic urticarial vasculitis syndrome. *Immunol Allergy Clin North Am* 2004;24:183-213.
2. Peroni A, et al. Urticarial lesions: If not urticarial, what else? The differential diagnosis of urticaria. *J Am Acad Dermatol* 2010;62(4):557-570.
3. Wisnieski JJ. Urticarial vasculitis. *Curr Opin Rheumatol* 2000;12:24-31.

Case # 7

Case Presented by Adrienne Schupbach, MD, Steven Mandrea, MD and Sophie M. Worobec, MD

History of Present Illness:
This 40 year old African American female presented with a two year history of nodules on her lower extremity. She initially developed a small dark spot on her left leg, which progressively enlarged. Additional nodules subsequently appeared on her left leg and right buttock. She denied any associated pain or itching. An outside biopsy in 2008 was suggestive of lymphocytoma cutis. She was treated with clobetasol cream twice daily, along with a three week course of doxycycline for empiric treatment of Lyme disease. She had a second biopsy in 2009 which was read as granulomatous dermatitis. Hydroxychloroquine was initiated, but was discontinued after less than one month due to blurry vision.

Past Medical and Surgical History:
Diabetes mellitus, hyperlipidemia, hypertension, obstructive sleep apnea, morbid obesity

Medications:
Simvastatin, metformin, losartan, glyburide, and phentermine

Family History:
Son with psoriasis

Review of Systems:
The patient denies fevers, chills, night sweats, weight loss, swollen glands, shortness of breath, or weakness.

Physical Examination:
On the left upper lateral thigh is a 10 cm x 6 cm indurated, pink-brown, pebbly plaque with a hyperpigmented rim. A similar 8 cm x 4 cm indurated plaque is noted on the left distal thigh. There is a 3-4 cm hyperpigmented, thin plaque on the left posterior mid calf and on the right inferior lateral buttock. There is no cervical or supraclavicular lymphadenopathy or organomegaly.

Laboratory Data:
The following were positive or abnormal:
Hemoglobin A1C 11.8% (4.5-5.9)

The following were negative or within normal limits:
Lyme IgG and IgM antibodies, tissue for borrelia species DNA by polymerase chain reaction, blood culture for mycobacteria, rapid plasma reagin, purified protein derivative, antinuclear antibody, anti-Ro and anti-La antibodies, thyroid stimulating hormone, angiotensin-converting enzyme, lipid panel

Histopathology:
Left lateral buttock, right upper lateral thigh, and right lower lateral thigh, skin: Sections show a dermal nodular and diffuse mixed inflammatory infiltrate composed of numerous enlarged histiocytes, along with lymphocytes and plasma cells. Emperipolesis is identified in multiple foci. Enlarged histiocytes stain positive for CD68 and S-100. The CD1A stain is negative. Special stains for microorganisms are negative.

Diagnosis:
Cutaneous Rosai-Dorfman disease

Treatment and Course:
The patient has not yet been able to return to clinic for further evaluation. Additional diagnostic tests, including a complete blood count with differential, erythrocyte sedimentation rate, complete metabolic panel, and serum protein electrophoresis, along with a chest x-ray, have been ordered for further work-up.

Discussion:
Rosai-Dorfman disease (RDD) or Sinus histiocytosis with massive lymphadenopathy, is a rare, benign, idiopathic proliferative disorder of histiocytes affecting lymph nodes as well as extranodal sites. Cervical lymph nodes are most commonly involved, with painless, bilateral, massive cervical lymphadenopathy. Patients often also have fever, leukocytosis, elevated erythrocyte sedimentation rate, and polyclonal hypergammaglobulinemia. Extranodal involvement is common, occurring in approximately 40% of patients. The skin is the most common extranodal site involved. Skin lesions are variable, often presenting as yellow to red-brown papules, plaques, or nodules. The disease has a male predominance, and most commonly occurs in blacks and whites in the first or second decades of life.

The purely cutaneous form without systemic or nodal disease, cutaneous Rosai-Dorfman disease (CRDD), is rare, occurring in only 3% of patients with RDD. In contrast to the systemic form, there is a marked female predominance, an older age of onset, and an increase in Asians. The cutaneous lesions and histologic features in purely CRDD are indistinguishable from the cutaneous lesions seen in RDD with lymph node involvement. Skin lesions may be solitary or multifocal, and most frequently affect the extremities and face. In contrast to classic RDD, the purely cutaneous form is typically not associated with constitutional symptoms or laboratory abnormalities. However, rarely, uveitis has been associated with CRDD.

Histologic features of both forms include a mixed inflammatory infiltrate composed of histiocytes, plasma cells, lymphocytes, and neutrophils. The histiocytes are large with abundant pale, eosinophilic cytoplasm and typically stain positive for S-100 and CD68 and negative for CD1a. Emperiopolesis is characteristic, with inflammatory cells found within the cytoplasm of the histocytes.

Both forms of the disease tend to follow a benign course and often resolve spontaneously. Various treatments of the cutaneous manifestations of RDD and CRDD have been described with variable effectiveness. Surgical excision is ideal for solitary lesions. Alternative therapies include topical, intralesional, and systemic steroids, acitretin, dapsone, hydroxychloroquine, thalidomide, cryotherapy, pulsed dye laser and intense pulsed light, interferon, and local radiation.

Essential Lessons:
- Cutaneous Rosai-Dorfman disease (CRDD) is a rare, benign, idiopathic histiocytosis localized to the skin without systemic or nodal involvement.
- Histologic features include a histocyte rich inflammatory infiltrate staining positive for S-100 and negative for CD1a, with emperipolesis.

References:

1. Fumerton R, et al. Refractory cutaneous Rosai-Dorfman disease responsive to cryotherapy. *Cutis* 2011;87:296-99.
2. Rubenstein MA, et al. Cutaneous Rosai-Dorfman disease. *Dermatol Online J* 2006;12(1):8.
3. Brenn T, et al. Cutaneous rosai-dorfman disease is a distinct clinical entity. *Am J Dermatopathol* 2002;24(5):385-91.
4. Lu CI, et al. Clinical and histopathologic spectrum of cutaneous Rosai-Dorfman disease in Taiwan. *J Am Acad Dermatol*. 2004;51(6);931-9.
5. Wang KH, et al. Cutaneous Rosai-Dorfman disease: clinicopathological profiles, spectrum and evolution of 21 lesions in six patients. *Br J Dermatol* 2006;154(2);277-86.
6. Fening K, et al. Cutaneous rosai-dorfman disease persisting after surgical excision: report of a case treated with aceitretin. *J Clin Aesthet Dermatol* 2010;3(9);34-6.

Case # 8

Case Presented by Karl Vance, MD, Helen Chen, MD, PhD and Sophie Marie Worobec, MD

History of Present Illness:
This 53 year old female presented in December 2010 with a six month history of subcutaneous nodules on the arms, trunk, hips and buttocks. These were asymptomatic aside from new lesions on the buttocks which were occasionally tender. The patient described the lesions as initially presenting as deep subcutaneous nodules, most of which would spontaneously resolve, but some would evolve into a red scaly plaque. A skin biopsy from the right arm from 11/19/10 was suspicious, though not definitive for cutaneous T-cell lymphoma (CTCL).

