Chicago Dermatological Society

October 2012
Monthly Educational Conference

Program Information
Continuing Medical Education Certification
and
Case Presentations

Wednesday, October 10, 2012

David Fretzin Lecture

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

Program

Conference Locations

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

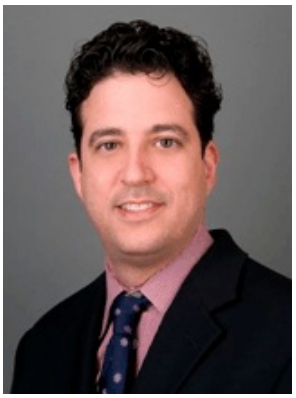
8:00 a.m.	**Registration Opens** *Student Center West, 2nd floor Foyer*
9:00 a.m. - 10:00 a.m.	**Resident Lecture** – *SCW Chicago Room A-C* "Critical Appraisal of Dermatologic Drug Safety" *Joel M. Gelfand, MD, MSCE*
9:30 a.m. - 10:45 a.m.	**Clinical Rounds** Patient & Poster Viewing *Dermatology Clinic, Suite 3E* Slide Viewing *Student Center West, Room 213 A/B*
11:00 a.m. - 12:00 p.m.	**General Session** - *SCW Chicago Room A-C* FRETZIN LECTURE: "Clinical Practice Implications of Co-morbidity Risk in Psoriasis Patients" *Joel M. Gelfand, MD, MSCE*
12:00 p.m. - 12:40 p.m.	**Box Lunches & visit with exhibitors** *SCW - 2nd Floor Foyer*
12:40 p.m. - 1:00 p.m.	**CDS Business meeting** – *SCW Chicago Room A-C*
1:00 p.m. - 2:30 p.m.	**Case Discussions** – *SCW Chicago Room A-C*
2:30 p.m.	**Meeting adjourns**

Mark the Date!

Next CDS monthly meeting – Wednesday, November 14, 2012 at Northwestern University; Elise A. Olsen, MD; Duke University Medical Center; Durham, NC

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

Guest Speaker



JOEL M. GELFAND, MD, MSCE

Associate Professor of Dermatology
Department of Dermatology
Perelman School of Medicine,
University of Pennsylvania; Philadelphia, PA

Delivering the David Fretzin Lecture

Dr. Gelfand received his medical degree at Harvard Medical School in 1998, and a Master of Science in Clinical Epidemiology at the University of Pennsylvania (2003). His clinical specialties are psoriasis and general dermatology.

Dr. Gelfand's research is focused on epidemiology, clinical trials, drug safety, and psoriasis. His epidemiology research focuses on the natural history of psoriasis and the risk of various health outcomes associated with psoriasis such as malignancy, diabetes/metabolic disorders, atherosclerosis/myocardial infarction, and psoriatic arthritis. His clinical trials research focuses on improving efficiency of trials through use of efficient statistical designs and the creation and validation of surrogate endpoints to predict early on in the course of treatment which patients will have a clinical response. Dr. Gelfand also serves as an investigator on a number of industry initiated clinical trials of novel therapies for psoriasis and other common skin conditions. He is the author of numerous research publications, reviews and textbook chapters.

Continuing Education Credit

Chicago Dermatological Society

"Chicago Dermatological Society Monthly Conference"

October 10, 2012 *Chicago, IL*

Participants must attend entire session to receive full credit. Please complete the CME claim form included in your meeting materials and return to the COS registration table before you leave the conference. A certificate will be sent to you following the meeting. Also, we ask that you complete the evaluation form and return to the CLUB registration table. The information collected as part of this process represents an important part of the CME planning process.

The Colorado Foundation of Medical Care (CFMC) will retain a record of attendance on file for six years. CFMC contact information: 303-695-3300, ext. 3372

JOINT SPONSOR STATEMENT

This Continuing Educational activity is Joint-sponsored by the **Colorado Foundation for Medical Care, Office of Continuing Education** and the **Chicago Dermatological Society**. **CFMC is accredited by the ACCME to provide continuing medical education for physicians.**

GOAL/PURPOSE

To broaden the clinical knowledge of dermatologists with respect to diagnostic.

SESSION OBJECTIVES

Upon completion of sessions, participants will be able to apply new knowledge and skills in the area of physician learning.

1. Describe psoriasis associations with major co-morbidities.
2. Identify directionality of psoriasis associations with co-morbidities.
3. Recognize implications co-morbid disease has for the care of patients with psoriasis.

.CREDIT STATEMENTS

CME CREDIT

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 joint sponsorship of the Colorado Foundation for Medical Care, Office of Continuing Education (CFMC OCE) and Chicago Dermatological Society. CFMC is accredited by the ACCME to provide continuing medical education for physicians.

The Colorado Foundation for Medical Care designates this Live Activity for a maximum of 4.5 *AMA PRA Category 1 Credit(s) ™*. Physicians should claim only the credit commensurate with the extent of their participation in the activity.

OTHER HEALTH CARE PROFESSIONALS

This educational activity has been planned and implemented following the administrative and educational design criteria required for certification of health care professions continuing education credits. Registrants attending this activity may submit their certificate along with a copy of the course content to their professional organizations or state licensing agencies for recognition for 4.5 hours.

DISCLOSURE STATEMENTS

Joel M. Gelfand	Consultant	Amegen, Abbott, Novartis, Genentech

All other members of the faculty and planning team have nothing to disclose nor do they have any vested interests or affiliations. **It is the policy of the Chicago Dermatological Society and Colorado Foundation for Medical Care (CFMC) that the faculty discloses real or apparent conflicts of interest relating to the topics of the educational activity.**

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Department of Dermatology

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Case Presented by David Smart, MD
and Lawrence S. Chan, MD

History of Present Illness:
This 67 year old male presented to our clinic for a malignancy screening. The patient had started using Melanotan II six months prior to presentation, and since then had noted new dark moles as well as darkening of existing moles. He reported self-injecting the compound (Melanotan II) subcutaneously twice a week for its sunless tanning properties, as well for its libido enhancement effects. He acquired the Melanotan II online from a company in Europe. Prior to injections the patient reported being able to tan, but only after burning. In addition, he denied use of tanning beds, but acknowledged a history of blistering sunburns.

Past Medical and Surgical History:
Bipolar disorder, herpes simplex viral infection and gastroesophageal reflux

Medications:
Aripiprazole, lamotrigine, trazodone, acyclovir, and omeprazole

Social History:
The patient is a retired ophthalmologist, reports occasional alcohol intake, and does not smoke.

Review of systems:
The patient reported a brief flushing sensation, headache, and nausea immediately after each injection with Melanotan II.

Physical Examination:
The patient has blue eyes and is overall tanned. He has multiple brown and dark brown small asymmetric macules and papules, many of them irregularly pigmented, scattered mainly over the back, chest, and abdomen. Fewer lesions are noted over the face, ears and extremities.

Histopathology:
Left helix, skin: There is a nodular proliferation of basaloid nests at the dermal-epidermal junction and in the superficial dermis, with peripheral palisading. The nests are separated from the surrounding stroma by clefting. There is hyperpigmentation and increased melanophages across the entire lesion. There is no increased proliferation of melanocytes.

Upper back, lower back and abdomen, skin: Two of the three biopsies show early junctional lentiginous proliferations of small nests of melanocytes. This is associated with a superficial dermal infiltrate of melanophages. The third lesion shows proliferation of nested melanocytes at the dermal-epidermal junction and in the superficial dermis. This is associated with slightly increased parakeratosis suggestive of external trauma.

Diagnosis:
Pigmented basal cell carcinoma and new nevi in the setting of Melanotan II use

Treatment and Course:
The patient was referred to Mohs micrographic surgery for removal of the basal cell carcinoma. It was recommended that he avoid self-injecting products that are not FDA-regulated until more information and guidelines on its use become available. He was counseled on sun protection.

Discussion:

Melanotan I and Melanotan II are synthetic analogues of alpha-melanocyte stimulating hormones (α-MSH), and are potent non-selective melanocortin receptor (MCR) agonists with high affinity for MC1R, MC3R, MC4R, and MC5R subtypes. The melanocortin peptide hormones are thought to participate in the regulation of a variety of physiologic systems. They induce skin pigmentation by stimulating melanocyte proliferation and melanogenesis via stimulation of MC1R, increase libido and produce penile erections by binding to the MC3R in the central nervous system, and decrease appetite and increase lipolysis by binding to MC4R and MC5R respectively. They also have vasopressor effects resulting in increased blood pressure.

Melanotan I, also called afamelanotide, is more resistant to enzymatic breakdown than the natural analogue α-MSH, and represents a more potent stimulus of MC1R. Melanotan II is also more potent, but is less receptor-specific and associated with more side effects, including increased libido and penile erections.

First synthesized over thirty years ago, the α-MSH analogues are currently being studied as potential therapeutic options for photoprotection and prevention of non-melanoma skin cancer, and for the treatment of photosensitive skin diseases such as solar urticaria, polymorphic light eruption, and erythropoietic protoporphyria.

With the promise of weight loss, tanning, and increased libido, it is not surprising that over the last decade an unregulated "black" market has developed for Melanotan I and II, where they have been referred to as "Sun tan jabs" or "Barbie drugs". Serious concerns exist regarding the quality of these preparations. Furthermore, most users inject the compounds subcutaneously, adding concerns of needle contamination and potential infection. The unlicensed distribution brings to light another concerning phenomenon made possible by a global marketplace through the internet, wherein illicitly-manufactured medications are successfully and robustly distributed, while still in preclinical and clinical trial stages.

To date there have been 2 reports of melanoma and melanoma in situ arising in Melanotan II users, 1 report of melanoma in a Melanotan I user, and 6 reported cases of eruptive, changing, or dysplastic nevi. Easy access to these drugs through online sources and its growing popularity seem likely to lead to similar new cases. However, it should be noted that both in vitro and in vivo studies to this point have failed to show carcinogenic potential.

Essential Lesson:

- Melanotan I and II are melanocortin receptor agonists that represent potential treatment options in photosensitive conditions, and can be associated with new and darkening pigmented lesions.

References:

1. Evans-Brown M, et al. Use of melanotan I and II in the general population. *BMJ* 2009;338:b566.
2. Hadley ME, Dorr RT. Melanocortin peptide therapeutics: historical milestones, clinical studies and commercialization. *Peptides* 2006; 27(4):921-30.
3. Heuso-Gabriel L, et al. Nevos displasicos eruptivos tras el consumo de Melatonan. *Actas Dermosifiliogr*. 2012;103:329-42.
4. Langan EA, et al. Melanotropic peptides: more than just 'Barbie drugs' and 'sun-tan jabs'? *Br J Dermatol* 2010;163(3):451-5.
5. Mahiques-Santos L. Melatonan. *Actas Dermosifiliogr*. 2012;103:257-259.
6. Ong S, Bowling J. Melanotan-associated melanoma in situ. *Australas J Dermatol*. 2012 Jun 22.

Case Presented by Amanda LaReau, MD
and Iris K. Aronson, MD

History of Present Illness:

This 24 year old Hispanic female was hospitalized for fever spiking to 102.5° F and recurrent weeping sores with increased drainage from her groin, perineum, inframammary skin and umbilicus. She complained of pain in the affected areas without itch or burning sensation. Her axillae were not involved. She had a recent history of eye pain, oral ulcers, pretibial lesions, reactive arthritis, and 20 pound unintentional weight loss over three months but denied vaginal discharge, urinary discomfort, diarrhea, bloody stools or other genitourinary or gastrointestinal complaints. The patient had been previously treated for presumed hidradenitis suppurativa and chronic folliculitis since the age of 13. She reports that "boils and open wounds" would come and go with prior treatments that included topical, oral and intravenous antimicrobials, incision and drainage, oral contraceptives and spironolactone.

