Chicago Dermatological Society

December 2009
Monthly Educational Conference

Program Information
Continuing Medical Education Certification
and
Case Presentations

Wednesday, December 9, 2009

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

Program

Venue Information

See site map on following pages

UIC DERMATOLOGY DEPARTMENT CLINIC
1801 W. Taylor, Suite 3E
- Registration for practicing members & guests (*8 - 10 a.m. only)*
- Patient viewing

STUDENT CENTER WEST (SCW)
828 S. Wolcott, 2nd Floor
- Registration
- Committee meetings
- Slide viewing
- Lectures, business meeting & case discussions
- Lunch
- Exhibitors

Committee Meetings

8:00 a.m.	CDS Plans & Policies Committee - *SCW Room 213 A/B*
9:00 a.m.	IDS Board of Directors - *SCW Room 216 A/B*

Program Activities

9:00 a.m. - 10:00 a.m.	Registration for Members & Guests *Dermatology Clinic (moves to SCW 2nd floor foyer at 10 a.m.)*
10:00 a.m. - 2:30 p.m.	Registration for Members & Guests *SCW - 2nd Floor Foyer*
8:00 a.m. - 2:30 p.m.	Registration for Residents/Fellows *SCW - 2nd Floor Foyer*
9:00 a.m. - 10:00 a.m.	*RESIDENT LECTURE – SCW Chicago Room A-C* "Dermatitis Herpetiformis: A Model for Cutaneous Manifestations of Gastrointestinal Disease" – *Russell P. Hall, III, MD*
9:30 a.m. - 10:45 a.m.	*CLINICAL ROUNDS* Patient viewing – *Dermatology Clinic* Slide viewing – *SCW Room 206 A/B*
11:00 a.m. - 12:00 p.m.	*GENERAL SESSION - SCW Chicago Room A-C* *David Fretzin Lecture:* "Dapsone: Uses and Abuses" – *Russell P. Hall, III, MD*
12:00 p.m. - 12:30 p.m.	Box lunches & visit with exhibitors
12:30 p.m. - 1:00 p.m.	IDS Presentation: The State of Affairs for Health Care Reform, A Washington Report – *SCW Chicago Room A-C*
1:00 p.m. - 1:05 p.m.	CDS Business meeting – *SCW Chicago Room A-C*
1:05 p.m. - 2:35 p.m.	Case Discussions – *SCW Chicago Room A-C*
2:35 p.m.	Meeting adjourns

Next meeting – Wednesday, February 17, 2010; Hosted by Stroger/Cook County Hospital, to be held at the Stephens Convention Center in Rosemont

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

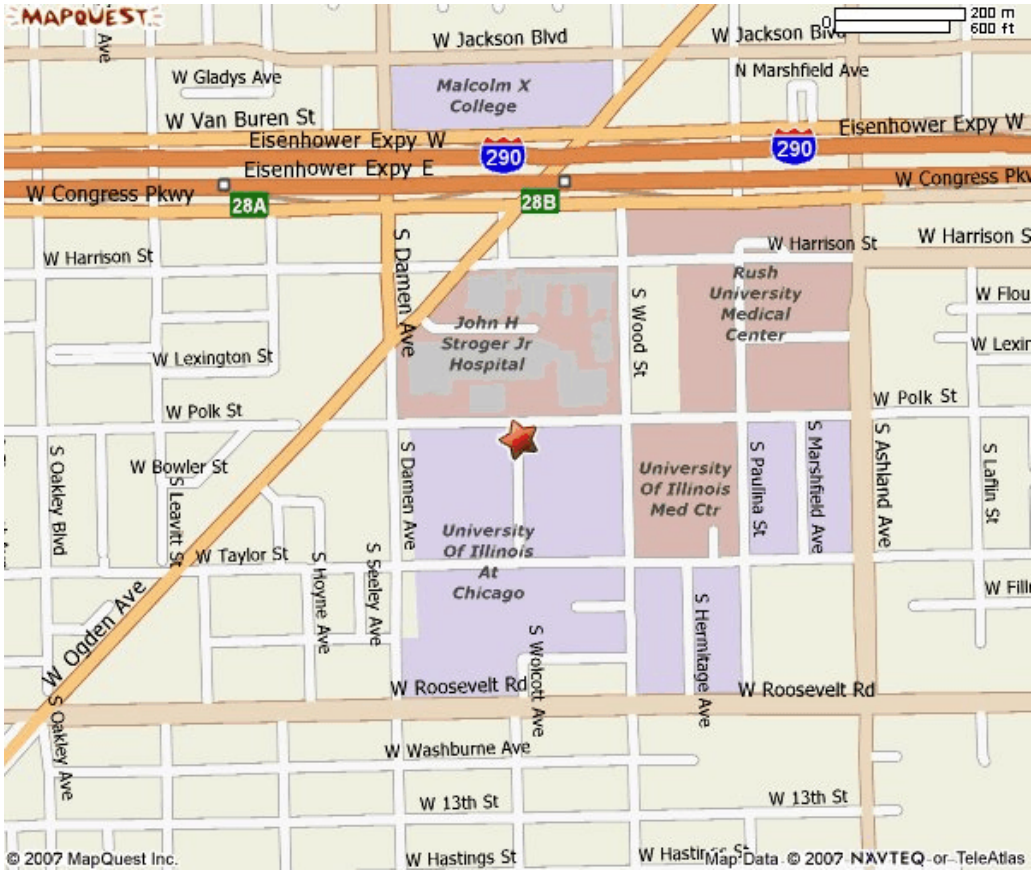
University of Illinois - Chicago

12/08

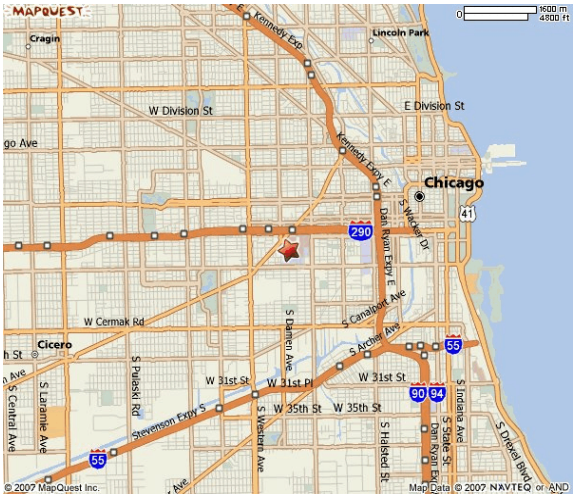
- UIC Student Center West - 828 S. Wolcott Ave., 2nd Floor
  Registration (residents throughout, practicing physicians after 10 a.m.), lectures, slide viewing and committee meetings
- UIC Outpatient Care Center, Dermatology Clinic - 1801 W. Taylor, Suite 3E
  Patient viewing (practicing physician registration 8 - 10 a.m. only)

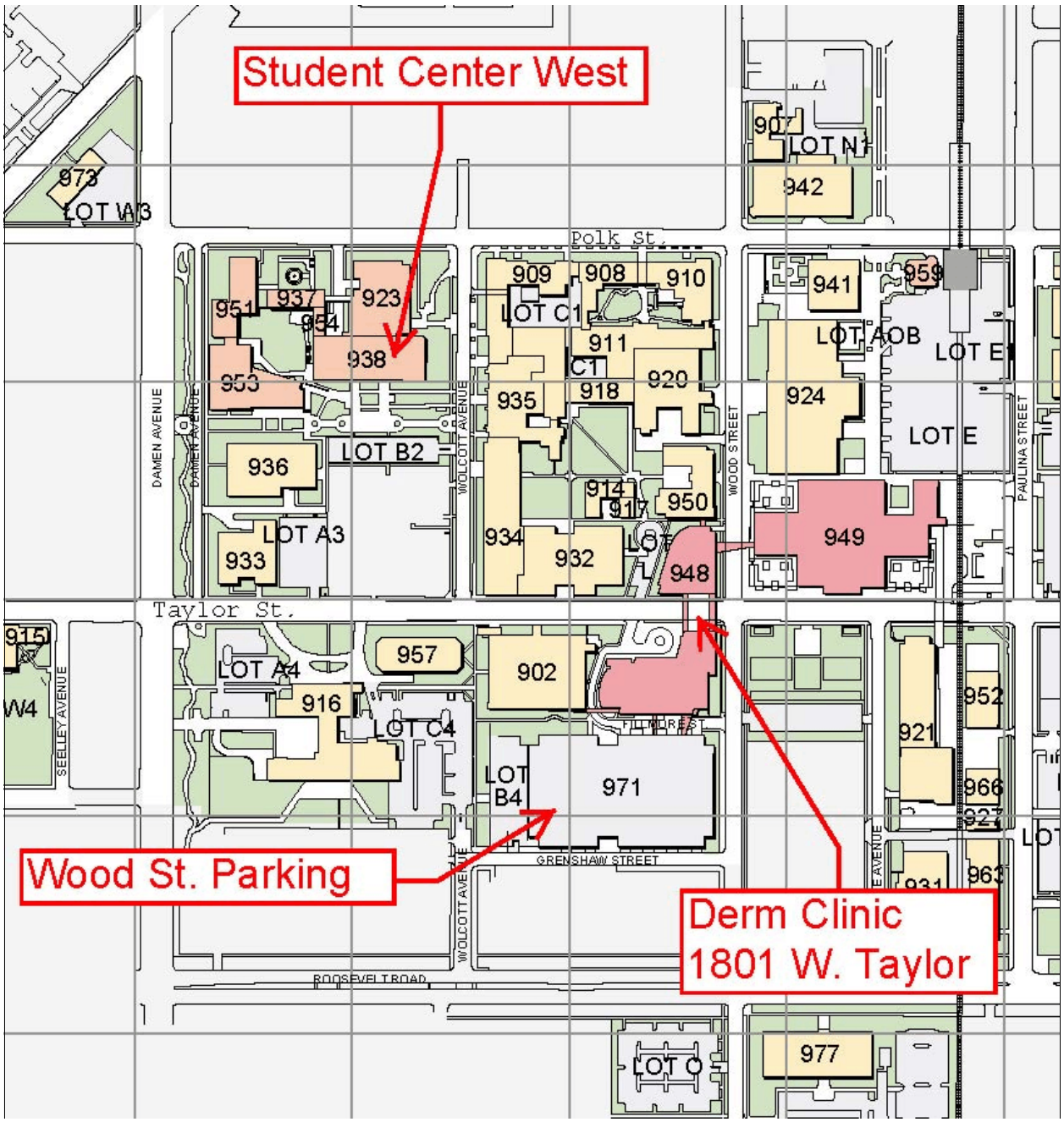
UIC parking – Use the Wood Street Parking Structure, 1100 S. Wood (Wood & Grenshaw, just south of the UIC Outpatient Care Center)

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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CME Information

This activity is jointly sponsored by the Chicago Medical Society.

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

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

Commercial Support: There were no educational grants secured for this CME activity. We are pleased to acknowledge the participation of our exhibitors: Abbott Laboratories; Amgen Inc.; Astellas Pharma US; Centocor; CPC Pathology; Gazelle Medical Solutions; and Graceway Pharmaceuticals.

CME Credit Documentation

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

Evaluation Forms

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

CME Disclosure of Financial Interests

Speaker - Dr. Hall has disclosed the following financial relationships: Research grants - Genentech; Centocor; Spectral Images.

Program Planning Committee Participants

- Benjamin Dubin, MD, program chair, has no significant financial relationships to disclose.
- Richard Paul, CDS executive director, has no significant financial relationships to disclose.
- Roger L. Rodrigues, MD, Chairman, Chicago Medical Society's CME Subcommittee on Joint Sponsorship, has no significant financial relationships to disclose.
- Bapu P. Arekapudi, MD, Member of Chicago Medical Society's CME Subcommittee on Joint Sponsorship, has no significant financial relationships to disclose.
- M. Anita Johnson, MD, Member of Chicago Medical Society's CME Subcommittee on Joint Sponsorship, is a shareholder with the following: Pfizer, Merck, Abbott Laboratories, Bristol Meyers Squibb, and Zimmer Holdings, Inc.
- Marella L. Hanumadass, MD, Member of Chicago Medical Society's CME Subcommittee on Joint Sponsorship, has no significant financial relationships to disclose.
- Hugo A. Alvarez, MD, Member of Chicago Medical Society's CME Subcommittee on Joint Sponsorship, has no significant financial relationships to disclose.
- Cecilia Merino, Chicago Medical Society, Director of Education, has no significant financial relationships to disclose.

Guest Speaker

David Fretzin Lecture

Russell P. Hall III, MD

Interim Chair, Department of Dermatology, Duke University Medical Center, Durham, NC

Dr. Hall is the J. Lamar Callaway Professor of Dermatology, professor of immunology, and the interim chair of the Department of Dermatology at Duke, newly created in 2009. He joined Duke's faculty as assistant professor of medicine in 1984 after residencies in internal medicine and dermatology at the University of Missouri–Columbia and Johns Hopkins, as well as five combined years in the Dermatology Branch of the National Cancer Institute. He previously served as the deputy editor for the Journal of Investigative Dermatology and is currently the secretary–treasurer for the Society for Investigative Dermatology.

Educational Items

Course Director: Benjamin Dubin, MD

Target Audience: Practicing dermatologists, dermatology residents and fellows

Objectives: At the conclusion of this learning activity, the participant should be able to:

1. Describe the pharmacology of dapsone and similar medications, and the idiosyncratic and pharmacologic adverse effects.
2. Explain the clinical conditions that are most appropriate to treat with dapsone vs other drugs.
3. Discuss the appropriate evaluation of patients before and during the selected treatment in order to minimize adverse effects.