Past Medical & Surgical History & Medications:
Hypertension and diabetes mellitus treated with nebivolol and olmesartan, prior infectious mononucleosis

Allergies:
Penicillin

Review of Systems:
The patient denies fevers, chills, night sweats, weakness, fatigue, shortness of breath, cough, hematuria, or pruritus. She exercises regularly, and had an intentional 25 pound weight loss. Eastern Cooperative Oncology Group performance status 0, Karnowsky functional performance score 90

Physical Examination:
Several tender, indurated, deep seated nodules and erythematous plaques with or without surface changes of moderate peripheral scale are noted on bilateral buttocks, thighs, arms and the back. No palpable hepatosplenomegaly and no palpable cervical, axillary, or inguinal lymphadenopathy

Laboratory Data:
The following were positive or abnormal:
Peripheral blood absolute lymphocyte count 1000 cells/ul (1300-4200), CD4:CD8 ratio 5.35 (1.1-2.4), CD4 count 434 cells/ul (693-1319) CD8 count 81 cells/ul (267-787) CD3 count 515 cells/ul (1240-1840), ferritin 305ng/ml (5-114), lactate dehydrogenase 196 IU/l (90-180)

The following were negative or within normal limits:
Complete blood count, comprehensive metabolic panel, lipid panel, peripheral blood T-cell and B-cell gene rearrangements were negative for a dominant clone

Microbiology:
Skin and subcutaneous tissue and lung tissue cultures for aerobic and anaerobic bacteria, fungi, mycobacteria and viruses had no growth. Urine histoplasma antigen, serum epstein barr virus PCR, and cryptococcus antigen were negative.

Histopathology:
Right posterior thigh, skin (2/17/11): Sections show a superficial and deep multinodular lymphoid infiltrate, extending into the subcutis. Lymphoid cells are small to intermediate size, with scant to moderate amount of cytoplasm. There is also a mixed infiltrate of histiocytes and eosinophils. Many of the small blood vessels are swollen with plump endothelial cells. Some of the lymphocytes have enlarged nuclei and irregular nuclear contours and small nucleoli. A few mitotic figures are identified. A very extensive panel of immunohistochemical stains was performed. The lymphocytic infiltrate consists of predominantly CD2 positive, CD4 positive, and CD5 positive T cells with partial loss of CD3 and CD7. The CD 30 and CD 56 stains are negative. The T-cell receptor-alpha-beta gene rearrangement is positive. Viral and fungal stains are negative. Multiple subsequent skin biopsies showed similar findings with an atypical lymphoid infiltrate and variable mixed histiocytic infiltrate.

Bone marrow biopsy (1/14/11): Mildly hypocellular bone marrow with trilineage hematopoesis, no morphologic or immunophenotypic evidence of T-cell lymphoma, or monoclonal B cell population

Lung biopsy, transbronchial (2/22/11): A few lymphoid aggregates composed of small mature lymphocytes, no definitive morphologic evidence of T-cell lymphoma. T-cells express CD7.

Lung biopsy, VATS (8/29/11): Organizing pneumonia pattern with mild CD7 loss and CD4:CD8 ratio 5:1. A T-cell lymphoproliferative lesion cannot be concluded based on the T lymphocyte immunoprofile. Although there is a mild CD7 loss and increased CD4:CD8 ratio, these changes are also associated with reactive T-cell infiltrates. Flow cytometry is negative for immunotypic evidence of a T-cell lymphoma.

Radiology:
CT chest, abdomen and pelvis (1/14/11): Multiple pulmonary crescentic and nodular opacities, numerous subcutaneous nodules, hepatic steatosis, indeterminate right renal lesions
CT chest (8/1/11): Unfavorable change with increased number and size of ground glass nodules

Diagnosis:
Peripheral T-cell lymphoma, not otherwise specified

Treatment and Course:
A multi-disciplinary team decided not to start CHOP-type (cyclophosphamide, doxorubicin, vincristine, and prednisone) chemotherapy while the pulmonary findings were investigated. Bexarotene was started at a dose of 75 mg po daily and titrated up to 225 mg daily with a goal dose of 525 mg daily. Hypertriglyceridemia and hypothyroidism subsequently developed, and are currently controlled with fenofibrate and levothyroxine respectively. There is persistent lymphopenia (600-500 cells/uL) since starting bexarotene. Cutaneous lesions are stable, and further work-up by infectious diseases and pulmonology for the lung lesions is pending.

Discussion:
Peripheral T-cell lymphomas (PTCLs) are a rare and diverse group of hematologic malignancies, representing about 12% of all non-Hodgkin lymphomas. They are classified based on morphologic, immunophenotypic, genetic and clinical features as specific entities or not otherwise specified (NOS.) PTCL-NOS are among the most aggressive non-Hodgkin lymphomas, and have a 5 year overall survival rate near 30%. Extra-nodal disease is common, with the skin, GI tract, liver and bone marrow frequently involved.

Standard therapy for PTCL is CHOP-type chemotherapy, though this is largely based on studies performed on B-cell lymphomas. No randomized controlled trials have demonstrated that this, or any other treament is the best option. Two drugs have FDA approval for the second line treatment of PTCL: pralatrexate, an antifolate, and romidepsin, a histone deacetylase inhibitor. Experimental treatment modalities include stem-cell transplantation, monoclonal antibodies, nucleoside analogs, proteasome inhibitors and signaling inhibitors. A clinical trial of pralatrexate and bexarotene versus bexarotene alone has been agreed to as a post-marketing requirement of the pralatrexate FDA approval for PTCL.

Essential Lessons:
- PTCLs are a diverse group of lymphomas with frequent involvement of the skin and poor prognosis.
- Treatment options include CHOP-type chemotherapy, pralatrexate, romidepsin and bexarotene.

References:

1. Savage KJ. Peripheral T-cell lymphomas. *Blood Rev* 2007;21(4):201-16.
2. Foss FM. Peripheral T-cell lymphoma. *Blood* 2011;117(25):6756-67.
3. Malik et al. Folotyn (pralatrexate injection) for the treatment of patients with relapsed or refractory peripheral T-cell lymphoma: food and drug administration drug approval summary. *Clin Cancer Res* 2010;16:4921-4927.
4. Piekarz et al. Phase 2 trial of romidepsin in patients with peripheral T-cell lymphoma. *Blood* 2011;117(22): 5787-8.

Case # 9

Case Presented by Shruthi Reddy, MD, Ronald Berne, MD and Iris Aronson, MD

History of Present Illness:
This 76 year old female presented with a 20 year history of progressive, dry callused hands and broken fingernails with minimal growth. She developed severe itching after breaking her left arm 5 years before presentation which caused her to scratch, rub, bite, pick and use a nail file to her fingernails, fingers and calluses. She had been using an unknown topical steroid cream thought to be desonide twice a day and was treated with light therapy both with no improvement.

Past Medical and Surgical History:
Depression and left arm fracture status post surgical repair

Medications:
Escitalopram and unknown steroid cream

Allergies:
No known drug allergies

Family History:
Daughter with similar but less severe nail changes

Review of Systems:
The patient reports fevers, chills and night sweats with a 30 pound weight loss over a 4 month period prior to presentation that has since improved. She denies nausea, vomiting, cough or arthralgias.