Past Medical History:

Gravida 0 (G0), episcleritis, aphthous ulcers, erythema nodosum, reactive arthritis, pilonidal cyst, methicillin resistant *Staphylococcus aureus* furunculosis, asthma, eczema

Medications:

Drospirenone/ethinyl estradiol, hydrocodone/acetaminophen, diphenhydramine, albuterol inhaler

Allergies:

Vancomycin and imipenem-cilastin – develops morbilliform rash; Iodine contrast – develops renal dysfunction

Family History:

No history of skin conditions. The patient's father has history of inflammatory bowel disease, and his gastrointestinal symptoms are well controlled on mesalamine.

Social History:

The patient is currently unemployed and was previously a legal assistant. She denies any sexual exposures or history of sexually transmitted infection. She additionally denies alcohol, tobacco, or illicit drug use.

Physical Examination:

The patient is febrile to 102.5° F and tachycardic to 144 beats per minute but otherwise normotensive and breathing well. Her face, scalp, neck, oral mucosa, and axillae are clear. The inframammary folds, periumbilical skin, and inguinal folds extending to medial thighs, labia, perineum and gluteal cleft are symmetrically involved with large eroded, edematous and violaceous plaques with clear to milky discharge and bordered by numerous perifollicular pink erosions. There is vulvar edema of the labia majora and labia minora.

Laboratory Data:

The following were positive or abnormal:

White blood cell count 14.8 k/μl (3.9-12)
Absolute neutrophils 11.k/μl (1.3-7.5)
Hematocrit 33.8 % (35-49)
Platelets 452 k/μl (150-450)
Erythrocyte sedimentation rate 71 mm/hr (<20)
C-reactive protein 8.7 mg/dl (<0.8)
Urinalysis with 148 white blood cells (<5)
Albumin 2.6 g/dl (3.4-5.0)
Protein 5.8 g/dl (6.0-8.0)
Ferritin 119 ng/ml (5-116)
Total complement activity (CH50) 215 units (60-144)
Complement C3 212 mg/dl (<152)
IgA 682 mg/dl (<436)
IgG 1674 mg/dl (<1643)

The following were negative or within normal limits:
Comprehensive metabolic panel, lactic acid, creatine kinase, lactate dehydrogenase, liver enzymes, Vitamin B, folate, iron, mean corpuscular volume, red blood cell distribution width, thyroid stimulating hormone, hepatitis B, rapid plasma reagin (RPR), HIV 1/2, anti-nuclear antibody (ANA), nicotinamide adenine dinucleotide phosphate-oxidase (NADPH) activity, Cryptococcus antibody, Histoplasma antibody, Blastomyces antibody, QuantiFERON®-TB Gold test, and urine hCG.

Diagnostic Procedures and Tests:
Tissue culture, Periumbilical: Rare diphtheroids. No anaerobes, yeast, fungus, virus, or acid fast bacilli.
Blood culture, two sets: No growth of yeast or bacteria. Nasal culture: No growth of *Staph aureus*.
Urine culture: <10,000 colony forming units of bacteria. Chest X-ray: Clear.

Histopathology:
Periumbilical, skin: There is a predominantly superficial dermal mixed inflammatory cell infiltrate with numerous multinucleated giant cells forming small epithelioid granulomas. Neutrophils and eosinophils are present. This is associated with erosion of the overlying epidermis with scale and crust. Sparse periadnexal inflammatory infiltrate is also present in the deeper dermis. The special stains for microorganisms, including Gomori methenamine silver, Warthin–Starry, and Fite stain, are all negative.

Periumbilical, skin, direct immunofluorescence: Negative for immune complex deposition.

Diagnosis:
Cutaneous Crohn's disease without prior evidence of gastrointestinal involvement

Treatment and Course:
The patient was started on prednisone at 60 milligrams by mouth daily with plan for taper and additionally discharged on clindamycin for a one-month course to treat superinfection. Esophagogastroduodenoscopy, small bowel follow through, wireless capsule endoscopy, and colonoscopy were performed without evidence of inflammatory bowel disease or malignancy. Rectal biopsy was inconclusive for inflammatory bowel disease (IBD). Serology studies also were not consistent with IBD, with antineutrophil cytoplasmic antibodies (ANCAs), anti-*Saccharomyces cerevisiae* antibodies (ASCA), and anti-*Escherichia coli* outer membrane porin (anti-OmpC) not detected.

Once clinical improvement was maintained on a daily oral dose of 10 milligrams of prednisone, she was started on metronidazole 500 milligrams by mouth twice daily, which was well tolerated. Continued clinical improvement was observed at one-month follow-up after starting metronidazole. Once prednisone was fully tapered off and six months of oral metronidazole was completed, over 90% healing of erosions was observed. However, she recently presented with relapse of disease, oral ulcers, abdominal cramping and bloating. Therefore prednisone was restarted and the tumor necrosis factor antagonist, infliximab, is being considered as an alternative systemic treatment. She continues to apply topical metronidazole gel, nystatin, triamcinolone 0.1% ointment, dexamethasone swish and spit, and fluticasone inhaler twice a day to affected areas.

Discussion:
Cutaneous Crohn's disease describes the presentation of non-caseating granulomas in the skin that are incontiguous with intestinal Crohn's disease, often referred to as "metastatic Crohn's disease." It is relatively rare, with less than 100 cases reported in the literature and over 80% reported in adults (two-thirds are women with a mean age of onset of 35). Cutaneous Crohn's disease is more commonly associated with colorectal rather than small intestinal disease, but not all patients have gastrointestinal findings or symptoms. Approximately 20% of the reported cases had skin manifestations that preceded the diagnosis of intestinal Crohn's disease by 3 months to 8 years. Our patient similarly presented with a

long history of skin findings without prior evidence of gastrointestinal involvement. It is of interest to note that she did manifest other associated findings of typical Crohn's disease such as episcleritis, aphthous ulcers, erythema nodosum, and reactive arthritis.

Crohn's disease is thought to be the result of an imbalance between pro-inflammatory and anti-inflammatory mediators, leading to an exaggerated Th1- and Th17-mediated response to certain commensal enteric bacteria. Cutaneous Crohn's disease typically manifests with genital involvement, found in approximately two-thirds of affected children and one-half of affected adults. Labial or scrotal swelling and dusky erythema are common presenting signs. Non-genital disease similarly presents with dusky erythema and edema followed by ulceration with undermined edges mostly affecting the lower extremities, abdomen, and flexural areas.

Histologically, the findings are the same as those seen in intestinal lesions with non-caseating epithelioid granulomas and surrounding lymphocytes found in the superficial and deep dermis with few scattered multinucleated Langhans-type giant cells. There is a sparse perivascular lymphohistiocytic infiltrate. Other features include the presence of eosinophils and ulceration of the overlying epidermis.

The differential diagnosis of cutaneous Crohn's disease includes other granulomatous disorders such as cutaneous sarcoidosis (not usually associated with ulceration, eosinophils, vasculitis, or dermal edema), foreign body reactions, mycobacterial infections, and deep fungal infections. Other infections, including actinomycosis, granuloma inguinale, or cellulitis, may mimic it. Ulcerated lesions may be misdiagnosed as pyoderma gangrenosum, whereas inverse psoriasis is usually not eroded. Hidradenitis suppurativa and benign familial pemphigus (Hailey-Hailey) typically have axillary involvement. The presence of granulomas makes necrolytic migratory erythema less likely. Behcet's disease has the dominant feature of uveitis.

Cutaneous Crohn's disease tends to be chronic, with severity of disease unrelated to the activity, if any, of the patient's intestinal disease. There is no consensus for its treatment. Like intestinal disease, surgery is often discouraged due to wound dehiscence and disease recurrence. There are a number of reports describing oral metronidazole 250-500 milligrams three to four times daily for one to six months as an effective treatment with or without topical or intralesional corticosteroids. Its mechanism of action in cutaneous Crohn's disease is thought to be due to its immunosuppressive and anti-inflammatory properties. Other options include systemic agents such as oral corticosteroids, sulfasalazine, azathioprine, and 6-mercaptopurine. Four biologics are FDA-approved for Crohn's disease: three TNF antagonists (certolizumab, adalimumab, and infliximab) and an integrin receptor antagonist (natalizumab).

Essential Lesson:

- Cutaneous Crohn's disease often presents with erythematous edematous plaques on genital skin.
- A minority (about 20%) of patients with cutaneous lesions have no preceding diagnosis of gastrointestinal Crohn's disease.
- The disease tends to be chronic, with severity of disease unrelated to the activity, if any, of the patient's intestinal disease.

References:

1. Boerr LA, et al. Cutaneous metastatic Crohn's disease: treatment with metronidazole. *Am J Gastroenterol* 1987; 82(12):1326-7.
2. Bolognia JL, et al. Chapter 93: Non-infectious Granulomas *in* Dermatology, Third Edition. Elsevier Limited, 2012: 1570-71.
3. Corbett SL, et al. Vulvar inflammation as the only clinical manifestation of Crohn disease in an 8-year-old girl. *Pediatrics* 2010; 125(6):e1518-22.
4. Khaled A, et al. Vulvoperineal Crohn's disease: response to metronidazole. *Skinmed* 2010; 8(4):240-1.

Case #3

Case Presented by Amanda Cooper, MD
Todd Davis, MD and Iris K. Aronson, MD

UNKNOWN CASE

This 78 year old female presented with a rash affecting her trunk and intertriginous areas.

Case #4

Case Presented by Juliana Choi, MD, PhD
and Aleksandar Krunic, MD, PhD

History of Present Illness:
This 24 year old male presented for removal of "hair growing inside his mouth" 15 months after surgical resection of a tumor on the left side of the jaw. In 2009, the patient was diagnosed with ameloblastoma of the left mandible and he underwent left hemimandibular resection and reconstruction using a free fibula flap with accompanying skin paddle. The skin paddle was harvested over the posterior border of the left fibula and placed together with the bony fragment to reconstruct the defect of the mandibular bone and mucosa. The skin was expected to mucosalize and replace lost gingival epithelium. The mandibular resection and reconstruction was successful, but the patient noticed persistent hair growth from the transplanted skin paddle which interfered with chewing and produced a "foreign body sensation" in the mouth. In 2011, the patient was referred to dermatology for consultation for intraoral hair removal.

Past Medical History:
Ameloblastoma of the left mandible treated with left hemimandibular resection and left mandible reconstruction with free fibula flap in December 2009
Endo-osseous implant placement for masticatory insufficiency in anticipation of restorative work for placement of missing teeth in August 2010
Right radial shaft fracture due to a gunshot wound in 2002

Medications and Allergies:
None and no known drug allergies

Social History:
The patient has smoked one pack per week for the past ten years and uses alcohol occasionally.

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

Physical Examination:
The first bicuspid, second bicuspid, first molar, and second molar were absent from the left lower mandibular arch, and overlying this region was a light tan to pink mucosalized skin graft with multiple long terminal hairs.

Diagnosis:
Intraoral hypertrichosis following left mandibular reconstruction with free fibula osteocutaneous flap

Treatment and Course:
Different treatment options were discussed with the patient including laser epilation and thermolysis and the decision was made to proceed with thermolysis. After local infiltrative anesthesia and left mandibular block (1% lidocaine with epinephrine 1:100,000), the patient was treated with a re-usable epilation needle with the Hyfrecator®2000 electrosurgical unit (at settings of 5-8 watts, 3000 volts, 500 ohms, 32.3 kilohertz repetition rate, 500 kilohertz frequency, and duty cycle of 30 seconds on and 30 seconds off) every 2 months for a total of 9 treatments. Since the mandibular resection and reconstruction, the patient has demonstrated full range of motion of his mouth and upon completion of electro-epilation, he has nearly complete reduction of hair growth and is able to eat without difficulty.

