Chicago Dermatological Society

September 2016 Educational Conference

Program & Speaker Information
CME Certification
Case Presentations

Wednesday, September 28, 2016
Stephens Convention Center – Rosemont, IL

Conference Host:
Division of Dermatology
Loyola University Medical Center

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Program

Host: Loyola University
Wednesday, September 28, 2016
Stephens Convention Center, Rosemont

8:00 a.m.	**Registration & Continental Breakfast with Exhibitors** *Foyer outside Ballroom #24*
8:30 a.m. - 10:30 a.m.	**Clinical Rounds** Slide viewing/posters Patient viewing
9:00 a.m. - 10:00 a.m.	**Basic Science Lecture** "The History of Dermatology" *David H. Peng, MD, MPH*
10:00 a.m. - 10:30 a.m.	**Break and Visit with Exhibitors**
10:30 a.m. - 12:00 p.m.	**Resident Case Presentations & Discussion**
12:00 p.m. - 12:15 p.m.	**MOC Self-Assessment Questions**
12:15 p.m. - 12:45 p.m.	**Box Lunches & visit with exhibitors**
12:55 p.m. - 1:00 p.m.	**CDS Business Meeting**
1:00 p.m. - 2:00 p.m.	**General Session** “Toxic Epidermal Necrolysis: Where we think we are” and “D.R.E.S.S. Syndrome: An update” *David H. Peng, MD, MPH*
2:00 p.m.	**Meeting adjourns**

Mark the Date!
Next CDS monthly meeting – Hosted by UIC
Wednesday, October 26; Student Center West, University of Illinois Campus; Chicago

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

Guest Speaker

DAVID H. PENG, MD, MPH

Chair, Department of Dermatology, Keck School of Medicine of University of Southern California
Los Angeles, CA

David Peng, MD, MPH, came to the Keck School after three years at Stanford University School of Medicine, where he served as associate professor and director of the Department of Dermatology's Residency Training Program. He also served as chief of the Stanford Dermatology Clinics, director of the Medical Dermatology Program and director of the Allergic Contact Dermatitis Program in the Department of Dermatology. He originally joined the Keck School's faculty in 2004 and was appointed visiting assistant professor of clinical medicine, associate residency program director in the division of dermatology, and director of the Contact Dermatitis Clinic. Peng received his bachelor's degree from the University of California, Berkeley, and medical degree from the University of California, San Diego (UCSD). He completed his internship at UCLA, where he also earned a master of public health degree before returning to UCSD for his residency in dermatology.

CME Information

This educational activity is jointly provided by AXIS Medical Education, Refine Me CE and the Chicago Dermatological Society

Overview

The Chicago Dermatological Society was established in 1903 and has strived to provide meaningful educational opportunities to dermatologists in the Chicago area for more than a century. Guest speakers from across the country share their expertise with CDS members, as well as residents in training medical students doing their dermatology rotation. CDS schedules six day-long meetings each year which are "hosted" by one of the dermatology residency programs in the city. In addition to two lectures given by the guest speaker, the residents of the host institution present cases which are offered for audience discussion. In addition, live patients, posters and microscopic slides prepared by the residents are made available during the "clinical rounds" portion of the meeting. CDS also offers a 15-minute session that qualifies for "Maintenance of Certification" self-assessment questions under the auspices of the American Board of Dermatology.

Target Audience

This activity has been designed to meet the educational needs of dermatologists. CDS members, residents in training and medical students engaged in their dermatology rotation are invited to attend.

Learning Objectives

At the conclusion of the 2016/17 series of meetings, the participant should be able to:

1. Discuss key factors in the diagnosis and treatment for viral diseases and bacterial infections.
2. Describe the manifestation of skin cancers and the efficacy of treatments available to the dermatologist.
3. List the therapeutic options available to the dermatologist for a variety of skin diseases, both medical and surgical, and discuss how new emerging treatments can be successfully incorporated into a dermatology practice.

Physician Accreditation Statement

This activity is planned and implemented by AXIS Medical Education, Refine Me CE and the Chicago Dermatological Society. AXIS Medical Education is accredited by the Accreditation Council for Continuing Medical Education (ACCME), the Accreditation Council for Pharmacy Education (ACPE), and the American Nurses Credentialing Center (ANCC) to provide continuing education for the healthcare team.

Credit Designation for Physicians – AXIS Medical Education designates this live activity for a maximum of 4.75 *AMA PRA Category 1 Credit(s)*™. Physicians should claim only the credit commensurate with the extent of their participation in the activity.

Attendees are required to submit a CME claim form upon departure from the conference. Please leave your form, along with the attached evaluation form, at the registration table when you leave the meeting. Thank you for your attention to this important item.

Disclosure of Conflicts of Interest

AXIS Medical Education requires instructors, planners, managers and other individuals and their spouse/life partner who are in a position to control the content of this activity to disclose any real or apparent conflict of interest they may have as related to the content of this activity. All identified conflicts of interest are thoroughly vetted by AXIS for fair balance, scientific objectivity of studies mentioned in the materials or used as the basis for content, and appropriateness of patient care recommendations. All speakers are expected to follow the "first slide" rule to repeat their conflict of interest disclosures during their talk.

Today's guest speaker, David Peng, MD, MPH, has no relevant conflicts of interest to disclose, nor do the residents presenting cases at this meeting. Likewise, the following planning committee members have no conflicts of interest to disclose: Alix Charles, MD, program chair and CDS president; Julie Moore, MD, CDS past-president; Richard Paul, CDS Executive Director; Ronald Viggiani, MD and Dee Morgillo, MEd, MT(ASCP), CHCP, AXIS Medical Education.

AXIS Contact Information

For information about the physician accreditation of this program please contact AXIS at 954-281-7524 or info@axismeded.org.

Americans with Disabilities Act

In compliance with the Americans with Disabilities Act, we will make every reasonable effort to accommodate your request. For any special requests, please contact the CDS at: Rich@ChicagoDerm.org.

Disclaimer

Participants have an implied responsibility to use the newly acquired information to enhance patient outcomes and their own professional development. The information presented in this activity is not meant to serve as a guideline for patient management. Any procedures, medications, or other courses of diagnosis or treatment discussed in this activity should not be used by clinicians without evaluation of patient conditions and possible contraindications on dangers in use, review of any applicable manufacturer's product information, and comparison with recommendations of other authorities.

Dislosure of Unlabeled Use

This educational activity may contain discussion of published and/or investigational uses of agents that are not indicated by the FDA. The planners of this activity do not recommend the use of any agent outside of the labeled indications. The opinions expressed in the educational activity are those of the faculty and do not necessarily represent the views of the planners. Please refer to the official prescribing information for each product for discussion of approved indications, contraindications, and warnings.

Case Presentations

Prepared by
Loyola University
Residents

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NOTES

CHICAGO DERMATOLOGICAL SOCIETY **CASE #1**

Presented by Jennifer Eyler MD[1], Kelli Hutchens MD[2], Wendy Kim DO[1]
[1]Division of Dermatology, Loyola University Medical Center
[2]Department of Pathology, Loyola University Medical Center

HISTORY OF PRESENT ILLNESS

A 2-week old male presented to the dermatology clinic with a rash on the left inner thigh present since 3 days after birth. The rash started with small red bumps, some of which developed into blisters, crusted over, and slowly resolved. The rash was asymptomatic. He was otherwise healthy.

PAST MEDICAL HISTORY

The baby was born full term via spontaneous vaginal delivery without complications.

PRENATAL HISTORY

Mother had a urinary tract infection during the first trimester of pregnancy. No other complications or lab abnormalities.

MEDICATIONS

None

FAMILY HISTORY

Mother and father have eczema and seasonal allergies.

SOCIAL HISTORY

The baby lives with his mother, father, 2-year old sister, and dogs.

PHYSICAL EXAMINATION

Physical examination demonstrated a well-nourished Caucasian male infant in no distress. There were many 2-4mm pink papules and pustules on an erythematous base in a blaschkolinear distribution on the left flank, left medial thigh, and extending to the left medial knee. The remainder of his skin was uninvolved.

DERMATOPATHOLOGY

Two adjacent punch biopsies were performed on the left medial thigh for hematoxylin-eosin and direct immunofluorescence. Hematoxylin-eosin staining showed eosinophilic spongiosis and dyskeratotic keratinocytes. There was superficial and mid-dermal perivascular inflammation with eosinophils. Direct immunofluorescence showed a negative or non-diagnostic staining pattern.

DIAGNOSIS

Incontinentia Pigmenti in a Male Patient

TREATMENT AND COURSE

The baby was referred to genetics, ophthalmology, and neurology. His karyotype was normal. His ophthalmologic exam was normal. Neurology ordered an MRI of the brain which was normal.

