CHICAGO DERMATOLOGICAL SOCIETY **CASE #1**

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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**

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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]
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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**

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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**

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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

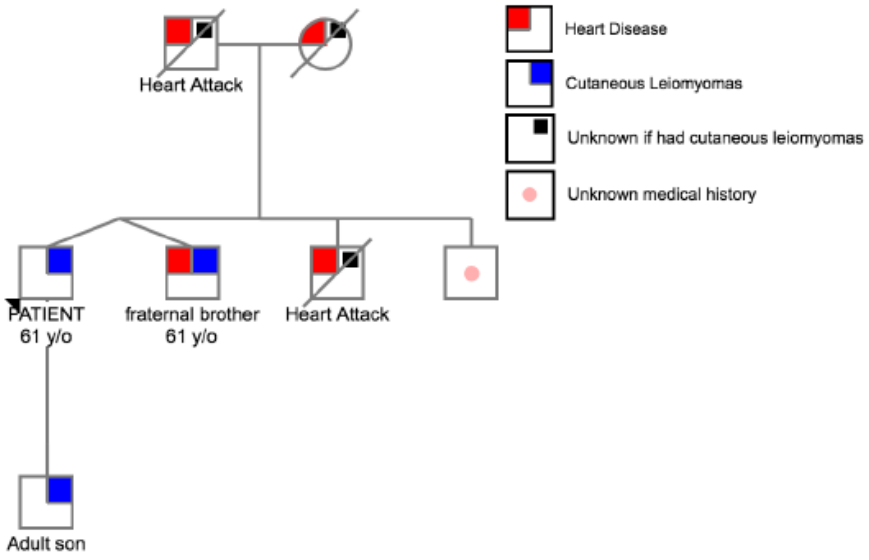
MEDICATIONS

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**

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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**

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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**

Presented by Daniel Opel MD[1], Jodi Speiser MD[2], Kelli Hutchens MD[2], Kumaran Mudaliar MD[2], and Wendy Kim DO[1]
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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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Case 1

Case Presented by Leigh Stone, MD, Ramya Tripuraneni, MD and Michelle Bain, MD

History of Present Illness:
A two year old male with multiple developmental disabilities was referred to dermatology clinic for diffuse congenital skin findings. His mother reported that he was born after an uncomplicated pregnancy and that she noted discoloration of most of his skin on his first day of life. She denied any change in appearance or progression of the lesions since his birth.

Past Medical History:
Global developmental delay, epilepsy, hypotonia, and recurrent aspiration pneumonia

Medications:
Levetiracetam

Allergies:
No known drug allergies

Family History:
No one in the patient's family had a history of similar skin findings, including two siblings. His maternal aunt had epilepsy and developmental delay. His maternal uncle died at age 38 due to stroke; he also had a history of epilepsy and developmental delay.

Social History:
The child lived at home with his parents and siblings. The family was noted to have poor compliance with medical appointments.

Review of Systems:
The mother reported speech delay and difficulty walking.

Physical Examination:
The patient has Blaschkoid hypo- and hyperpigmented linear patches on his trunk as well as the upper and lower extremities, a high forehead, wide-set eyes, broad nasal root, low-set ears, invasion of philtral skin onto the vermillion of the upper lip, and decreased scalp hair density.

Diagnostic Procedures and Tests:
02/14 Microarray: normal male microarray. Microarray analysis using a whole genome oligonucleotide array detected no clinically significant abnormalities.

08/15 Chromosome Analysis of Skin: abnormal mosaic male karyotype. 55% of the cells examined contained an isochromosome 12p.

Diagnosis:
Pallister-Killian syndrome

Treatment Course:
The patient is responding well to physical, speech, and behavioral therapy as well as follow up with multiple medical specialties including genetics, neurology, and ophthalmology. However, compliance has been a continued issue.

Discussion:
Pallister-Killian syndrome (PKS) is a rare, sporadic, multisystem disorder caused by tissue-limited mosaic tetrasomy of 12p. In PKS, tetrasomy is produced by the presence of an isochromosome, which is comprised of two extra copies of 12p arranged in mirror image. The isochromosome is created by a non-disjunction event, thought to occur most often during maternal meiosis II.