Discussion:

The free fibula flap (FFF) is the gold standard osteocutaneous flap for mandibular reconstruction. The FFF has several advantages including ample bone length which can tolerate multiple osteotomies and allow for shaping, strong vascular supply for anastamoses, high content of cortical bone for dental implant placement, and low morbidity of the donor region. Usually the FFF is harvested with an accompanying skin paddle which is used intraorally to fill soft tissue defects. However, the fibular skin compared to mucosa is thick, hair-bearing, and desquamative. Many flaps mucosalize but in some patients the hair follicles survive in the transplanted tissue and produce intraoral hypertrichosis.

Several treatment options to decrease intraoral hypertrichosis following flaps have been attempted. These have included surgical revision as well as removal of the skin paddle. Also, other mandibular reconstructive options such as an osteo-adipofascial flap by Smith et al. have been recommended. Although without the risk for intraoral hypertrichosis, this flap may still provide suboptimal results since the adipofascial flap may not completely mucosalize and may produce contraction especially when used to reconstruct not just the mandible but also the labial gingiva. Furthermore, since flaps with hair growth imply adequate vascularization of the grafted tissue, less invasive methods to decrease intraoral hypertrichosis were sought.

Laser and electro-epilation are the main methods of hair reduction and removal. Laser epilation produces permanent hair reduction, but often does not produce complete ablation of hair follicles, which is desirable in the case of intraoral hypertrichosis. Furthermore, Chaine et al. described one case of intraoral hair growth after FFF in which treatment with laser epilation failed and the patient was later treated with skin paddle revision. Other methods of electro-epilation, such as galvanic or direct current electrolysis, have a risk for additional scarring and mucosal burns due to the caustic effect of sodium hydroxide which is produced by the direct current to chemically destroy the hair follicle. In addition, for locations that are difficult to reach such as the intraoral cavity, electro-epilation by thermolysis remains a viable option. The use of this procedure for intraoral hair growth has not been previously described.

In thermolysis, a high-frequency alternating current is passed through a fine, thin, long epilation needle which is inserted to the level of the hair bulb. This technique removes hairs one-by-one and is most effective on anagen hairs. On average, hair may regrow in 20-40% of the treated follicles and therefore multiple treatments are necessary. This case demonstrates successful use of thermolysis to treat intraoral hair growth and has been shown to be efficacious after multiple treatment sessions.

Essential Lessons:

- Intraoral hair growth on the skin paddle of free fibula flaps after mandibular reconstruction can be distressing to patients.
- Thermolysis is a treatment option for permanent hair removal in small localized areas that are difficult to lase such as the intraoral cavity.

References:

1. Chaine A, et al. Postoperative complications of fibular free flaps in mandibular reconstruction: an analysis of 25 consecutive cases. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod.* 2009;108(4):488-495.
2. Chim H, et al. Reconstruction of mandibular defects. *Semin Plast Surg*. 2010 May;24(2):188-197.
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5. Smith ML, et al. Fibula osteo-adipofascial flap for mandibular and maxillary reconstruction. *Head Neck.* 2011; 1-6.
6. Wanitphakdeedecha R, Alster TS. Physical means of treating unwanted hair. *Dermatol Ther*. 2008;21(5):392-401.

Cases Presented by Amanda Marsch, MD
Inderjit Gill, MD, James Seehafer, MD, Michael Bukhalo, MD, and Iris K. Aronson MD

Patient A

History of Present Illness:

A 53 year old female presented with a pruritic, burning, and painful eruption on her lower legs that had been present for over one year. The eruption waxed and waned in severity, and was associated with intermittent "sores". There was history of swelling in her legs that worsened with prolonged standing. After an evaluation by a vascular surgeon, she underwent endovenous laser ablation therapy twice for suspected venous insufficiency and initially noted some improvement. She had also been taking aspirin and dipyridamole over the past year and noted some improvement with this as well. Additional prior treatments included topical mupirocin and clobetasol.

Past Medical and Surgical History:

Hepatitis A and B, venous insufficiency, endovenous laser ablation therapy in December 2010 and February 2011, meningioma s/p removal 1993, hypertension.
No prior history of blood clots.

Medications:

Aspirin, dipyridamole, amlodipine, diovan, and oxcarbazepine

Allergies:

Penicillin

Family History:

No venous thromboses, cerebrovascular accidents, skin cancer or other skin disorders. Father died of lung cancer - he was a smoker. She had many relatives with venous varicosities.

Review of Systems:

The patient denied any fevers, chills, night sweats, weight loss, or joint pains.

Physical Examination:

The patient has hyperpigmented stellate and retiform patches with atrophic white macules located predominately on the pretibial area, medial and lateral malleoli, and dorsal feet. There are also scattered pinpoint petechiae on the pretibial areas bilaterally. There are no ulcerations present. Patient had a photograph taken at her previous dermatologist's office, which demonstrated numerous pinpoint crusty punched-out ulcerations over the aforementioned areas.

Laboratory Data:

The following were positive or abnormal:
Cholesterol 222 mg/dL (<150 mg/dL)
HDL 40 mg/dL (>40 mg/dL)
LDL 154 mg/dL (<100 mg/dL)
Homocysteine 12.7 µmol/L (<10.4 µmol/L)

The following were negative or within normal limits:
Complete blood count, complete metabolic profile including liver function tests, thyroid stimulating hormone, uric acid level, serum amylase, urinalysis, phosphatidylserine antibodies, cryoglobulin screen, antinuclear antibody assay, cytoplasmic and peri-nuclear anti-neutrophil cytoplasmic antibodies, cardiolipin antibodies, protein C, protein S, antiphospholipid antibody panel, Factor V Leiden, plasminogen activator inhibitor-1, lipoprotein A

Diagnostic Procedures and Tests:

11/2011 Venous and Arterial Ultrasound with Doppler, Lower Extremities: no evidence of peripheral arterial disease. Venous Doppler showed no evidence of DVT bilaterally but did show superficial venous insufficiency bilaterally.

Histopathology:

Right shin, skin: The superficial dermal blood vessels are dilated. This is associated with extensive extravasation of red blood cells. The lumens of the small blood vessels are occluded and fibrin thrombi are easily identified. There is, however, no active inflammation in the vessel wall. The overlying epidermis is hyperplastic with focal spongiosis, scale and crust. This is also associated with increase in dermal fibrosis, extending into superficial subcutis.

Diagnosis:

Livedoid vasculopathy (atrophie blanche)

Treatment and Course:

Aspirin/dipyridamole was continued. Pentoxifylline along with vitamins B12, B6, folic acid, and rutoside were added after hyperhomocysteinemia was identified and compression stockings were recommended. The patient initially continued to get new petechiae but no ulcerations therefore her pentoxifylline, aspirin, and dipyridamole doses were increased. Her aspirin was eventually discontinued due to development of a possible gastric ulcer. After these dose adjustments she did not develop further cutaneous ulcerations. She continued to have intermittent tingling in her legs but denied pain. Recommendation for the addition of clopidogrel was made but the patient elected not to start this medication since she was improving.

Patient B

History of Present Illness:

This 67 year old female with a history of psoriasis presented for an evaluation of an ulcerated lesion on her right ankle for 5 months duration. The patient stated that she has had erythema and pain in the medial aspect of her right ankle for the past 1-2 years, which intermittently develop very small ulcers, and take months to heal. The lesions were very painful. Over the preceding 4 months, she noted increased erythema and pain while many of the smaller ulcers coalesced into a larger ulceration. The right ankle ulcers had clear to whitish discharge and mild bleeding. Past treatments included betamethasone 0.05% ointment, pimecrolimus topical 1% cream, tacrolimus topical 0.1% ointment and a water-based emulsion. She had also recently been put on doxycycline and gabapentin for pain control as well as prednisone 40mg tapered by 10mg every four days. In the past she had also tried pentoxifylline but could not tolerate this medication due to development of a rash. She denied a history of lower extremity swelling or blood clots.

Past Medical History:

Psoriasis, arthritis, hypothyroidism. No prior history of blood clots.

Medications:
Doxycycline, gabapentin, levothyroxine, folic acid, pilocarpine, multivitamin, calcium, fish oil, glucosamine, raloxifene

Allergies:
Pentoxifylline- rash

Family History:
No blood clots, skin cancer or other skin disorders. No family history of autoimmune disorders.

Review of systems:
The patient denied any fevers, chills, night sweats, or weight loss.

Physical Examination:
The patient has a large area of erythema with multiple small ulcerations centrally over her right medial malleolus. Some of the ulcerations are coalescing and have a yellow discharge. Surrounding the erythema are several small ivory-white depressed plaques. Her left medial ankle also has multiple ivory-white depressed plaques, at sites of previous ulcerations.
Dorsalis pedis pulses are 2+ bilaterally.

Laboratory Data:
The following were positive or abnormal:

06/2011	Phosphatidylserine IgG antibody 19 U/ml (0-10 U/ml)
01/2012	Phosphatidylserine IgM antibody 12 U/ml (<10 U/ml negative, 10-20 U/ml equivocal, >20 U/ml positive)

The following were negative or within normal limits:
Complete blood count, serum protein electropheresis, hepatitis A IgM antibody, hepatitis B profile, hepatitis C screen, anti- cardiolipin antibodies, anti-beta 2 glycoprotein antibodies, cytoplasmic and peri-nuclear anti-neutrophilic cytoplasmic antibodies, phosphatidylserine IgA antibodies, Protein S, Protein C, anti-nuclear antibody panel, cryoglobulins, Factor V Leiden

Diagnostic Procedures and Tests:

06/2011	Venous and arterial duplex, lower extremities: no evidence of peripheral arterial disease or thrombi; ankle brachial index within normal limits bilaterally

Diagnosis:
Livedoid vasculopathy (atrophie blanche)

Treatment and Course:
Gabapentin was continued for pain management and doxycycline was continued as an anti-inflammatory agent. She was started on aspirin 81 mg, dipyridamole, B vitamins, and nicotinamide. The patient was not able to tolerate compression stockings and previously had an allergic reaction to pentoxifylline. The ulcers were healing after approximately 1 month of this therapy; there were no new lesions, although she continued to have burning sensations in the affected areas. Though the patient's ulcers had improved, they were not completely healed on this regimen. Raloxifene was discontinued due to concern that this estrogen modulator may predispose the patient to thrombosis. Later on in her course, her aspirin dose was titrated up but the patient developed a rash which after being biopsied was suspected to be due to the aspirin. Her aspirin and dipyridamole were discontinued and replaced with clopidogrel. This led to complete resolution of her ulcers and symptoms. The patient remains symptom-free to date.

Patient C

History of Present Illness:

This 59 year old female with a history of peripheral arterial disease and bilateral lower extremity stent placement was referred to us for evaluation of her lower extremity lesions that had been present for 4 months. The patient complained of lower leg swelling and a painful black, crusted lesion on her lateral right leg and multiple red bumps evolving into crusty lesions on both lower extremities. She had recently taken some new medications, including cyclobenzaprine, diclofenac and gabapentin and she was told that she may have had an allergic reaction to one of these medications although she notes that her leg lesions had been present before starting these medications. Previous medications which were not helpful for her leg symptoms included desoximetasone cream, clobetasol ointment, biafine, and a course of cephalexin.

Past Medical and Surgical History:

Peripheral arterial disease with bilateral lower extremity stent placement, non-alcoholic steatohepatitis, brain aneurysm with coil placement, cerebrovascular accident in 2007 thought to be secondary to aneurysmal bleeding, hypertension, hypercholesterolemia, multiple operations including knees bilaterally, right shoulder, bladder sling, appendectomy, bilateral carpal tunnel and hysterectomy
No prior history of blood clots.