DISCUSSION

Incontinentia pigmenti (IP) is a rare X-linked dominant genodermatosis caused by a loss-of-function mutation in the NEMO gene (nuclear factor κB essential modulator) resulting in a deletion of exons 4-10. The NEMO gene mutated in IP is mapped to Xq28. Disruption of the NEMO gene leads to diminished NF-κB activity which increases the susceptibility of cells to apoptosis. IP predominantly affects female infants and is usually lethal in males in utero. Expressivity of IP varies greatly due to the effects of lyonization in females and the resulting functional mosaicism. The extent of expression reflects the percentage of progenitor cells harboring the mutated X chromosome.

The clinical features of IP are associated with abnormalities in ectodermal tissue including skin, hair, nails, teeth, eyes, and central nervous system. Dermatologic manifestations are usually the presenting sign of IP. The lesions follow Blaschko's lines and are classically divided into 4 stages: vesicular, verrucous, hyperpigmented, and atrophic. The vesicular stage occurs in approximately 90% of cases, most often during the first 2 weeks of life. The lesions present as superficial vesicles on an erythematous base in a linear distribution typically sparing the face. The verrucous stage occurs in approximately 70% of patients between 2 and 6 weeks of life. Nearly all patients with IP experience the hyperpigmented stage between 12 and 26 weeks, with whorls and streaks of brown to gray pigmentation following the lines of Blaschko. These lesions do not typically correlate with the location of the 2 prior stages and do not represent postinflammatory hyperpigmentation. The hyperpigmented stage can persist for years or decades. The atrophic stage appears in approximately 28% of patients as pale, hairless, atrophic patches. Less commonly it can appear as hypopigmented patches without atrophy. This stage is commonly permanent. The distribution of lesions along Blaschko's lines represents the death of cells carrying the mutated gene along the lines of embryonic cellular migration. Some of the stages may occur concurrently with others or not at all.

Additional clinical manifestations include vertex alopecia, nail dystrophy, dental abnormalities, ophthalmic anomalies, and central nervous system deficits. Dental abnormalities are the most common non-cutaneous manifestation, occurring in more than 80% of patients, with the most common finding being absence of teeth. Most patients with IP have normal vision, however both retinal and nonretinal manifestations can occur and are often associated with neurologic deficits. Slightly more than 30% of IP patients are thought to have central nervous systemic deficits which can significantly impact quality of life. These deficits can include seizure disorder, spastic paralysis, motor retardation, microcephalus, and developmental delay. The overall severity of IP is related to ocular and neurologic impairment, in particular blindness and psychomotor retardation.

Skin biopsy from the vesicular stage classically demonstrates spongiotic dermatitis with eosinophil-filled intraepidermal vesicles and massive intraepidermal and dermal eosinophilia. A skin biopsy obtained during the verrucous stage would include

hyperkeratosis, papillomatosis, and dyskeratosis. Melanin deposition in the papillary dermis is classically seen in the hyperpigmented stage. During the atrophic stage a skin biopsy would include an atrophic epidermis with a loss of rete ridges and the pilosebaceous apparatus. Patients with IP typically show a marked peripheral blood leukocytosis and eosinophilia during the early stages of disease.

Despite its X-linked dominant inheritance pattern, rare cases of IP have been identified in male patients. Three proposed mechanisms for the survival of affected males include 47, XXY karyotype (Klinefelter syndrome), hypomorphic mutations, and somatic mosaicism. The 47, XXY karyotype establishes a heterozygous genotype that is compatible with survival in the setting of a mutated X chromosome. Hypomorphic mutations are milder mutations with a less deleterious effect on NEMO activity and function. Somatic mosaicism is the most reliable explanation for the survival of male patients. It results from a postzygotic mutation occurring during the blastocyst stage of embryogenesis that does not completely inactivate NF-κB and allows survival. This ultimately results in milder features of disease with better outcomes.

The clinical phenotype of male IP has not been well characterized. However, it has been noted that males tend to have more localized disease than females. Unilateral presentation is a distinctive occurrence in males. Data suggest that male patients with IP that survive to birth are not at an increased risk for neonatal or infantile mortality, and there is potential for survival into reproductive age and adulthood.

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CHICAGO DERMATOLOGICAL SOCIETY **CASE #2**

Presented by Amanda Champlain MD[1], Kumaran Mudaliar MD[2], James Swan MD[1,3], Laura Winterfield MD[1]
[1]Division of Dermatology, Loyola University Medical Center
[2]Department of Pathology, Loyola University Medical Center
[3]Section of Dermatology, Edward Hines Jr. Veterans Affairs Hospital

HISTORY OF PRESENT ILLNESS

A 17 year old woman with a history of anorexia nervosa presented to Dermatology for evaluation of a rash that began 4 weeks prior. The rash initially appeared on the dorsal feet and ankles, and then subsequently spread to involve the arms, dorsal hands, and neck. She complained of associated burning pain. The rash was previously treated with fluticasone cream, triamcinolone lotion, mupirocin ointment, and a 1 week course of prednisone with no improvement. On review of systems, the patient noted nausea, decreased appetite, fatigue, and depression.

PAST MEDICAL HISTORY

Anorexia nervosa
Raynaud's disease

MEDICATIONS

None

ALLERGIES

None

FAMILY HISTORY

Non-contributory

SOCIAL HISTORY

High school student. No tobacco, alcohol, or illicit drug use.

PHYSICAL EXAMINATION

Superficial confluent erosions in a photodistribution affecting the jaw, anterolateral neck, upper chest, antecubital fossae, and dorsal hands. Bilateral upper extremities with hyperpigmentation and desquamating scale. Bilateral dorsal feet and ankles with few lichenified hyperpigmented plaques. Oral commissures with erosions.

DERMATOPATHOLOGY

A punch biopsy of the right lateral ankle showed an interface as well as superficial and deep perivascular dermatitis with mild basement membrane thickening.

ADDITIONAL STUDIES

Complete blood count with differential WNL
Complete metabolic panel WNL

Antinuclear Antibody (ANA) < 1:40

DIAGNOSIS

Pellagra secondary to anorexia nervosa

TREATMENT AND COURSE

Treatment was initiated with niacin 500 mg PO twice daily for 3 days, then 500 mg daily thereafter. Liberal emollient use, avoidance of sun exposure, and consultation with a nutritionist was recommended. The patient responded quickly to niacin supplementation with resolution of cutaneous disease within 3 weeks.

DISCUSSION

Pellagra is a systemic disease caused by a deficiency of niacin or its precursor amino acid tryptophan. It was first described in the 18th century as a condition affecting impoverished inhabitants of southern Europe who subsisted primarily on maize. Pellagra was first recognized in the United States in 1902, although it wasn't until 1926 that Dr. Joseph Goldberger discovered dietary modification could induce the symptoms of pellagra and identified niacin as the deficient factor. Potential etiologies of pellagra include malnutrition, malabsorption disorders, chronic alcoholism, carcinoid syndrome, Hartnup disease, and medications such as isoniazid, 5-fluorouracil, 6-mercaptopurine, and azathioprine.

Niacin (also known as vitamin B_3 or nicotinic acid) is a water-soluble vitamin essential for cell function and metabolism. *In vivo* niacin is converted to an amide form (niacinamide or nicotinamide) that is a component of the pyridine nucleotide enzymes nicotinamide adenine dinucleotide (NAD) and nicotinamide adenine dinucleotide phosphate (NADP). These coenzymes facilitate numerous reduction-oxidation reactions in cells. Inadequate amounts of NAD and NADP cause dysfunction in tissues with high energy use or turnover such as the integumentary, neurologic, and gastrointestinal systems. The photosensitivity characteristic of pellagra may be due to deficient urocanic acid and excess kynurenic acid, which reduces the skin's protection from ultraviolet rays and induces phototoxicity, respectively.

Pellagra is clinically characterized by the classic triad of dermatitis, diarrhea, and dementia. Untreated disease results in multiorgan failure and death. Cutaneous manifestations include a photosensitive eruption, perineal lesions, and hyperpigmentation and lichenification over bony prominences. It initially presents as a photodistributed, sunburn-like, sharply demarcated erythema affecting the face, neck, chest, and dorsal hands and feet. Occasionally, vesicles and bullae are present. Characteristic cutaneous involvement of the photoexposed neck is known as "Casal's necklace." Skin lesions may be painful, burning, or itchy. In later stages the acute erythema changes to a dusky brown discoloration with dry scale. The scale is described as having a "shellac-like" or "flaky paint" appearance. Other clinical features include cheilitis, angular stomatitis, glossitis, anorexia, abdominal pain, diarrhea, irritability, depression, fatigue, and memory loss. Pellagra is a clinical diagnosis; there is no adequate test to directly measure niacin levels.