Nearly half of PKS patients exhibit cutaneous findings, specifically linear patches of hyperpigmentation or hypopigmentation and can appear as a whorled pattern following the lines of Blaschko. PKS represents one of the many chromosome mosaicisms that can present with Blaschkoid dyschromia, historically referred to by the descriptive rather than diagnostic term Hypomelanosis of Ito.

Distinct craniofacial features are associated with PKS and include fronto-parietal alopecia, sparse eyebrows, philtral skin projecting onto the upper lip vermillion, depressed nasal bridge, large mandible, bifid uvula, and a short neck. Systemic features that can be associated with PKS include decreased vision, structural brain malformations, epilepsy, structural cardiac defects, lung hypoplasia secondary to a diaphragmatic hernia, intestinal malrotation, displacement of the anus, and a growth pattern unique to PKS which consists of an accelerated prenatal growth period followed by a decelerated postnatal growth period. Like many mosaic conditions, PKS has a vast spectrum of disease severity ranging from intrauterine death to very mild forms. The overall neurologic prognosis is poor with significant mental and motor retardation being common.

For diagnosis, the genetic changes of PKS may be detected by karyotype of cultured skin fibroblasts as was done in this case. Alternatively, fluorescent in situ hybridization (FISH) can be employed with chromosome 12 specific DNA probes in order to identify isochromosome 12p. It is typically not detected in rapidly dividing cells such as those found in the peripheral blood. However, there are limited reports of cases being identified in peripheral lymphocytes. The diagnosis is highest among amniocytes and bone marrow cells with a detection rate of 100%, followed by a detection rate of 50-100% in fibroblasts and 0-2% in lymphocytes. Prenatal detection by chorionic villous sampling, amniocentesis, and cordocentesis is also possible.

At this time, treatment of PKS is supportive and requires a multidisciplinary approach.

Essential Lesson:
- Pallister-Killian syndrome is caused by mosaic tetrasomy of 12p resulting from an isochromosome.
- Almost half of Pallister-Killian patients have cutaneous findings, which fit under the descriptive rather than diagnostic term Hypomelanosis of Ito.
- Additionally, Pallister–Killian syndrome is characterized by facial dysmorphism, heart defects, congenital diaphragmatic hernia, hypotonia, intellectual disability, and epilepsy.
- In all patients presenting with Blaschkoid pigmentary changes, consider obtaining a skin biopsy with subsequent karyotyping of cultured fibroblasts.

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Case Presented by Iona Chapman, MD
and Milena J. Lyon, MD

UNKNOWN

This 49 year old female presented with multiple stellate necrotic plaques and overlying hemorrhagic bullae.

Case 3

Case Presented by Lorelei E. DiTommaso, MD
Benjamin Garden, MD, and Iris K. Aronson, MD

History of Present Illness:
A 46 year old cognitively impaired female was referred by rheumatology due to concern for vitiligo. The patient's mother stated that over the past year the skin on the patient's chest started to lighten, and in recent months had progressed to include the arms, face, back, and legs. There had been no improvement with hydrocortisone cream.

Past Medical History:
Cognitive impairment, recent pneumonia, inflammatory arthritis (undergoing work-up with orthopedics and rheumatology)

Medications:
Montelukast, omeprazole, and cetirizine

Allergies:
No known drug allergies

Family History:
Niece: Systemic lupus erythematosus

Review of Systems:
The patient's mother reported weakness, chronic cough in recent months, fatigue, dysphagia, and joint pain. She denied fevers, chills, shortness of breath, constipation, or diarrhea.

Physical Examination:
The patient has diffuse depigmented patches with uniform peri-follicular pigmentary retention on the scalp, face, upper chest, upper back, and upper and lower extremities. There is periungual loss of pigment as well as mild sclerodactyly of both hands. Diffuse skin tightening is observed on the face, torso, upper and lower extremities proximal to the elbows and knees. On the volar tip of the right fourth digit, there is a three millimeter atrophic macule, consistent with a scar.