Medications:

Acetaminophen/hydrocodone, clopidogrel, aspirin, hydrochlorothiazide, losartan, atenolol, fenofibrate, calcium, vitamin D, potassium gluconate, vitamin E, multi-vitamin, silver sulfadiazine cream

Allergies:

Tape-develops rash, lisinopril, intravenous dye, shellfish- rash

Family History:

No history of blood clots, skin cancer or other skin disorders. Father had a cerebrovascular accident.

Review of systems:

The patient denied any fevers, chills, night sweats, weight loss, or joint pains.

Physical Examination:

On the lower extremities, there are violaceous papules with overlying crust (most prominently near her ankles), superficial erosions and punched-out ulcers with surrounding erythema. Cayenne pepper macules are scattered bilaterally. There is a reticulated erythema around the knees as well as on the abdomen and lower back.

Laboratory Data:

The following were positive or abnormal:
Protein S activity 138 (65-129)
Homocysteine 16 µmol/L (<10.4 µmol/L)

The following were negative or within normal limits:
Serum protein electrophoresis, Hepatitis B and C panel, anti-nuclear antibody assay, antiphospholipid antibodies, anti-cardiolipin antibodies, Factor V Leiden, protein C, alpha-1 anti-trypsin, C4 and C3 levels, CH50, cryoglobulins, cytoplasmic and peri-nuclear anti-neutrophil cytoplasmic antibodies, basic metabolic panel, partial thromboplastin time, fibrinogen, anti-phosphotidylserine prothrombin complex antibody, plasminogen activator inhibitor-1, lipoprotein A, prothrombin G20210A gene mutation

Diagnostic Procedures and Tests:

10/2011 Arterial and venous duplex, lower extremities: arterial patency within normal range; no evidence of thrombi; ankle brachial index within normal limits bilaterally

Diagnosis:

Livedoid vasculopathy (atrophie blanche)

Treatment and Course:

The patient was continued on clopidogrel which she was taking for her peripheral arterial disease. She was started on aspirin and pentoxifylline. She initially could not tolerate compression stockings secondary to pain. She was referred to the wound care clinic and continued to follow-up there for her leg ulcers. After discovery of her elevated serum homocysteine level, the patient was started on folic acid, vitamin B6, and vitamin B12. The patient continued to improve on this regimen with resolution of her ulcerative lesions and improvement in pain after approximately two and a half months on this treatment. She was eventually able to tolerate compression stockings. She remained symptom-free at her recent one year follow-up appointment.

Discussion:

Livedoid vasculopathy (LV) is a term that encompasses livedoid vasculitis, segmental hylanizing vasculitis, livedo reticularis with summer ulcerations and PURPLE (painful purpuric ulcers with reticular pattern of the lower extremities). It is a disorder characterized by blood vessel occlusion and it is most commonly associated with hypercoagulable disorders although it can also be associated with inflammatory conditions such as lupus or polyarteritis nodosa. Conditions creating Virchow's triad (endothelial injury, hypercoagulability, stasis) appear to play a role in this disorder and they include hyperhomocysteinemia, Factor V Leiden mutation, antiphospholipid antibody syndrome, and also stasis, as varicose veins may be found in up to 75% of patients with LV.

LV mainly affects young to middle-aged women and follows a chronic, relapsing course. Primary lesions consist of petechia, purpura, or lenticular macules. Eventually, these lesions progress to asymmetrical, painful leg ulcers that may heal leaving white, depressed scars, known as *atrophie blanche*. It is important to note that atrophie blanche is not specific for LV and may be found in a number of other conditions such as venous stasis as well as autoimmune diseases. It most commonly affects the lower legs and has a predilection for the malleolar area.

Key histopathologic findings include deposition of fibrinoid material in the vessel lumen, vessel wall hyalinization and infarction, and the absence of vasculitis. Although typically a distinct clinical entity, biopsy may be necessary to exclude vasculitis, which would preclude the diagnosis.

Suggested laboratory and diagnostic work-up include but are not limited to: prothrombin time (PT), partial thromboplastin time (PTT), complete metabolic profile, complete blood count, anti-thrombin activity, protein C and S activity, anti-cardiolipin antibodies, lupus anticoagulant, prothrombin gene mutation, factor V Leiden mutation, fibrinogen, homocysteine (assess acquired or inherited), tissue plasminogen activator, plasminogen activator inhibitor-1, serum protein electrophoresis, Hepatitis B and C panels, cytoplasmic and peri-nuclear anti-neutrophilic cytoplasmic antibodies, cryoglobulins, HIV, anti-nuclear antibody panel, rheumatoid factor, anti-phospholipid antibodies, and lower extremity arterial and venous duplex.

Treatment should focus on identifying an underlying cause. Pain management and resolution of cutaneous ulcerations should be the primary endpoints. First line treatments include antiplatelet therapy such as dypyridamole with or without aspirin and clopidogrel. Pentoxifylline is often used to reduce blood viscosity and increase circulation. When a pro-thrombotic state is identified, anticoagulants may be used such as warfarin or heparin. General consensus is to keep the INR between 1.5 and 2.0 although other studies used guidelines consistent with that used for atrial fibrillation. Recommended doses for heparin therapy are not established. Other treatments include drugs stimulating endogenous fibrinolytic activity such as the anabolic steroids ethylestrenol and danazol. Recently, recombinant tissue plasminogen activator (rt-PA) has been used, but in combination with heparin. Phototherapy with PUVA has been used for cases demonstrating pro-inflammatory states, such as elevated erythrocyte sedimentation rate (ESR) or C-reactive protein (CRP). Other drugs used in case reports include cyclosporine, hyperbaric oxygen therapy, and intravenous immunoglobulin. Oral rutoside (a bioflavonoid) in combination with ascorbic acid may also be considered in some patients, as this treatment has been used successfully for other related dermatological diseases such as pigmented purpuric dermatoses. Additionally, rutoside and its derivatives have been shown to inhibit thrombus formation both in-vitro and in-vivo.

Extensive laboratory work-up (as listed above) should be pursued in an effort to identify a possible underlying cause or contributing factor. For example, there has been a report of a patient with LV who was found to have hyperhomocysteinemia secondary to vitamin B6 and B12 deficiencies and exacerbated by renal insufficiency. After correction of the patient's vitamin deficiencies with oral supplementation, in addition to anticoagulation therapy, the patient's LV improved significantly and her homocysteine, vitamin B6 and vitamin B12 levels normalized. Additionally, one study evaluated 34 LV patients and identified 8 of these patients to have pro-coagulant conditions based on laboratory studies. These patients were treated with either warfarin or heparin and 7 of 8 patients achieved remission of their LV symptoms for 6-9 months.

Essential Lesson:

- Livedoid vasculopathy is a thrombotic disorder and is one of the causes of atrophie blanche.
- The work-up for livedoid vasculopathy is extensive, due to the many possible underlying etiologies.

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Case #6

Case Presented by Adrienne Schupbach, MD
and Iris K. Aronson, MD

UNKNOWN CASE

This 31 year old male presented with a painful rash on his chest.

Case #7

Case Presented by Eliana Krulig, MD
David Fretzin, MD and Lawrence S. Chan, MD

History of Present Illness:
This 64 year old African American male presented with a four year history of multiple lesions on his face and scalp. He stated that his lesions waxed and waned, but had been constantly present for one year prior to evaluation. Facial lesions were asymptomatic, whereas scalp lesions were occasionally itchy but responded to the application of salicylic acid 3% solution. The patient denied any recent illness.

Past Medical/ History:
Diabetes, hypertension, dyslipidemia, coronary and peripheral artery disease, benign prostatic hyperplasia

Medications:
Glipizide, carvedilol, hydrochlorothiazide/lisinopril, simvastatin, salicylic acid 3% solution

Family History:
Mother had breast cancer. Siblings and children are otherwise healthy.

Social History:
The patient is a veteran with a 20 pack-year smoking history. He reports occasional alcohol intake and marijuana use.

Review of systems:
He reported weight loss of greater than 25 lbs over the prior 2 years, attributed to decreased appetite. He denied fever, chills, weakness, fatigue, shortness of breath, cough, hemoptysis, nausea, vomiting, abdominal pain, diarrhea, hematuria, or headache.

Physical Examination:
Over the forehead and bilateral cheeks, there are multiple firm, skin-colored, well-defined, subcutaneous nodules, ranging from 3 to 6 mm. Some of the lesions are mildly erythematous. Similar larger lesions are noted throughout the scalp, many with evidence of excoriation and hyperkeratosis. A 2 cm non-tender firm lymph node is palpated on the right posterior cervical chain. There are no other palpable lymph nodes. The remaining skin, nail, and mucosal examinations are normal.

Diagnostic Procedures and tests:
The following were positive or abnormal:
Creatinine 1.4 mg/dl (0.67-1.17), lactate dehydrogenase 242 U/l (81-234).

The following were negative or within normal limits:
Complete blood count with differential, complete metabolic panel, rapid plasma reagin, QuantiFERON®-TB Gold test, serum protein electrophoresis, computed tomography of the head, chest, abdomen and pelvis, skeletal bone survey, thyroid stimulating hormone, free T4, morning cortisol, adrenocorticotropic hormone, testosterone, luteinizing hormone, follicle-stimulating hormone

Histopathology:
Right forehead, skin: There is a nodular infiltrate of histiocytes predominantly in the deep dermis. This is surrounded by an infiltrate of lymphocytes and scattered eosinophils. The histiocytes in the center are enlarged with abundant amphophilic cytoplasm and small nucleoli. These histiocytes stain positive for CD 68, CD1a and S100. The overlying epidermis is unremarkable. There is no evidence of epidermotropism. Additional imunohistochemical stains show a mixed population of T and B cells. Multiple special stains for microorganisms are all negative.

Diagnosis:
Indeterminate cell histiocytosis

Treatment and Course:
The patient completed consultations with surgery, endocrinology, infectious disease, and hematology-oncology departments. He underwent a lymph node biopsy of the posterior neck, which was suggestive of a reactive process, and a separate skin biopsy obtained from a similar scalp nodule was consistent with an epidermal inclusion cyst. Given a negative malignancy work up and no evidence suggestive of systemic involvement, a bone marrow biopsy was not indicated. The patient decided to follow a conservative management. He uses fluocinonide solution as needed for his scalp pruritus and continues to follow up with our service regularly. Upon subsequent evaluations, resolution of some of the facial subcutaneous nodules has been noted.

Discussion:
Indeterminate Cell Histiocytosis (ICH) is a rare condition characterized by the proliferation of indeterminate cells. Due to its immunophenotypic profile, it is thought to represent an overlap between Langerhans Cell Histiocytosis (LCH) and Non-Langerhans Cell Histiocytosis (non-LCH). Initially described by Wood et al. in 1985, less than 50 cases have been reported to date.

Indeterminate cells (IC) are considered by some authors to represent dermal precursors of Langerhans cells (LC). They are referred to as "indeterminate" since their immunohistochemistry pattern is positive for S-100 and CD1a, which are markers of Langerhans cells, as well as CD68, a macrophage/monocyte marker. Ultrastructurally these cells lack Birbeck granules, but as electron microscopy is rarely employed, langerin immunostaining (CD207) can be used as a surrogate marker, which is expected to be negative in cases of ICH.

Although IC are closely related to LC, ICH clinically resembles non-LCH. It remains a controversial diagnosis, and authors argue whether this is a distinct entity or represents a variation of a non-LCH. Clinical presentation can vary widely from a single lesion to generalized involvement. This condition is usually seen in adults, and has no gender predilection. Patients present with asymptomatic yellow, red, or red to brown monomorphic firm papules ranging from 3 to 10 mm in size. Extracutaneous and systemic symptoms are not typically seen, but conjunctiva and bone involvement have been documented. In addition, there are a few cases of ICH that have been followed by the development of leukemia.