Histopathology varies with stage of disease and is often nonspecific. Possible histologic features include hyperkeratosis, parakeratosis, acanthosis, and increased epidermal pigmentation. Initial lesions may demonstrate vacuolar change of the upper epidermis. Later stage lesions may show an epidermal psoriasiform hyperplasia.

The syndrome is cured with niacin or niacinamide supplementation. Niacinamide is preferred as it does not cause flushing observed with niacin administration. A recommended initial dose of oral niacinamide is 100 mg every 6 hours until major symptoms resolve, then 50 mg every 8 hours until complete resolution of cutaneous disease. Additionally, patients should consult with a nutritionist and increase intake of dietary sources of niacin such as eggs, poultry, fish, red meat, peanuts, legumes, seeds, and whole grain cereals. A liquid or soft diet may be necessary in patient with dysphagia due to significant glossitis. Emollient use can be recommended to reduce discomfort, and sun avoidance is advised. Symptoms respond dramatically to treatment with improved mentation in 24-48 hours and resolution of cutaneous disease in 3-4 weeks.

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CHICAGO DERMATOLOGICAL SOCIETY **CASE #3**

Presented by Carly Webb MD[1], Kumaran Mudaliar MD[2], Jodi Speiser MD[2], Rebecca Tung MD[1]
[1]Division of Dermatology, Loyola University Medical Center
[2]Department of Pathology, Loyola University Medical Center

HISTORY OF PRESENT ILLNESS

A 72-year-old South Asian male presented to the outpatient dermatology clinic for evaluation of hypopigmented patches of four weeks' duration. The patient was bothered by his appearance, but the lesions themselves were asymptomatic. Since their onset, individual lesions remained stable in size but were increasing in number. The eruption was located on the scalp and face. He had no history of similar skin issues. He denied any new systemic symptoms as well as any personal or family history of autoimmune disease or pigmentary disorders.

PAST MEDICAL HISTORY

Chronic myelogenous leukemia, diagnosed in 2003 (currently in remission)
Carcinoma in-situ of prostate
Coronary artery disease s/p multiple stent placements
Chronic Kidney Disease, Stage III
Atrial Fibrillation
Hypertension
Actinic Keratoses (upper cutaneous lip) s/p cryosurgery

MEDICATIONS

Dasatinib
Imatinib (took for 10 years; not currently taking)
Aspirin
Clopidogrel
Rosuvastatin
Metoprolol succinate XL
Valsartan
Pantoprazole
Ferrous sulfate

ALLERGIES

Tetracyclines (rash)

FAMILY HISTORY

No known autoimmune disease
No known pigmentary disorders

SOCIAL HISTORY

No tobacco, alcohol, or illicit drug use
Lives part time in Pakistan

PHYSICAL EXAMINATION

Physical examination revealed a well-appearing middle-aged male. Cutaneous examination was notable for hypopigmented and depigmented patches of varying sizes and with indistinct borders on the superior forehead, frontal scalp, melolabial cheeks, and chin. Confetti-like depigmentation was present on the bilateral helices, tragii, conchal bowls, and earlobes, most fully appreciable on Wood's lamp examination. All scalp hair and the majority of his facial hair was depigmented. There were no additional areas of pigment loss identified on the skin by regular or Wood's lamp examinations.

DERMATOPATHOLOGY

Histopathology of a representative lesion on the left frontal scalp demonstrated a significant decrease in melanocyte number, which was highlighted by MART-1 staining. No fungal organisms were identified with Periodic Acid-Schiff (PAS) staining.

LABORATORY STUDIES

Laboratory Study	Patient Result	Reference Range
TSH (UU/ML)	3.47	0.40-4.60
FREE T4 (NG/DL)	1.1	0.80-1.70
VITAMIN D, 25-OH (NG/ML)	32	30-80
IRON (UG/DL)	90	40-150
TRANSFERRIN (MG/DL)	261	180-329
FERRITIN (NG/ML)	48	22-322

DIAGNOSIS

Focal cutaneous depigmentation in the setting of chronic dasatinib therapy

TREATMENT AND COURSE

As our patient's CML precluded cessation of dasatinib therapy, we treated his pigment loss with mometasone 0.1% cream alternating with dovonex 0.005% cream. He was also started on vitamin D2 (ergocalciferol) supplementation, as well as a daily multivitamin and B complex vitamin, with modest improvement in his skin findings.

DISCUSSION

Dasatinib is a second generation tyrosine kinase inhibitor most commonly used to treat imatinib-resistant CML and other hematological malignancies. However, its therapeutic indications are expanding to include treatment of various solid tumors, particularly soft tissue sarcomas. Dasatinib inhibits most Bcr-Abl mutant forms, in addition to Src, c-Kit, and platelet-derived growth factor receptor-β (PDGFR-β) tyrosine kinases.

While hypopigmentation has been reported to occur in up to 41% of patients treated with imatinib and other first generation tyrosine kinase inhibitors, pigmentary abnormalities are much less commonly seen with the second generation tyrosine kinase inhibitors. The cutaneous side effects most commonly reported with dasatinib use include a nonspecific

morbilliform drug eruption, skin irritation, and skin exfoliation. Pustular and acneiform eruptions, neutrophilic panniculitis, and dyschromia have also been reported, albeit rarely.

The cutaneous and histopathologic features of dasatinib-associated dyschromias are nonspecific. In the majority of cases, patients present with hypopigmentation or depigmentation of the hair and/or skin. Skin lesions consist of hypopigmented or depigmented macules and patches, which appear to have a predilection for the head and neck. Time to pigment loss is variable, ranging from one month to several years after initiating dasatinib therapy, and these effects appear to be dose-dependent. Pigment loss is potentially reversible with cessation of therapy, with repigmentation reported to begin within 4-8 weeks of stopping dasatinib. If dasatinib is continued, however, pigment loss tends to be progressive. In one case, a patient who initially presented with hypopigmentation experienced transient hyperpigmentation following withdrawal of dasatinib, highlighting the likely mechanistic role of c-kit modulation in dasatinib-associated dyschromias, as discussed below.

Pigment loss associated with dasatinib therapy likely results from this drug's inhibition of c-kit, a proto-oncogene encoding a class III tyrosine kinase receptor found on an array of cell lines, including melanocytes. Its ligand is stem cell factor (SCF). The interaction of stem cell factor with the c-kit receptor plays a role in melanocyte survival, proliferation, and migration. Therefore, interference with this pathway, i.e., via treatment with tyrosine kinase inhibitors, negatively affects melanocyte survival and migration; this results in the clinical manifestations of pigment loss from the hair and skin.

We present this case of focal cutaneous depigmentation in the setting of chronic dasatinib therapy to highlight a rare cutaneous side effect of a medication that is being utilized with increasing frequency for treatment-resistant hematologic malignancies and solid tumors. We encourage clinicians to consider this entity in the differential diagnosis of vitiligo in patients treated with tyrosine kinase inhibitors.

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CHICAGO DERMATOLOGICAL SOCIETY **CASE #4**

Presented by Ashish Arshanapalli MD, Daniel Opel MD, Samantha Gordon MD, Patricia Todd MD, Rebecca Tung MD
Division of Dermatology, Loyola University Medical Center

HISTORY OF PRESENT ILLNESS

A 16 year-old Eurasian boy with no significant past medical history presented with lesions on his penis. He said the lesions had been present for over five years. They were asymptomatic, and he did not have similar lesions anywhere else on his body. One of the lesions had been biopsied in the past and was found to be a syringoma. Electrocautery and cryosurgery were used in an attempt to treat the syringomas, but they were persistent despite treatment. The patient requested removal of these lesions and refused referral to urology or plastic surgery.

PAST MEDICAL HISTORY

None significant

MEDICATIONS

None

ALLERGIES

No known drug allergies

FAMILY HISTORY

No history of syringomas, melanoma, or non-melanoma skin cancers

SOCIAL HISTORY

The patient lives at home with his parents. He denies tobacco, alcohol, or illicit drug use.

PHYSICAL EXAMINATION

The patient was well appearing teenage male. There was a cluster of small, white, dermal 1-3 mm papules coalescing into a plaque on the mid-dorsal penile shaft and extending bilaterally.

DERMATOPATHOLOGY

An excisional biopsy was performed on the dorsal penis. Hematoxylin-eosin staining showed multiple ductal structures lined by cuboidal epithelium extending into the deep reticular dermis. Some of the ducts demonstrated dilatation, and there was also a background dense fibrous stroma.