University of Illinois at Chicago
Department of Dermatology

FACULTY

Lawrence S. Chan, MD, *Head of the Department*
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DERMATOPATHOLOGY

Helen Chen, MD
Patricia Fishman, MD
David Fretzin, MD

DERMATOLOGY RESIDENTS

Third Year

Tanya Bulj-Stevens, MD
Sabrina Guillen Fabi, MD
Rikk Lynn, MD
Caroline Schmitt, MD
Amber Stevenson, MD

Second Year

Joanne Montgomery, MD
Jonathan Pewitt, MD
Marie Reichle, MD

First Year

Shruthi Reddy, MD
Carmen Schwartz, MD
Brendan Thomas, MD

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Case # 1

Case Presented by Joanne Montgomery, MD
and Lawrence Chan, MD

History of Present Illness:
This 40 year old African American woman presented with a pruritic blistering eruption which began approximately two years prior. The eruption started on the face with subsequent spread to the trunk and extremities. On presentation, the most prominent involvement was over her anterior lower legs. She noted severe itching with blister formation after scratching. The patient denied photosensitivity and was taking no medications prior to onset of the eruption. She was initially seen by an outside dermatologist and was placed on triamcinolone 0.1% cream, tetracycline 500 mg twice daily, niacin 500 mg twice daily, and hydroxyzine as needed for itching. She noted minimal improvement with this regimen.

Past Medical and Surgical History:
None

Medications:
Tetracycline, niacin, hydroxyzine, triamcinolone 0.1% cream

Allergies:
No known drug allergies

Family History:
Non-contributory

Review of Systems:
Occasional nausea and diarrhea; no fever, chills, weight changes, chest pain, shortness of breath, arthralgias or myalgias.

Physical Examination:
There are scattered excoriated hyperpigmented patches and thin plaques over the face, back, chest, abdomen, and arms. Over bilateral pre-tibial surfaces are prominent, well-demarcated, hyperpigmented confluent plaques with multiple overlying superficial blisters and erosions. There is no mucosal involvement.

Laboratory Data:
The following were negative or within normal limits:
Complete blood count, complete metabolic panel, glucose-6-phosphate dehydrogenase (G6PD) level, antinuclear antibody

Histopathology/Immunopathology:
Back, lesional skin: Multiple sections show intraepidermal vesiculation with acantholysis involving predominantly the mid-epidermis. This is associated with both intraepidermal and superficial dermal infiltrate of mixed inflammatory cells including neutrophils.

Direct immunofluorescence, back, peri-lesional skin: There is strong deposition of IgG on keratinocyte cell surfaces. IgA and C3 were not detected.

Indirect immunofluorescence: Serum test on monkey esophagus showed IgG epithelial cell surface binding autoantibodies at a titer of 1:80.

Diagnosis:
Pemphigus herpetiformis

Treatment and Course:
The patient was started on dapsone 50 mg daily with improvement of her pruritus and diminished blister formation. Attempt was made to increase the dose to 100 mg daily, however she experienced persistent flu-like symptoms necessitating dose reduction back to 50 mg daily. Over the course of the next three months, the patient's blisters resolved completely, leaving only post inflammatory changes.

Discussion:
Pemphigus herpetiformis (PH) is a rare, clinically distinct variant of pemphigus which classically combines the physical characteristics of dermatitis herpetiformis with an immunofluorescence pattern typical of pemphigus. Although reports of similar cases, described as "dermatitis herpetiformis with acantholysis," can be found in the literature as early as 1955, criteria and naming of this disorder did not occur until 1975.

Skin lesions are frequently described as similar to dermatitis herpetiformis, including erythematous, edematous, annular or gyrate plaques studded with fragile vesicles or blisters. The trunk and proximal limbs are most commonly affected, with occasional report of mucosal involvement. Clinical presentation can be quite variable, and patients are often initially diagnosed with other blistering disorders, such as dermatitis herpetiformis, pemphigus foliaceous, bullous pemphigoid, or linear IgA bullous dermatosis. This variability is evident in our patient, as her most prominent and persistent lesions were localized over the bilateral pre-tibial surfaces. Other hallmarks of PH are intense pruritus and marked response to sulfones, including dapsone.

Histologically, PH varies significantly between cases and multiple biopsies are often required to confirm the diagnosis. Acantholysis is frequently mild or absent, however spongiosis and infiltration of the epidermis with eosinophils and/or neutrophils is commonly reported. In contrast to the variable clinical and histological findings, direct immunofluorescence consistently reveals IgG deposition on keratinocyte cell surfaces, most prominently in the upper epidermis.

Essential Lessons:
- Pemphigus herpetiformis is a clinically distinct variant of pemphigus characterized by intense pruritus.
- Pemphigus herpetiformis should be distinguished from other forms of pemphigus, as these patients often respond to dapsone, a medication with fewer side effects than many other potential therapies.

References:

1. Floden CH, Gentale H. A case of clinically typical dermatitis herpetiformis (M. Duhring) presenting acantholysis. *Acta Derm Venereol (Stockh)* 1955;35:128.
2. Jablonska S, et al. Herpetiform pemphigus, a variable pattern of pemphigus. *Int J Dermatol* 1975;14:353-9.
3. Maciejowska E, Jablonska S, Chorzelski T. Is pemphigus herpetiformis an entity? *Int J Dermaol* 1987;26:571-7.
4. Robinson ND, et al. The new pemphigus variants. *J Am Acad of Dermatol* 1999;40(5);649-71.
5. Santi CG, et al. Pemphigus herpetiformis is a rare clinical expression of nonendemic pemphigus foliaceus, fogo selvagem, and pemphigus vulgaris. *J Am Acad Dermatol* 1996;34:40-6.

Case # 2

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

History of Present Illness:
This 14 year old female presented with complaints of thin hair, thickened nails, and dry skin. Her hair had been thin and slow-growing since birth, but during the year prior to presentation the patient had developed scattered gray hair shafts on her scalp. She reported scant eyebrow hair and eyelashes, along with scant and brittle axillary and pubic hair. She complained of thickened and easily broken fingernails, but stated that her toenails were unaffected. The patient did acknowledge significant misalignment of the teeth, but denied any abnormalities of sweating or thickening of the palms or soles.

Past Medical and Surgical History:
Surgical repair of a cleft lip and palate, bilateral otoplasty for protruding ears

Medications:
None

Allergies:
No known drug allergies

Family History:
The parents are first cousins, healthy, with two other healthy children, all with normal skin, hair, and nails.

Social History:
The patient is a high school student doing well academically.

Review of Systems:
The patient denied any fevers, chills, night sweats, weight loss, joint pains, or rashes.

Physical Examination:
The scalp hair is thin, dry, brittle, and wavy, with several intermixed gray hair shafts of varying lengths. The eyebrows are short, brittle, and scantly distributed over each eye, with the eyelashes also noted to be short. There is a surgical scar from a cleft lip and palate repair. The central and lateral incisors are spread apart from one another, and one incisor is cone-shaped in appearance. The fingernails are thickened with yellow discoloration. The left foot has a bulbous fifth toe. There is diffuse xerosis of the arms and legs. Microscopic examination of several scalp hairs reveals variation of diameter within individual hair shafts.

Laboratory Data:
None

Diagnosis:
Unknown ectodermal dysplasia

Treatment and Course:
The likely autosomal recessive nature of the patient's condition and implications for future offspring were discussed with the patient and her parents. Consultation with a geneticist was arranged, at which time testing for mutations in selected exons of the tumor protein p73-like gene was negative. At this time, no curative treatment currently exists for the patient's condition.

Discussion:

Ectoderm is the outer germ layer in the embryo that ultimately differentiates into several important tissues and structures, which include the skin, skin appendages, teeth, and components of the nervous system. Rarely, different inheritable defects resulting in abnormalities of the ectodermal structures may occur, and the term "ectodermal dysplasias" is used to describe this large group of inherited disorders. Approximately 160 different ectodermal dysplasias have been described, and each type may be classified into one of eleven subgroups based on the presence of hair (1), tooth (2), nail (3), and sweating defects (4). These conditions are always present at birth and do not progress to more severe forms with age.

The above patient's presentation meets the criteria for categorization into subgroup 1-2-3, which contains approximately 15 conditions. Of those conditions, the above case shares similarities with (a) Fried's tooth and nail syndrome (OMIM 189500), which is characterized by scanty eyebrows, thin nails, hypotrichosis, occasional clefting of the lip, and branchial cysts, and (b) odontoonychodysplasia with alopecia, having features of hypotrichosis, hypodontia, and dystrophic toenails, but seems to most closely resemble (c) ectodermal dysplasia with pili torti and syndactyly (OMIM 225060), which often presents with a cleft lip and palate, sparse scalp hair, malformed protruding ears, and partial syndactyly of the fingers and toes, though cases in which syndactyly is absent have been reported.

The tumor protein p73-like (TP73L) gene produces a p53 homolog protein, also known as tumor protein p63, p53-related protein p63, and KET. Within mice, this gene product has been detected in several different tissues, including proliferating basal cells within the epidermis, and seems to be a key regulator of stem cells in the stratified epidermis. As a result, mutations in this gene have been found to be associated with several ectodermal dysplasias, including ectrodactyly–ectodermal dysplasia–cleft lip and palate syndrome (OMIM 604292), ankyloblepharon–ectodermal dysplasia–clefting syndrome (OMIM 106260), and Rapp–Hodgkin syndrome (OMIM 129400). Of note, all of these syndromes are categorized into subgroup 1-2-3-4, which is expected given that mutations of the TP73L gene generally result in hair, tooth, nail, and sweating defects. With regard to our case, negative testing for mutations in the TP73L gene is expected given that the patient's clinical presentation falls into subgroup 1-2-3.

Essential Lesson:

- Ectodermal dysplasias may be classified based on the presence of hair, tooth, nail, and sweating defects.

References:

1. Burns T, et al. Rook's Textbook of Dermatology. Seventh Edition. Oxford: Blackwell Science, 2004;12-40.
2. Fried K. Autosomal recessive hidrotic ectodermal dysplasia. *J Med Genet* 1977;14:137-139.
3. "Online Mendelian Inheritance in Man." http://www.ncbi.nlm.nih.gov/omim/. Retrieved 2009-10-30.
4. Other genodermatoses *in* Dermatology, Second Edition. Bolognia JL editor in chief. Spain: Elsevier Limited, 2008;857-82.
5. Pinheiro M, Freire-Maia N. Ectodermal dysplasias: a clinical classification and a causal review. *Am J Med Genet* 1994;53:153-62.
6. Pinheiro M, Freire-Maia N, Gollop T. Odontoonychodysplasia with alopecia: a new pure ectodermal dysplasia with probable autosomal recessive inheritance. *Am J Med Genet* 1985;20:197-202.
7. Yi R, et al. A skin microRNA promotes differentiation by repressing 'stemness.' *Nature* 2008;452:225-9.

Case # 3

Case Presented by Shruthi Reddy, MD
and Michelle Bain, MD

History of Present Illness:
This 4 year old male with common variable immunodeficiency presented with a 9 month history of multiple asymptomatic flesh-colored bumps on the extremities. The eruption resolved with prednisone and lesions recurred after it was discontinued. Molluscum contagiosum was diagnosed at an outside institution and cantharidin was subsequently applied to 120 lesions causing an exuberant reaction with no resolution. A shave biopsy performed at an outside institution was bisected with half consistent with lichen nitidus and the other with granuloma annulare.

Past Medical and Surgical History:
Born at 33 weeks gestational age with intrauterine growth restriction, common variable immunodeficiency, autoimmune hemolytic anemia, neutropenia, recurrent sinusitis with sinus surgery, otitis media with tympanic membrane perforation status-post bilateral myringotomy and adenoidectomy

Medications:
Sulfamethoxazole/trimethoprim, azithromycin

Allergies:
No known drug allergies

Family History:
Denies consanguinity; no family history of immunodeficiency or skin disorders

Review of Systems:
No fevers, chills, nausea, vomiting, or night sweats

Physical Examination:
On the face, arms, hands, legs, feet, and buttocks are numerous pink scaly umbilicated papules and indurated plaques, some with cratiform center and crusting.

Laboratory Data:
The following were positive or abnormal:
IgA 10 mg/dL (50-210), IgM <25 mg/dL (50-200), white blood cell count 3.2 k/uL (5-15), hematocrit 32.5% (36-44), % neutrophil 75.6 (30-50), % lymphocyte 9.4 (30-60), % monocyte 12.7 (4-8), absolute lymphocytes 0.3 k/uL (1.5-9), absolute eosinophils 0.1 k/uL (0.2-0.6), absolute CD3 151 cells/uL (1610-4230), absolute CD4 93 cells/uL (900-2860), absolute CD8 33 cells/uL (630-1910), absolute CD19 0 cells/uL (400-1440).

The following were negative or within normal limits:
IgG 691 mg/dL (540-1440), complete metabolic panel, hemoglobin, platelets, and antinuclear antibody

Histopathology:
Right buttock, skin: Multiple sections show extensive dermal granulomas with central necrosis, associated with psoriasiform epidermal hyperplasia. There is also a dermal perivascular and interstitial infiltrate of neutrophils, histiocytes, and giant cells. The Gomori's methenamine silver stain for fungi, along with the Acid-fast and Fite stains for mycobacteria are all negative.

Diagnosis:
Common variable immunodeficiency with cutaneous granulomas

Treatment and Course:
The patient was treated with multiple courses of rituximab, intravenous immunoglobulin, and prednisone for the hemolytic anemia and panhypogammaglobulinemia for his CVID with no resolution of cutaneous granulomas. Flurandrenolide tape, clobetasol ointment, and diprosone cream were applied with no improvement. The patient is planning to start hydroxychloroquine per an immunologist at Mayo Clinic.

Discussion:
Common variable immunodeficiency (CVID) is the most common primary immunodeficiency characterized by hypogammaglobulinemia, poor or absent antibody response, and recurrent bacterial infections. Prevalence ranges from 1:50,000 to 1:200,000 individuals. The usual age of onset is 20 to 30 years but children can present as early as 2 years. Granulomatous complications of different organs including the skin can occur. However, isolated cutaneous granulomas in CVID are rare and are mainly described in association with visceral granulomas. Clinical features are non-specific, typically consisting of infiltrated erythematous scaly, excoriated, or ulcerated papules, nodules, or plaques on the face and extremities.