Laboratory Data:
The following were positive or abnormal:
Antinuclear antibody: dual homogenous and anti-centromere patterns, both >1:10,240 (≥1:160 clinically significant titer) on indirect fluorescence assay
Anti-topoisomerase I (Scl-70) antibody: 351 AU/mL (≥41 positive)
Erythrocyte sedimentation rate: 58 mm/hr (1 – 10)
Hemoglobin 10.1 g/dl (13.2 – 18)
Albumin 2.9 g/dl (3.4-5)
Urine analysis: protein 30 g/dL
Brain natriuretic peptide 558 pg/mL (>100 high)

The following were negative or within normal limits:
Complete metabolic panel, ferritin, Vitamin B12, angiotensin-converting enzyme level, complement 3 level, complement 4 level, anti-neutrophil cytoplasmic antibody, C-reactive protein, creatinine kinase, aldolase, quantiferon gold, as well as antibodies to dsDNA, Smith, cyclic citrullinated peptide, and ribonucleoprotein.

Diagnostic Procedures and Tests:

06/15 Computed Tomography, Chest: Mild interstitial lung disease, axillary and mediastinal adenopathy, cardiomegaly, and pulmonary arterial hypertension.

08/15 Transthoracic Echocardiogram: Severely enlarged right ventricle, reduced right ventricular function, dilated right atrium, tricuspid regurgitation, and elevated pulmonary artery systolic pressure.

Diagnosis:

Diffuse cutaneous systemic sclerosis

Treatment Course:

The patient was started on pentoxyphylline, prednisone, ambrisentan, and mycophenolate mofetil. However, there was disease progression involving the viscera, with worsening of pulmonary fibrosis, pulmonary hypertension, and subsequent cor pulmonale. Two months later, the patient died from septic shock secondary to a gastrointestinal infection.

Discussion:

Systemic sclerosis (SSc) is a progressive and debilitating disease that includes a wide spectrum of diverse cutaneous findings, typified by skin thickening, as well as varying degrees of multisystem involvement. It is important for the physician to be aware of this disease spectrum as the diagnosis of SSc rests largely on clinical findings. In an effort to increase diagnostic sensitivity, particularly for patients with early and limited disease, the American College of Rheumatology and European League Against Rheumatism updated the 1980 classification criteria in 2013. Classification criteria may be met with 91% sensitivity and 92% specificity. Skin manifestations included in the criteria are skin thickening, telangiectasias, Raynaud's phenomenon, abnormal nailfold capillaries, as well as digital edema, sclerodactyly, ulcers, and pitting scars.

Though not included in the aforementioned criteria, cutaneous pigmentary changes have long been recognized as an associated feature of SSc. In 1898, Sir William Osler was the first to publish the observation of dyspigmentation, which he noted in three out of the eight patients with SSc for whom he was investigating treatment with thyroid extract. Thereafter, a large case series from the Mayo Clinic of 727 patients with SSc, from 1935 – 1958, reported 222 patients (30.5%) with pigmentary changes. Interestingly, pigmentary changes were found to occur later in the disease, with only eight patients presenting with hyperpigmentation as the initial manifestation of SSc. Decades later, in 1983, a case series reported the first histologic features from skin biopsies of depigmented skin in seven patients with SSc. Haematoxylin and eosin (H&E) stain revealed minimal or absent melanin-laden melanosomes within the papillary dermis, rare melanocytes, and an abundance of Langerhans cells in the lower third of the epidermis. Observing pigmentary retention overlying blood vessels within larger field of depigmentation in three patients with SSc, Jawitz et al. in 1984 used thermography to test, inconclusively, the hypothesis that temperature variations may be causative in this phenomenon. Overall, the pigmentary alterations reported in the literature include the following: vitiligo-like depigmentation with perifollicular pigment retention (leukoderma of scleroderma, "salt and pepper" sign) most commonly on the central face and upper trunk, diffuse hyperpigmentation, localized hyper- or hypopigmentation especially in areas of pressure, and retention of pigment overlying superficial veins within larger patches of depigmentation.