DIAGNOSIS

Syringomas

TREATMENT AND COURSE

The patient underwent a novel technique for the cosmetic micro-excision and closure of his penile syringomas. The technique involved pre-application of topical anesthesia (lidocaine

2.5%/prilocaine 2.5%) under a waterproof occlusive dressing for 30 minutes before small volumes of anesthetic (lidocaine 1% with 1:100,000 epinephrine) as well bupivacaine 0.25% were locally infiltrated, very slowly, with a 32-gauge needle. The cluster of lesions were then excised as a fusiform ellipse with an initial incision with a scalpel (#15 stainless surgical with blade with polymer coating) followed by excision using Castroviejo ophthalmic scissors. Wound edge apposition was achieved with 5-0 fast-absorbing chromic suture with no subcutaneous sutures. This was followed by application of 2-octyl cyanoacrylate skin adhesive (Dermabond Advanced®, Ethicon, Somerville, NJ) along the incision line. Of note, the patient was on a course of minocycline for concomitant inflammatory acne. The minocycline was continued pre and post-operatively. The patient had no wound care tasks or follow-up appointments for suture removal, and at 12 weeks post-op he was satisfied with the cosmetic result from the procedure. He wanted to schedule further excisions for his remaining cosmetically distressing lesions.

DISCUSSION

Syringomas are benign adnexal neoplasms that arise from primarily eccrine glands. Histologically, they have ductal differentiation. They tend to arise in clusters or as solitary lesions during adolescence, and they tend to affect the eyelids, upper trunk, or genital skin. They are typically asymptomatic and pose no malignant potential. Syringomas rarely spontaneously resolve, so treatment is needed if the patient is suffering from cosmetic impairment. Common treatment modalities include cryosurgery with liquid nitrogen, electrodessication, trichloroacetic acid, carbon dioxide laser ablation, and surgical excision.

The skin of the eyelid and genitals is delicate and cosmetically sensitive, and therefore special considerations must be taken into account when treating syringomas in these areas. Cosmetic surgery is most successful when techniques maximize tissue healing and minimize tissue damage, and it is further improved when the patient has fewer tasks involved in their wound care. This is all achieved through proper instrument use and delicate tissue handling, in addition to proper suture selection and technique. We present a technique concept for increasing wound healing and minimizing scar formation and wound care tasks for lesions in sensitive areas, including the eyelid, periorbital space, and genital skin. The technique was first practiced on silicone models, with subsequent successful use in the removal of multiple grouped penile syringomas in a 16 year-old male.

For excision of the lesions, we used Castroviejo ophthalmic scissors, which minimize risk of scarring. This was made evident by a study looking at patient satisfaction after removal of periorbital syringomas with Castroviejo scissors, where 95% of patients reported good to excellent esthetic results. Using these scissors, we were able to perform micro-excisions, and this technique of excising superficially allowed for the avoidance of subcutaneous sutures, which can induce granuloma formation. This technique also reduces the risk of hypertrophic scarring.

For wound closure, 5-0 fast absorbing plain gut suture was our suture of choice. According to Moy et al, the ideal wound closure technique should provide maximal wound eversion and maintain tensile strength throughout the healing process, be technically

simple and fast to perform, and allow precise wound edge adaptation without leaving suture marks. Our choice thus was aligned with this, as fast absorbing chromic sutures allow for more precise adjustment of wound edge apposition and eversion.

Wound care is often a challenge in the genital, eyelid, and periorbital areas, as there may be friction or discomfort with medication over thin skin. We therefore chose to use topical 2-octyl cyanoacrylate skin adhesive (Dermabond Advanced®, Ethicon, Somerville, NJ) along our incision lines in order to protect and reinforce the sutured incisions. A previous report showed successful healing of Mohs excisional defects in an elderly man when cyanoacrylate was directly applied to the base of wounds. Other reports show cyanoacrylate as equivalent to epidermal sutures in linear repairs of facial wounds following Mohs surgery.

In the 16-year-old patient with penile syringomas whom this technique was successfully used on, minocycline may also have played a role in minimizing inflammation and promoting uniform healing. A recent randomized controlled animal study found a significant decrease in hypertrophic scarring following iatrogenic wound creation in subjects that were treated with minocycline. This is believed to be secondary to minocycline's role as a matrix metalloproteinase (MMP) inhibitor, given MMP's involvement in scar formation.

We feel that this technique can be applied to most genital lesions, eyelid, and periorbital regions, especially in relation to the removal of syringomas or other small papules in that area. The use of Castroviejo ophthalmic scissors in performing micro-excisions minimizes the risk of scarring and proved key to the success of our delicate tissue technique, in addition to avoiding subcutaneous suturing and the use of a cyanoacrylate adhesive. The patient had no wound care tasks or future appointments for suture removal, which is optimal for lesions in sensitive, high friction areas or in patients who may be less inclined to participate in wound care, such as teenagers or the elderly. Furthermore, the use of antibiotics such as minocycline should be further explored in order to minimize scarring, reduce inflammation, promote healing, and achieve cosmetically desirable results.

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CHICAGO DERMATOLOGICAL SOCIETY **CASE #5**

Presented by Dana Griffin MD[1], Michael Dreifke MD[1], Lori Asztalos MD[1], Anthony Peterson MD[1], James Swan MD[1,2], Rebecca Tung MD[1], David Eilers MD[1,2]
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DERMATOLOGY CASE FILES:

"Would you mind taking a look at _____?"

CHICAGO DERMATOLOGICAL SOCIETY **CASE #6**

Presented by Lori Asztalos MD[1], Amanda Champlain MD[1], Kumaran Mudalier MD[2], Madhu Dahiya MD[3], David Eilers MD[1,4]
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HISTORY OF PRESENT ILLNESS

A 61-year-old Caucasian male presented with a 20-year history of painful skin nodules. They appeared in adulthood and are present predominantly on the trunk and extremities. The patient reports shooting 10/10 pain that is aggravated by cold temperature.

PAST MEDICAL HISTORY

Non-contributory

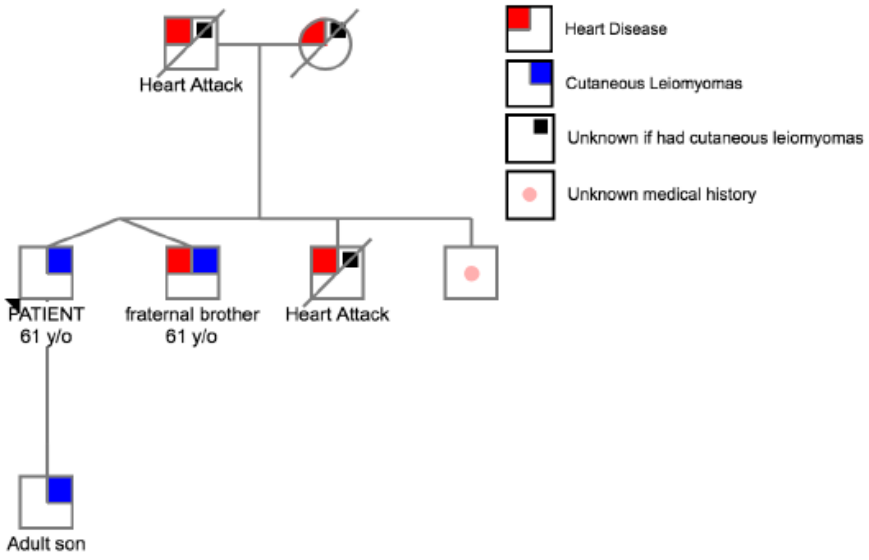
MEDICATIONS

Sildenafil citrate 502 mg prn

ALLERGIES

No known drug allergies

FAMILY HISTORY



PHYSICAL EXAMINATION

The patient's cutaneous exam was notable for firm red-brown to flesh-colored dome-shaped painful dermal papules and nodules in a grouped or linear configuration on the trunk and extremities.

DERMATOPATHOLOGY

Punch biopsy showed an un-encapsulated dermal proliferation composed of interweaving fascicles of spindle cells with elongated central nuclei, perinuclear vacuoles and eosinophilic cytoplasm. There was no nuclear atypia or mitotic activity. Stains for smooth muscle actin and desmin were positive.

Immunohistochemical assay for fumarate hydratase (FH) or S-(2-succinyl) cysteine antibody was unavailable.