Physical Examination:
Over both dorsal hands, wrists, and distal forearms are multiple flesh-colored to pink-tan firm waxy papules, some with a warty appearance and some coalescing into horizontal linear plaques. There is erythema and scaling over both palms with sharply demarcated erythematous thickening and erosions of the distal digits extending to the ventral hands. Absence of most fingernails is noted with residual pterygium formation.

Laboratory Data:
The following were positive or abnormal:
Serum protein electrophoresis (11/2010): Immunofixation shows a polyclonal increase in IgA, no monoclonal proteins seen [IgM 69 (60-263), IgA 683 (68- 378), IgG1 310 (768-1632)]

The following were negative or within normal limits:
Serum protein electrophoresis (1/2009), complete blood count with differential, comprehensive metabolic panel, antinuclear antibody, thyroid stimulating hormone, free T4, total and free T3, urine protein electrophoresis (Bence Jones Protein)

Histopathology:
Left extensor wrist, skin: Multiple sections show superficial dermal proliferation of fibroblasts associated with increased interstitial mucin. There is also a mild infiltrate of histiocytes and lymphocytes. The colloidal iron stain highlights markedly increased mucin deposition.

Diagnosis:
Acral persistent papular mucinosis

Treatment and Course:
The patient was seen by a local hematologist/oncologist and per the patient, repeat blood work was within normal limits. She was also seen by a local neurologist and reports no abnormalities were found. She

continues to traumatize the hands and is unable to follow-up for further work-up and treatment considerations.

Discussion:

Acral persistent papular mucinosis (APPM) is a rare subtype of localized lichen myxedematosus (LM), a disorder characterized by lichenoid papules, nodules and/or plaques due to dermal mucin deposition and a variable degree of fibrosis. Clinically, APPM is characterized by symmetric, asymptomatic, chronic, ivory to flesh colored, 2-5mm papules on the dorsa of the hands, extensor wrists and distal forearms. In most cases, the lesions increase in number but there are no associated thyroid disorders, paraproteinemia and systemic abnormalities. APPM has a marked female predominance with a female to male ratio of 27:7 and a mean age of 49.6. The etiology remains unknown, but the primary event likely stems from an increased intracellular metabolism in the dermal fibroblast. Histologically, the lesions show focal mucin deposition in the papillary and mid-dermis interspersed with sparse thin collagen fibers that never reach the deep reticular dermis. The deposition of mucin is well-circumscribed and spares a grenz zone.

The term APPM was first coined by Rongioletti, et al. in 1986 to describe a clinically and histologically distinct form of cutaneous mucinosis; however, in 1953, Montgomery and Underwood had described similar lesions as discrete papular subtype of lichen myxedematosus (DPLM) as did Woerdeman in 1960. DPLM is characterized by similar papules but distributed asymmetrically mainly on the trunk and extremities with more diffuse mucin deposition. The cases described as DPLM were later reclassified as APPM in 1989 because of the acral location of the lesions, the benign and persistent course and no systemic abnormalities; controversy exists, however, as to the reclassification and whether APPM should be considered a variant of DPLM or a completely distinct form of cutaneous mucinosis. Other subtypes of LM include nodular, self-healing papular mucinosis and papular mucinosis of infancy.

The differential diagnosis includes granuloma annulare, molluscum contagiosum, acrokeratoelastoidosis, keratoelastoidosis marginalis of the hands, hereditary papulotranslucent acrokeratoderma, focal acral hyperkeratosis, degenerative collagenous plaques of the hand, lichen amyloidosis and malignant atrophic papulosis, as well as other forms of mucinosis. The locations of lesions and histologic findings help differentiate APPM from the other conditions.

No treatment is necessary but topical and intralesional corticosteroids, tacrolimus 0.1% ointment, and electrofulguration has been tried with variable success. Spontaneous resolution has not been reported in APPM even with 4 or 12 years follow-up.

Over the years, classification of APPM has been a challenge due to the scarcity of cases and lack of clinical and histological information presented in the cases. The classification of APPM and other forms of LM has yet to be completely elucidated and remains controversial.

Essential Lessons:

- APPM is a rare subtype of localized lichen myxedematosus characterized by symmetric, flesh colored, 2-5mm papules localized to the dorsa of the hands, extensor wrists and forearms.
- Histologically, lesions show focal mucin deposition in the papillary and mid-dermis.
- Classification of APPM and other forms of LM remains controversial.

References:

1. Abalde T, et al. Atypical acral persistent papular mucinosis. *Int J Dermatol* 1999;38(6):470-3.
2. Harris, JE, et al. Acral persistent papular mucinosis. *J Am Acad Dermatol* 2004;51(6):982-8.
3. Luo, DQ, et al. Acral persistent papular mucinosis: a case report and literature review. *J Dtsch Dermatol Ges* 2011;9(5):354-9.
4. Rongioletti F, et al. Updated classification of papular mucinosis, lichen myxedematosus, and scleromyxedema. *J Am Acad Dermatol* 2001;44(2):273-81.

Case # 10

Case Presented by David Smart, MD
and Wiley Smith, MD

History of Present Illness:
This 85 year old male with a history of chronic lymphocytic leukemia, currently in partial remission for the last 2 years, presented to dermatology with an 11 month history of mildly pruritic papules on his scrotum. Since onset, the papules have steadily increased in both size and number, and spread to involve the majority of the scrotum and extended to the left crural fold. The patient has no history of similar lesions in the past.

Past Medical and Surgical History:
Chronic lymphocytic leukemia (stage II, partial remission), gout, hypertension, gastroesophageal reflux disease, hyperlipidemia, diabetes

Medications:
Allopurinol, atenolol, finasteride, glipizide, hydrochlorothiazide, lisinopril, omeprazole, and tamsulosin

Allergies:
Terazosin

Family History:
Negative for skin disease

Social History:
The patient uses alcohol occasionally and denies smoking.

Review of Systems:
Negative review of systems

Physical Examination:
There are numerous pink to white/yellow firm superficial nodules covering the majority of the scrotum, many with a central yellow keratotic plug. The lateral left chest and right superior calf each have a small pink, dome-shaped, smooth papule with central umbilication.

Laboratory Data:
The following were positive or abnormal:
White blood cell count 21.1 k/ul (4.0-11.0), monocytes 21% (2-12%), hemoglobin 12.7 g/dl (13.0-17.0), Creatinine 1.4 mg/dl (0.8-1.3), glomerular filtration rate 45 ml/min (>60)

The following were negative or within normal limits:
Platelet count, blood urea nitrogen, sodium, potassium, chloride, bicarbonate, liver function tests

Histopathology:
Scrotum, skin: Sections show an endophytic proliferation of squamous epithelium with numerous intracytoplasmic eosinophilic inclusion bodies (molluscum bodies) maturing toward the surface. The epithelial cells have pale bluish-purple cytoplasm. There is mild inflammatory infiltrate in the surrounding dermis.

Diagnosis:
Molluscum contagiosum

Treatment and Course:
No medical treatment has yet been initiated.