Histopathology reveals a dense dermal proliferation of histiocytes with admixed lymphocytes. Histiocytes often have an oncocytic appearance, with occasional spindled, scalloped or vacuolated cell variants. Eosinophils are occasionally observed and epidermotropism is rare. Touton giant cells can be present. As previously mentioned, immunohistochemistry of the proliferating cells demonstrates an S-100 +, CD1a +, CD68 +, and langerin - phenotype.

The clinical course of ICH is most often either self-limited or non-progressive, and conservative management is preferred. However, if extensive or disfiguring disease occurs, treatment with systemic medication is indicated. Although evidence supporting any particular treatment is limited, PUVA, broad-band UVB, low-dose methotrexate, systemic steroids, thalidomide, total skin electron beam therapy, and chemotherapy with cyclophosphamide, vinblastine, 2-chlorodeoxyadenosine, or etoposide, have been variably effective. Solitary lesions can be managed with surgical excision. Careful follow up is recommended due to its possible association with leukemia.

Essential Lessons:

- ICH is thought to represent an overlap between Langerhans cell histiocytosis (LCH) and Non-Langerhans cell histiocytosis (non-LCH).
- Indeterminate cells immunohistochemistry pattern is positive for S100 and CD1a, which are LC markers, as well as CD68, which is a macrophage/monocyte marker.

References:

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3. Ratzinger G, et al. Indeterminate Cell Histiocytosis: Fact or Fiction? *J Cutan Pathol*. 2005;32(8):552-60.
4. Rezk SA, et al. Indeterminate Cell Tumor: A Rare Dendritic Neoplasm. *Am J Surg Pathol*. 2008;32(12):1868-1876.

Case #8

Case Presented by Steven Kahn, MD
Nicole Hartsough, MD, Paula Lapinski, MD, and Iris K. Aronson, MD

Patient A

History of Present Illness:
This 43 year old African American female presented with a 7 year history of a photosensitive rash on her upper arms. Her rash was pruritic and intermittent in nature. She complained of occasional sun sensitivity but denied any facial rash as well as oral ulcers. She had previously only tried hydrocortisone lotion for her rash.

Past Medical & Surgical History:
Hernia repair 1973

Medications:
None

Allergies:
No known drug allergies

Family History:
Brother with asthma, sister with breast cancer, son with eczema

Social History:
The patient is a restaurant manager, lives with her husband and 2 children, smokes 5 cigarettes per day, and drinks 1-2 glasses of wine per day.

Review of systems:
The patient denied any fevers, chills, night sweats, shortness of breath, or weight loss. She noted occasional knee pain.

Physical Examination:
The patient has several scattered 1-5 cm atrophic areas, some appearing violaceous and indurated, on the bilateral shoulders and proximal upper extremities.

Patient B

History of Present Illness:
This 34 year old female presented with a history of intermittent eyelid swelling which had not improved with antibiotics. Approximately one year after the onset of this symptom, she developed a persistent, growing pimple on her left cheek which was biopsied and read as rosacea. She was referred to rheumatology for a workup of sarcoidosis. A chest radiograph was performed and was negative for any signs of sarcoidosis. The patient was treated with a course of steroids by rheumatology which decreased the redness and size of the skin lesion. She then developed a persistent palpable mass on her right nose and cheek.

Past Medical & Surgical History:
Bilateral bunionectomy

Medications:
Vitamin D

Allergies:
No known drug allergies

Family History:
Sister with lichen planus, grandmother with lupus erythematosus

Social History:
The patient is an oncology nurse and she denies smoking, alcohol intake, or illicit drug use.

Review of systems:
The patient denied any fevers, chills, night sweats, shortness of breath, weight loss, muscle pains, or joint pains.

Physical Examination:
The patient has an atrophic area of the left medial cheek. There is a small ice-pick scar medially to this area. She has a 6x8 mm hyperpigmented macule on the left bridge of her nose. Her right medial cheek appears swollen with a 1 cm erythematous thin plaque medially with rolled borders. No atrophy is evident at the proximal extremities. There are no palpable cervical, post-auricular, occipital, submental, or axillary lymph nodes.

Case #9

Case Presented by Karl Vance, MD
Kristen Pytinia, MD, MPH, Anuja Antony MD, MPH and Aleksandar Krunic, MD, PhD

History of Present Illness:
The patient is a 50 year old female who presented with an ulcer on the right cheek which had grown over the past 3 years. She noted pain, occasional itch, and occasional drainage from the lesion. As the lesion grew, she developed difficulty closing the right eye and a right-sided facial droop which prompted her to seek medical attention.

Past Medical & Surgical History:
None

Medications:
Ibuprofen

Allergies:
No known drug allergies

Family History:
No known history of skin cancer, other skin diseases, or other malignancies.

Review of systems:
The patient denied fevers, chills, night sweats, change in hearing, change in vision, or difficult phonation.

Physical Examination:
On the right cheek overlying the parotid gland and extending to the pinna there is a 4.5x7cm deep ulceration with irregular borders and granulation tissue at the base. There is a pronounced right-sided facial droop. There is no palpable lymphadenopathy.

Laboratory Data:
The following were normal or within normal limits:
Complete blood count, comprehensive metabolic panel.

Microbiology:
Wound cultures for bacteria, fungus, and mycobacteria grew normal skin flora.

Histopathology:
Right cheek, skin: There is proliferation of baseloid cells with a highly infiltrative growth pattern. The neoplastic cells infiltrate through subcutaneous adipose tissue, invading skeletal muscle. Perineural invasion is identified in multiple foci.

Diagnosis:
Aggressive basal cell carcinoma

Treatment and Course:
Mohs surgery was performed utilizing the moat technique to clear the peripheral margin. She was then brought to the operating room by our otolaryngology colleagues who performed a wide local excision including the parotid gland, auriculectomy, lateral temporal bone resection, partial mandibulectomy, removal of the zygomatic arch, and right-sided level II/III neck dissection. This was followed by repair

by plastic surgery with a right radial forearm free flap, gold weight placement to the right upper eyelid, nerve graft to the right frontal branch of the facial nerve, and a temporalis sling to suspend the right oral commisure. Perineural involvement was confirmed on pathology of the surgical specimen, and zero of 19 lymph nodes had tumoral involvement, resulting in a final grade of pT2N0M0 and stage II. Due to perineural invasion and involvement of the temporal bone, a multidisciplinary team recommended adjuvant radiation. She received 6000 centigray to the tumor bed in 200 centigray fractions. She has responded well to the treatment and repair.

Discussion:

Basal cell carcinoma (BCC) is the most common malignancy with over 1,000,000 new cases in the United States annually. Most are small, well-defined lesions that are easily cured with a wide variety of treatment modalities including electrodessication and curettage, cryodestruction, wide local excision, Mohs surgery, topical chemotherapy, intralesional chemotherapy, and radiation therapy. Less than 1% of tumors may enlarge substantially, involve deep underlying tissues such as bone, or exhibit perineural invasion. These tumors are often referred to as "aggressive," "advanced," or "severe" BCCs though no specific criteria of those terms are widely accepted. Tumors overlying embryonic fusion planes such as the medial canthus, philtrum, mid-lower lip and chin, meilolabial fold, preauricular cheek, and retroauricular sulcus often exhibit extensive subclinical extension. Advanced BCCs often display aggressive histologic subtypes such as morpheaform, micronodular, or metatypical.

Aggressive BCCs can often not be completely removed with Mohs surgery, and a multidisciplinary approach is preferred. In our experience, the "moat" technique (also referred to as the "ring of Mohs" or "spaghetti" technique) is the optimal method to clear the peripheral margin before the central bulk of the tumor is extricated in the operating room. A narrow (2-4 mm) ribbon of skin is removed circumferentially around the tumor, and the lateral margin is examined with frozen sections with additional layers taken until there is no evidence of residual tumor. A moat is thus created between the central bulk of the tumor and the uninvolved skin surrounding it.

Radiation therapy plays a limited though important role in treatment of BCCs. It is often reserved for patients with extensive tumors and significant comorbidities who are not candidates for general anesthesia, or as adjuvant treatment for lesions with perineural invasion, involvement of underlying bone, or in whom it is not possible to obtain a clear surgical margin. While radiation therapy has the advantage of not requiring surgical reconstruction, the cosmetic outcome tends to deteriorate with time, and thus is not preferred in younger patients. Radiation is contraindicated in patients with Gorlin's syndrome.

Essential Lessons:

- Aggressive basal cell carcinomas are rare, and often require a multi-disciplinary approach.
- The "moat" technique is recommended to histologically clear the peripheral margin before the patient is brought to the operating room to extricate the tumor.

References:

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Case #10

Case Presented by Karl Vance, MD
Claudia Hernandez, MD and Aleksandar Krunic, MD, PhD

Patient A

History of Present Illness:
The patient is a 17 year old male who presented with an 18 month history of "growths" within the red colored parts of his professional tattoos. They were occasionally pruritic, but otherwise asymptomatic.

Past Medical & Surgical History:
None

Medications:
None

Allergies:
No known drug allergies

Family History:
Non-contributory

Physical Examination:
Bilateral ventral forearms with extensive dark blue-black tattoos depicting letters and flowers. Exophytic, erythematous, crusted plaques localized to the red colored portions of the tattoos.

Laboratory Data:
None

Histopathology:
Right arm, skin: Sections demonstrate a dense, band-like infiltrate of small lymphocytes in the upper dermis admixed with numerous histiocytes and fewer eosinophils. Necrotic keratinocytes are focally evident at the base of the epidermis. The reticular dermis shows an infiltrate of similar composition with much less density in a perivascular, peri-eccrine and focally interstitial distribution. Immunohistochemistry shows a predominance of CD3+/CD4+ helper T-cells with fewer CD3+/CD8+ cytotoxic T-cells and very few CD20 positive B-Cells. CD163 highlights numerous histiocytes.

Diagnosis:
Pseudolymphomatous tattoo reaction

Treatment and Course:
Treatment options including surgical excision, topical or intralesional corticosteroids, and oral hydroxychloroquine were discussed. The patient was reluctant to consider surgical excision due to the risk of jeopardizing the shape of the tattoo and scarring. He also declined intralesional steroids due to concerns regarding dyschromia. Oral hydroxychloroquine 200 mg by mouth daily was initiated, and he is scheduled for follow-up.

Patient B

History of Present Illness:

The patient is a 29 year old female who presented with a rash on her chest and right upper arm localized to tattoos on these areas. She had been diagnosed with pulmonary sarcoidosis 6 months prior to presentation, and was taking oral prednisone 16 mg daily. She had not attempted to treat the eruption.

Past Medical & Surgical History:

Pulmonary sarcoidosis confirmed by lung biopsy and computed tomography, and seasonal allergies

Medications:

Prednisone 16mg by mouth daily, prednisolone eye-drops, fluticasone nasal spray

Allergies:

No known drug allergies

Family History:

Non-contributory

Review of systems:

The patient denied fevers, chills, night sweats, weakness, fatigue, shortness of breath, cough, or visual changes.

Physical Examination:

Right arm and upper chest with numerous flesh colored papules coalescing into plaques confined to areas with dark blue-black and red tattoos. Several small papules on bilateral alar grooves and a 10cm atrophic scaly patch with decreased follicular density on the crown of the scalp.

Laboratory Data:

The following were positive or abnormal:
Angiotension Converting Enzyme 237 u/l (9-67)

Histopathology:

Right arm, skin: There are multiple superficial and deep epithelioid granulomas. They are surrounded by sparse lymphocytic infiltrate in the periphery. The overlying epidermis is unremarkable. Hemosiderin-laden macrophages are also identified in the superficial dermis. The Gomori methenamine silver stain for fungi and Fite stain for mycobacteria are both negative.