DIAGNOSIS

Multiple painful leiomyomas in the setting of hereditary leiomyomatosis and renal cell cancer (HLRCC)

TREATMENT AND COURSE

Treatment was initiated with gabapentin 300 mg TID and intralesional botulinum toxin A. Only 1 group of leiomyomas was injected at each visit with 2 groups total injected to date, per patient preference. The visual analogue scale (VAS) was used to assess pain before and after ice provocation at baseline and at each subsequent visit of botox and non-botox treated groups of leiomyomas.

After 7 weeks, reported pain decreased from 5 (chest), 10 (back), and 3 (arm) to 1, 2, and 0 respectively. The ice challenge demonstrated 10/10 pain after 6 sec (chest), immediately (back) and 7 sec (arm) prior to therapy and immediately (chest), 2 sec (back) and 8 sec (arm) at the 7-week follow-up visit.

The patient was also evaluated by urology and had an MRI that was negative for renal tumors. He is scheduled to see genetics for possible genetic testing.

DISCUSSION

Cutaneous leiomyomas are rare benign smooth muscle neoplasms that usually arise from the erector pili muscle (piloleiomyoma) and rarely from vascular smooth muscle (angioleiomyoma) or dartos muscle (genital leiomyoma). They may arise sporadically or inherited in the setting of hereditary leiomyomatosis and renal cell cancer (HLRCC), formerly known as Reed's syndrome.

HLRCC affects 180 families worldwide. It is caused by an autosomal dominant (AD) heterozygous inactivating germline mutation on chromosome 1q42.3-43, which codes for FH. FH catalyzes the conversion of fumarate to malate in the Kreb's cylcle. Tumor formation is suspected to be secondary to deceased levels of enzymatic activity and a subsequent increase in intracellular levels of fumarate. The elevated fumarate levels lead to upregulation of hypoxia-inducible factor and HIF-mediated transcription pathways, providing angiogenesis for neoplastic growth.

HLRCC is characterized by multiple cutaneous leiomyomas, early-onset multiple uterine leiomyomas, and early-onset type-2 papillary renal cell carcinoma. Most patients (90-100%) will have at least some clinical manifestation of the disease by age 45 years.

Clinical criteria for a likely diagnosis of HLRCC includes: (1) histologically confirmed multiple cutaneous leiomyomas OR (2) at least two of the following: surgical treatment for symptomatic uterine leiomyomas before age 40, type-2 papillary renal cell carcinoma before age 40 or a first-degree family member who meets one of these criteria.

Cutaneous leiomyomas are often extremely painful either spontaneously or in response to pressure, emotion, or cold. Episodes of pain can be so intense that they provoke nausea, vomiting, hypotension, micturition and pallor, greatly impacting quality of life. Lesions favor the extensor surfaces of the extremities and trunk and often cluster around Blaschko's lines arranged in a linear, segmental, and/or zosteriform pattern.

Cutaneous leiomyomas usually present before the development of renal cell cancer, ranging from 10 to 47 years with a mean age of 25 years. The development of renal cell cancer has been reported in as young as 10 years of age, although the majority are reported between ages 30-40 years. Uterine leiomyomas usually present in patients younger than 30 years of age compared with 40s in the general population.

Therapeutic options for painful cutaneous lesions include surgical and medical management. Surgical interventions include excision, electrodessication, cryotherapy, carbon dioxide laser ablation, and intralesional botulinum toxin. Both excisional and destructive options have high recurrence rates, ranging from 6 weeks to more than 15 years. Botulinum toxin has only been reported in small case reports and case serious, but shows encouraging results. Patient in these studies required injections about every 3 months for continued pain control. Its effects are two-fold: (1) preventing acetylcholine release from nerve endings via inhibition of synaptosomal associated protein (SNAP-25), thus reducing muscle spasms and (2) inhibition of other neuropeptides such as substance P and glutamate, thus reducing central pain signals.

Medical management includes medications that either block smooth-muscle contraction (nifedipine, phenoxybenzamine, nitroglycerine, doxazosin, calcium channel blockers) or target nerve activity (gabapentin, capsaicin and topical analgesics). Recently antidepressants have been shown to be effective as well.

Management usually requires a multidisciplinary approach and should include a dermatologist, gynecologist, urologist and geneticist. If HLRCC is suspected, appropriate genetic counseling is often recommended for both the patient and family members given the AD inheritance pattern. The diagnosis is confirmed with either Immunohistochemistry testing for FH and 2-succinate dehydrogenase (if available) and/or molecular genetic testing of the FH gene. FH mutation testing is often recommended prior to renal cancer surveillance in order to avoid unnecessary investigations.

Long-term surveillance for development of new or recurrent leiomyomas and renal tumors is prudent; however there are no consensus guidelines for surveillance. Recommendations from expert opinion include: (1) full-body skin exams every 1-2 years, (2) Annual gynecologic examination for women, and (3) Annual radiological invention, preferably abdominal MRI for renal evaluation vs alternating CT with MRI to balance radiation

exposure and cost. Renal cell cancer associated with HLRCC is only reported to occur in 10-16% of patients, however it is often associated with an aggressive clinical course and may metastasize even when the tumor is small, warranting annual radiological intervention.

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CHICAGO DERMATOLOGICAL SOCIETY **CASE #7**

Presented by Jayla Gray MD[1], Daniel Opel MD[1], Dariusz Borys MD[2], Kumaran Mudaliar MD[2], Wendy Kim, DO[1]
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HISTORY OF PRESENT ILLNESS

An infant male born at 38 weeks gestational age via Cesarean section was transferred to Loyola University Medical Center NICU on day 1 of life for further evaluation of a congenital mass on his back. He had an unremarkable prenatal course. Upon arrival in the NICU, dermatology was consulted, and punch biopsy was obtained. Hematology-Oncology was also consulted due to concern for malignancy

PAST MEDICAL HISTORY

Full term (38 weeks gestational age) via Cesarean section due to placenta previa.

MEDICATIONS

None

ALLERGIES

No known drug allergies.

FAMILY HISTORY

The patient's mother, father and 9-year-old brother are healthy. The patient's maternal grandfather has prostate cancer. There is no family history of bleeding disorders, clotting, leukemia, lymphoma, or congenital malformations.

SOCIAL HISTORY

The patient lives with his mother, father, older brother and pet dog. There is no smoking in the home.

PHYSICAL EXAMINATION

The baby was well appearing. On the right lower back there was a mobile, firm 4.5 cm x 3 cm erythematous ulcerated nodule and an adjacent 2 cm x 2.3 cm violaceous nodule with hypertrichosis. There was no cervical, retroauricular, supraclavicular, axillary, or inguinal lymphadenopathy.

DERMATOPATHOLOGY

Histologic sections showed a neoplasm composed of hypercellular areas of monomorphic round to ovoid spindled cells forming intersecting fascicles as well as hypocellular areas of monomorphic small cells on a myxoid background. Some vessels show a hemangiopericytoma-like pattern. Some areas show prominent mitotic figures. These morphologic findings are most consistent with congenital fibrosarcoma.

Immunohistochemistry was performed at Mayo Clinic. The neoplastic cells were negative for myogenin, myoD1, wide spectrum cytokeratin, pancytokeratin, GFAP, SOX10, and p63. Fluorescence in-situ hybridization for ETV6 gene rearrangement mutation was negative.

ADDITIONAL STUDIES

CBC with differential was normal. CMP was normal except for elevated AST of 136.
Newborn metabolic screen was negative or normal.
Karyotype was normal.

DIAGNOSIS

Congenital Infantile Fibrosarcoma

TREATMENT AND COURSE

At 4 weeks of life, the patient was admitted to the hospital. He underwent complete excision with clear margins of the flank mass with wound closure including split thickness skin graft by plastic surgery. The patient is following with orthopedic oncology for local surveillance with serial examinations and occasional pulmonary surveillance with plain radiograph of the chest. The postoperative course was uncomplicated.

DISCUSSION

Fibrosarcoma is a rare, malignant, rapidly growing, spindle cell tumor that originates in the connective tissue. There are two sub-types of fibrosarcoma in children: the congenital infantile subtype and the childhood subtype. The congenital infant subtype occurs most commonly in the first 2 years of life and tends to follow a more benign course. The childhood subtype occurs in older children or adolescents and tends to be more aggressive.