Discussion:
Molluscum contagiosum (MC) is a contagious disease caused by infection with a poxvirus. Poxviridae are large double stranded DNA viruses characterized by their cytoplasmic replication. There are two molecular subtypes of the MC virus both of which cause infection and are clinically indistinguishable.

MC is generally a benign and self-limited process, but can be relatively chronic, lasting several months to years before spontaneous resolution. The virus is transmitted either by skin-to-skin contact between hosts or less commonly by fomites. The virus can also be spread autologously, via the scratching or shaving of lesions.

The disease is common in children and can be found almost anywhere on the skin, including rare involvement of the mouth or on the palms and soles. It also occurs in adults and is generally considered to be a sexually transmitted disease when seen in immunocompetent hosts. Therefore lesions in adults are more commonly distributed on the lower abdomen, inner thighs, perineum and genitalia. MC lesions most often manifest as firm, smooth papules with central umbilication. These papules are generally asymptomatic, but can be pruritic and an associated dermatitis is common. MC has been observed with increasing frequency and severity in patients with acquired immunodeficiency syndrome (AIDS), and extensive or atypical presentations have been reported in patients receiving chemotherapy, corticosteroids, and in those with congenital or other acquired immunodeficiencies. In these patients, widespread, large, nodular, and occasionally deforming lesions can be seen. These cases also tend to be progressive, refractory, and rapidly recurring.

Diagnosis is typically made clinically, but biopsy is sometimes necessary for atypical morphology to confirm the diagnosis. Histological evaluation demonstrates multiple molluscum bodies (Henderson-Patterson bodies), which are large inclusion bodies in epidermal keratinocytes.

Many treatment options are available, including cantharidin, liquid nitrogen, curettage, manual expression, laser, topical salicylic acid and imiquimod, among others. There have also been several reports of giant molluscum in immunocompromised patients causing significant deformity clearing with systemic cidofovir.

Essential Lesson:
- Molluscum contagiosum can present with atypical morphology, especially in patients who are immunocompromised.

References:

1. 1. James WD, et al. Viral diseases *in* Andrews' Diseases of the Skin: Clinical Dermatology Eleventh Edition. James WD editor in chief. Canada: Elsevier, 2011: 387-389
2. Erickson C, et al. Efficacy of Intravenous Cidofovir in the Treatment of Giant Molluscum Contagiosum in a Patient With Human Immunodeficiency Virus. *Arch Dermatol.* 2011;147(6): 652-654.
3. Mancini AJ, Shani-Adir A. Other Viral Diseases *in* Dermatology. Second Edition. Bolognia JL editor in chief. Spain: Mosby Elsevier, 2008: 1229-1232
4. Schwartz JJ, Myskowski PL. Molluscum contagiosum in patients with human immunodeficiency virus infection. A review of twenty-seven patients. *J Am Acad Dermatol* 1992; 27: 583-8.
5. Feldmeyer L, et al. Molluscum contagiosum folliculitis mimicking tinea barbae in a lung transplant recipient. *J Am Acad Dermatol*. 2010; 63(1): 169-71

Case # 11

Case Presented by Eliana Krulig, MD
and Claudia Hernandez, MD

History of Present Illness:
This 18 year old black male with history of congenital lymphedema of his right hand presented for evaluation of multiple cutaneous verrucous lesions. The patient underwent right hand surgery for lymphedema nine years prior to presentation, but noted worsening after surgery. One year later he developed multiple skin lesions all over his affected hand. The lesions progressively grew larger in number and size but have now stabilized. He occasionally wore a lymphedema sleeve which helped with the swelling. He denied any other treatments, or symptoms including pain, burning, and pruritus.

Past Medical and Surgical History:
Right hand congenital lymphedema, right hand surgery in 2002, history of multiple infections on the right hand and arm (last episode in 2007)

Medications:
None

Allergies:
No known drug allergies

Family History:
Maternal history of hypothyroidism

Social History:
The patient is currently a senior in high school. He denies tobacco or alcohol use.

Review of Systems:
The patient denies pain, itching, bleeding, or similar lesions in other areas.

Physical Examination:
Distally from right mid forearm extending into the hand and fingers there is moderate non-pitting edema. Multiple clear 2-4 mm vesicles, comingled with white to yellow verrucous papules are noted over dorsal hand and palmar surface.

Histopathology:
Right dorsal hand, skin: Multiple sections show a well-circumscribed area with ectatic, thin-walled lymphatic channels. These lymphatics have single layer of endothelial lining and a small amount of pale eosinophilic material in the lumen. There is moderate epidermal hyperplasia and hyperkeratosis in adjacent and overlying epidermis.

Diagnosis:
Lymphangiomas in the setting of congenital lymphedema

Treatment and Course:
No medical treatment has been initiated. Continued compliance with lymphedema sleeve was encouraged.

Discussion:

Lymphatic malformations are a group of conditions that develop secondary to hyperplasia of the lymphatic network, and can be classified as microcystic, macrocystic or combined, depending on the size of the abnormal proliferating lymphatic channels. The skin, mucous membranes, and subcutaneous tissues are the most commonly affected sites. The microcystic type is also referred as lymphangioma circumscriptum.

Lymphangioma circumscriptum can be congenital, presenting within the first two years of life, or can arise as a complication of conditions that alter the local lymphatic system. The literature reports associations with surgery, radiation therapy, Crohn's disease, infections, and chronic lymphedema. Our case is likely secondary to the combination of congenital lymphedema, recurrent local infections, and surgery. Clinically, it presents with persistent clustered vesicles containing clear or hemorrhagic fluid. The vesicles may be discrete or grouped into structures resembling "frog spawn," and can bleed or ooze colorless fluid intermittently. Vulvar lymphangiomas commonly present as verrucous lesions that can be mistaken as genital warts.

Histopathologic evaluation is diagnostic, revealing a proliferation and dilation of lymph vessels in the dermis or deep soft tissue lined by endothelial cells. Hyperkeratosis and collarette of acanthotic epidermis extends around the dilated lymph vessels. Lesions are often much more extensive than clinically visible, hence evaluation by magnetic resonance is recommended. Given the deeper component of the lymphangiomas, treatment is difficult and lesions tend to recur. Reported modalities include surgical excision, lasers, sclerotherapy, and radiofrequency ablation, among others.

Essential Lessons:

- Acquired lymphangiomas can arise in the setting of chronic lymphedema.
- Clinical manifestation of lymphangiomas can range from clear-fluid filled superficial vesicles to verrucous papules and plaques.