Cutaneous granulomas in CVID are histologically differentiated into nonnecrotizing (sarcoid-like), caseating (tuberculoid) or, rarely, necrobiotic palisading. Pathogenesis is unknown but may include an unrecognized infectious agent or altered cell-mediated and humoral immune response resulting in excess cytokine release. Tumor necrosis factor-alpha (TNF-α), the key cytokine produced by activated monocytes and macrophages, appears to be elevated in patients with CVID associated granulomatous disease and may suppress the effects of T and B lymphocytes, leading to granuloma formation. Low dose steroids are the mainstay of treatment, however they are not always effective. Steroid sparing treatments, including the TNF-α antagonists, hydroxychloroquine, anti-CD20, and cyclosporine have been tried with mixed results and should be used with caution due to the increased risk of infection and malignancy.

Essential Lessons:
- Isolated cutaneous granulomas is a rare occurrence in CVID.
- Cutaneous granulomas can be differentiated histologically into nonnecrotizing, caseating, and necrobiotic.

References:

1. Artac H, et al. Sarcoid like granulomas in common variable immunodeficiency. *Rheumatol Int* 2009. Epub 2009 Mar 27.
2. Hatab AZ, Ballas Z. Caseating granulomatous disease in common variable immunodeficiency treated with infliximab. *J Allergy Clin Immunol* 2005;116:1161-2.
3. Knight AK and Cunninghma-Rundles C. Inflammatory and autoimmune complications of common variable immune deficiency. *Autoimmun Rev* 2006; 5(2):156-9.
4. Lin J, et al. Etanercept treatment of cutaneous granulomas in common variable immunodeficiency. *J Allergy Clin Immunol* 2006;117(4):878-82.
5. Mitra A, et al. Cutaneous granulomas associated with primary immunodeficiency disorders. *Br J Dermatol* 2005;153:194-9.
6. Pujol RM, et al. Cutaneous granulomatous lesions in common variable immunodeficiency: complete resolution after intravenous immunoglobulins. *Dermatol* 1999;198:156-8.

Case # 4

Case Presented by Tanya Bulj-Stevens, MD
and Lawrence Chan, MD

History of Present Illness:
This 71 year old African American male was referred for evaluation of multiple rapidly growing nodules within a thermal burn scar. Four weeks prior to initial presentation he was burned after spilling hot coffee on his right arm. He initially developed redness, burning pain, and itching, but denied blister formation. Several weeks after the accident, multiple nodules began to develop within the scar.

Past Medical and Surgical History:
Seizure disorder, depression, benign prostate hypertrophy. The patient denied any history of ultraviolet phototherapy or radiation therapy.

Medications:
Citalopram, phenytoin

Allergies:
No known drug allergies

Family History:
No family history of skin cancer

Review of Systems:
Occasional joint pains; no nausea, vomiting, fever, chills, cough, or weight loss

Physical Examination:
Over the right dorsal arm is a hyperpigmented patch with multiple overlying firm pink papules and several larger pink nodules, some with eroded crateriform centers. The remaining skin and mucosal examinations were normal. There is no significant photodamage in the overall skin examination.

Histopathology:
Right arm, skin: Multiple sections show exo-endophytic proliferation of well differentiated keratinocytes. The nests of epithelial cells are keratinizing at the base of the biopsy. This is associated with a dermal robust infiltrate of lymphocytes and numerous eosinophils. Intraepithelial eosinophilic abscesees are identified. Excision of the lesion shows similar morphology. The base of the lesion is very well differentiated with no significant cytological atypia.

Diagnosis:
Multiple keratoacanthomas arising within a burn scar

Treatment and Course:
After the initial biopsy, the patient returned for excision of several larger nodules. The remaining adjacent smaller lesions have regressed in size. He was advised to closely follow up in dermatology clinic to monitor for new or recurrent lesions.

Discussion:

Keratoacanthomas (KA) typically occur spontaneously as a single rapidly growing tumor in sun-exposed areas in elderly patients. They appear as firm dome-shaped papules or nodules with crateriform centers. Multiple KAs are rarely seen, however they have been reported to arise in sites of previous cutaneous trauma. We report a case of sudden appearance of multiple KAs several weeks after thermal burn.

Although skin trauma may be a contributing factor, the actual induction mechanism of keratoacanthoma remains unclear. Genetic factors appear to play a role in certain conditions involving KAs. For example, Ferguson-Smith type of multiple KAs has been noted to have a familial tendency with childhood onset. Interaction between genetic predisposition and various cofactors, such as UV-light exposure, chemical carcinogens, radiation therapy, and various forms of antecedent trauma, including surgery, grafting, thermal burns, laser resurfacing, and vaccination may also play an important role in pathogenesis of KAs. Some have proposed the idea of the necessary involvement of an initiating factor (i.e. sunlight or a chemical carcinogen) with subsequent trauma acting as the promoter to induce tumor formation. Overall, there is a predilection for these lesions to arise in sites of trauma.

The differential diagnosis for KAs is broad, including seboacanthoma, exophytic pilomatricoma, cutaneous metastatic disease, verrucous carcinoma, deep fungal infection, halogenoderma and giant molluscum contagiosum. The most frequent consideration in the clinical and histologic differential diagnosis of the KA, however, is squamous cell carcinoma (SCC). Clinically, KAs are characterized by a rapid onset and regression within months without tendency to form regional or distant metastasis. They display distinct histological features including a keratin-filled crater lined by a proliferating squamous epithelium and prominent keratinization of the squamous cells producing a glassy appearance. Intraepidermal abscesses are common in KA and rarely seen in SCC. Cytological atypia is absent to mild and mitotic figures are rare, in contrast to the more pleomorphic and aggressive appearance of SCC. Regression is immunologically mediated and activated by a variety of molecular mechanisms.

Solitary KAs are usually treated by complete excision. Mohs micrographic surgery is the method of choice for treating large KAs or KAs located in critical anatomic areas. Other treatments described in literature include cryosurgery, radiation therapy, laser surgery, intralesional bleomycin, intralesional 5-fluorouracil, intralesional methotrexate, as well as intralesional interferon alfa-2a. Systemic treatments are reserved for multiple, surgically non-resectable or recalcitrant lesions and include retinoids, methotrexate, 5-fluorouracil, cyclophosphamide and epidermal growth factor receptor antagonists.

Essential Lessons:

- Keratoacanthoma must be considered in the differential diagnosis of rapidly growing nodules within a scar, as it shows predilection for sites of cutaneous trauma.
- The pathogenesis of keratoacanthoma is uncertain and remains to be elucidated.

References:

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2. Hendricks WM. Sudden appearance of multiple keratoacanthomas three weeks after thermal burn. *Cutis* 1991;47:410-2.
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Case # 5

Case Presented by Amber Stevenson, MD
and Iris Aronson, MD

UNKNOWN CASE

This 16 year old previously healthy female presented to dermatology for evaluation of new onset progressive, painful genital ulcerations.

Case # 6

Case Presented by Sabrina Guillen Fabi, MD and Lawrence Chan, MD

History of Present Illness:
This 22 year old man presented in October 2008 with a 2 month history of a pruritic, painful, draining plaque over his right elbow that he noted 2 weeks after returning from Iraq. He complained that it was increasing in size and had shown no signs of resolution.

Past Medical and Surgical History:
None

Medications:
None

Allergies:
Penicillin

Social History:
The patient is a U.S. Marine who is presently on active duty.

Review of Systems:
He denied fevers, chills, sweats, weight loss, epistaxis, mucosal involvement, or difficulty breathing.

Physical Examination:
Over the right proximal elbow was an approximately 1.5 cm erythematous, hyperkeratotic, scaly plaque with central ulceration and overlying serosanguinous crust. There was no axillary lymphadenopathy.

Laboratory Data/Diagnostic Procedures and Tests:
The following were positive or abnormal:
Tissue culture of lesional skin on diphasic Novy-MacNeal-Nicolle (NNN) media grew *Leishmania* and polymerase chain reaction (PCR) idenitified *Leishmania major (L major)* as the species

The following were negative or within normal limits:
Tissue cultures of lesional skin for anaerobes, acid- fast bacilli, and fungi

Histopathology:
Right proximal elbow, skin: There is a mixed dermal inflammatory cell infiltrate including lymphocytes, plasma cells, and histiocytes. The cytoplasm of histiocytes is filled with numerous small organisms, measuring 2 to 4µm in diameter. These organisms are highlighted by the Giemsa stain. Both the Gomori's methenamine silver for fungi and the Fite stain for acid-fast bacilli are negative.

Diagnosis:
Cutaneous leishmaniasis

Treatment and Course:
Given that the patient had limited cutaneous involvement near the elbow joint and was not showing evidence of spontaneous resolution after 4 months, treatment was initiated. The patient underwent a 1 month treatment course of ketoconazole 600 mg daily. Within 3 weeks of treatment, there was marked improvement in the appearance and symptoms of the plaque. After 4 months of treatment, the plaque had resolved with evidence of post-inflammatory hyperpigmentation.

Discussion:

Leishmaniasis is caused by more than 20 species of *Leishmania*, which are intracellular protozoan parasites that are divided into Old World (Africa, Asia, Southern Europe, and the Middle East) and New World (Latin America) species. *Leishmania* are transmitted by the sand fly from the genera *Lutzmyia* (Old World) and *Phlebotomus* (New World). Some species primarily cause cutaneous disease (*L major and L tropica*), while others primarily cause visceral disease (*L infantum, L amazonesis, L brazilensis and L donovani).* The global incidence of leishmaniasis has increased in recent years because of leisure- and military-related travel. Cutaneous leishmaniasis (CL) is one of the top 10 causes of skin disease in tourists from tropical countries. Despite the relatively high incidence, diagnosis is often delayed, which, depending on the sub-type, can lead to mucosal spread.

Diagnosis of CL is based on the clinical finding of a non-healing ulcerated or verrucous scaly plaque in a patient who has returned from an endemic area. Several conditions need to be considered in the differential diagnosis, including arthropod bite, atypical mycobacterioses, subcutaneous mycoses, cutaneous myiasis, and basal cell carcinoma. The diagnosis is confirmed by a skin biopsy demonstrating the presence of amastigotes in dermal macrophages. NNN media or chick embryo media is required for culturing *Leishmania*, which is positive in approximately 40% of cases. The gold standard for diagnosis is presently PCR, as it speciates the organism allowing for species-specific treatment.

Although CL often spontaneously heals with significant scarring, it can proliferate to become more invasive mucocutaneous leishmaniasis (ML). Therefore, treatment may be considered to prevent this complication. Although the decision of whether or not to treat requires a careful assessment of the individual patient, criteria are suggested to determine whether a patient may benefit from systemic therapy. The criteria include: 1) Lesion localization to the face (cosmetically evident sites) or close proximity to joints, 2) Lesions which have not healed for many months, 3) Lesions measuring more than 4-5 cm in diameter or multiple lesions, 4) Lesions suggesting local evidence of dissemination, 5) Most species of New World leishmaniasis, and 5) Chronic ear infection of *L mexicana* (chiclero ulcer).

Pentavalent antimonials are considered the gold standard for treatment of CL of the New World and for severe Old World Leishmaniasis, but are unfortunately associated with many adverse effects and prove difficult to administer because they are only available in parenteral forms. Pentamidine is an alternative parenteral drug, associated with less toxicity. Miltefosine, available orally, is a phosphocholine analog that shows efficacy in treatment of Old World and New World CL and ML. In a small nonrandomized trial of 15 patients with *L major* and *L tropica*, miltefosine at a dose of 2.5 mg/kg/day for 28 days had a 100% cure rate after the end of treatment and an 87% cure rate after 6 months; unfortunately its adverse effects and cost limit its use. The imidazoles and structurally-related triazoles have anti-leishmanial activity, and are generally better tolerated and can be given orally. A comparative study treating 64 patients with ketoconazole 600 mg/daily for adults and 10 mg/kg/day in children for 30 days, showed an 89% cure rate 6 weeks after treatment. Other effective treatment modalities include cryotherapy (up to 3 sessions at 3 week intervals), as well as twice daily application of an ointment with 15% paromomycin plus 12% methylbenzethonium chloride for 20 days, which demonstrated a 74.2% cure rate.

Essential Lesson:

- Speciation of leishmaniasis with PCR is imperative as treatment of certain species may be different and suboptimal treatment may cause a prolonged course or disfiguring scars.

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1. Blum JA, Hatz CF. Treatment of cutaneous leishmaniasis in travelers 2009. *J Travel Med* 2009;16(2):123-31.
2. Palumbo E. Current treatment for cutaneous leishmaniasis: a review. *Am J Ther* 2009;16(2):178-82.
3. Salmanpour R, Handjani F, Nouhpisheh MK. Comparative study of the efficacy of oral ketoconazole with intra-lesional meglumine antimoniate (Glucantime) for the treatment of cutaneous leishmaniasis. *J Dermatolog Treat* 2001;12(3):159-62.

**Cases Presented by Marie Reichle, MD, Edmund Chow, MD,
Iris Aronson, MD, and Aleksandar Krunic MD, PhD**

Patient A

History of Present Illness:

This 63 year old African American male presented with a one year history of slowly progressive hand swelling, thickening, and fissuring as well as small papules on his nose, lips, and eyelids. The hands were intermittently painful and sensitive to cold. The papules at his oral commissures made eating uncomfortable but were otherwise asymptomatic.

Past Medical and Surgical History:

Hyperlipidemia, arthritis, history of transaminitis, bilateral total hip arthroplasties, excision of laryngeal nodules in 2008

Medications:

Triamterene, omeprazole, multivitamin, fish oil, K-Swiss laxative

Allergies:

No known drug allergies

Family History:

Negative for malignancy

Review of Systems:

The patient reported decreased hand strength, dyspnea on exertion, and orthopnea. He denied weight loss, fatigue, gastrointestinal symptoms, paresthesias, and lymphadenopathy.

Physical Examination:

There are small, waxy, flesh-colored and purpuric papules at the upper eyelids, nostrils, and columella. The vermillion lips have waxy, flesh-colored, confluent papules. The volar finger surfaces have large areas of skin-colored soft plaques with cerebriform folds and mild fissuring.