Congenital infantile fibrosarcoma, while rare, is one of the more common soft tissue sarcomas found in infants. It typically presents as a rapidly growing, asymptomatic mass around the time of birth that appears as a round, dome-shaped, skin-colored, erythematous, or erythematous to blue tumor that is solid and fixed to the deep tissue planes. Surface telangiectasia, bleeding, and/or ulceration may be observed. Most commonly the tumor affects the superficial and deep soft tissues of the distal extremities. However, tumors affecting the head and neck region are more frequent in infants than older children and are suggested to have a more aggressive behavior with higher risk of metastasis. Coagulopathy has been associated with congenital infantile fibrosarcoma in some cases and may manifest as overt bleeding, anemia or thrombocytopenia. This can lead to misdiagnosis as a vascular lesion. Congenital-infantile fibrosarcoma has potential to spread to other surrounding soft tissues such as fat, muscles, tendons, nerves, joint tissue or blood vessels. Regional or distant metastasis is rare with a 5-year survival probability exceeding 80%. Delayed local recurrence is more common with reported rates between 17% and 43%. Thus, long-term follow up is very important in these patients.

The differential diagnosis for congenital-infantile fibrosarcoma includes several benign and malignant tumors, such as rhabdomyosarcoma, congenital hemangioma, infantile fibromatosis, and myofibromatosis. The ETV6-NTKR gene fusion, derived from a

chromosomal t(12;15)(p13;q25) rearrangement, has been recognized as a diagnostic marker for congenital infantile fibrosarcoma. Several studies have shown the majority of cases of congenital fibrosarcoma had a detectable ETV6-NTRK gene fusion while none of the other histologically similar malignant or benign spindle cell tumors expressed this fusion gene.

Imaging features of congenital infantile fibrosarcoma are nonspecific, and differentiation of malignant soft-tissue tumors is not possible based on imaging alone. Imaging studies reveal a large soft tissue mass with a heterogeneous enhancement pattern and variable osseous erosion. A large percentage of cases have also shown tumoral hemorrhage on MRI.

Macroscopically these tumors are soft to firm, grey to tan, poorly circumscribed masses that infiltrate the surrounding soft tissues and can have the appearance of being well-circumscribed due to compression of the adjacent tissue. They frequently have variable areas of myxoid changes, hemorrhage, and necrosis.

Microscopically congenital-infantile fibrosarcoma can be identical to the adult-type of fibrosarcoma, but often it tends to be less mature in appearance. This tumor appears as a densely cellular neoplasm composed of intersecting fascicles of primitive ovoid and spindle cells with little pleomorphism. Mitotic activity is variable. Commonly focal areas of prominent hemangiopericytoma-like pattern of vasculature, myxoid stroma or round to ovoid immature cellular proliferation with minimal collagen will be seen. Stains for S-100 protein, EMA, keratin, myogenin, and myoD1 should be negative.

Historically, the treatment of choice was surgery, including wide local excision or amputation depending on the location of the tumor. This was in conjunction with long-term follow-up as local recurrence and metastasis has been reported. However, more recent data suggests, that initial surgery should be used only when complete and conservative resection of the tumor is possible. Neoadjuvant chemotherapy should be used in cases where immediate complete resection would cause significant morbidity such as functional or cosmetic consequences. Neoadjuvant chemotherapy to shrink tumors prior to surgical excision allows for less risky and less mutilating surgeries to be completed and has been found to be successful in most cases with risk of metastasis being very low and treatment failures being mostly local relapses with similar incidence in patients treated with neoadjuvant chemotherapy plus resection compared to complete resection alone.

Chemotherapy was found to be especially useful in cases in which the ETV6-NTRK3 gene fusion is detected, suggesting the ETV6-NTRK3 gene fusion may indicate tumor sensitivity to chemotherapy. However, the role of post-resection chemotherapy for microscopic margins is still unclear.

We present this case of congenital infantile fibrosarcoma on the back of a newborn to highlight the clinical presentation, diagnosis, disease course and treatment for this rare type of congenital malignant tumor.

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CHICAGO DERMATOLOGICAL SOCIETY **CASE #8**

Presented by Michael Dreifke MD[1], James Swan MD[1,2], Laura Winterfield MD[1]
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HISTORY OF PRESENT ILLNESS

A 17-year-old boy with a recent diagnosis of acute myelogenous leukemia (AML) status post induction chemotherapy was admitted for a planned matched donor allogenic stem cell transplantation. His course had been complicated by neutropenic fever, thrombocytopenia, anemia, and multiple infections including a strep viridans line infection, typhilitis, chin abscess, and most recently with a suspected fungal pneumonia. The planned bone marrow transplantation was postponed due to worsening nausea, vomiting, fevers, productive cough, and shortness of breath. Prophylatic fluconazole was discontinued and the patient was started on empiric caspofungin, voriconazole, meropenem, and vancomycin. Throat swab, blood, urine, and sputum cultures for bacteria and fungus were repeatedly obtained, but unremarkable. Sputum smears for acid-fast bacilli were negative, and galactomannan testing for aspergillosis was negative. Following a bronchoscopy for further work up of a suspected fungal pneumonia a “linear bruise” was noted on the patient’s lower lip. Over the course the next week the lesion continued to expand eventually encompassing over half of the patients lower mucosal lip. The patient complained of worsening chills and tenderness at the affected site. He denied drainage, bleeding, trouble eating, speaking, or swallowing. He also denied similar lesions elsewhere on his body. Dermatology was ultimately consulted for further work up of the now necrotic lesion in the setting of suspected fungal pneumonia.

PAST MEDICAL HISTORY

Anxiety disorder
Acute myelogenous leukemia

FAMILY HISTORY

Father- Hodgkin’s lymphoma
Mother- hyperparathyroidism
Maternal grandmother- lung cancer

MEDICATIONS

Acetaminophen 650mg q6 hour prn
Capsofungin 150mg IV daily
Docusate sodium 100mg daily
Famotidine 20mg daily
Lorazepam 1mg prn
Meropenem 500mg IV daily
Ondansetron 8mg prn
Prochlorperazine 10mg prn
Tramadol 50mg daily
Vancomycin 1g IV daily

Voriconazole 250mg IV daily

ALLERGIES
No known drug allergies

SOCIAL HISTORY
Tobacco- never
Alcohol- never
Illicits- never

REVIEW OF SYSTEMS
Positive for fevers, chills, nausea, vomiting, shortness of breath, productive cough, visual disturbances

PHYSICAL EXAMINATION
Outer and inner lower mucosal lip extending to the lower cutaneous lip with a black necrotic plaque with surrounding violaceous patches. No evidence of open erosions/ulcerations or drainage.

DERMATOPATHOLOGY
Numerous fungal organisms noted within both superficial and deep dermal vessels as well as in the vessels of the subcutaneous adipose tissue.

LABORATORY STUDIES

Laboratory Study	Patient Result	Reference Range
WBC	0.1	3.5-10.5 k/uL
RBC	3.17	3.80-5.70 m/uL
Hemoglobin	9.1	11.5-15.5 gm/dL
Hematocrit	26.4	34.0-46.5%]
Platelet count	48	150-400 k/uL
Absolute neutrophil count	0.0	1.5-7.0 k/mm3
Sodium	126	136-144 mm/L
Creatinine	0.55	0.6-1.4 mg/dL
Calcofluor fungal smear	Non-septate hyphae	

BRONCHOSCOPY
Endobronchial changes consistent with acute bronchitis

IMAGING
Chest X-Ray: Extensive consolidation in the left upper lobe and diffuse interstitial and alveolar opacity throughout the right lung. Findings consistent with a multifocal pneumonia.
CT Head: New hemorrhagic transformation of a previously seen infarct involving the left posterior temporal lobe. Bilateral posterior infarcts.
CT Sinus: No evidence of paranasal sinus mucosal disease.

MR Brain/stem with and without contrast: Multiple foci of restricted diffusion. Consistent with acute ischemic change, most likely embolic in nature.

DIAGNOSIS

Disseminated Mucormycosis

TREATMENT AND COURSE

Upon obtaining the results of the fungal smear and angioinvasive hyphae seen on histology, voriconazole was discontinued and the patient was started on amphotericin B deoxycholate. The capsofungin and prior antibiotic regimen were continued for presumed zygomycetes lung infection given the results of the lip biopsy. Despite treatment, his neutropenic fevers continued and oxygen requirements continued to increase, ultimately requiring BiPAP. Three days following the initiation of amphotericin B, the patient had a respiratory code requiring intubation and initiation of acute respiratory distress syndrome (ARDS) protocol including stress dosed steroids. The following day the patient went into cardiac arrest and resuscitation attempts were unsuccessful.

DISCUSSION

Mucormycosis, formerly zygomycosis, is an opportunistic infection caused by Mucorales fungi, a saprophytic fungus located in soil, manure, and decaying organic material. There are three genera known to be human pathogens: Rhizopus, Absidia, and Mucor. And six recognized clinical presentations: Rhinocerebral, cutaneous, pulmonary, gastrointestinal, central nervous system, and a miscellaneous form typically involving the mediastinum, kidneys, and bone. Distinct from other filamentous fungi, which tend to target only immunosuppressed patients, Mucorales infects a heterogeneous patient population. In fact, up to 53% of reported cases of mucormycosis were identified in immunocompetent individuals. That being said, the risk of disseminated mucormycosis is three times more likely in those with immune dysfunction, which has significant implications for survival.