Radiology:

02/2012	Computed tomography, chest: Scattered nodular opacities and extensive lymphadenopathy compatible with sarcoidosis

Diagnosis:

Sarcoidosis within a tattoo

Treatment and Course:

The patient was prescribed triamcinolone 0.1% ointment to the affected areas twice daily. A multi-specialty management plan using oral immunosuppresive agents including prednisone, azathioprine, or methotrexate was under discussion until she became pregnant. Significant thinning of the papules was noted at follow up.

Discussion:

Complications of tattooing are rare, and include infection, allergic reaction to the tattoo ink, granuloma formation, flare of an underlying skin disease within the tattoo, and transmission of an infectious disease. Hypersensitivity reactions may take on a lichenoid, eczematous, or granulomatous clinical and histological appearance. Infections including bacterial, viral, mycobacterial, and fungal have been reported, as has the development of malignancies including melanoma, basal cell carcinoma, squamous cell carcinoma, keratoacanthoma, and dermatofibrosarcoma protuberans.

Pseudolymphomatous reaction, while rarely reported in tattoos, can be secondary to many different stimuli (medications, injected foreign substances, vaccinations, infections, arthropod assault, and photosensitivity) or may be idiopathic. Histologically, a superficial and deep nodular or diffuse infiltrate of polyclonal lymphocytes admixed with histiocytes and occasional plasma cells and eosinophils is seen. Rarely, a band-like and perivascular dermal infiltrate, at times with epidermotropism, may be seen, though this is more typical for malignancy.

Pseudolymphomatous tattoo reaction typically appears from 6 months to 6 years after tattooing, and is most commonly seen within red ink. Other dyes, like green and blue, have also been linked to its development. Treatment options include topical and intralesional corticosteroids, surgical excision or oral hydroxychloroquine. Laser therapy is not usually successful due to the incomplete removal of triggering pigment. Although pseudolymphomatous reactions may spontaneously regress, close follow up is advised due to the rare potential for malignant transformation.

Sarcoidosis is a granulomatous disease of unknown etiology that may affect any organ of the body, though the lungs and lymph nodes are most commonly involved. Cutaneous manifestations are present in about 25% of patients and include erythema nodosum, plaques, maculopapular eruptions, subcutaneous nodules and lupus pernio. Histologically, non-caseating granulomas are seen composed of epitheliod histiocytes with minimal lymphocytic infiltration.

Rarely, sarcoidosis may appear within tattoos. This has been described in patients with known systemic sarcoidosis, as a harbinger for underlying systemic disease, as well as in patients without systemic involvement. The etiology of sarcoidal tattoo reactions is unclear, and may represent the Koebner phenomenon, scar sarcoidosis, or an immunologic response to the tattoo ink. None of these postulates are completely satisfactory however, as the former cannot explain the appearance of sarcoidal granulomas in tattoos that are decades old, and the latter does not account for the manifestation as part of systemic sarcoidosis.

Treatment options for sarcoidosis within a tattoo include topical, intralesional and oral corticosteroids, anti-malarials, immunosuppressive agents, and excision.

Essential Lessons:

- Pseudolymphomatous tattoo reaction is a rare complication that mimics lymphoma, though has low malignant potential.
- Sarcoidosis may occur within tattoos in patients with known systemic disease, as a harbinger for underlying disease, or without underlying systemic sarcoidosis.

References:

1. Mataix J and Silvestre JF. Cutaneous adverse reactions to tattoos and piercings. *Actas Derosifilogr*. 2009;100:643-56.
2. Ali AM, et al. Sarcoidosis appearing in a tattoo. *J Cutan Med Surg*. 2008;12(1):43-8.
3. Desai NA and Smith ML. Body art in adolescents: Paint, Piercings and Perils. *Adolesc Med.* 2011;022:97-118.
4. Blumental G, et al. Pseudolymphomatous reaction to tattoos. Report of three cases. *J Amer Acad Dermatol.* 1982;4:485-8.
5. Patrizi A, et al. Tattoo-associated pseudolymphomatous reaction and its successful treatment with hydroxychloroquine. *Acta Derm Venereol*. 2009;89:327-8.

Cases Presented by Sonoa Au, MD
Claudia Hernandez, MD, Carlotta Hill, MD, and Sophie M. Worobec, MD

Patient A

History and Physical:

This 56 year old female presented with a two year history of a pruritic and painful rash on her face accompanied by swelling. The eruption was exacerbated by sunlight, heat, and wind. She briefly benefited from short courses of prednisone administered by her primary care physician (PCP), but her rash always recurred after cessation of therapy. Diphenhydramine and hydroxyzine provided some relief from her pruritus. Of note, she complained of worsening shortness of breath. A recent chest CT showed non-specific reticulonodular opacities throughout the right upper lobe and to a lesser extent the left lower lobe. A mildly prominent right perihilar lymph node was also noted. Physical examination shows significant swelling of her face with multiple coalescing erythematous to purple nodules on her central face, forehead, cheeks and chin.

Histopathology:

Right upper lip and left chin, skin: There is dermal nodular proliferation of histiocytes, forming epithelioid granulomas. This is associated with a rim of lymphocytes in the periphery. There are numerous giant cells. Multiple special stains for microorganisms, including Periodic acid-Schiff, Fite and Gomori methenamine silver stain are all negative.

Diagnosis:

Leonine facies due to sarcoidosis

Treatment and Course:

White awaiting histopathology results she was started on desonide 0.05% ointment to the affected areas, and her PCP initiated another course of prednisone and amoxicillin . After diagnosis, she was referred to pulmonology, ophthalmology, cardiology and rheumatology for a comprehensive work-up.

Patient B

History and Physical:

This 48 year old female from Greece presented with a twelve year history of swelling, numbness and tingling of her hands and feet. Over the years, she gradually developed swelling and changes in her facial features and was initially misdiagnosed and treated for scleroderma. Eventually she developed madarosis and a collapse of the bridge of her nose. Physical examination shows swelling of her face with thickening and furrowing of her skin and prominent supraciliary arches. There is a complete loss of the eyebrows and her nasal architecture demonstrates saddle nose deformity and perforation of the nasal septum. Several peripheral nerves in her upper extremities are thickened and pinprick examination shows diffuse cutaneous anesthesia.

Histopathology:

Left lower arm: There is multinodular infiltrate of histiocytes throughout the entire dermis, extending into subcutis. Many of the histiocytes have foamy cytoplasm with a bluish hue. This is mixed with small clusters of neutrophils. The overlying epidermis is slightly hyperplastic with scale and crust. Fite stain highlights numerous bacilli in the granulomas.

Diagnosis:

Leonine facies due to Hansen's disease, lepromatous type

Treatment and Course:
The patient was started on rifampin, clofazimine and dapsone. She was also intermittently treated with thalidomide and prednisone due to severe relapsing erythema nodosum leprosum. Her skin showed a bluish discoloration from treatment with clofazimine. Her nasal deformity caused severe nasal airway obstruction and she underwent reconstructive surgery by Otolaryngology. Over the next few decades, her disease course was complicated by iridocyclitis, chronic lower extremity neurotrophic ulcers, cellulitis and osteomyelitis which eventually required amputation of a great toe.

Patient C
History and Physical:
This 52 year old female presented with a one year history of enlarging pruritic nodules on her face. She had been treated with a variety of oral antibiotics and topical acne medications without improvement. Physical examination shows multiple fairly well circumscribed hyperpigmented patches, plaques, and nodules on the face bilaterally, many with follicular prominence and surrounding hyperpigmentation. She also has scattered follicular papules, patches and plaques on her trunk and extremities.

Histopathology:
Left chin and right cheek, skin: There is a dense superficial and deep dermal perivascular and perifollicular infiltrate of predominantly lymphocytes. There is extensive infiltration of lymphocytes within the follicular epithelium, associated with focal mucinous degeneration. Some of the lymphocytes have enlarged nuclei, more open chromatin, and irregular nuclear contours. The colloidal iron stain highlights focal increase of mucin within the follicular epithelium.

Diagnosis:
Leonine facies due to folliculotropic mycosis fungoides

Treatment and Course:
The patient was initially started on PUVA with modest improvement, and then was switched to interferon-alpha which caused depression. She was then treated with oral and topical bexarotene, extracorporeal photopheresis, betamethasone dipropionate 0.05% ointment, hydrocortisone valerate 0.2% ointment and intralesional triamcinolone injections that demonstrated a fluctuating course in the size and number of her lesions. Most recently, she underwent external beam radiation therapy with dramatic regression of her facial lesions.

Discussion:
Leonine facies is defined by thickening and furrowing of the skin that leads to a "lion-like" appearance. While this condition is most commonly associated with Hansen's disease, a variety of infiltrative processes and bony abnormalities can cause these features. Infiltrative processes include scleromyxedema, systemic amyloidosis, lipoid proteinosis, mastocytosis, chronic actinic dermatitis and sarcoidosis; infections like lepromatous leprosy and leishmaniasis; and neoplasms like cutaneous lymphoma and leukemia cutis. Bony disorders include Paget's disease, fibrous dysplasia and renal osteodystrophy.

Leonine facies is classically associated with lepromatous leprosy, which is the form of Hansen's disease with depressed cell-mediated immunity and high numbers of bacilli. Widespread infiltrative papules, plaques and nodules are filled with Virchow cells containing numerous bacilli. The face is a commonly involved area and infiltration of the forehead produces the appearance of leonine features. Our patient also showed common late sequelae including madarosis and saddle nose.

Folliculotrophic mycosis fungoides (FMF) is a distinct variant of cutaneous T-cell lymphoma that is characterized by folliculotrophic infiltrates of neoplastic T-cells. A variety of lesions including follicular papules, plaques and tumors commonly affect the head and neck region. Infiltrated plaques involving the eyebrow area lead to alopecia, as seen in our patient, and this is a common and characteristic finding. Coalescence of these tumors and plaques can produce leonine facies. Malignancy-associated leonine facies can be from direct infiltration of neoplastic cells, or caused by changes in the dermis or subcutaneous fat induced by the primary cancer.

There are only a few reports on leonine facies caused by sarcoidosis: one patient had concurrent complete heart block, another had laryngeal and bony involvement and the third only had cutaneous disease. As with the other infiltrative processes described above, treatment of the underlying condition usually improves the appearance of leonine facies.

Essential Lesson:

- Leonine facies can be caused by a variety of infiltrative processes and bony abnormalities.
- Malignancy-associated leonine facies can be from direct infiltration of neoplastic cells, or caused by changes in the dermis or subcutaneous fat induced by the primary cancer.

References:

1. Chodkiewicz HM, Cohen PR. Systemic mastocytosis-associated leonine facies and eyebrow loss. *South Med J.* 2011; 104(3):236-8.
2. Ito T, et al. Folliculotropic mycosis fungoides and a leonine clinical appearance of the face. *Dermatol Online J.* 2008;14(9):6.
3. Kendrick CG, et al. Cutaneous sarcoidosis presenting as leonine facies. *Cutis.* 2004;73(1):57-62.
4. Vocks E, et al. An unusual cutaneous T cell lymphoma presenting as leonine facies. *Eur J Dermatol.* 2000;10(4):309-12.

Case #12

Case Presented by Juliana Choi, MD, PhD
Steven Mandrea, MD and Michelle Bain, MD

History of Present Illness:
This 10 week old female presented with a blistering rash since birth on her arms, legs, and trunk. Outside hospital medical records from her birth documented "multiple stages of papules, pustules, vesicles, and healed slightly hyperchromatic lesions." Prior treatments included intravenous acyclovir, cefotaxime, and ampicillin, as well as nystatin cream, and hydrocortisone 2.5% ointment. No improvement was noted with these treatments. She does not scratch and appears to be unaffected by these lesions.