For the dermatologist, knowledge and attention to pigmentary changes, as well as the cutaneous findings beyond fibrosis, may aid in diagnosis of SSc. Some patients may experience acute swelling of the distal upper and lower extremities prior to the onset of fibrosis. Nailfold capillary anomalies, such as enlarged loops, avascular areas, and neoformation are common, and were found in >90% in a case-control study of 75 patients with SSc compared to twenty healthy subjects. Other commonly described cutaneous findings include telangiectasias, most often on lips and palms, which are often described as matted or squared off. Calcinosis cutis most commonly near the joints and the distal extremities, diminished hair growth in areas of fibrosis, Raynaud's phenomenon, and ulcerations of the tips of digits are additional well-described cutaneous manifestations. As opposed to limited cutaneous systemic sclerosis, diffuse cutaneous SSc follows a more rapidly progressive course, owing to early internal organ involvement. Overall, pulmonary disease is the leading cause of death. Autoantibodies associated with a less favorable prognosis include anti- topoisomerase I, anti-U3RNP, and anti-T_h/T_o. Management of SSc is challenging, and therapies may be of limited efficacy due to the debilitating and often progressive nature of the disease. Evidence-based treatment options for cutaneous fibrosis in SSc include methotrexate, cyclophosphamide, mycophenolate mofetil, and even autologous hematopoietic stem cell replacement. Current investigations into cytokine-based therapies, particularly TGF-β, owing to its role in inducing endothelial damage and fibroblast activation, could in theory provide disease modification, especially in patients with early disease.

Essential Lesson:

- Systemic sclerosis is a debilitating and often progressive disease, typified by symmetrical fibrosis and variable organ involvement with a spectrum of cutaneous features.
- Pigmentary changes are a poorly understood but well-established feature of the disease, though not included in the current disease classification criteria.
- Pigmentary features include "salt and pepper" sign, hyperpigmentation particularly in areas of pressure, and pigmentary retention overlying superficial veins within larger patches of depigmentation
- Dermoscopy to assess nailfold capillary anomalies is an important component in screening for systemic sclerosis.

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Case Presented by Lisa Blackwood, MD
and Milena J. Lyon, MD

UNKNOWN

This 31 year old male presented with a one year history of multiple, rapidly-growing papules that began on the right chest and subsequently spread to the right arm.

Case 5

Case Presented by Artem Sergeyenko, MD
and Iris K. Aronson, MD

History of Present Illness:
A 72 year old male presented for evaluation of his left hand. The patient reported that he first noticed a small firm lump on his palm in 2013 that was originally diagnosed as a Dupuytren's contracture. Over the next few months, the mass continued to grow and eventually started to bleed. After inconclusive imaging, biopsies, and aspirations by orthopedic surgery, and continued growth, the patient was referred to dermatology for further evaluation.

Past Medical and Surgical History:
Hypertension and myectomy in 2011

Medications:
Atenolol and lisinopril

Allergies:
Sulfa drugs – rash

Family History:
No history of skin cancer or skin diseases

Review of Systems:
The patient denied fevers, chills, nausea, vomiting, diarrhea, shortness of breath, cough, or weight loss.

Physical Examination:
The left central palm has a three centimeter by two centimeter heterogeneous, exophytic, pink nodule with areas of blue and violaceous discoloration with surrounding hemorrhage. The dorsal left hand between the third and fourth metacarpophalangeal joints has a three centimeter by two centimeter ulceration with active hemorrhagic weeping. The entire left hand appears edematous.

Diagnostic Procedures and Tests:
10/14 Magnetic Resonance Imaging, left hand with and without contrast: Large hematomas of the hand with areas of nodular enhancement raise the possibility of tumor dorsal to the third proximal phalanx abutting the extensor tendon, and between the third and fourth proximal phalanges. This could represent a sarcoma or a giant cell tumor, among other etiologies.