References:

1. Bond J, et al. Lymphangioma circumscriptum: pitfalls and problems in definitive management. *Dermatol Surg* 2008; 34(2):271-5.
2. Dagenais F, et al. Spontaneous chylothorax associated with primary lymphedema and a lymphangioma malformation. *Ann Thorac Surg* 1999; 67(5):1480-2.
3. Harwood CA and Mortimer PS. Acquired vulval lymphangiomata mimicking genital warts. *Br J Dermatol* 1993; 129(3):334-6.
4. Mu XC, et al. Acquired vulvar lymphangioma mimicking genital warts. A case report and review of the literature. *J Cutan Pathol* 1999; 26(3):150-4.
5. Niti K and Manish P. Microcystic lymphatic malformation (lymphangioma circumscriptum) treated using a minimally invasive technique of radiofrequency ablation and sclerotherapy. *Dermatol Surg*; 36(11):1711-7.
6. Patel GA and Schwartz RA. Cutaneous lymphangioma circumscriptum: frog spawn on the skin. *Int J Dermatol* 2009; 48(12):1290-5.
7. Radhakrishnan K and Rockson SG. The clinical spectrum of lymphatic disease. *Ann N Y Acad Sci* 2008; 1131:155-84.
8. Stewart CJ, et al. Acquired lymphangiectasia ('lymphangioma circumscriptum') of the vulva: a report of eight cases. *Pathology* 2009; 41(5):448-53.
9. Thelenberg G. Primary sporadic lymphedema with circumscribed lymphangioma. *Hautarzt* 1980; 31(9):491-4

Case # 12

Case Presented by Brendan Thomas, MD
and Iris Aronson, MD

History of Present Illness:
This 20 year old female presented with an approximately two week history of worsening pain and discoloration of the left upper arm following an intramuscular injection of promethazine for migraine headache relief. Upon initial presentation to an outside hospital, concern for necrotizing faciitis prompted an emergent exploratory surgery with no evidence of necrosis found.

Past Medical and Surgical History:
Migraine headaches

Medications:
Intramuscular promethazine

Allergies:
No known drug allergies

Family History:
None

Social History:
The patient denies smoking, alcohol, or illicit drug use.

Review of Systems:
Non-contributory

Physical Examination:
The left upper lateral arm was characterized by an approximately 14cm x 8cm reticulated, purpuric patch within which the prior surgical incision was appreciated.

Diagnosis:
Nicolau syndrome

Treatment and Course:
After evaluation by the dermatology consult service, the patient was started on subcutaneous heparin injections twice daily, pentoxifylline 400mg po three times daily, and intravenous hydromorphone as needed for pain control. As the pain continued to worsen, a left upper extremity computed tomography (CT) scan and repeat exploratory surgery were performed, both revealing no abnormalities in the underlying fascia or muscle. Immediately following this second surgery, the patient noted decreased pain and was ultimately switched from hydromorphone to gabapentin 100mg po three times daily. By postoperative day three, the patient had noted significant improvement in the arm discoloration and pain, at which time the heparin and pentoxifylline were discontinued and she was discharged home.

Discussion:
Nicolau syndrome, also known as embolia cutis medicamentosa, is a cutaneous condition that occurs most commonly following intramuscular injections of various medications. Less commonly, the

condition has been reported after subcutaneous and intraarticular injections. Clinically, patients present with significant pain at the injection site, followed by a well demarcated, reticulated, bluish discoloration of the overlying skin. The pathophysiology of these changes is not well understood, but they have been reported to occur following the administration of numerous medications, including promethazine, interferon beta, and vitamin K.

The diagnosis is usually made clinically and should always be differentiated from necrotizing fasciitis. In the latter, there is severe local pain and redness of the skin, with symptoms out of proportion to the clinical presentation. Treatment of Nicolau syndrome is predominately supportive. Immediately following the triggering insult therapies to improve vascularity of the area may be implemented. The use of oral pentoxyfylline, subcutaneous heparin, and hyperbaric oxygen have all been reported in the treatment of Nicolau syndrome. Surgical debridement may also help enhance wound healing when ulceration has occurred, and antibiotics usage is recommended when secondary infection of the compromised area occurs.

Essential Lessons:

- Nicolau syndrome most commonly occurs from intramuscular injections of medicine.
- Oral pentoxyfylline and subcutaneous heparin may help improve the impaired vascularity.

References:

1. James, W, et al. Andrews' Diseases of the Skin: Clinical Dermatology. Tenth Edition. Saunders, 2005.
2. Faucher L and Marcoux D. What syndrome is this? Nicolau syndrome. *Pediatr Dermatol* 1995;12(2):187-90.
3. Luton K, et al. Nicolau Syndrome: three cases and review. *Int J Dermatol* 2006;45(11):1326.
4. Nischal K, et al. Nicolau syndrome: an iatrogenic cutaneous necrosis. *J Cutan Aesthet Surg* 2009;2(2):92-5.

Case # 13

Case Presented by Amanda Silverio, MD
and Lawrence Chan, MD

Patient A

History of Present Illness:
This 61 year old Hispanic male presented with thickening and darkening of an area of skin on his right lower abdomen more than a year after experiencing a painful, itchy rash in that area. At initial presentation, he noted a 2 week history of red blisters along the distribution of pain and itching but the blisters resolved before presenting to clinic. He completed a course of acyclovir, which resolved the painful sensation. Over the next 15 months, there was residual itching and development of a dark, indurated area not improved by clobetasol 0.05% ointment twice daily or calcitriol 3mcg/g ointment daily.

Past Medical and Surgical History:
Obesity, hypertension, diabetes mellitus, peripheral neuropathy, hyperlipidemia, osteoarthritis

Medications:
Clobetasol 0.05% ointment, calcitriol 3mcg/g ointment, insulin with meals and twice daily, metoprolol, hydrochlorothiazide, rosuvastatin, and hydrocodone/acetaminophen as needed for joint pain

Allergies:
No known drug allergies

Family History:
No history of skin diseases or cancer

Review of Systems:
The patient reports chronic shortness of breath and chronic joint pain. He denies fevers, chills, weight loss, oral erosions, difficulty swallowing, myalgias, fatigue, or Raynaud's phenomenon.

Physical Examination:
On the right lower abdomen in the same location as the previous blistering eruption is a 15.5cm x 5cm reddish brown annular indurated plaque with erythematous border and 1cm central area of hypopigmentation. There is a 4mm hyperpigmented macule consistent with previous biopsy site. No scale, vesicles, erosions or tenderness to palpation noted.

Laboratory Data:
The following were negative or within normal limits: Antinuclear antibody

Histopathology:
Right lateral abdomen, skin (12/21/09): Sections show intraepidermal vesiculation with prominent viral cytopathic changes, including multinucleation, nuclear molding and margination of chromatin. This is associated with superficial and mid-dermal perivascular and periadnexal inflammatory cell infiltrate.

Right lateral abdomen, skin (11/22/10): Sections show superficial and deep dermal perivascular and periadnexal interstitial infiltrate of lymphocytes and a few plasma cells and eosinophils. Dermal collagen is slightly thickened.

Diagnosis:
Localized morphea arising at site of prior herpes zoster outbreak

Treatment and Course:
The patient continues to use clobetasol 0.05% ointment twice daily alternating with calcitriol 3mcg/g ointment daily with improvement of pruritus but hyperpigmentation and induration remain stable.