Past Medical History:
Born full term via vacuum-assisted vaginal delivery

Medications:
None

Family History:
No history of a similar blistering condition; older brother is unaffected; mother without a history of rash or infection during pregnancy

Review of systems:
No reported fevers, chills, alopecia, nail dystrophy, strabismus, nystagmus, seizures, paralysis, motor retardation, or difficulty feeding. She is meeting all developmental milestones.

Patient's Physical Examination:
The patient has hyperpigmented reticulated patches with intermixed coalescing clear fluid-filled vesicles in a blaschkoid distribution on bilateral arms, axillae, buttocks, inguinal folds, legs, and flanks extending anteriorly to the chest and abdomen and posteriorly to the back. A few verrucous hyperpigmented plaques are on bilateral buttocks and legs. Nikolsky sign is negative. No alopecia and no teeth were observed. All nails were normal.

Mother's Physical Examination:
The patient's mother has a brown irregular patch above the intergluteal fold consistent with a nevus. She does not have evidence of alopecia, peg teeth, or nail dystrophy.

Laboratory data:
The following were positive or abnormal:
Eosinophil percentage 9% (0-6), absolute eosinophil count 1.5 thousand/µL (0.0-0.9)

The following were negative or within normal limits:
Blood culture, urine culture, herpes simplex PCR of skin, rectum and conjunctiva

Histopathology:
Right forearm, skin: There is mild epidermal hyperplasia with focal dyskeratosis, associated with superficial dermal perivascular and interstitial infiltrate of scattered eosinophils. Some of the eosinophils extend close to the base of epidermis.

Diagnosis:
Incontinentia pigmenti

Treatment and Course:

The patient's mother reported that a few areas developed a darker discoloration and she continued to develop new areas with blisters. The patient continued to appear unaffected by these lesions. The family was counseled regarding the 25% risk of the mother giving birth to another child with incontinentia pigmenti. It was discussed that blisters may continue to erupt over the next few years but these would likely spontaneously resolve leaving residual discoloration. The patient was seen by ophthalmology and no abnormalities were detected and follow-up in 3 months was recommended. She was also seen by dentistry but due to her age X-rays were not obtained and a follow-up appointment was scheduled when the patient is 6 to 12 months of age. The patient was also referred to neurology and genetics but she has not yet been evaluated; the importance of a neurologic exam was repeatedly stressed. She has not demonstrated any neurologic symptoms to date.

Discussion:

Incontinentia pigmenti (IP), also known as Bloch-Sulzberger syndrome, is a rare X-linked dominant genodermatosis due to a mutation in the NEMO/IKKγ (nuclear factor kappa B essential modulator or inhibitor kappa B kinase γ-subunit) gene on chromosome Xq28. This gene is required for the activation of a transcription factor that regulates the expression of many genes including cytokines and chemokines. Activation of nuclear factor kappa B confers protection against apoptosis induced by the tumor necrosis family of cytokines.

Nearly all patients present with dermatologic findings. Cutaneous lesions follow lines of Blaschko and are characterized by four distinct phases: vesicular/inflammatory, verrucous, hyperpigmented, and hypopigmented/atrophic. The phases can overlap, occur *in utero*, or may be skipped. Therapy for cutaneous lesions is not required as spontaneous resolution usually occurs.

Although most patients present with skin manifestations, the severity of IP is related to extracutaneous findings. About one-third of patients demonstrate ocular involvement which can range from strabismus and cataracts to retinal detachment and blindness. Neurologic involvement is seen in one-third of patients with the most common manifestations being seizures, paralysis, developmental delays and mental retardation. Also, dental abnormalities including partial anodontia and conical or peg-shaped teeth can be observed.

The diagnosis of IP is clinical and in 1993 Landy and Donnai proposed diagnostic criteria for sporadic and inherited IP based on the associated cutaneous and extracutaneous findings. After the diagnosis of IP is made, it is imperative that patients be promptly evaluated by ophthalmology and neurology.

Essential Lesson:

- Incontinentia pigmenti usually presents with dermatologic findings.
- After diagnosis, prompt evaluation by ophthalmology and neurology is warranted.

References:

1. Berlin AL, et al. Incontinentia pigmenti: A review and update on the molecular basis of pathophysiology. *J Am Acad Dermatol.* 2002;47(2):169-187.
2. Goldberg MF. The skin is not the predominant problem in incontinentia pigmenti. *Arch Dermatol.* 2004;140(6):748-750.
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4. Hsieh DT, Chang T. Incontinentia pigmenti: skin and magnetic resonance imaging findings. *Arch Neurol*. 2011; 68(8):1080-1081.

Case #13

Case Presented by Whitney Fancher, MD
Iris K. Aronson, MD, and Claudia Hernandez, MD

Patient A

History of Present Illness:

This 83 year old Hispanic male presented to our clinic with a complaint of a longstanding, asymptomatic dark "mole" on his right cheek which had been present for about 15 years and had not recently changed. He had a history of basal cell carcinoma excised from his upper back in Mexico in 2002. He had no other concerning lesions or skin complaints and review of symptoms was negative. There was no family history of skin cancer.

Physical Examination:

The patient has a 1.5 cm x 1.5 cm, well demarcated, dark brown to black, variegated, irregular patch with a 0.6 x 0.6 hypopigmented macule located on the right preauricular cheek.

Histopathology:

Right lateral cheek, skin: There is a broad, asymmetrical, and poorly-circumscribed proliferation of melanocytes as irregular nests and solitary units in the epidermis and superficial dermis, filling up the papillary dermis. This is associated with dermal infiltrate of lymphocytes and numerous melanophages. The immunohistochemical stain for Melan-A highlights numerous melanocytes above the basal layer. The dermal nests fail to mature as they descend. At higher magnification, many melanocytes have enlarged nuclei and prominent nucleoli. Dermal melanocytes extend to a maximum depth of 0.5 mm. The surgical margins are free.

Diagnosis:

Lentigo maligna melanoma

Treatment and Course:

The melanoma was completely excised; the patient has been lost to follow-up.

Patient B

History of Present Illness:

This 73 year old Hispanic male presented with a complaint of an itchy and progressively enlarging "pimple" on his scalp present for one year. The patient denied pain or bleeding of the lesion and denied additional skin complaints. Medical history was significant for non-alcoholic steatohepatitis induced cirrhosis status post liver transplant in June 2010. His medications included sirolimus and mycophenolate mofetil. He had no personal or family history of skin cancer, and review of systems was negative.

Physical Examination:

The patient has a 1.5 cm x 2.0 cm erythematous hyperkeratotic plaque on his left anterior scalp.

Histopathology:

Left anterior scalp, skin: The epidermis is thickened, with full thickness atypia of keratinocytes. There are numerous mitotic figures, including atypical mitoses, throughout the entire lesion.

Diagnosis:

Squamous cell carcinoma in-situ

Treatment and Course:
The patient underwent Mohs micrographic surgery with complete removal of the lesion with negative margins.

Patient C

History of Present Illness:
This 25 year old Indian female presented with a dark lesion on her forehead which started as a black spot four years prior and had been progressively enlarging. The lesion was intermittently itchy with occasional bleeding after scratching. She had no medical history, no personal or family history of skin cancer, and review of systems was negative.

Physical Examination:
The patient has a 1.3 cm x 1.3 cm smooth black plaque with superior regression on her left forehead above her eyebrow. There is no regional lymphadenopathy.

Histopathology:
Left forehead, skin: There is proliferation of basaloid nests at the dermal-epidermal junction, associated with hyperpigmentation of the epithelial cells. There is peripheral palisading of the basaloid cells.

Diagnosis:
Pigmented superficial basal cell carcinoma

Treatment and Course:
The lesion was excised with negative margins.

Patient D

History of Present Illness:
This 62 year old Asian female presented with a pigmented perianal nodule with central ulceration noted on routine colonoscopy. The lesion was noted eight years earlier and was described as a small mole that progressively enlarged and felt like an open wound. The patient stated that her primary care physician was aware of this lesion but did not think it was malignant. Aside from the perianal lesion, colonoscopy results were normal. She denied additional skin complaints and had no medical or family history of skin cancer, and review of systems was negative.

Physical Examination:
The patient has a 2.0 cm x 3.0 cm hyperpigmented irregular nodule with central ulceration located 2 cm from her anus at the 12 o'clock position.

Histopathology:
Perianal skin: There is a nodular proliferation of basaloid cells with peripheral palisading and brisk mitosis. The scattered individual melanocytes in the basaloid nests have thickened dendrites. There is, however, no evidence of nesting of melanocytes. Markedly increased deposition of melanin is present throughout the entire lesion. The inferior margin of specimen is involved and the deep margin is within 1 mm of basal cell proliferation

Diagnosis:
Pigmented basal cell carcinoma

Treatment and Course:
Due to high suspicion of melanoma, the patient was referred to surgical oncology for evaluation, diagnostic biopsy, and wide local excision once the diagnosis was established. However after her initial excision she was found to have positive margins and requires further excision which is pending.

Discussion:
Skin cancer is the most common form of cancer in the United States. Larger amounts of pigmentation in Blacks, Asians, and Hispanics result in greater ultraviolet light protection and lower skin cancer risk. Despite lower risk, minorities have been found to be more likely to develop greater tumor depth and higher rates of metastases. This is likely due to diagnosis occurring at more advanced stages and atypical presentations with occasional involvement of non-sun exposed areas.

Many individuals of color perceive themselves as having little to no skin cancer risk which in all likelihood influences their decision not to seek out skin cancer screening or practice prevention. Minorities have documented deficits in the utilization of many cancer screening tests, yet the issue of skin cancer is compounded by poor risk awareness in many primary care physicians. In single-ethnicity focus groups conducted in Chicago, persons who self-identified as black, Hispanic, or Asian had lower skin cancer screening rates by physicians than did Caucasians and often did not find skin cancer to be relevant in skin of color. As it is projected that by 2050 half of the U.S. population will be composed of Asians, and Hispanics, it is important to raise awareness of and address the risks of skin cancer in these populations. Preventative measures including education of the public and primary care physicians, regular and thorough physician-performed skin exams, and promotion of regular self skin exams in these populations will decrease the morbidity and mortality seen in many ethnic groups.

Essential Lesson:
- Morbidity and mortality due to skin cancer is much higher in ethnic populations.
- Dermatologists must address misconceptions regarding skin cancer amongst patients of color and stress the importance of performing regular total body skin exams, including the acral, perianal and genital regions.

References:

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2. Cormier JN, et al. Ethnic differences among patients with cutaneous melanoma. *Arch Intern Med.* 2006;166(17):1907-14.
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Case #14

Case Presented by David Smart, MD
Milena Lyon, MD and Sophie Worobec, MD

History of Present Illness:
This 46 year old African American female presented to dermatology with loss of pigment of the skin surrounding her fingernails. Pigment loss began after acrylic nail placement approximately 6 months prior to presentation. She continued to use acrylic nails for 3-4 months following the appearance of these white patches and then discontinued their use approximately 2 months prior to presentation. No change in her skin lesions was noted after discontinuing the use of acrylic nails. The lesions were asymptomatic. She denied any erythema or pruritus prior to the white patches appearing. She has been using acrylic nails for many years and has been going to the same nail technician for 2 years prior to this event. Her nail technician reported not having changed the chemicals or materials used.