Laboratory Data:

The following were positive or abnormal:
Urine free lambda light chains 12.3 mg/dL (0.02-0.67), urine kappa/lambda ratio 0.12 (2.04-10.37), urine total protein 165 mg/day (10-140), serum IgM 29 mg/dL (60-263), serum IgG 701 mg/dL (768-1,632)

The following were negative or within normal limits:
Complete blood count, peripheral smear, beta 2 microglobulin, lactate dehydrogenase, serum protein electrophoresis, serum IgA, basic metabolic panel, ionized calcium, uric acid, thyroid stimulating hormone, urinalysis

Diagnostic Procedures and Tests

Bone marrow aspirate: Immunoglobulin heavy chain gene rearrangement study by polymerase chain reaction negative

Bone survey: No lytic lesions

Echocardiogram: Bright myocardium, reduced biventricular systolic function, severely decreased left ventricular ejection fraction at 25% (50-70), left ventricular restrictive filling pattern, tricuspid and mitral valve regurgitation, pulmonary hypertension, and mildly increased size of ventricles and atria. The findings are consistent with cardiac amyloidosis.

Histopathology:
Left hand, skin: There is extensive deposition of pale pink material in a perivascular distribution. The pink material is highlighted by the Congo red stain.

Bone marrow biopsy: The biopsy is hypercellular for the patient's age with rather extensive hemorrhage. There is an interstitial infiltrate of lymphocytes and plasma cells, with plasma cells accounting for approximately 5-10% of marrow cellularity. Multiple small blood vessels display a thickened wall with hyalinized appearance. Nodular deposit of pink material is identified in one focus. The pink material stains strongly positive for Congo red. The plasma cells are highlighted by the CD 138 stain.

Vocal fold nodule biopsy: polypoid fragments of tissue from vocal cord showing significant stromal deposits of amyloid.

Diagnosis:
Primary systemic amyloidosis

Treatment and Course:
This patient was diagnosed with primary systemic amyloidosis with cutaneous and cardiac involvement. Due to amyloid deposition within myocardium and low ejection fraction, autologous stem cell transplant with high-dose melphalan conditioning could not be performed. He is currently being treated with bortezomib, lenalidomide, and dexamethasone. If repeat echocardiogram shows improvement of cardiac function, stem cell transplant with melphalan conditioning may be considered.

Patient B
History of Present Illness:
This 72 year old female presented with a four month history of hand papules and nodules. She complained of hand paresthesias and tenderness.

Past Medical and Surgical History:
Asthma, hypertension, osteoarthritis, history of sarcoidosis diagnosed by pulmonary lymph node biopsy in 1990, bilateral carpal tunnel release surgery in 2009

Medications:
Fluticasone / salmeterol inhaler, diltiazem, hydrochlorothiazide / losartan

Allergies:
Naproxen, ibuprofen

Family History:
Negative for malignancy and autoimmune diseases

Review of Systems:
She complained of bilateral hand paresthesias, which had improved since her carpal tunnel release surgeries. She had intermittent abdominal bloating. She denied fatigue, weight loss, and weakness.

Physical Examination:
The volar finger surfaces have soft, tender, flesh-colored papules and nodules.

Laboratory Data:
The following were positive or abnormal:
Presence of serum abnormal protein band 0.9 g/dL (0), presence of serum monoclonal free lambda light chains (0), kappa quantitation 422 mg/dL (629-1350), lambda quantitation 1010 mg/dL (313-723), kappa/lambda ratio 0.42 (1.47-2.95), serum alpha-1 globulins 0.4 g/dL (0.1-0.3), serum beta globulins 1.5 g/dL (0.8-1.4), serum gamma globulins 0.5 g/dL (0.6-1.6), urine protein / creatinine ratio 372 (21-161), presence of abnormal protein band in urine beta globulins 4 mg/dL (0), white blood cells 11,000 cells/uL (3.8-10.8), absolute eosinophils 726 cells/uL (15-500)

The following were negative or within normal limits:
Complete metabolic panel, hemoglobin, platelets, serum IgA, serum IgG, serum IgM, serum alpha-2-globulins, urine albumin, urine alpha-1-globulins, urine alpha-2-globulins, urine gamma globulins, antinuclear antibody, anti-double stranded DNA antibody, anti-topoisomerase I antibody, anti-Smith antibody, anti-ribonucleoprotein antibody, anti-Ro antibody, anti-La antibody, rheumatoid factor, anti-cyclic citrullinated peptide

Diagnostic Procedures and Tests:
Bone marrow aspirate: Cytogenetic analysis reveals normal female karyotype without evidence of acquired clonal abnormality. Myeloma fluorescent in situ hybridization is normal.

Abdominal ultrasound: Multiple nodules in the liver, bilateral renal cysts

Histopathology:
Right hand, skin: There is extensive perivascular and interstitial deposition of pale pink amorphous material, with some artifactual separation. There is no significant inflammatory cell infiltrate. The overlying epidermis displays mild reactive changes. The pink material is highlighted by the Congo red stain.

Bone marrow biopsy: There is a clonal population of lambda restricted, CD138-positive plasma cells, accounting for approximately 15% of marrow cellularity. Congo red stain is negative for amyloidosis.

Diagnosis:
Primary systemic amyloidosis

Treatment and Course:
Evaluation for additional organ involvement is ongoing. Treatment has not yet been initiated, but there are plans for treatment with a thalidomide-containing regimen.

Discussion:
In primary systemic amyloidosis (AL amyloidosis), clonal plasma cells produce serum monoclonal immunoglobulin light chains, which are deposited into various organs. AL amyloidosis is a rare disorder with an annual incidence of 6-9 per million, affecting men more than women (2:1). The median age at presentation is sixty-seven years, and presentation will depend on the predominately affected organs.

Diagnosis depends on AL amyloid on biopsy, presence of serum or urine monoclonal protein, and a compatible clinical picture. If AL amyloidosis is suspected, screening for monoclonal light chains should be performed by either urine and serum immunofixation (90% sensitivity) or by immunoglobulin free light chain assay (99% sensitivity). Bone marrow biopsy is performed to exclude multiple myeloma and shows less than 30% plasma cells in AL amyloidosis patients. Clonal plasma cells in bone marrow are usually detected when examined by flow cytometry, immunofluorescence, or immunohistochemistry.

The affected organ which is most easily accessible should be biopsied to check for amyloid deposition. Preferable sites include the skin, labial salivary glands, rectum, duodenum, and subcutaneous fat. On

histology, amyloid is highlighted by Congo red stain and exhibits apple green birefringence under polarized light. Congo red staining is 100% specific for amyloidosis if properly performed and read. If no paraproteinemia is present, typing of amyloid is of great importance. This is generally performed by immunohistochemistry and allows AL amyloid to be distinguished from other forms.

After diagnosis, additional organ involvement should be determined. A complete history and physical exam, echocardiography, urine studies, and blood studies including beta-2 microglobulin, brain natriuretic peptide, and troponin will assess disease extent. ^{123}I-labeled serum amyloid P scintigraphy identifies amyloid deposition in organs with 90% sensitivity and 93% specificity. Numerous organs may be affected, producing corresponding signs and symptoms. Amyloid deposition in myocardium (37% of cases) leads to poor contraction and congestive heart failure. The most common cause of death is fatal arrhythmia due to involvement of the conduction system. Renal involvement (27%) results in proteinuria, nephritis, and azotemia with associated edema, weight loss, and fatigue. Peripheral nerve involvement (15-21%) results in paresthesias or neuropathy, especially involving the median nerves. Hepatic deposition (15-24%) may manifest as hepatomegaly. Intestinal amyloid (7%) may cause diarrhea, weight loss, or upper gastrointestinal pseudo-obstruction. Salivary gland infiltration leads to xerostomia. Life-threatening spontaneous hemorrhage may occur from arterial deposition.

Cutaneous involvement may occur in 21-40% of AL amyloidosis cases. Periorbital and perinasal asymptomatic, waxy, smooth papules are most commonly seen. Cutaneous AL amyloidosis may also manifest as waxy plaques with diffuse infiltration of the palms and volar fingers. Amyloid purpura is seen in 17% of patients. Involved or uninvolved skin develops petechiae spontaneously, after straining, or following trauma. The most specific finding for AL amyloidosis is macroglossia, which occurs in 9-19% of AL amyloidosis patients causing dysphonia and dysphagia. Patients may also have localized rubbery, purpuric plaques in the oral mucosa. Uncommon dermatological manifestations include scleroderma-like changes, cerebriform-like skin changes, bullae, nail dystrophy, paronychia, acquired cutis laxa, alopecia, and external auditory canal involvement.

Without treatment, median survival for AL amyloidosis patients is 12-18 months, with a median of only 6 months if congestive heart failure is present. The oldest treatment regimen combines melphalan with prednisone or dexamethasone. Stem cell transplantation after chemotherapy is often employed, although this has a high mortality rate due to patients' widespread organ dysfunction and poor tolerance to fluid shifts. Other reported treatment regimens include various combinations of the following: thalidomide, lenalidomide, cyclophosphamide, vincristine, carmustine, bortezomib, etanercept, colchicine, and dimethyl sulfoxide. No treatment regimens have consistently been effective in treating AL amyloidosis. Treatment of systemic disease may result in improvement of cutaneous findings.

Essential Lessons:

- Cutaneous involvement in primary systemic amyloidosis occurs in up to 40% of cases.
- Cutaneous primary systemic amyloidosis may appear as waxy, purpuric, papules, nodules, or plaques affecting periorbital, perinasal, or volar hand skin where it may rarely present in a cerebriform pattern.

References:

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Case # 8

Case Presented by Jonathan Pewitt, MD
and Iris Aronson, MD

History of Present Illness:
This is a 57 year old African American male who presented with an ulceration of the right hip. The patient reported that the lesion started 4 months earlier as a dark red "bruise" that subsequently developed a painful ulceration with crusting and bleeding. He was admitted to an outside hospital where vancomycin was initiated to treat an "abscess." A subsequent biopsy of the ulcer was read as diffuse dermal angiomatosis. At the time of presentation, he was treating the ulcer with Neosporin and daily dressing changes.

Past Medical and Surgical History:
Diabetes mellitus, chronic renal failure on hemodialysis, deep vein thrombosis of the right leg, glaucoma, atrial fibrillation, gout, hypertension

Medications:
Hydrocodone/acetaminophen, sevelamer, acetaminophen, naproxen, warfarin, cinacalcet, allopurinol, vitamin B complex/vitamin C/biotin/folic acid, acetazolamide, furosemide

Allergies:
Pencillin, valsartan

Review of Systems:
Patient reports muscle aches with walking and swelling of the legs. He denies fever, chills, weight loss, or joint pains.

Physical Examination:
Overlying the right anterolateral hip is a 15 cm x 5 cm well-demarcated, shallow ulceration with sloped borders. The base of the lesion has pink granulation tissue interspersed with creamy white fibrinous exudate and small scattered areas of black necrotic eschar. There is mild serosanginous drainage. Erythema and induration extend diffusely around the ulcer margin, which is tender to palpation.

Laboratory Data:
The following were positive or abnormal:
Hemoglobin 7.7g/dL (11.7-16.0), hematocrit 24.5% (38-55%), BUN 31mg/dL (6-20), creatinine 8.4 mg/dL (0.6-1.6), calcium 11.5mg/dL (8.6-10.6)

The following were negative or within normal limits:
Basic metabolic profile except as above, complete blood count except as above

Histopathology:
Right hip, skin: Multiple sections show diffuse dermal proliferations of small blood vessels associated with a moderate lymphohistiocytic infiltrate. Proliferating vessels permeate between collagen bundles. The overlying epidermis displays psoriasiform hyperplasia. The immunohistochemical stains for CD31 and CD34 highlight the relatively well-formed dermal blood vessels with a diffuse growth pattern throughout the dermis. Immunostaining for CD68 shows the presence of reactive histiocytes. The immunostain for HHV-8 is negative.

Diagnosis:
Diffuse dermal angiomatosis

Treatment and Course:
The wound was widely excised with primary closure and subsequently healed well. Excised tissue showed evidence of dystrophic calcium occurring within the wall of a medium-sized artery in the subcutaneous tissue.

Discussion:
Diffuse dermal angiomatosis (DDA) is a rare variant of cutaneous reactive angiomatosis. The reactive angiomatoses are benign processes that involve the endothelial cells and pericytes. The pathogenesis of cutaneous reactive angiomatosis is thought to be secondary to tissue hypoxia from systemic conditions that result in occlusion or inflammation of the vascular network. DDA, in particular, is associated with peripheral vascular atherosclerosis, arteriovenous fistulas, and more recently with calciphylaxis.

The clinical presentation consists of painful, violaceous, purpuric plaques that often ulcerate. The most common location is the lower extremities, but it has been described on the breasts and the forearm distal to hemodialysis arteriovenous fistulas as well. No internal organ involvement has been reported. The differential diagnosis includes other benign reactive angiomatoses, other vascular proliferations, and the benign or malignant vascular tumors. Included in the reactive angiomatoses are reactive angioendotheliomatosis, acroangiodermatitis, reactive intravascular histiocytosis, glomeruloid reactive angioendotheliomatosis and angiopericytomatosis.

The characteristic histological finding in DDA is proliferation of extravascular endothelial cells interstitially dispersed between collagen bundles throughout the dermis forming small, well developed blood vessels. The proliferating cells may show a partial spindled appearance and have vacuolated cytoplasm with surrounding extravasated erythrocytes and hemosiderin. DDA differs from reactive angioendotheliomatosis because the latter condition is a proliferation of endothelial cells within vascular lumina. There is a lack of atypia and frank spindling as well as negative staining for human herpes virus 8, which differentiates DDA from Kaposi sarcoma. Angiosarcoma, with a similar infiltrative architecture would show cellular atypia, crowded endothelial cells lining irregular vessels and solid papillary clusters.

Management involves correcting the underlying vascular abnormality. A consultation with vascular surgery for appropriate imaging and corrective surgery is indicated. After revascularization surgery, the lesions tend to resolve. Alternative therapies have included systemic steroids, and in one case involving the breast, isotretinoin reduced the symptoms, but did not heal the lesion.