Patient B

History of Present Illness:
This 38 year old Hispanic female presented with a 10 year history of skin discoloration and thickening at her buttocks where she had received gluteal silicone injections. According to the patient, in 2001 she visited a cosmetologist in Chicago to obtain 3 sessions of gluteal silicone injections. After the 3rd session, she noted fever, chills, and an "allergic reaction" at the injection sites with severe pruritus. Over the next year, she developed firmness and "granulomas" at previous injection sites. She tried massage therapy without improvement. In 2004, a mass was removed at her left groin but was complicated by a fluid collection spreading upwards from her gluteal region to lower back. In 2009, she went to Nicaragua where a mass was removed from her back, and in the subsequent year 7 masses were removed from her buttocks. She continues to have a non-healing surgical wound at her right hip. A local plastic surgeon recommended whole excision of the affected areas on her buttocks, but she opted to perform conservative wound therapy instead with an at-home wound vacuum. She also uses baby soap and Vaseline lotion on affected areas.

Past Medical and Surgical History:
Asthma

Medications:
Montelukast, dephenhydramine, and folic acid

Allergies:
Codeine – develops warmth and tingling sensation throughout body

Family History:
No history of skin diseases or skin cancer; aunt with thyroid cancer

Review of Systems:
The patient reports generalized pruritus with dry skin. She denies fevers, chills, weight loss, oral erosions, shortness of breath, joint pain, myalgias, fatigue, or Raynaud's phenomenon.

Physical Examination:
Well-defined hyperpigmented, indurated plaques without tenderness to palpation at lateral and posterior buttocks bilaterally. Linear scars measuring 5cm at left gluteal cleft, 1.8cm at right gluteal cleft, and 8cm at right hip. There is a 2x1.5cm deep wound with yellow granulation tissue and tenderness to palpation located over the right hip scar. No muscle atrophy, weakness, or joint contractions noted.

Laboratory Data:
The following were positive or abnormal:
Aspartate transaminase (AST) mildly high at 45 mcg/L (10-40)

The following were negative or within normal limits:
Complete blood count with differential, comprehensive metabolic panel (except for AST noted above), wound culture for bacteria/fungi/mycobacteria, Human immunodeficiency virus (HIV) 1 and 2 ELISA

Imaging:
Magnetic resonance imaging, spine: peri-vertebral mass does not impinge on spinal cord

Histopathology:
Right buttock, skin: Punch biopsy of skin without the usual tapered appearance. Sections show markedly thickened dermis with increased deposition of eosinophilic material, both vascular and interstitial. In mid-dermis, there are foci of residual foreign body granulomatous inflammation with "swiss cheese" appearance consistent with changes produced by deposits of liquid silicone. Polarization reveals no

evidence of polarizable foreign material. Overlying epidermis is unremarkable. Congo red stain is negative. Masson Trichrome stain strongly highlights the fibrous tissue.

Diagnosis:
Localized morphea arising at site of prior silicone injections

Treatment and Course:
The patient was prescribed betamethasone 0.05% ointment and calcipotriene 0.005% ointment twice daily for the past six months with some improvement of hyperpigmentation and induration. She was recently switched to fluocinonide 0.05% ointment instead of betamethasone 0.05% ointment due to change in insurance coverage. Generalized pruritus improved with loratadine and pseudoephedrine. Open wound at right hip scar continues to drain, and she is applying rifampin spray and neomycin ointment to the wound as well as using an at-home wound vacuum. There is still a mobile fluid collection at her lower spine.

Discussion:
Morphea, or localized scleroderma, is characterized by excess collagen deposition mostly in the deep dermis and subcutaneous fat that can lead to significant morbidity from scar-like sclerosis. The definitive etiology of morphea is not known, but prior localized trauma has been thought to be a potential mechanism. Recent investigations have focused on the possible role of *Borrelia burgdorferi* infection or of post-irradiation trauma in patients with breast cancer. However, there are few reported cases of localized morphea developing at the site of regressed herpes zoster or at the site adjacent to a leaking silicone-gel breast implant.

In the case of secondary unrelated cutaneous lesions arising in areas of resolved herpes zoster lesions, the term "isotopic response" was coined for such reactions by Wolf et al. in 1995. Varicella zoster reactivation could induce vascular, neurologic, and immunologic change that can make the skin more susceptible to the development of morphea in that area. Various studies have shown that interleukin-4 (IL-4) and transforming growth factor-beta (TGF-beta) are elevated in the skin of patients with morphea. Immune dysregulation from reactivation of the varicella zoster virus has been thought to induce local dominance of these two cytokines, which have been shown to activate fibroblasts and induce fibrosis.

It is known that injection of foreign substances (silicone or liquid paraffin) into the skin for cosmetic purposes can lead to chronic inflammation and the formation of foreign body granulomas with calcification. Silicone polymers are immunogenic and, when injected into soft tissue, can induce initially a perivascular lymphocytic infiltrate with immunoglobulin deposition around the walls of small vessels. This leads to microvascular injury, reduction in number of blood vessels, and fibroblastic reaction in the dermis- all consistent with changes seen in morphea. Of note, silicone injections have also been implicated in causing systemic sclerosis[13] but recent meta-analyses did not substantiate this claim.

Clinical features of the most common type of morphea, plaque-type, include an erythematous or violaceous plaque that centrifugally expands, leaving a hypopigmented, sclerotic central area. Initially, the area can go unrecognized by the patient since there may be an absence of associated symptoms but subsequent pruritus and "skin tightening" are often noted. Hair and sweat glands are often lost. Post-inflammatory hyperpigmentation may become prominent. The course is variable (average is 3-5 years) and relapse can occur.

Histologically, the area of central sclerosis will reveal densely packed collagen bundles replacing vascular and pilosebaceous structures in the mid and deep reticular dermis, often extending involvement to the subcutis. Eccrine glands and ducts are compressed and "trapped" by surrounding packed collagen. The inflammatory border will reveal a perivascular infiltrate of mostly CD4+ T-cells and sometimes include plasma cells, eosinophils, and macrophages. The epidermis may be normal. Clinicopathological correlation is necessary in order to distinguish between the characteristically similar changes of morphea and systemic sclerosis seen histopathologically. Raynaud's phenomenon is usually not associated with

morphea but is regularly present in systemic sclerosis. One must also distinguish lichen sclerosus as another type of inflammatory skin disease leading to scar-like sclerosis but mostly affecting the epidermis and superficial dermis.

Although effective treatment is available for the visceral complications of systemic sclerosis, treatment options for isolated cutaneous disease remain unsatisfactory. Spontaneous resolution can occur but may require several years (average is 3-5 years) and relapse is possible. To target the early inflammatory stage, topical or intralesional corticosteroid can help the lesion regress due to anti-inflammatory effects. Topical vitamin D analogues, topical tacrolimus, or topical imiquimod have also been used with successful responses. Psoralen, especially with UVA1, and broadband ultraviolet irradiation have shown some efficacy. In our cases, potent topical corticosteroid and topical vitamin D resulted in some improvement of signs and symptoms, yet long-term follow-up has not yet been established. In the second patient case, physical therapy has been encouraged since joints are affected.

Essential Lessons:

- In our observation, direct contact between silicone gel and dermal elements can induce an immunogenic response, resulting in sclerodermatous reactions.
- Varicella zoster reactivation can induce vascular, neurologic, and immunologic change in a localized area that can make the skin more susceptible to the development of morphea in that area.
- Current treatment options for morphea remain limited in efficacy. Topical or intralesional corticosteroid and topical vitamin D analogues are still first-line therapies. Other topical immunomodulators and phototherapy have shown some success.