Past Medical and Surgical History:
Hypertension, allergic contact dermatitis

Medications:
Lisinopril, hydrochlorothiazide

Allergies:
Bactrim

Patch test results:
10/15/2010: Benzocaine 1+, 4-Phenylenediamine 2+, Ethylenediamine Dihydrochloride 3+, Budesonide 2+, Amerchol L101 (lanolin) 2+

Family History:
No history of skin disease

Social History:
Patient uses alcohol occasionally, and does not smoke.

Physical Examination:
There are sharply demarcated depigmented patches of the periungual skin of the fingers. Longitudinal pigmented bands are present on several fingernails.

Treatment and Course:
The patient was treated with desoximetasone 0.25% ointment twice daily to the affected areas and advised to continue to avoid acrylic nails. Mild repigmentation was noted after 6 weeks.

Diagnosis:
Chemical leukoderma

Discussion:

Chemical leukoderma (CL) is an acquired depigmentary disorder caused by exposure of the skin to particular chemicals. The skin becomes depigmented in areas that were exposed to the chemical; the phenolic/catecholic derivatives are the largest class of such chemicals. The diagnosis can be made clinically based on a history of repeated exposures to a particular chemical corresponding to the areas of depigmented skin.

The first recognized cases of CL occurred in individuals who worked with rubber gloves or other garments that contained monobenzyl ether of hydroquinone. Most reported cases are caused by exposure to derivatives of phenols and catechols. A few common materials containing these derivatives include: soap and rubber antioxidants, germicidal detergents, lacquer resins, deodorants, motor and synthetic oils, paints, adhesives, latex gloves, insecticides, and photographic chemicals. However, other responsible compounds reported include sulfhydryls, cinnamic aldehyde, p-phenylenediamine, mercurials, arsenics, azelaic acid, and corticosteroids among others.

Phenols and catechols are structurally similar to tyrosine and thought to induce CL by competing with this endogenous substrate for enzymes such as tyrosinase-related protein-1 (TYRP1). TYRP1 catalytically converts phenol and catechols resulting in reactive oxygen species. Theoretically, CL may be the result of a genetic inability of melanocytes to respond to TRYP1 related oxidative stress, as only a subset of patients develops CL with exposure to a certain compound.

Treatment includes avoidance of the inciting agent, which can lead to repigmentation. In persons with vitiligo who develop CL, repigmentation occurs in only 20% of lesions. However, persons without a history of vitiligo who develop CL have a better prognosis, with repigmentation occurring in 75% of lesions. Resistant patches of CL have been effectively treated with modalities commonly used in vitiligo, such as topical corticosteroids and narrow-band ultraviolet B phototherapy.

Essential Lesson:

- Chemical leukoderma should be distinguished from cases of idiopathic vitiligo.

References:

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Case # 15

Case Presented by Sonoa Au, MD, Whitney Fancher, MD and Iris K. Aronson, MD

History of Present Illness:
This 61 year old Caucasian female presented with a one year history of an asymptomatic periorbital rash. She only occasionally used mascara and denied any change in cosmetic routine. She had recently been complaining of increasing muscle aches and fatigue. Her dermatologist was concerned about possible dermatomyositis, and her creatinine kinase was found to be elevated at 286 ng/ml. However, a left deltoid muscle biopsy was negative for myositis. She was being followed by an oncologist for gammopathy thought secondary to monoclonal gammopathy of undetermined significance or smoldering myeloma.

Past Medical and Surgical History:
Gammopathy, deep vein thrombosis complicated by pulmonary embolism thought to be secondary to estrogen replacement therapy 1996, hypertension, gastroesophageal reflux disease, hysterectomy, torn rotator cuff, hip replacement, appendectomy

Medications:
Ramipril, spironolactone, celecoxib, omeprazole, and aspirin

Allergies:
Penicillin – rash

Family History:
Son with asthma and allergies, brother with diabetes

Social History:
Drinks alcohol occasionally, denies tobacco use

Review of Systems:
The patient reported dry skin, fatigue, muscle ache and intentional weight loss. She denied fevers, chills, vomiting, diarrhea, shortness of breath, or chest pain.

Physical Examination:
The patient's bilateral upper eyelids have yellow-brown hyperpigmented patches between the eyebrows and eyelashes with scattered petechiae and purpuric 2-3 mm macules within. The upper lip is normal but there are some faint white patches on the lower lip and some scattered pinpoint pink papules at the vermillion border.

Laboratory Data:
The following were positive or abnormal:
Erythrocyte sedimentation rate 39 mm/hr (< 25), creatinine kinase 450 ng/ml (35-165), serum IgG 2880 mg/dL (694-1618), M-Protein 2.3 g/dL (0).
Serum protein electrophoresis detected IgG Lambda elevated at 2.1g/dL. Lambda free light chain was elevated at 12.30 mg/dL and 28 mg/dL (0.57-2.63). Urine protein electrophoresis detected monoclonal lambda light chains and a corresponding heavy chain.

The following were negative or within normal limits:
Complete metabolic panel, complete blood count, aldolase, C-reactive protein, urinalysis, Autoantibodies: Jo-1, ANA, ssDNA, dsDNA, Sm, RNP, SSA/SSB, chromatin, Scl-70, centromere, RF, CCP, ANCA, and anticardiolipin.

Diagnostic Procedures and Tests:

- Skeletal Survey: Unremarkable with no lytic lesions
- Muscle Biopsy, Left Deltoid: Negative for dermatomyositis
- Bone Marrow Biopsy: Aspirate smears showed increased plasma cells comprising at least 30% of marrow cellularity; however, the bone marrow biopsy shows very small focal collections of plasma cells accounting for less than 5% cellularity. This discrepancy in the extent of plasma cell infiltration is due to patchy distribution of plasma cells. Based in the findings on the bone marrow aspirate, the possibility of an early multiple myeloma should be considered.
- Multiple Myeloma Fluorescence In -Situ Hybridization Panel: normal
- Upper and Lower Gastrointestinal Endoscopy: Amyloid deposits were found in the stomach and intestines but not in the esophagus

Histopathology:

Right upper eyelid, skin: There is dermal nodular deposition of pale pink amorphous material with fissures. The dermal small blood vessels have thickened walls with increased pink amorphous material. This is associated with extensive extravasation of RBCs. Congo red stain is strongly positive.

Diagnosis:

Primary systemic amyloidosis due to monoclonal gammopathy of undetermined significance

Treatment and Course:

The patient underwent four cycles of bortezomib at 1.3 mg/m^2 and weekly dexamethasone. She reported that her levels of serum IgG and lambda free light chain have decreased. A repeat bone marrow biopsy showed similar findings and stained positive for amyloid. Her skin disease has not progressed and a cardiac work-up including an echocardiogram was negative. Currently she is in contact with an amyloidosis support group, but has no plans to pursue a bone marrow transplant.

Discussion:

Light chain amyloidosis (AL), the most common type of systemic amyloidosis, is a plasma cell dyscrasia characterized by the pathologic production and deposition of misfolded proteins in a variety of tissues resulting in progressive organ damage. Most patients have an isolated monoclonal gammopathy or smoldering myeloma. The most frequently affected organs are the heart and kidneys, while the gastrointestinal tract and nervous system are also commonly involved. Renal involvement, manifested by heavy proteinuria with nephrotic syndrome and impaired renal function, are found in 2/3 of patients at diagnosis while cardiac involvement is present in 50% at diagnosis. Between 25% and 40% of patients have mucocutaneous involvement. The most common presenting symptoms are fatigue, weakness, dyspnea, and edema, and AL amyloidosis should be suspected in any patient with non-diabetic nephrotic syndrome, non-ischemic cardiomyopathy, hepatomegaly or increased alkaline phosphatase, or a monoclonal gammopathy with unexplained dyspnea, fatigue, edema, weight loss, orthostasis, or paresthesias.

As cutaneous manifestations can give an early indication of underlying amyloidosis and plasma cell dyscrasia, it is important to be aware of common presentations. Waxy papules, nodules, and plaques classically on the periorbital region or palms and volar fingertips represent skin infiltration by amyloid protein. Other common findings include petechiae, purpura, and ecchymoses especially at flexural regions, such as eyelids, nasolabial folds, neck, axillae, umblicus, anogenital area, and mouth. Bullous lesions, alopecia, and nail changes are also common findings. Macroglosia is seen in 10-20% of patients, and macroglossia together with carpal tunnel syndrome is a classic presentation. Less commonly, diffuse cutaneous infiltration can cause a sclerodermoid appearance.

Evaluation for AL amyloidosis includes investigation for an underlying clonal plasma cell disorder via bone marrow apsirate or biopsy, serum and urine electrophoresis and immunofixations, and serum free light chain testing. Definitive diagnosis of systemic amyloidosis depends upon demostration of amyloid in tissue. If mucocutaneous lesions suspicious for amyloid deposition are present, skin is the recommended tissue to sample as skin biopsy is easy to perform and carries low risk. If no specific mucocutaneous lesions are present, aspiration of abdominal fat or rectal mucosal biopsy may be performed as amyloid deposits are found in up to 80-90% of these specimens in patients with amyloidosis.

The differential diagnosis for AL amyloidosis is broad and depends on the clinical presentation. Waxy papules on the face may be confused with adnexal tumors; periorbital purpura may resemble dermatomyosis or lupus; bullous lesions may resemble porphyria cutanea tarda or epidermolysis bullosa acquisita; sclerodermoid appearing lesions may mimic morphea or other sclerodermal diseases.

Histopathologically, amyloid deposition is found in the dermis and subcutis, often around appendages, within blood vessel walls, and around individual fat cells. H&E stains show masses of eosinophilic, amorphous material, and congo red staining produces an orange-red color by light microscopy and the characteristic ‘apple-green’ (can actually appear blue-green) birefringence under polarized light. A number of other stains (crystal violet, methyl violet, periodic acid-Schiff, Sirius red, dylon, thioflavin T), immunohistochemical stains (immunoglobulin gamma light chain, transthyretin, keratin, AA protein), and tandem mass spectrometry can also be performed to identify and differentiate between different types of amyloid protein.

Treatment for AL amyloidosis depends on the extent of organ involvement with the goal being eradication of the monoclonal plasma cells and suppression of the pathologic light chains. Median survival is thirteen months in untreated individuals but is highly variable and dependent on the extent of organ involvement with patients who have cardiac involvement carrying a worse prognosis. Treatment is individualized, determined by patient’s age, organ dysfunction- primarily extent of cardiac disease, and regimen toxicities. Alkylator-based chemotherapy, most often with melphalan, is effective in almost two-thirds of patients. Treatment of choice in younger patients with minimal or no cardiac involvement is high-dose IV melphalan followed by autologous stem cell transplantation (SCT). In patients not eligible for SCT (older patients or those with extensive cardiac disease), dexamethasone combined with either oral melphalan or cyclophosphamide and thalidomide have shown to produce hematologic response and increase survival. Newer targeted agents such as lenalidomide and bortezomib alone or with melphalan and corticosteroids have proved beneficial as well.

Essential Lesson:

- AL amyloidosis is a plasma cell dyscrasia causing pathologic production and deposition of misfolded proteins in a variety of tissues resulting in progressive organ damage; the heart and kidneys are the most frequently affected organs.
- The most common presenting symptoms are fatigue, weakness, dyspnea, and edema.
- It is important to be aware of the variety of cutaneous manifestations of amyloidosis as early diagnosis and treatment portend prolonged survival.
- Skin biopsy is an easy and low-risk procedure to aid in diagnosis.
- H&E stains show masses of eosinophilic, amorphous material, and congo red staining produces an orange-red color by light microscopy and 'apple-green' birefringence under polarized light.
- Treatment is based on age, organ -especially cardiac- involvement, and treatment toxicity; IV melphalan followed by stem cell transplant, oral melphalan plus dexamethasone, and targeted agents lenalidomide and bortezomib are the most commonly used therapies.

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