Essential Lessons:
- Diffuse dermal angiomatosis is a rare benign reactive process to tissue hypoxia that is diagnosed on histological exam.
- Correction of the underlying process via vascular surgery will allow the ulceration to heal.

References:

1. Draper BK, Boyd AS. Diffuse dermal angiomatosis. *J Cutan Pathol* 2006;33(9):646-8.
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Case # 9

Case Presented by Caroline Schmitt, MD
and Iris Aronson, MD

History of Present Illness:
This 62 year old female initially presented in 2001 with a three year history of itchy, shiny, red bumps in clusters on the lower back and painful sores in the mouth and vaginal area. Biopsy at an outside institution showed interface dermatitis deemed consistent with discoid lupus. She had previously been treated with potent topical steroids, intramuscular methotrexate, intravenous solumedrol, cyclosporine, oral metronidazole, hydroxychloroquine, and tacrolimus 0.1% ointment. Since disease onset, the patient had variable involvement of the scalp, dorsal hands, trunk, and oral mucosae. These sites showed some improvement with therapy, but her vulvar disease was persistent.

Past Medical and Surgical History:
Hypertension, hysterectomy for fibroids, herpes labialis, right great toe arthroplasty with titanium implant

Medications:
Tacrolimus 0.1% ointment, conjugated estrogens, metoprolol

Allergies:
No known drug allergies

Family History:
The patient's mother has thyroid disease.

Review of Systems:
The patient denies odynophagia, hematuria, melena, or ophthalmologic symptoms. She does complain of dyspareunia and dysuria.

Physical Examination:
On the lower back are multiple scattered violaceous-to-tan variably scaly 3-5 mm papules. Over the vertex scalp is an atrophic pink alopecic patch. The periodontal gingiva show smooth red erosions with partially adherent white membranes. On the posterior vaginal introitus are two roughly symmetric apposed smooth erythematous patches.

Laboratory Data:
The following were negative or within normal limits:
Hepatitis C and B serology, complete blood count, complete metabolic panel, fasting lipid panel, antinuclear antibody, and erythrocyte sedimentation rate

Histopathology/Immunopathology:
Back, skin: There is a dense superficial dermal lichenoid infiltrate composed predominantly of lymphocytes, associated with areas of subepidermal clefting. The epidermis is mostly atrophic, with areas of hypergranulosis and hyperkeratosis. Multiple dyskeratotic keratinocytes are identified along the basal layer. On direct immunofluorescence, multiple single and grouped cytoids at the basement membrane zone and upper dermis stain with IgG, IgM, and fibrin.

Vulva, mucosa: There is a dermal lichenoid infiltrate associated with hyperkeratosis, hypergranulosis, and numerous dyskeratotic cells in the overlying epidermis.

Diagnosis:
Lichen planus with recalcitrant erosive vulvar disease

Treatment and Course:
In addition to the trials of therapy administered prior to the patient's presentation, she has been treated with the following medications concurrently with potent topical steroids and tacrolimus 0.1% ointment:

Isotretinoin 20 mg daily for four months
Prednisone 20-40 mg daily for five months; subsequently with 2-4 week tapered courses for flares
Metronidazole 500 mg two-to-three times daily for four months (multiple courses)
Mycophenolate mofetil 1000 mg BID (maximum dose) for one year
Methotrexate 15 mg (maximum dose) for six months

Despite some response of the oral and cutaneous lesions to these treatments, the patient's vulvar erosions have been recalcitrant. She declined a trial of thalidomide.

Discussion:

Lichen planus (LP) is an idiopathic inflammatory dermatosis classically characterized by pruritic purple papules on the skin whose histologic correlate is a band-like lymphocytic infiltrate causing liquefactive degeneration of the epidermal basal layer. Vulvovaginogingival syndrome, first described by Pelisse in 1982, is an uncommon variant of LP in which the labial and vaginal mucosae appear erythematous, tender, and denuded of epithelium in association with desquamative gingivitis. Chronic genital disease can lead to loss of normal vulvar morphology with scarring, adhesion formation, and vaginal stenosis.

Genital involvement of LP may be part of more widespread mucocutaneous disease, but is often its most bothersome manifestation, causing dyspareunia, itching, burning, pain, and vaginal discharge. Reports of malignant transformation of vulvar LP further highlight the need for efficacious therapy for these patients. Unfortunately, for those who do not respond readily to first-line ultrapotent topical steroids, there are no consistently efficacious treatment alternatives. In a prospective study of 114 women with erosive LP of the vulva, no systemic therapy was found to be reliably effective, including minocycline, erythromycin, acitretin, cyclosporine, azathioprine, hydroxychloroquine, thalidomide, and colchicine. Griseofulvin, once thought to be a safe alternative for classic LP, was recently shown to be ineffective in oral erosive disease.

It is unclear why patients do not respond to systemic immunosuppressants given that LP is thought to be a T-cell-mediated autoimmune disease. An alternative immunomodulatory strategy, extracorporeal photophoresis (ECP), was found to induce partial or complete remission in eleven women with erosive genital LP in two series. Efalizumab is another novel alternative therapy, recently shown to clear LP in patients with oral erosive disease, but is presently unavailable in the United States. Finally, rituximab was reported to successfully treat a patient with esophageal involvement of mucocutaneous LP. We are considering ECP, as well as a repeat, more prolonged trial of cyclosporine for this patient, and welcome suggestions for additional potential therapies.

Essential Lesson:

- Erosive lichen planus of the vulva is a difficult-to-treat, uncommon variant of LP with significant morbidity and potential for malignant transformation.

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Case # 10

Case Presented by Rikk Lynn, MD
and Aleksandar Krunic, MD, PhD

History of Present Illness:
This 38 year old African American female presented with a growth on her left upper chest. The lesion had been present for over ten years with no prior history of trauma to the area. Recently, the lesion had been increasing in size with some tenderness and itching.

Past Medical History:
Hyperlipidemia

Medications:
Simvastatin

Allergies:
No known drug allergies

Review of Systems:
The patient denies fevers, chills, night sweats or weight loss.

Physical Examination:
The patient has a 3.5 cm x 3.0 cm well-demarcated, firm, reddish-brown plaque with multiple nodular areas. There is no cervical or axillary lymphadenopathy.

Laboratory Data/Diagnostic Procedures and Tests:
FISH cytogenetics: positive for fusion of the collagen 1 alpha 1 (17q21) and platelet-derived growth factor beta chain (22q13) loci

Histopathology:
Left superior lateral chest, skin: There is dermal and subcutaneous proliferation of slender, monotonous spindle cells in a storiform configuration. The overlying epidermis is unremarkable. These spindle cells infiltrate into adipose tissue and adnexal structures. There is moderate cytological atypia with hyperchromatic chromatin. The CD34 is strongly and diffusely positive in the constituent spindle cells.

Diagnosis:
Dermatofibrosarcoma protuberans

Treatment and Course:
After histological confirmation of the diagnosis, the patient was sent for Mohs consultation. Given the size of the tumor, if was felt that surgery would result in an extensive defect; therefore, neoadjuvant treatment with Imatinib mesylate was initiated in collaboration with Hematology-Oncology after confirmation of the t(17:22) cytogenetic translocation. The patient has currently undergone two months of treatment with Imatinib 400mg by mouth twice daily. There has been symptomatic improvement of the lesion as well as a reduction in the erythema. Consideration for Mohs is anticipated to occur at a future date.

Discussion:
Dermatofibrosarcoma protuberans (DFSP) is a locally aggressive sarcoma of intermediate malignancy that favors young to middle-aged adults. DFSP occurs on the trunk in 50-60% of patients, the proximal extremities in 20-30%, and the head and neck in 10-15%. Initially, it presents as a slowly growing, asymptomatic, skin-colored indurated plaque that eventually develops violaceous to red-brown nodules measuring from one to several centimeters in diameter.

On histological examination, DFSP typically appears as a well-differentiated fibrosarcoma characterized by a dense array of uniform cells with spindle-shaped nuclei. The tumor cells are typically arranged into irregular, interwoven fascicles, forming a storiform pattern. DFSP generally stains positively for CD34 and negatively for factor XIIIa.

Complete surgical excision, including Mohs micrographic surgery, is the accepted treatment for DFSP. This tumor is characterized by its local invasion and tendency to recur; however, recurrences with Mohs surgery are only up to 5% for recurrent tumors and less than 1% for primary tumors. Achieving local control by performing an adequate initial resection is important because locally recurrent and neglected lesions have a propensity for deep fascial, muscular, and bone invasion.

More than 90% of DFSPs are characterized cytogenetically by either the reciprocal t(17;22) translocation or more frequently a supernumerary ring chromosome containing sequences from chromosomes 17 and 22. The translocation fuses the platelet-derived growth factor beta chain (PDGFB) on chromosome 22 with the strongly expressed collagen 1 alpha 1 (COL1A1) gene on chromosome 17. The formation of the COL1A1-PDGFB gene results in constitutive production of a functional fusion protein. The identification of this translocation led to the hypothesis that a specific inhibitor of platelet derived growth factor receptor (PDGFR), such as Imatinib, might have activity against the disease.

Multiple studies have shown that binding of Imatinib results in inhibition of DFSP proliferation and apoptosis induction. Imatinib is currently approved for the treatment of adult patients with unresectable, recurrent, and/or metastatic DFSP who are not eligible for surgery. It has not yet been clearly defined whether neoadjuvant treatment improves the results after tumor resection or if an adjuvant use can reduce the risk of local recurrence. Han et al. recently reported four patients treated with neoadjuvant Imatinib prior to Mohs and found an average reduction in tumor size of 36.9% and local cure after Mohs of 100% at four year follow up. Larger prospective studies are needed to confirm and expand on these results.

Essential Lessons:

- DFSP is a locally aggressive sarcoma of intermediate malignancy.
- More than 90% of DFSP are characterized by a translocation involving chromosomes 17 and 22.
- Imatinib, an inhibitor of PDGFR, represents a novel treatment for unresectable, recurrent, and/or metastatic disease. It is still to be determined whether neoadjuvant use of Imatinib is useful.

References:

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Case # 11

Case Presented by Sabrina Guillen Fabi, MD and Claudia Hernandez, MD

History of Present Illness:
This 6 year old boy presented with a 3 month history of asymptomatic, hypopigmented patches over his lower back. His mother denied any other area of involvement or poliosis. Six months prior, he experienced pain, photophobia, and blurry vision of both eyes, which was not preceded by trauma. Ophthalmology diagnosed him with granulomatous panuveitis of both eyes.

Past Medical and Surgical History:
Granulomatous panuveitis, cataracts, increased intraocular pressure of both eyes

Medications:
Methotrexate 12.5 mg intramuscularly weekly, timolol 0.5% ophthalmic solution, difuprednate 0.5% ophthalmic suspension, preservative-free ophthalmic lubricating drops

Allergies:
No known drug allergies

Family History:
Maternal grandfather and uncle with vitiligo. No known history of ophthalmologic, dermatologic, or neurologic disease.

Social History:
The patient is undergoing speech therapy due to delayed speech, otherwise normal developmental milestones.

Review of Systems:
On presentation, the patient complained of headaches, dizziness, tinnitus, and nausea. He denied loss of consciousness, confusion, ataxia, hearing loss, fevers, vomiting, and arthralgias.

Physical Examination:
Cutaneous: Multiple, ovoid, hypopigmented patches over the mid-lumbosacral back. The remainder of the skin and hair examination was unremarkable.

Ocular: Slit lamp examination of both eyes revealed 3+ cells/3+ flare in the anterior chamber and 3+ cells in the anterior vitreous, consistent with panuveitis. Fundoscopic exam demonstrated bilateral optic nerve head edema and exudative retinal detachments of both maculas. Folds in the retina indicated sub-retinal fluid/exudation. Peripherally, both eyes exhibited Dalen-Fuchs nodules (collections of epithelioid cells lying between Bruch's membrane and the retinal pigment epithelium).

Laboratory Data/Diagnostic Procedures and Tests:
The following were positive or abnormal:
Fluorescein angiogram of both eyes revealed multiple areas of pin-point leakage from both maculas, consistent with hyperopic shifts.

The following were negative or within normal limits:
Complete blood count with differential, complete metabolic panel, hepatitis C, hepatitis B, rapid plasma reagin, angiotensin-converting enzyme, and QuantiFERON®-TB Gold test

Histopathology:
Lumbosacral back, skin (lesional and nonlesional): Compared with normal skin, hematoxylin and eosin staining shows a reduced number of melanocytes in sections of lesional skin. Also, there is a mild

superficial perivascular dermal infiltrate of lymphocytes. Melan-A stain of normal skin shows a normal number of melanocytes in a normal distribution. Immunohistochemical stain of Melan-A shows a marked reduction of melanocytes in lesional skin.

Diagnosis:
Vogt-Koyanagi-Harada Syndrome

Treatment and Course:
The patient was referred to neurology where he had normal neurologic, audiologic, and vestibular examinations. Topiramate, an anti-convulsant used for migraine prophylaxis, was offered to ameliorate the patient's headaches and dizziness but was declined by his mother. The patient's panuveitis has been controlled with a tapering course of oral prednisone, intramuscular methotrexate injections, homatropine ophthalmic drops, and ophthalmic lubricating drops. The patient has subsequently developed cataracts and increased intraocular pressure of both eyes, which is being treated with timolol maleate 0.5% ophthalmic solution.

Discussion:
Vogt-Koyanagi-Harada Syndrome (VKHS) is a multisystem disorder that has ophthalmic, neurologic, and cutaneous manifestations. The disease commonly manifests in the third to fourth decades of life and primarily affects Asian, Middle Eastern, Hispanic, and Native American populations. The pathogenesis has not been clearly elucidated, but studies have suggested that it is an immune-mediated condition.