References:

1. Bolognia J, Jorizzo J, Rapini R. *Dermatology*. Elsevier Limited, 2008;2;1469-76.
2. Prinz JC, et al. "Borrelia-associated early-onset morphea": a particular type of scleroderma in childhood and adolescence with high titer antinuclear antibodies? Results of a cohort analysis and presentation of three cases. *J Am Acad Dermatol* 2009;60:248-55.
3. Verbov J. Post-irradiation morphoea. *Br J Dermatol*. 1989;121:819-20.
4. Noh TW, et al. Morphea developing at the site of healed herpes zoster. *Ann Dermatol* 2011;23:242-5.
5. Lopez N, et al. Wolf's isotopic response: zosteriform morphea appearing at the site of healed herpes zoster in a HIV patient. *J Eur Acad Dermatol Venereol* 2009;23:90-2.
6. Forschner A, et al. Morphea with features of lichen sclerosus et atrophicus at the site of a herpes zoster scar: another case of an isotopic response. *Int J Dermatol* 2005;44:524-5.
7. Granel B, et al. Localized morphea after silicone-gel filled breast implant. *Dermatology* 2001;202:143-4.
8. Di Lorenzo G, et al. Morphea after silicone gel breast implantation for cosmetic reasons in an HLA-B8, DR3-positive woman. *Int Arch Allergy Immunol* 1997;112:93-95.
9. Lazar AP, Lazar P. Localized morphea after silicone gel breast implantation: more evidence for a cause-and-effect relationship. *Arch Dermatol* 1991;127:263.
10. Gabriel SE, et al. Risk of connective tissue disease and other disorders after breast implantation. *N Engl J Med* 1994;330:1697-1702.
11. Naoum C, et al. A histological and immunohistochemical study of medical- grade fluid silicon. *Dermatol Surg* 1998;24:867-870.
12. Janowsky EC, Kupper LL, Hulka BS. Meta-analyses of the relation between silicone breast implants and the risk of connective-tissue diseases. *N Engl J Med* 2000;342:781-790.
13. Mancuso G, Berdondini RM. Localized scleroderma: response to occlusive treatment with tacrolimus ointment. *Br J Dermatol* 2005;152:180-182.
14. Dytoc M, Ting PT, Man J, Sawyer D, Fiorillo L. First case series on the use of imiquimod for morphoea. *Br J Dermatol* 2005;153:815-820.
15. Grundmann-Kollmann M, et al. PUVA-cream photochemotherapy for the treatment of localized scleroderma. *J Am Acad Dermatol* 2000;43:675-678.

Case # 14

Case Presented by Shruthi Reddy, MD
and Claudia Hernandez, MD

History of Present Illness:
This 68 year old female presented with a nodule at the base of the neck since 2005. She noted intermittent bleeding, but no change in the size of the lesion over the years. No other lesions were reported by the patient.

Past Medical and Surgical History:
Papillary thyroid carcinoma status post total thyroidectomy and radioablative iodine treatment in 2002, tracheal resection for recurrent papillary thyroid carcinoma on left trachea in 2005, anxiety, diabetes mellitus, hyperlipidemia, hypertension, and glaucoma

Medications:
Sorafenib, cyproheptadine, levothyroxine, lisinopril, metoprolol, pilocarpine, and simvastatin

Allergies:
No known drug allergies

Family History:
No skin cancers or skin conditions

Review of Systems:
The patient denies dysphagia, fevers, chills, nausea, or vomiting.

Physical Examination:
On the upper chest is a 7 x 8 mm indurated, erythematous keratotic nodule with central hemorrhagic crust.

Histopathology:
Upper chest, skin: Sections show a multinodular proliferation of epithelial cells with a papillary configuration. At higher magnification, many of the cells have nuclear grooves and overlapping nuclei with ground glass appearance. Psamomma bodies are also present.

Diagnosis:
Metastatic thyroid carcinoma to the skin

Treatment and Course:
Treatment with sorafenib was continued per hematology-oncology. She reported a new, asymptomatic lesion on the umbilicus first noted in August 2010. In November 2010, the lesion was biopsied and also found to be metastatic papillary thyroid carcinoma. With the development of metastasis to the umbilicus and activity of neoplastic processes involving the right lung field and left lobe of the liver on serial positron emission tomography (PET) scans, sorafenib was changed to sunitinib. At follow-up, she was found to have multiple peritoneal and omental soft tissue nodules, compatible with metastatic disease on computed tomography (CT) scan of the abdomen in February 2011. Since April 2011, she has been on and off of sunitinib secondary to thrombocytopenia and hypertension and the umbilical mass has not been excised.

Discussion:

Thyroid carcinoma is the most common endocrine malignancy with papillary thyroid carcinoma (PTC) being the most common subtype. PTC most commonly metastasizes to the regional lymph nodes in the neck (40% of cases) while distant metastases, usually to the lung, bone, or central nervous system occur in about 10% of patients. Cutaneous metastases are rare occurring in less than 1% of all patients with PTC and usually occur in the setting of disseminated disease. Occasionally, skin metastases may be the initial presentation of an occult thyroid carcinoma. Some authors believe follicular carcinoma of the thyroid has a higher propensity to spread to the skin, followed by PTC. Others believe PTC is the most common thyroid malignancy to metastasize to the skin. The most frequent site of cutaneous involvement is the scalp, occurring in approximately two thirds of cases with equal incidence in men and women. Cutaneous metastasis may present as flesh colored or erythematous to purple plaques or nodules that are almost always asymptomatic and rarely ulcerate.

Biopsy of suspicious lesions will readily provide a diagnosis. The usual histological feature of PTC is a complicated, branching, tree-like pattern formed by papilliform fibrovascular stroma. A follicular architecture is also common and may predominate. The stroma is lined by one or more layers of epithelial cells that contain "ground glass" chromatin. Psammoma bodies are laminated, spherical, calcified structures characteristic of papillary carcinoma and found in approximately 25% of cases.

Immunoperoxidase staining is helpful in determining the tissue of origin in metastatic tumors to the skin. Antibodies to thyroid transcription factor (TTF-1), a 38 kDa homeodomain containing, DNA binding protein, is a useful screen for metastatic thyroid carcinomas and helps distinguish pulmonary and thyroid carcinoma from other primary carcinomas. Thyroglobulin, a 670 kDa glycoprotein synthesized in the cytoplasm of follicular thyroid epithelium, is found in normal thyroid tissue, goiters, thyroiditis, and some carcinomas, but not in lung carcinomas. With immunoperoxidase staining, thyroglobulin is detectable in about 95% of papillary tumors.

In general, PTC tends to have a relatively benign clinical course with slow progression and a good prognosis. However, low compliance and delayed treatment may lead to disseminated disease and cutaneous metastasis, which portends a poor prognosis. The average length of survival with cutaneous metastasis is 19 months, ranging from 1 month to 7 years.

Essential Lessons:

- Cutaneous metastasis of thyroid carcinoma is a rare manifestation of thyroid carcinoma with poor prognosis.
- A flesh colored skin nodule on the scalp in a patient with thyroid carcinoma should be concerning for metastatic thyroid carcinoma to the skin.