The first case report describing a patient with mucormycosis (then zygomycosis) was in 1885, and since 1940, there have been over 1050 individual case reports of mucormycosis. The global incidence is estimated as 3500 cases per year and steadily increasing the last two decades. There is a slightly higher prevalence of infection among males, which may be related to the protective affects of estrogen, as has been observed in paracoccidioidomycosis studies. The overall mortality of mucormycosis is roughly 54%. However, non-disseminated cases are associated with 35% mortality, whereas mortality rates in disseminated cases reach over 95%.

Previous studies illustrate that the primary sites of infection vary as a function of the hosts underlying condition. Sinus involvement constitutes the majority of infections in patients with diabetes, whereas more than half of primary cutaneous cases affect those with no underlying condition. Pulmonary disease comprises more than half of all bone marrow transplant patients and those with malignancy. Hematogenous dissemination from skin to other organs occurs in 20% of patients. However, unlike other filamentous fungi, hematogenous dissemination from other organs to the skin is extremely rare, occurring in less than 3% of cases. Independent risk factors for hematogenous dissemination include

deferoxamine use, human immunodeficiency virus, prematurity, and hematologic malignancy.

Mucormycosis infection results from traumatic inoculation or inhalation of spores. It is well established that iron metabolism has a key role in the organisms' establishment, survival, and progression. Circulating iron in the form of siderophores are abundant in those experiencing hemorrhage, acidemia, and in patients receiving multiple blood transfusions. Mucorales' angioinvasive capabilities are related to its ability to induce its own endocytosis in mammalian cells by binding to host Glucose Regulated Protein (GRP78), a stress related protein that is over expressed in high iron and glucose states. This self-induced endocytosis damages endothelial cells leading to thrombosis and eventual necrosis. Clinically, this manifests as hemoptysis, melena, and in cutaneous cases, as erythema, vesicles, pustules, ulceration, and necrosis.

The gold standard for diagnosis is biopsy and culture growth. Given the inverse relationship between time to diagnosis and survival, it is important to initiate treatment as soon as the diagnosis is suspected. Given that culture growth is positive in less than 50% of pre-mortem cases, the importance of histological confirmation cannot be overstated. Mortality rates decreased sharply in the 1960's, when amphotericin B deoxycholate became widely available, but has essentially remained unchanged for the last 50 years. Amphotericin has fundamentally been the only agent active against most Mucorales species. In recent years there has been a significant shift towards concomitant surgical debridement with systemic antifungal therapy as the standard of care.

The case discussed today illustrates the challenge and unfortunate outcome that establishing a timely diagnosis can have. The patient had had an extensive but negative infectious workup prior to our service being consulted for evaluation of the lip lesion. Given the extremely low rates of hematogenous spread from solid organs to skin, as discussed above, it is more likely that traumatic and incidental inoculation from the bronchoscopy seeded the lower lip. As recognition of specific host groups and their risk factors increases, earlier diagnosis and intervention may ultimately help improve survival outcomes of this devastating infection.

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CHICAGO DERMATOLOGICAL SOCIETY **CASE #9**

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HISTORY OF PRESENT ILLNESS

A 62 year-old male with a long history of hidradenitis suppurativa (HS) presented with ulcers and indurated plaques on the buttocks and thighs. The patient's history of HS started in his twenties, which he believed to have stemmed from prior military vaccinations. Since his initial diagnosis, he had been treated with antibiotics (clindamycin, doxycycline, and rifampin); retinoids (isotretinoin, and acitretin); and surgical excision of the axilla, inguinal, and perineal regions. The patient's last surgery was in 2011. After a 7 year loss to follow-up, the patient resumed care at the VA and was noted to have developed thickened, rolled borders at the periphery of his longstanding perineal ulceration that were not present at his last visit. He had been performing his own dressing changes since he was last seen.

PAST MEDICAL HISTORY

Diabetes, Type 2
Anemia
Hypertension
Hyperlipidemia

MEDICATIONS

Acitretin
Insulin
Omeprazole
Lactulose
Gabapentin
Ferrous sulfate
Lisinopril

ALLERGIES

Penicillin
IV contrast

FAMILY HISTORY

Mother passed at 75 from myocardial infarct
Father passed at 36 from colon cancer
3 brothers and 3 sisters are alive and well

SOCIAL HISTORY

The patient has a 2.5 pack per day smoking history for 25 years. He previously drove a truck for a living. He does not have children and lives alone with pets in Indiana.

PHYSICAL EXAMINATION

The patient appeared to be in discomfort. He had an elaborate bandage system overlying his perineum. The patient's right axillae had tender, erythematous subcutaneous abscesses with scant drainage upon applying pressure. His bilateral buttocks had a very large ulceration down to the subcutaneous tissue with firm rolled borders that were weeping with serosanguinous drainage and extremely tender to touch. Additionally, at 6 o'clock, the patient had a well-defined, large fungating verruciform mass.

DERMATOPATHOLOGY

Histopathology of the left and right buttock demonstrated nests of squamous epithelial cells extending into the dermis. Keratin pearls are present in between large, cells with an abundance of eosinophilic cytoplasm consistent with invasive well differentiated squamous cell carcinoma.

LABORATORY STUDIES

Laboratory Study	Patient Result	Reference Range
Hgb	8.1	13-17
WBC	24.52	4-11.0

ADDITIONAL STUDIES

Computer tomography angiography of the abdomen and pelvis with contrast demonstrated a large infiltrative anal and perineal neoplasm with associated sacrococcygeal bony destruction and ilioinguinal lymphadenopathy. Compared to previous imaging done on this patient, three new hepatic lesions, worrisome for metastasis, were observed. At the lung base, emphysematous changes were observed with few scattered 2-3 mm lung nodules.

DIAGNOSIS

Metastatic squamous cell carcinoma in the setting of HS.

TREATMENT AND COURSE

After the patient's presentation, he was biopsied and found to have squamous cell carcinoma (SCC). The initial plan was for the patient to undergo surgical resection of the region with subsequent radiation. However, during the pre-operative evaluation, as noted above, the patient was noted to have 3 worrisome liver masses as well as sacrococcygeal bone destruction and ilioinguinal lymphadenopathy suggestive of widespread metastasis, likely of his SCC. As such, the patient was transferred to hospice and given palliative radiation.

DISCUSSION

HS is a debilitating and chronic disease that affects approximately 1% of the population. Often beginning in the second to third decade of life, HS has shown a female predominance and a reduction in quality of life on par with mild to moderate psoriasis and

alopecia. While the exact etiopathogenesis has not been elucidated, follicular occlusion is believed to be a central contributor. Furthermore, a number of factors, including smoking, obesity, and bacterial agents have been found to worsen the condition.

HS is characterized by a persistent gradual course in often otherwise healthy males and females. Early lesions include the double comedone and small subcutaneous nodules. Repetitive follicular rupture with foul smelling purulent discharge and subsequent reepithelialization gives way to more involved lesions including deep abscesses, sinus tracts, and scarring. The painful, draining lesions in particular can cause significant economic and psychological morbidity, often leading to job loss and family desertion. The aforementioned lesions most commonly afflict the axillary region, followed by the inframammary, inguinal, and perineal regions, with the perineum being associated with the highest morbidity.

Typically, HS can be identified clinically. Commonly related conditions include anemia, the other members of the follicular occlusion disorders (acne conglobata, dissecting cellulitis of the scalp, and pilonidal cyst), as well as Crohn's disease. Additionally, acanthosis nigricans, dowling-degos disease, keratitis-ichyosis-deafness syndrome, and pachyonychia congenita have been associated with HS.

The treatment of HS is challenging and often requires employing a number of differing modalities including but not limited to antibiotics, retinoids, immunomodulators, and surgery. In particular, surgery is regarded by many as one of the more effective treatment modalities for intractable HS. While HS recurrence in the resected area may be as high as 50% and distant disease may confound results, surgical resection still represents a useful approach when used prudently. In those patients with difficult-to-control HS, it is particularly important to schedule regular follow-up appointments to prevent downstream complications.