During embryogenesis, the neural-crest cell derived melanocytes migrate into the epidermis, hair follicles, uveal tract of the eye (choroid, ciliary body, and iris), leptomeninges, and cochlea. The destruction of these melanocytes explains the constellation of findings seen in VKHS, which include vitiligo, poliosis, bilateral choroiditis, uveitis, aseptic meningitis, vertigo, dysacousia, and hearing loss. Although uveitis and fundal pigmentary abnormalities may be seen in 2 out of 3 patients with vitiligo, it rarely leads to the degree of visual acuity loss seen in VKHS.

Diagnostic criteria divide VKHS into complete, incomplete, and probable disease. All require bilateral ocular disease not preceded by trauma. Further categorization depends on having integumentary and/or neurological and auditory findings. Other conditions to consider when leukoderma is accompanied by ophthalmic and neurologic symptoms include Alezzandrini syndrome, sarcoidosis, secondary syphilis, Hansen's disease, and tuberculosis.

Vitiligo is a late manifestation of the syndrome preceded by the ocular findings, auditory findings, and meningismus of VKHS. It can be treated with topical steroids, topical calcipotriene, narrow-band ultraviolet B, and excimer laser. Early and aggressive treatment of the ocular disease in VKHS is most important, as ocular complications are quite common and include cataract formation, glaucoma, subretinal neovascularization, and atrophy of the retinal pigment epithelium. Treatment of the ocular inflammatory disease includes systemic corticosteroids, cyclosporine, cyclophosphamide, chlorambucil, azathioprine and methotrexate.

Essential Lesson:

- Melanocytes are not only found in the epidermis and hair follicle but also in structures of the eye, meninges, and inner ear. Destruction of cutaneous melanocytes may be accompanied by inflammation in other melanocyte-containing structures.

References:

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Case # 12

Case Presented by Rikk Lynn, MD
and James Feinberg, MD

History of Present Illness:
This 78 year old man presented with discoloration of his right arm. The patient had fallen one year prior and sustained a distal right radial fracture and he recalled extensive bruising. The patient then had a second fall three months later and re-fractured his right radius at the same sight. Again, he had considerable bruising with partial resolution, but he noted a distinct area that remained permanently discolored.

Past Medical History:
Diabetes mellitus, hypertension, hyperlipidemia, anemia, rosacea, psoriasis

Medications:
Atenolol, felodipine, simavastain, niacin, metformin, minocycline, calcipotriene 0.005% cream, metronidazole 0.75% cream

Allergies:
No known drug allergies

Review of Systems:
The patient denies any arthralgias, myalgias, or history of easy bruising.

Physical Examination:
There is a large non-confluent, blue-green patch involving the right extensor forearm. A few smaller patches extend onto the right flexor forearm.

Histopathology:
Right forearm, skin: There is superficial and deep perivascular and interstitial deposition of dark brown pigment, predominantly within the cytoplasm of macrophages. The pigment is positive with both iron and argentaffin stains.

Diagnosis:
Minocycline pigmentation

Treatment and Course:
The patient had sustained a fracture of his right distal radius in January 2008 after a fall. He then suffered another fall in April of 2008 and re-fractured his radius. Both fractures were treated with closed reduction and casting. One week after the second fracture the patient had been taken off tetracycline and switched to minocycline for treatment of his rosacea. The patient believed the discoloration over his arm was just a bruise and did not seek any treatment until nearly one year after his original fracture. The patient was seen in February of 2009 and had a biopsy of the forearm performed at this time that was consistent with minocycline pigmentation. His minocycline has since been discontinued with no changes in the discoloration thus far.

Discussion:
Minocycline is a commonly used antibiotic in dermatology. It is a tetracycline derivative that is a highly lipid soluble, yellow crystalline material that turns black with oxidation. Drug-induced discoloration of the skin can be accompanied by darkening of the nails, sclera, oral mucosa, thyroid, bones and teeth. Incidence of this has varied from 2.4% to 14.8% in limited longitudinal studies.

Minocycline associated hyperpigmentation has been divided into three types. Type I consists of blue-black discoloration localized to sites of inflammation or scarring, including those due to acne or trauma. Some authors limit this type to areas only involving the face. Type II is characterized by blue-gray macules and patches that appear within previously normal skin, most commonly on the arms, anterior legs, and ankles; lesions can range from 1 mm to 10 cm in size and are sometimes misdiagnosed as ecchymoses. Type III develops on healthy skin, similar to type II, but type III pigmentation appears as diffuse muddy brown discoloration that is more prominent in sun-exposed areas.

Histologic findings also vary depending on the clinical type. Type I discoloration shows intra- and extracellular iron-containing pigment within the dermis that may represent hemosiderin and/or a minocycline derivative plus chelated iron. Type II specimens reveal melanin- and iron-containing pigment granules in the dermis and subcutis. Type III is associated with increased melanin in the basal layer of the epidermis and in dermal macrophages without the presence of iron.

Type I pigmentation is thought to be the most common and is unrelated to cumulative or daily dose of minocycline exposure, while type II is less common and type III is the least common. The incidence of types II and III pigmentation is thought to correlate with the duration and cumulative dose of treatment. Both types occur most often when cumulative doses are greater than 100 grams. These three types of minocycline induced pigmentation, while distinct, are not mutually exclusive, and patients affected by minocycline often demonstrate more than one clinical pattern of pigmentation.

The association of minocycline-induced pigmentation and trauma has been well-established. In most reported cases, minocycline exposure precedes the source of injury. Our patient's presentation is unique in that minocycline exposure occurred after the fracture of his radius and still resulted in marked discoloration.

Resolution usually occurs spontaneously after discontinuing the medication, but it may take months or even years for complete resolution. For types I and II, laser therapy, similar to that used for tattoo removal, may improve the discoloration.

Essential Lessons:

- Minocycline is a commonly used antibiotic and can result in three variants of discoloration both clinically and histologically.
- These three types of minocycline induced pigmentation, while distinct, are not mutually exclusive, and patients affected by minocycline often demonstrate more than one clinical pattern of pigmentation.
- This case is unique in that the minocycline exposure occurred after the onset of injury.

References:

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2. Eisen D, Hakim MD. Minocycline-induced pigmentation, incidence, prevention and management. *Drug Saf*. 1998; 18:431-40.
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4. Youssef S, Langevin KK, Young LC. Minocycline-induced pigmentation mimicking persistent ecchymosis. *Cutis* 2009; 84:22-6.

Case # 13

Case Presented by Jonathan Pewitt, MD
and Michelle Bain, MD

History of Present Illness:
This is a 20 year old African American female who presented with a life long history of atopic dermatitis. She sought treatment for hyperpigmentation and flaring of dyshidrotic eczema on her hands and feet. She gave a personal and strong family history of nail-patella syndrome. She has been followed for open-angle glaucoma related to the syndrome.

Past Medical and Surgical History:
Multiple eye surgeries related to open-angle glaucoma, current vision in left eye 20/400 with worse vision in the right eye

Medications:
Bimatoprost ophthalmic solution, brimonidine ophthalmic solution, dorzolamide-timolol ophthalmic solution, triamcinolone 0.1% ointment

Allergies:
No known drug allergies

Family History:
Mother and maternal aunts, uncles, cousins and grandfather with nail-patella syndrome. One 16 year old cousin passed away from complications of kidney disease.

Social History:
Student at University of Illinois at Chicago, nonsmoker, no alcohol or illicit drugs

Review of Systems:
No fever, chills, nausea, vomiting, diarrhea, swelling of the hands or face, weight loss or night sweats

Physical Examination:
There are corneal opacities bilaterally affecting the right cornea more than the left. There is horizontal nystagmus bilaterally. Both elbows have bony abnormalities with antecubital fossae webbing and restricted extension. There are a few deep seated palmar and plantar vesicles. The bilateral thumbnails have ulnar sided hypoplasia. Lunulae are absent on all fingernails except a small triangular lunula of the right ring fingernail. The anterior ankles, dorsal feet, and popliteal fossae have hyperpigmented and lichenified plaques.

Laboratory Data:
The following were positive or abnormal:
Urinalysis protein 30 mg/dL (negative), leukocyte esterase moderate (negative), urinary red blood cells 147 (0-2), urinary white blood cells 71 (0-5)

The following were negative or within normal limits:
Basic metabolic profile

Diagnostic Procedures and Tests:
Elbow radiograph: bilateral luxation of hypoplastic radial heads

Knee radiographs and pelvis radiographs: within normal limits

Diagnosis:
Nail-patella syndrome

Treatment and Course:
For her atopic dermatitis, she was started on betamethasone dipropionate augmented ointment to the feet twice daily and triamcinolone 0.1% ointment to the hands twice daily. She was instructed to avoid corticosteroid contact with the eyes to prevent increasing intraocular pressure and cataract formation. Consults were placed for nephrology and orthopedic surgery; she is followed regularly by ophthalmology.

Discussion:
Nail-patella syndrome (NPS), also known as Hereditary Osteo-Onychodysplasia, is an autosomal dominant disease with complete penetrance and variable expressivity. It is caused by a mutation in the LMX1B gene on chromosome 9q34. Over 140 mutations in LMX1B have been reported. LMX1B encodes a LIM-homeodomain transcription factor important in normal dorsoventral limb development and collagen formation. LMX1B is involved in skeletal development, differentiation of anterior eye structures, and formation of glomerular basement membranes. Diagnostic clinical findings include fingernail dysplasia, absent or hypoplastic patellae, presence of posterior conical iliac horns, and deformation or luxation of the radial heads. Systemic findings of nephropathy and glaucoma are associated with this disease.

Cutaneous findings include absence of skin lines over the distal interphalangeal joints, webbing of the antecubital and popliteal fossae, digital webbing, skin laxity, palmoplantar hyperhidrosis, and nail dysplasia. Nail findings include hypoplastic or absent nails, longitudinal ridging with or without splitting, discoloration, pitting, thinning, koilonychia, and poorly formed or triangular lunulae. The triangular lunulae are pathognomonic. Ulnar aspects of nails tend to be affected more than radial, and lateral digits are more severely affected than medial. Nail findings are most often bilateral, symmetric, and may be present at birth. Toenails are less commonly affected.

Eye defects described include open-angle glaucoma, heterochromia of the iris with cloverleaf deformity, cataracts, microcornea, and hyperpigmentation of the pupillary margin of the iris, which is called Lester iris. The Lester iris occurs in 45% of patients with nail-patella syndrome and can be a useful diagnostic sign.

Defective LMX1B in the podocytes of kidneys results in abnormal type 4 collagen. This defect leads to faulty glomerular basement membranes and resultant chronic proteinuria. Nephropathy can develop in up to 40% of patients and lead to kidney failure in 8-10%. The earliest sign is typically microalbuminuria. Patients with NPS should have regular urinalysis to monitor kidney function.

Essential Lessons:
- Nail-patella syndrome is an autosomal dominant disease caused by a mutation in LMX1B.
- The disease has characteristic nail, skeletal, ocular, and renal findings. Newly diagnosed cases should be evaluated by ophthalmology and screened for renal pathology.

References:

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Case # 14

Case Presented by Brendan Thomas, MD
and Carlotta Hill, MD

History of Present Illness:
This 33 year old male presented initially in February 2009 with a one and a half year history of tingling and painful sensations in the hands along with burning sensations in his feet. For five months prior to presentation, he was unable to straighten his third through fifth fingers bilaterally. As sensation in his feet continued to decline, he developed redness, swelling, and pain of the left first toe. He was admitted to an outside hospital and diagnosed with osteomyelitis. It was during this admission from December 2008 to January 2009 that the patient's peripheral neuropathy was noted along with several pink plaques on his extremities. He was subsequently evaluated with electromyogram, sural nerve biopsy, and skin biopsy.

Past Medical History:
Seasonal allergies

Medications:
Loratadine

Allergies:
No known drug allergies

Family History:
There is no history of leprosy, skin cancer, or other skin conditions.

Social History:
The patient moved from India to the United States approximately four years prior to presentation.

Review of Systems:
The patient denied any fevers, chills, night sweats, or weight loss, but did admit to occasional fatigue.

Physical Examination:
The patient had normal appearing eyebrows. There were several, poorly demarcated, hyperpigmented, occasionally reticulated patches over the lateral and anterior neck, central back, arms, and ankles. Both the ulnar nerves and external popliteal nerves were palpable and tender bilaterally. Claw hand deformities were appreciated bilaterally. With testing, the bilateral third and fourth fingers had four out of five strength, and the bilateral fifth fingers had three out of five strength. Sensation to light touch and pain was absent in the hands extending to mid forearms and in the feet extending to mid lower legs.

Laboratory Data:
The following were negative or within normal limits:
Complete blood count with differential and comprehensive metabolic panel

Diagnostic Procedures and Tests:
Electromyogram: There is an advanced axonal sensorimotor polyneuropathy affecting the arms and legs. Bilateral ulnar nerve injury is severe.

Histopathology:
Left mid arm, skin: There is a very mild superficial dermal perivascular infiltrate of lymphocytes and histiocytes. Fite stain is negative.

Sural nerve biopsy: There is a dense perineural infiltrate of predominately lymphocytes on hematoxylin and eosin staining. Fite stain of nerve biopsy shows multiple foci of positive staining, slender bacilli compatible with mycobacterium.

Diagnosis:
Pure neuritic leprosy

Treatment and Course:
The patient was started on dapsone 100 mg daily and rifampin 600 mg daily, to which clofazamine 50 mg daily was later added. The patient is tolerating the medications well. On subsequent exams, he has shown clinical improvement with decreased nerve tenderness, slightly increased finger strength, and restoration of his ability to straighten fingers.

Discussion:
Pure neural leprosy is caused by *Mycobacterium leprae* and characterized clinically by peripheral nerve thickening, evidence of a nerve deficit, and absence of skin involvement. In India, pure neural leprosy is estimated to account for 3–8.2% of all diagnosed cases. In the United States, the incidence and prevalence of neuritic leprosy is much lower. This condition is more common in males, and the ulnar nerve is most commonly affected.

Pathophysiologically, leprous neuritis occurs due to decreased immunity and integrity of a patient's peripheral nerve–blood barrier. Recently, the Schwann cell was described as the target of *M. leprae*, which binds to proteins on the surface of the Schwann cell, ultimately leading to connections with the host cell's cytoskeleton. Clinically, this is manifested by early sensory complaints. Occasionally, cutaneous lesions may develop after the diagnosis of pure neuritic leprosy is established, and this supports the hypothesis that leprosy is neural in inception, from which the other types of leprosy are derived.