References:

1. Alwaheeb S, et al. Cutaneous manifestations of thyroid cancer: a report of four cases and review of the literature. *J Clin Patho* 2004;57(4):435-8.
2. Avram AM, et al. Choroidal and skin metastases from papillary thyroid cancer: case and a review of the literature. *J Clin Endocrinol Metab* 2004;89(11):5303-7.
3. Dahl PR, et al. Thyroid carcinoma metastatic to the skin: a cutaneous manifestation of a widely disseminated malignancy. *J Am Acad Dermatol* 1997;36(4):531-7.
4. Kim HS, et al. Cutaneous metastasis of thyroid cancer presenting as a nodulocystic mass with ulceration. *J Dermatol* 2009;36(10):559-60.

Case # 15

Case Presented by Steven Kahn, MD
and Michelle Bain, MD

History of Present Illness:
This 3 year old male presented at 21 months for pigment and textural changes on the right side of his body. The patient's mother noticed increased width of the right leg at birth as well as several darkly pigmented spots. The patient scratches his skin frequently and had only used baby lotion and soap with no other topical treatments. On presentation, the patient was already followed by pediatrics, genetics, endocrinology, and orthopedics.

Past Medical and Surgical History:
Normal spontaneous vaginal delivery at 40 weeks, birth weight 7lbs, 4oz, appropriately meeting developmental milestones

Medications:
None

Allergies:
No known drug allergies

Family History:
No history of skin diseases, hemihypertrophy, neurofibromatosis, or skin cancer

Review of Systems:
The patient's mother reports fever for 2 days, rhinorrhea, and cough, and denies nausea, vomiting, diarrhea, or joint pains.

Physical Examination:
On the right trunk are scattered, hypopigmented macules, some of which have a whorled configuration with a sharp demarcation at the midline chest and abdomen. Nine hyperpigmented macules with at least 6 having a diameter greater than 5mm are present on the right flank and back. The right arm has several faint, blaschkoid, hypopigmented patches with a slightly increased girth compared to the left arm. The right leg circumference at the calf is 21cm compared to 18.5cm on the left, and the right leg is approximately 1-2cm longer than the left leg. The right leg has soft, redundant skin and multiple overlying hyperpigmented to pink macules and papules.

Laboratory Data:
The following were positive or abnormal:
Prolactin 32.7ng/mL (2.6-13.1), insulin-like growth factor 1 <25ng/mL (25-248), insulin-like growth factor binding protein 3 947ng/mL (1444-4408)

The following were negative or within normal limits:
Phosphatase and tensin homolog (PTEN) sequencing and deletion/duplication testing, thyroid stimulating hormone 1.61mcIU/ml (0.35-4.0), thyroxine 1.0ng/dl (0.6-1.7), triiodothryonine 4.1pg/mL (2.4-4.2), alpha-fetoprotein 1.1 (<9.0)

Diagnostic Procedures and Tests:
06/09 Skeletal bone survey, lower extremities: the right femur measures 12.9cm and the left 13.2cm. The right tibia measures 9.5cm and the left measures 10cm. No fibrous dysplasia noted.
10/09 Magnetic resonance imaging, brain: hypoplasia of the anterior lobe of the pituitary gland.
11/10 Skeletal bone survey, lower extremities: the right femur measures 17.5cm. The right lower leg measures 15cm. The left femur measures 17.5cm. The left lower leg measures 15.5cm.
05/11 Ultrasound, abdomen: essentially unremarkable

Histopathology/Immunopathology:
Left lateral thigh, skin: Sections show unremarkable skin with mild dermal edema. There is no evidence of proliferation of spindle cells. The S100 stain is negative.

Diagnosis:
Isolated hemihyperplasia and café au lait macules

Treatment and Course:
The patient was initially treated with topical hydrocortisone 2.5% ointment, cetirizine 2.5mL daily, and white petrolatum. The patient's limb length discrepancy caused no gait disturbances, disability, or apparent limp. Alpha-fetoprotein testing and abdominal ultrasounds were performed every three months and were consistently unremarkable. Ophthalmologic exam was notable for pseudoestropia, but there were no signs of Lisch nodules. The patient's endocrinologist was concerned for growth hormone deficiency based on previous laboratory data, but the patient's growth had been appropriate with no signs of hypoglycemia. The patient was regularly followed by pediatrics, genetics, endocrinology, and orthopedics.

Discussion:
Isolated hemihyperplasia (IH) is a congenital disorder with asymmetric regional body overgrowth due to an underlying abnormality of cell proliferation in bone, soft tissue, or both. The diagnosis can be made by clinical exam after ruling out other causes of body asymmetry, including Beckwith-Wiedemann syndrome, Proteus syndrome, and neurofibromatosis type 1. Individuals with IH are at an increased risk for embryonal tumors, particularly Wilms tumor and hepatoblastoma. Recommendations for all children with IH include referral to a clinical geneticist for evaluation, abdominal ultrasound every 3 months until 7 years of age, serum alpha-fetoprotein measurement every 3 months until 4 years of age, and routine abdominal examination.

The major consideration in a patient presenting with multiple café au lait macules is neurofibromatosis type 1 (NF1). Diagnostic criteria for NF1 include the presence of two or more of the following: six or more café au lait spots larger than 5mm in the prepubertal child, skin-fold freckling (Crowe's sign), two or more neurofibromas or one plexiform neurofibroma, two or more iris Lisch nodules, optic glioma, characteristic skeletal dysplasia, and an affected first-degree relative. Axillary freckling, neurofibromas, and Lisch nodules may be difficult to identify in young children, as they tend to be age-dependent. The vast majority of patients with at least six café au lait spots who are followed for 3 or more years develop other signs of NF1, with skin-fold freckling and Lisch nodules being the most common features to appear. Segmental neurofibromatosis (SN) is extremely rare and refers to signs of NF1 confined to a specific region of the body possibly as a consequence of postzygotic mutation of the NF1 gene, leading to somatic mosaicism. Most patients with SN do not have a family history of neurofibromatosis, and SN involves the right side of the body more commonly than the left side.

Essential Lessons:
- Isolated hemihyperplasia is a congenital overgrowth disorder associated with an increased risk for embryonal tumors, including Wilms tumor and hepatoblastoma.
- Neurofibromatosis type 1 is the most common diagnosis established for children with multiple café au lait macules, who typically develop skin-fold freckling or Lisch nodules to fulfill diagnostic criteria.

References:

1. Arnsmeier SL, et al. Familial multiple café au lait spots. *Arch Dermatol* 1994;130:1425-1426.
2. Ballock RT, et al. Hemihypertrophy concepts and controversies. *J Bone Joint Surg Am* 1997;79:1731-1738.
3. Clericuzio CL and Martin RA. Diagnostic criteria and tumor screening for individuals with isolated hemihyperplasia. *Genet Med* 2009;11:220-222.
4. Korf BR, et al. Diagnostic outcome in children with multiple café au lait spots. *Pediatrics* 1992;90:924-927.
5. Morais P, et al. Segmental neurofibromatosis: a rare variant of a common genodermatosis. *Acta Dermatoven APA* 2010;19:27-29.