One such complication of HS is increased risk of malignancy, including buccal cancer, primary liver cancer, and squamous cell carcinoma. While the incidence of SCC arising from HS is low (1- 4.6%), and has a higher male to female predominance (4:1), once it occurs, the prognosis is poor. Interestingly, this occurs independently of differentiation as good histological prognosis does not correlate clinically. A review of the literature of SCC arising from HS lesions showed 48% of patients dying within 2 years of diagnosis. It is unclear as to what exactly causes such a poor prognosis, though late presentation of the SCC is a common theme. Loss to follow-up, late recognition, presence of HPV (particularly HPV-16), and characteristics of HS that increase the aggressiveness of the SCC have been proposed rationales. In particular, one hypothesis is that tumors may spread along deep tissue planes, and thus can be missed by superficial biopsies. As such, close follow-up and repeated biopsies should be performed for suspected malignancies, especially in chronic, longstanding HS. It should be recognized that even with resection of SCC, local and distant recurrence rates are close to ~50%.

We present this case to highlight an uncommon but frequently fatal complication of HS and to report an additional case of SCC arising from HS that has metathesized.

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CHICAGO DERMATOLOGICAL SOCIETY **CASE #10**

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HISTORY OF PRESENT ILLNESS

In October 2015, our patient developed erythematous subcutaneous nodules with overlying scale on her left leg. Skin biopsy was performed, which showed deep dermal supportive and necrotizing granulomatous inflammation. Within one month these lesions ulcerated and evolved into classic pyoderma gangrenosum. At the time, she was being treated by rheumatology with etancercept for chronic recurrent multifocal osteomyelitis (CRMO)/possible early synovitis, acne, pustulosis, hyperostosis, osteitis (SAPHO) syndrome. She had failed adalimumab therapy due to the development of presumed adalimumab induced psoriasis. She had been followed in our clinic since June of 2014 for routine folliculitis of the scalp as well as moderate inflammatory and comedonal acne.

PAST MEDICAL HISTORY

No significant past medical history except for above.

MEDICATIONS

Meloxicam 7/2015 - current
Doxycycline 6/2014 - 6/2015
Adalimumab 2/2015 - 8/2015
Etanercept 8/2015 - 10/2015
Prednisone 11/2015 - 7/2016
Dapsone 2/2016 – 9/2016

ALLERGIES

Clindamycin (rash), penicillins (serum sickness like reaction), levofloxacin (joint pain)

FAMILY HISTORY

Negative for psoriasis, inflammatory bowel disease or Crohn's disease, inflammatory bone lesions, immunodeficiencies, rheumatoid arthritis, systemic lupus. Father has a history of eczema.

SOCIAL HISTORY

She is in the 12th grade, lives with her parents and three younger siblings.

PHYSICAL EXAMINATION WITH TIME COURSE

- **7/8/2014**: frontal and superior scalp with clusters of small follicular based pustules on an erythematous base. Cheeks and forehead with scattered open and closed comedones, inflammatory papules and pustules on glabella and nasal dorsum
- **5/21/2015**: initially left and later right palm with pinpoint desquamating papules with >75% desquamation of palms

- **7/30/2015**: left anterior inner thigh, right posterior inner thigh with nonpruritic small erythematous scaly circular plaques. Both plantar feet with erythematous papules and pustules with desquamation
- **10/6/2015**: left distal shin with large, painful, erythematous nodule with overlying scaly plaque
- **10/20/2015:** left distal shin with weeping, tender nodule
- **11/3/2015**: left distal shin with large ulcerated erythematous nodule with violaceous rim and purulent base. Left proximal shin with a new bright red smaller ulcerated nodule with purulent base and scaly patch around the periphery with an isolated small pustule noted at the edge of the ulcer. It is non-tender and developed within a previous psoriatic patch. Palmoplantar psoriasis improving on hands but still present on feet
- **12/8/2015**: left medial and superior anterior leg with four well-demarcated ulcers with an erythematous rim. Pustulosis clear on hands, improving on feet. Psoriatic patches improved on thighs. Acne improved.

DERMATOPATHOLOGY

A punch biopsy was performed of a nodule on the left lower leg which showed deep dermal supportive and necrotizing granulomatous inflammation. No fungal or atypical mycobacterial organisms were identified on GMS, PAS, AFB, or PCR send-out studies

ADDITIONAL STUDIES

Chest XR 10/2015 – normal
MR Left Lower Extremity 11/2015: extensive soft tissue edema, no evidence of osteomyelitis
Venous Doppler 11/2015: no evidence of DVT

LABORATORY STUDIES

Laboratory Study	Patient Result	Reference Range
WBC (K/UL) -10/2015	11.3 (H)	3.5-10.5
Fecal calprotectin	negative	
SCL-70	negative	
SS-A	negative	
SS-B	negative	
Anti-Smith	negative	
Cardiolipin	negative	
B2-glycoprotein	negative	
Serum protein electrophoresis (SPEP)	WNL	
ANA	negative	
Anti-DNA	negative	
Complement C3	179(H)	79-152
CRP(MG/DL)	0.6	<0.8
ESR	34(H)	0-20
Deep fungal/AFB culture	negative	

DIAGNOSIS
Pyoderma gangrenosum in setting of a yet-to-be-identified autoinflammatory syndrome

TREATMENT AND COURSE
Our patient was initially treated for mild acne and folliculitis which improved with oral doxycycline, adapalene 0.1% gel and clindamycin 1% lotion. After initiation of adalimumab in February of 2015 for bone pain related to possible CRMO/SAPHO, she developed palmoplantar pustulosis and psoriasiform plaques which did not resolve despite a change in therapy to etanercept as well as aggressive topical therapy. Pyoderma gangrenosum developed on her leg. Prednisone was initiated and dapsone was added. Several attempts at weaning the prednisone resulted in worsening of the ulcers, and the patient and her family were apprehensive of alternative therapeutic options, such as Anakinra. Her left leg wounds eventually healed with meticulous wound care including daily vinegar soaks, topical clobetasol ointment, topical dapsone gel, Xeroform with Telfa and Coban wrap. She was eventually weaned off prednisone completely. Genetic testing from the Mayo Clinic was negative for PAPA (pyogenic arthritis, pyoderma gangrenosum, acne) syndrome in August 2016. She continues to follow with immunology and GI at the Mayo Clinic and further testing will be pursued to investigate underlying causes of her pyoderma gangrenosum.

DISCUSSION
Pyoderma gangrenosum (PG) is a rare inflammatory skin disease. In its classical presentation it manifests as single or multiple painful ulcers with violaceous, raised, undermined borders on the legs. PG can be associated with many conditions, notably inflammatory bowel diseases (20-30%), arthritis (20%) hematological malignancies (15-25%), or can be idiopathic. It may precede, coexist or follow many systemic diseases. PG may occur in the context of syndromes like PAPA (pyogenic arthritis, PG and acne) and SAPHO, as well as in the recently described entities such as PASH (PG, acne and suppurative hidradenitis), DIRA (deficiency of the interleukin-1-receptor antagonist) and DITRA (deficiency of the interleukin-36 receptor antagonist). PG is a neutrophilic dermatosis, which is hallmarked by an accumulation of neutrophils in the skin. The cutaneous manifestations of neutrophilic dermatoses are polymorphous and include pustules, abscesses, papules, nodules, plaques and ulcers.

Our patient's workup has not identified a unifying diagnosis for her pyoderma gangrenosum, psoriasiform dermatitis, and sterile osteomyelitis. Autoinflammatory diseases are a heterogeneous group of disorders clinically characterized by recurrent episodes of sterile inflammation in the affected organs, in the absence of high titers of circulating autoantibodies or autoreactive T cells. The classic monogenic autoinflammatory syndromes like PAPA are due to mutations of single genes which regulate the innate immune response.

DIRA and DITRA are two other recently identified autoinflammatory conditions. DIRA presents in the neonatal period with a severe neutrophilic pustular skin eruption, skin pathergy, and nail dystrophy, as well as elevated acute-phase reactants, sterile

osteomyelitis, and periostitis. DIRA is caused by loss of function of the IL-1 receptor (IL-1R) antagonist, the first endogenous cytokine receptor antagonist identified that blocks IL-1 signaling. Absence of the IL-1R antagonist results in unopposed proinflammatory signaling. The cutaneous and systemic features of DIRA bear similarity to features seen in pustular psoriasis and SAPHO syndrome, suggesting that IL-1 signaling may play a role in these conditions as well.

Our patient had PG of the left leg as well as psoriasiform dermatitis and recurrent sterile osteomyelitis of the jaw. At this time, her constellation of findings does not fit perfectly into one diagnosis. DIRA or DITRA are being considered, despite her age.

We present this case of a patient with pyoderma gangrenosum in the setting of a yet-to-be-described autoinflammatory syndrome for clinical interest and to raise awareness of the spectrum of how autoinflammatory diseases may present clinically.

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