With regard to diagnosis and treatment, early detection of this condition is critical to preventing the many sequelae of nerve damage. Generally, multidrug therapy with dapsone, rifampin, and clofazimine is an effective treatment for pure neural leprosy and will halt further progression of nerve damage. However, existing nerve deficits are not likely to significantly improve with therapy.

Essential Lessons:
- Pure neural leprosy is a rare form of disease caused by *Mycobacterium leprae* infection.
- Multidrug therapy with dapsone, rifampin, and clofazimine is generally an effective treatment.

References:

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Case # 15

Cases Presented by Carmen Schwartz, MD, Claudia Hernandez, MD, and Lawrence Chan, MD

Patient A

History of Present Illness:
This 51 year old male presented with a changing "birthmark" over his right scalp. Over the prior six months, he noticed that the lesion was no longer smooth in texture and there was a new bump developing within it. The area was otherwise asymptomatic.

Past Medical and Surgical History:
Non-contributory

Medications:
Aspirin

Allergies:
No known drug allergies

Family History:
No family history of skin cancer

Review of Systems:
The patient denies headache, vision changes, fevers, chills, weight loss, nausea, vomiting, arthralgias, headaches, or fatigue. He denies history of seizures, mental retardation, ocular lesions, or skeletal abnormalities.

Physical Examination:
Over the right superior parietal scalp, there was a 2.4 cm x 1 cm verrucous, pink plaque with an 0.8 cm x 0.8 cm exophytic, crusted nodule growing over the 3 o'clock position.

Laboratory Data/Diagnostic Procedures and Tests:
None

Histopathology:
Right parietal scalp, skin: Multiple sections show papillomatous epidermal hyperplasia with sebaceous glands directly attached to the lower epidermis. There is also prominent apocrine hyperplasia in the underlying dermis. Multiple foci of basaloid nests are identified, some of which are pigmented. In one focus, there are papillary projections protruding into the invaginations of surface epithelium. A lymphoplasmacytic infiltrate is identified in the surrounding stroma.

Diagnosis:
Syringocystadenoma papilliferum arising in nevus sebaceus

Treatment and Course:
The patient underwent staged excision. The syringocystadenoma papilliferum within the nevus sebaceus was completely excised in the first stage. He then underwent a second stage of excision with removal of the remaining nevus sebaceus.

Patient B

History of Present Illness:
This 29 year old male presented with a new, growing nodule on his scalp. The lesion arose within a plaque on his right scalp that had been present since birth. The area was asymptomatic.

Past Medical and Surgical History:
Asthma, allergic rhinitis

Medications:
Albuterol metered dose inhaler

Allergies:
No known drug allergies

Family History:
No family history of skin cancer

Review of Systems:
The patient denies fevers, chills, weight loss, nausea, vomiting, arthralgias, headaches, or fatigue. He has no history of seizures, mental retardation, ocular lesions, or skeletal abnormalities.

Physical Examination:
On the right frontotemporal scalp, there was a 3 cm x 1.5 cm cobblestoned, skin colored linear plaque with a 0.8 cm x 0.4 cm dark brown papule over the anterior pole.

Laboratory Data/Diagnostic Procedures and Tests:
None

Histopathology:
Right temporal scalp, skin: There is papillomatous epidermal hyperplasia with sebaceous glands directly attached to the lower epidermis. The apocrine glands in the underlying dermis are hyperplastic. In the adjacent skin, there is an expansile growth of basaloid nodules with extensive melanin deposition. These basaloid cells display minimal differentiation. Clefting from the surrounding stroma is identified focally.

Diagnosis:
Trichoblastoma arising in nevus sebaceus

Treatment and Course:
The patient underwent excisional biopsy of the nodule. He was informed that the nevus sebaceus extended to the surgical margins and was educated about the risk of malignant transformation in the residual lesion. Despite this, the patient has elected not to undergo complete excision, but instead to observe the area closely for any changes.

Discussion:

Nevus sebaceus (NS) is a common congenital hamartoma of the skin occurring in 0.3% of newborns. It combines epidermal, hair follicle, sebaceous, and apocrine gland abnormalities. NS is most commonly found on the scalp, followed by the forehead and retroauricular regions. In fewer than 5% of cases, it presents on the trunk. Two-thirds of cases are present at birth with the remainder occurring in infancy or early childhood. Males and females are equally affected.

Three clinically distinct stages are noted in NS. During early childhood, NS is often described as a slightly raised, finely papulated, pink to orange, alopecic plaque with a linear configuration distributed along the lines of Blaschko. During adolescence, lesions are noted to thicken and develop a pebbly or verrucous surface. In adulthood, secondary adnexal neoplasms may develop within the existing NS often presenting as new, pigmented papules or nodules. Neoplastic transformation occurs with an incidence of 10-30% and the risk of neoplastic transformation increases with age. The development of benign tumors before the age of 16 occurs in less than 5% of cases with most neoplasms developing in the fourth to seventh decade. The most common benign tumors associated with NS include trichoblastoma and syringocystadenoma papilliferum.

Trichoblastoma is a benign adnexal neoplasm comprised of a well-circumscribed basaloid epithelial proliferation arranged in lobules, cords, or sheets with surrounding fibrocellular stroma. Peripheral palisading of basaloid cells and primitive papillary mesenchymal bodies are also often present. Syringocystadenoma papilliferum is an uncommon adnexal neoplasm with varying clinical appearances. However, its histology is distinctive with duct-like invaginations and cyst-like cavities of varying shapes and sizes extending from the epidermal surface into the body of the lesion. A chronic plasmalymphocytic inflammatory infiltrate is found in the stroma surrounding these duct-like structures.

Other neoplasms that may develop within NS include trichilemmoma, sebaceous adenoma, apocrine adenoma, and poroma. Rarely, secondary sebaceous or apocrine carcinomas may develop. The incidence of basal cell carcinoma (BCC) arising in NS was estimated to be between 6 and 22%. However, this figure has been variable in the literature and more recently the incidence of BCC in NS has been decreased to approximately 0.8%.

The treatment of NS has traditionally been prophylactic excision due to the risk of malignant transformation; however, there has been controversy as to whether or not to excise the NS and at what age. Some studies support prophylactic excision prior to its rapid growth phase around the start of puberty, while others suggest careful clinical monitoring for changes. Numerous factors also need to be considered prior to excision, including its size and location, cosmetic significance, and the risk-to-benefit ratio of general versus local anesthesia for surgery later in childhood or adolescence.

Essential Lessons:

- Nevus sebaceus is a common congenital hamartoma with the potential to develop a variety of secondary adnexal neoplasms.
- Trichoblastoma and syringocystadenoma papilliferum are the most common benign neoplasms to develop within NS.

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Case # 16

Case Presented by Tanya Bulj-Stevens, MD
and Michelle Bain, MD

History of Present Illness:
This 48 year old Caucasian woman presented for evaluation of waxing and waning scalp folliculitis. The lesions are associated with pruritus and pain. She was previously treated by an outside dermatologist with mupirocin 2% ointment with no improvement.

Past Medical and Surgical History:
Type I diabetes mellitus, hypothyroidism, anemia of chronic disease, diabetic nephropathy, neurogenic bladder, gastroparesis, Sjogren's syndrome, coronary artery bypass graft, autosternectomy secondary to methicillin-resistant staphylococcus aureus infection, multiple eye surgeries, multiple hand surgeries, breast biopsies x 3 (all benign), laparoscopic cholecystectomy

Medications:
Alendronate, aspirin, isosorbide mononitrate, pantoprazole, levothyroxine, duloxetine, folic acid, fenofibrate, metoclopramide, clopidogrel, clonazepam, lorazepam, insulin, calcium, sodium bicarbonate, fiber, amlodipine, ramipril, alprazolam, nitroglycerin sublingual, vitamin B6, vitamin B12, luprolide, progesterone, bethanechol, nicotine patch, betamethasone dipropionate 0.05% cream, clobetasol dipropionate 0.05% ointment

Allergies:
Piperacillin-tazobactam

Family History:
No history of skin cancer

Social History:
No history of alcohol or illicit drugs; quit smoking

Review of Systems:
No nausea, vomiting, fever, chills, cough, night sweats, or weight loss

Physical Examination:
Over the scalp there are scattered follicular-based erythematous thin papules with surface crusting.

Histopathology:
Right scalp, skin: there is a dilated follicular infundibulum, filled with keratinous and cellular debris. The follicular epithelium is focally disrupted. The adjacent dermis displays degenerative changes in the connective tissue, associated with mild fibrosing inflammation. The Masson trichrome stain demonstrates vertically oriented collagen fibers penetrating the basal portion of follicular epithelium. The Elastic stain confirms the presence of vertically oriented collagen fibers within follicular epithelium and within the overlying keratin plug.

Diagnosis:
Perforating folliculitis

Treatment and Course:

The patient did not respond to topical antibiotics such as mupirocin ointment, nor to high potency topical steroids including betamethasone dipropionate and clobetasol. She was then started on tretinoin 0.1% micro gel, tazarotene 0.05% cream, and oral doxycycline 100 mg twice a day. Phototherapy was not started as the patient has a history of photosensitivity.

Discussion:

Perforating skin dermatoses are a group of papulonodular skin disorders characterized by keratotic plugs or crusts in which there is transepidermal elimination of collagen, elastic tissue or necrotic connective tissue. Perforating diseases include elastosis perforans serpiginosa (EPS), reactive perforating collagenosis (RPS), Kyrle's disease (KD), and perforating folliculitis (PF). RPS, in which primarily collagen fibers perforate the epidermis, and EPS, in which primarily elastic fibers perforate, both can be inherited. Perforating folliculitis is listed in many textbooks as the fourth perforating disease but, according to some authors, it does not appear to be a specific entitiy, since perforation of follicles occurs in a wide variety of diseases classified as folliculitis regardless of the underlying pathogenesis.

In addition to these four diseases, an acquired form of perforating dermatosis that usually develops in adulthood and is associated with diabetes mellitus and/or chronic renal failure has been reported for which the term acquired perforating dermatosis (APD) was proposed. A review of the literature suggests that there may be considerable clinical and histologic overlap among PF, KD, and APD.

The molecular mechanism of transepidermal elimination of dermal components in perforating skin dermatoses remains unclear. Ultrastructural investigations failed to detect major constitutional defects in dermal collagen or elastic fibers. Increased expression of TGF-beta3 and increased fibronectin levels have been found at sites of perforating lesions. It was recently demonstrated that the 67-kDa elastin receptor can be detected in the epidermis eliminating altered elastic fibers in EPS, suggesting that the elastin-keratinocyte interaction may play a role in transepidermal elimination in EPS. Some authors suggest that epidermal injury from scratching and microvasculopathy with subsequent tissue hypoxia may cause upregulation of matrix metalloproteinases and result in focal necrobiosis.

Treatment of generalized acquired perforating dermatosis or extensive perforating folliculitis is often difficult. There is a correlation between control of pruritus to prevent scratching and clearing of the lesions. Phototherapy is a particularly good choice for patients with APD since it often relieves their coexisting pruritus.

Essential Lessons:

- There is a need for more precise criteria for classification of perforating disorders as there is a considerable clinical and histologic overlap among perforating folliculitis, Kyrle's disease, and acquired perforating skin dermatoses.
- The precise pathogenesis for the perforating disorders is unknown.

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Case # 17

Case Presented by Shruthi Reddy, MD
and Sophie Worobec, MD

History of Present Illness:
This 46 year old African American man presented with total skin discoloration since birth consisting of dark and light areas. The discoloration had been stable since childhood. The patient recalled being evaluated at age 14 by a dermatologist and underwent multiple skin biopsies, however did not recall a diagnosis.

Past Medical and Surgical History:
Crohn's disease status post 4 small bowel resections with ileocolonic anastomosis, small bowel obstruction, jejunoileal stricture, urethral strictures status post urethroplasty and stenting, frequent urinary tract infections, large hiatal hernia with gastroesophageal reflux, depression

Medications:
Atenolol, cholestyramine, diphenhydramine, ferrous sulfate, folic acid, hydrochlorothiazide, lansoprazole, morphine, prednisone, sucralfate

Allergies:
Iodinated radiocontrast dye

Family History:
No known family history of skin discoloration or other skin conditions

Social History:
Denies use of tobacco, alcohol, or drugs; patient is currently incarcerated

Review of Systems:
Frequent nausea and abdominal pain and occasional diffuse pruritus. Denies fever or chills.

Physical Examination:
There are generalized hypopigmented and hyperpigmented macules and patches of varying shades, shapes, and sizes sparing the palms, soles, and oral mucosa. On the mid-back is a single oval 5 mm x 4 mm black slightly raised papule. No poikiloderma, atrophy or telangiectasias are present.

Laboratory Data:
The following were positive or abnormal:
Hemoglobin 11.6 g/dL (13.2-18.0), hematocrit 35.5% (38-55)

The following were negative or within normal limits:
White blood cell count with differential, platelets, complete metabolic panel, magnesium, phosphorus

Histopathology:
Upper abdomen, skin (hyperpigmented macule): There is increased melanin deposition within the keratinocytes. The melanocytes are normal in number and distribution. They are highlighted by Melan-A stain.

Lower abdomen, skin (hypopigmented macule): There is a reduced amount of melanin within the keratinocytes in the lesional area. The Melan-A stain shows no change in the number of melanocytes.

Diagnosis:
Dyschromatosis universalis hereditaria

Treatment and Course:
No treatment is available. The patient has not developed any skin malignancies to date.

Discussion:
Dyschromatosis universalis hereditaria (DUH) is a rare genodermatosis first described in 1933 by Ichikawa and Higari. It is most common in Japan, but has also been reported in other parts of Asia, Europe, South America, and Africa. Classification of hereditary dyschromatosis depends on the distribution of skin lesions and includes a generalized form, DUH, a localized form limited to the extremities, dyschromatosis symmetrica hereditaria (acropigmentation of Dohi), and a segmental form known as unilateral dermatomal pigmentary dermatosis. DUH is characterized by generalized asymptomatic hypo- and hyperpigmented macules of varying sizes and shapes. Eighty percent of individuals develop dyschromia before age 6 and approximately 20% have dyschromia at birth. No spontaneous regression with age has been reported. Associated problems include isolated reports of short stature, high-frequency deafness, erythrocyte, platelet and tryptophan metabolism abnormalities, insulin-dependent diabetes mellitus, X-linked oculocutaneous albinism, tuberous sclerosis, bilateral glaucoma, unilateral cataract, photosensitivity with neurosensory hearing defects, and grand-mal seizures.

DUH appears to be a disorder of melanosome production and transfer in epidermal melanin units rather than a disorder of melanocyte number. Despite normal numbers of morphologically intact and active melanocytes within hypopigmented and hyperpigmented skin, the melanin synthesis, number of melanosomes and transfer to keratinocytes differs within each area. DUH also may be related to interference of the neural reflex-melanoctye interaction early in embryonic life in genetically susceptible individuals. The inheritance pattern is varied with autosomal dominant transmission in most cases and reports of sporadic, autosomal recessive, and pseudodominant transmission. Gene loci responsible for DUH have been mapped to chromosome 6 in autosomal dominant forms and to chromosome 12 in one autosomal recessive form. However, the gene candidates for chromosome 6 or 12 have not been definitively identified. The most promising gene for the region on chromosome 12 is the pro-melanin-concentrating hormone (PMCH) gene as melanin-concentrating-hormone has been suggested to play a role in regulating skin pigmentation.

Essential Lesson:
- Dyschromatosis universalis hereditaria is a very rare genodermatosis characterized by generalized skin dyspigmentation. No other cases, to our knowledge, have been reported in North America.

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Case # 18

Case Presented by Carmen Schwartz, MD
and Aleksandar Krunic, MD, PhD

History of Present Illness:
This 49 year old female presented with a one year history of a fleshy, red nodule over her right temporal scalp. Over the preceding three months, several smaller lesions developed close to the initial growth, some of which were pruritic and tender.

Past Medical and Surgical History:
Partial thyroidectomy, hypothyroidism

Medications:
Levothyroxine

Allergies:
No known drug allergies

Family History:
No family history of skin cancer

Review of Systems:
The patient denies headaches, vision changes, fevers, chills, weight loss, shortness of breath, chest pain, arthralgias, hematuria, or fatigue.

Physical Examination:
On the right temporal scalp was a 2.4 cm plaque with overlying clusters of dome-shaped, pinkish-red nodules. Inferior to this plaque was a 4 mm shiny pink papule and inferoposterior to this were three 1-2 mm shiny pink papules. There was mild tenderness to palpation of the area. No scaling or induration was noted.

Laboratory Data:
The following were negative or within normal limits:
Complete blood count with differential including eosinophils

Diagnostic Procedures and Tests:
MRI of brain with and without contrast and MRA of head without contrast: Unremarkable with no evidence of intracranial vascular malformation

Histopathology:
Right temporal scalp, skin: There is dermal nodular proliferation of small blood vessels. The endothelial cells are plump with an epithelioid appearance. There is mild perivascular fibrosis. The vascular proliferation is associated with a dense dermal inflammatory cell infiltrate including numerous eosinophils.

Diagnosis:
Angiolymphoid hyperplasia with eosinophilia

Treatment and Course:
The patient underwent excisional biopsy of the large plaque. The patient is currently undergoing pulsed dye laser ablation of the remaining lesions.

Discussion:
Angiolymphoid hyperplasia with eosinophilia (ALHE) is an uncommon vascular proliferation of unknown etiology that most commonly arises in females during the third and fourth decade. Originally thought to be a part of a disease spectrum with Kimura's disease, ALHE is now regarded as a distinct entity.

ALHE presents most commonly on the head and neck, especially the periauricular area, with dome-shaped, smooth surfaced papules or nodules. Approximately 50% of patients will have multiple lesions that are anatomically grouped. Associated symptoms include pain, pruritus, spontaneous bleeding, or rarely pulsation. Peripheral eosinophilia is found in approximately 20% of patients with ALHE.

Histological characteristics of ALHE include irregularly shaped small blood vessel proliferations composed of enlarged endothelial cells with uniform nuclei and intracytoplasmic vacuoles. The endothelial cells are often described as having a cobblestone or hobnail appearance. A perivascular and interstitial infiltrate with eosinophils comprising 5-10% of the infiltrate is also present.

The etiology of ALHE is unknown. However, infection or trauma may precede the development of ALHE in some cases, suggesting a possible reactive hyperplastic process. Cases have also been reported in association with arteriovenous fistulae and malformations.

The treatment of ALHE can be challenging, as recurrence is noted in one-third of patients. Treatment options described include simple surgical excision or Mohs micrographic surgery. The most effective excisions are those that include the arterial and venous components at the base, as lesions may recur if an underlying AV shunt is not removed. Other treatment modalities include curettage and desiccation, cryotherapy, radiotherapy, pulsed dye laser, carbon dioxide laser, imiquimod, tacrolimus, interferon alpha-2b, indomethacin, corticosteroids (oral, intralesional, or topical), pentoxifylline, intralesional chemotherapeutic agents, and oral retinoids. No malignant transformation or fatal outcomes have been reported in ALHE.

Essential Lessons:
- Angiolymphoid hyperplasia with eosinophilia is an uncommon benign vascular proliferation arising on the head and neck, especially around the ears.
- It is histologically characterized by blood vessel proliferation and a dense inflammatory infiltrate with eosinophils and lymphocytes.

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Case # 19

Case Presented by Caroline Schmitt, MD
and Claudia Hernandez, MD

History of Present Illness:
This 39 year old Hispanic transgender male presented with an 8 month history of mildly pruritic, pink, coin-like lesions erupting on the right lower leg. There had been gradual progression in the number and size of the lesions since their onset. He reported a history of silicone injections to the face, buttocks, and calves for soft-tissue augmentation over the course of the past 15 years. Two months after onset of the lesions, he was treated at another institution with oral erythromycin, hydrocortisone 2.5% cream, and an unknown topical medication without improvement.

Past Medical and Surgical History:
Silicone injections in the cheeks, buttocks, legs, and lips; rhinoplasty; breast augmentation

Medications:
None

Allergies:
No known drug allergies

Social History:
The patient is a transgender homosexual male who has not undergone full gender-reassignment surgery.

Review of Systems:
The patient denies fever, weight loss, malaise, or arthralgias.

Physical Examination:
On the right medial and posterior calf are multiple shiny, pink-tan, minimally indurated plaques.

Histopathology:
Right leg, skin: There is diffuse dermal and subcutaneous granulomatous inflammation, with round to oval vacuoles of varying size surrounded by histiocytes and foreign body giant cells. Many of the histiocytes have foamy cytoplasm.

Diagnosis:
Silicone granuloma

Treatment and Course:
The patient was started on minocycline 100 mg daily and after one month of therapy he reported an arrest in the growth of existing lesions. No new lesions have been identified since starting therapy.

Discussion:
The use of silicone fluids for soft-tissue augmentation was first described in the 1950s and gained popularity in the 1960s. Because it is chemically inert and techniques had been developed to purify and sterilize it in its liquid and rubber forms, silicone promised to be a safe biomedical material with wide-ranging cosmetic and surgical applications. However, in the 1970s, two case series were published describing significant inflammatory reactions in patients treated with facial injections of "medical-grade" silicone. The average time to first complication observed in these and other reports was 8 to 10 years, with the majority of complications consisting of granulomas, nodularity, and migration of material.

Silicone granuloma, or siliconoma, is a foreign body reaction following injection or implantation of silicone. The inflammatory response presents as nodule formation, pain, erythema, ulceration, or induration. Foreign body granulomas can occur at the site of initial injection, sites to which silicone has migrated, or sites remote from any identifiable silicone material. Histopathology shows a collection of histiocytes with admixed multinucleated giant cells and variable other inflammatory cells and fibrosis, consistent with a granulomatous reaction pattern. The appearance of "Swiss cheese" spaces from dissolution of silicone during processing secures the diagnosis. Silicone granulomas have been described most commonly following augmentation mammoplasty and soft-tissue filling. They are also a rare complication in non-dermatological scenarios in which silicone liquids, tubing, or prostheses are employed, such as: arthroplasty, hemodialysis (from silicone roller-pump inserts), dacryocystorhinostomy, penile injections, tracheobronchial stenting, acupuncture and venipuncture (from coated needles), endoscopic subureteric injection for vesicoureteric reflux, and intravitreal tamponade.

Treatment of silicone granuloma is often unsatisfactory. Surgical excision or debridement of the silicone can be curative but is usually precluded by concerns regarding potential disfigurement. Therapies that have anecdotally been shown to benefit or cure this condition include oral and intralesional corticosteroids, allopurinol, pentoxifylline, minocycline, carbon dioxide laser, etanercept, isotretinoin, celecoxib, doxycycline, and topical imiquimod. We opted for a trial of minocycline based on multiple reports of successful treatment of patients with silicone granulomas related to prior soft-tissue augmentation. Beer specifically reported that siliconoma nodules on the face of a patient "returned to normal" one week after initiation of minocycline. Less dramatic improvement was described by Arin and Senet, whose patients showed regression of inflammatory symptoms over a period of months.

In the 1980s, Milojevic, Aronsohn, and Webster separately reported on thousands of patients treated with medical-grade silicone injections with very low complication rates (e.g. 2 granulomas out of 1677 facial injections in one study), supporting the safety of sterile, purified "medical grade" silicone. Proponents of silicone for soft-tissue augmentation argue that the higher rates of complication seen decades ago should be attributed to use of impure product, and that the medical-grade silicone presently available is safe for injection. Silicone oils are currently approved by the U.S. Food and Drug Administration for ophthalmologic use only.

Essential Lessons:

- The use of silicone for soft-tissue augmentation is controversial, and presently off-label, due to the history of complications (most commonly migration and foreign body granuloma) surrounding its use.
- Minocycline has anecdotally been described as an effective treatment for inoperable silicone granulomas.

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Case # 20

Case Presented by Joanne Montgomery, MD
and Sophie Worobec, MD

History of Present Illness:
This 28 year old Caucasian female presented with a 2-3 year history of a brown patch on the bottom of her right foot. Over the years, the lesion had enlarged in size and become slightly lighter in color. She denied itching or other symptoms and had no prior treatment to the area. The patient lives in Chicago and her only significant travel history was a trip to Aruba in 2003. She has no personal or family history of skin cancer.

Past Medical and Surgical History:
None

Medications:
Zolpidem

Allergies:
Penicillin

Family History:
No family history of skin cancer or other skin conditions

Social History:
The patient drinks alcohol and smokes cigarettes socially on weekends. She lives alone and works in a fashion design office.

Review of Systems:
Denies any fevers, chills, nausea, vomiting, joint pains, itching or other symptoms.

Physical Examination:
There is a 1.5 cm x1.6 cm well-defined, solitary, light brown, circinate patch on the plantar surface of the right midfoot composed of innumerable pinpoint brown macules. Dermatoscopy reveals a fibrillar pattern of uniform pigmentation.

Diagnostic Procedures and Tests:
The following were positive or abnormal:
Microscopy with potassium hydroxide (KOH) preparation showed septate yellow-brown branching hyphae.

The following were negative or within normal limits:
Fungal Culture showed no growth of fungi after 4 weeks.

Diagnosis:
Tinea nigra

Treatment and Course:
The patient was treated with terbinafine cream twice daily to the affected area. The lesion resolved completely after two weeks of therapy and has not recurred.

Discussion:

Tinea nigra is a relatively uncommon, non-inflammatory superficial mycosis caused by *Hortae werneckii*, formerly classified as *Phaeoannellomyces*, *Exophiala*, and *Cladosporium*. It most commonly occurs in tropical climates such as Central and South America, Africa, and Asia; however, there have been reports of infection in southeastern costal states of the United States. There are also reports of Tinea nigra in cities further inland, including Chicago, however these patients often have history of travel, frequently to Caribbean islands.

Tinea nigra infection presents after a 10-15 day incubation period with development of a solitary, well-demarcated brown, black, gray, or green patch. The overlying surface may be velvety or have mild scale. The patch is asymptomatic, non-erythematous and non-indurated, consistent with its non-inflammatory nature. Over weeks to months the lesion grows and may reach several centimeters in diameter. The palms and soles are most frequently affected; however, there are reports in the literature of involvement of the neck, chest wall, penis, nails, and dorsal hands and feet.

Microscopic examination with potassium hydroxide is usually diagnostic, revealing classic pigmented, thick, septate, branching hyphae. Skin biopsy is infrequently performed, however pigmented hyphae in the stratum corneum are visible with hematoxylin and eosin staining and are further highlighted with Periodic acid-Schiff stain.

The differential diagnosis of tinea nigra includes melanocytic nevi, melanoma, fixed drug eruption, post inflammatory hyperpigmentation, and pigmentation due to chemicals, pigments or dyes. Dermatoscopic examination of tinea nigra was first reported in the literature in 2001 as a tool to help differentiate it from melanocytic lesions, thus avoiding unnecessary biopsies. On dermatoscopy the pigment pattern appears homogenous and nonmelanocytic with fine, wispy, light brown strands or spicules that do not follow dermatoglyphic lines.

Treatment of tinea nigra is primarily topical. Effective treatment has been reported with topical miconazole 2%, ketoconazole 2%, terbinafine, thiabendazole, and ciclopirox, as well as superficial shaving of the lesion with a blade. Undecylenic acid, Whitfield's ointment, retinoic acid, and epidermal tape stripping have also been anecdotally reported to be efficacious. Recurrent infections are infrequent.

Essential Lessons:

- Tinea nigra is an uncommon non-inflammatory superficial mycosis that is effectively treated with topical therapy.
- Although KOH is frequently diagnostic, dermatoscopy can be used as an adjuvant tool to examine tinea nigra.

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