10/14 Computed Tomography Angiogram, left hand with contrast: Two large hematomas about the hand, one at the volar aspect of the third and fourth metacarpals and one at the dorsal aspect of the third proximal phalanx dorsally, extending between the third and fourth proximal phalanges. Vessels appear to course around these collections. The enhancing areas suggesting tumor, visualized on the magnetic resonance imaging, are not well seen on this exam. No vascular malformation.

Histopathology:
Left palmar hand, skin: The specimen shows a large, soft tissue neoplasm with extensive hemorrhage. The tumor consists mostly of irregular slit-shaped vessels lined by atypical epithelioid endothelial cells. At higher power, one appreciates the atypical features of the endothelial cells lining the slit-shaped vessels. Immunostaining of the cells shows focal positivity for CD31. Additional stains demonstrate diffuse nuclear positivity for ERG in the cytologically malignant epithelioid cells. There were also irregularly distributed SMA-positive spindle cells around some of these vessels. HHV-8 stain was negative.

Diagnosis:
Epithelioid angiosarcoma

Treatment Course:
After being diagnosed with an epithelioid angiosarcoma the patient underwent a full malignancy work-up that was negative for metastases. In January 2015, he underwent a left upper extremity amputation of the forearm and sentinel lymph node biopsy. The sentinel lymph nodes were negative for metastases. In October 2015, the patient developed a recurrence in the left forearm stump, based on repeat imaging. The patient was referred to Mayo Clinic where he underwent an above left elbow amputation in December 2015. After evaluation by oncology and radiation oncology, no further treatment with chemotherapy or radiation therapy was recommended.

Discussion:
Epithelioid angiosarcomas are rare and aggressive malignancies of endothelial origin. They are more prevalent in men and have a peak incidence in the seventh decade. Tumors most commonly occur in the deep soft tissues of the extremities, but have been reported to form in a variety of primary sites, including the skin, bone, thyroid, and adrenal glands. Tumors tend to be highly aggressive and demonstrate early nodal and solid organ metastases. Within two to three years of diagnosis, 50% of patients die of the disease, and the five-year survival rate is estimated to be 12-20%. The etiology remains unknown, but it has been linked to previous toxic chemicals, irradiation, or Thorotrast contrast media exposure, and may arise in the setting of arteriovenous fistulae or chronic lymphedema. Diagnosis is made with hematoxylin-eosin (H&E) stained sections and immunochemical stains; although, it is often a complex diagnosis and can often be mistaken for a poorly differentiated carcinoma or malignant melanoma. On H&E, one appreciates pleomorphic, polygonal epithelioid cells with eccentric nuclei, prominent nucleoli, abundant eosinophilic cytoplasm, and focal areas of irregularly-anastomosing vessel formation with cellular stratification in a papillary appearance. Additionally, mitotic figures, necrosis, and hemorrhage can also be appreciated. The tumor is often strongly positive for vimentin and CD 31, and can likely be positive for factor VIII, FLI-1, and CD34.

While radiation therapy is often utilized, surgery is the primary treatment modality. Despite wide excision, local recurrence is common. Tumor size is one of the most important prognostic features, with a worse prognosis for tumors greater than five centimeters. Evidence suggests that paclitaxel-based chemotherapeutic regimens may improve survival, and a combination of paclitaxel with sorafenib has been reported to induce remission in metastatic epithelioid angiosarcoma of parietal origin. Currently, no standardized treatment regimen for this condition exists.

Our case demonstrates the classic presentation, in terms of patient age, location, and anatomic location of epithelioid angiosarcoma. The histopathologic diagnosis can be subtle and requires

appropriate use of immunohistochemical stains to confirm the diagnosis. Finally, the recurrent and recalcitrant nature of the disease, despite wide resection, was also apparent in our patient.

Essential Lessons:

- Epithelioid angiosarcoma is an aggressive tumor that requires appropriate use of histochemical stains to facilitate diagnosis.
- Despite wide excision, epithelioid angiosarcoma is a disease with a very high recurrence rate.
- Metastatic epithelioid angiosarcoma treatment with paclitaxel-based chemotherapy has promising results, but standardized therapeutic regimens have not been established for this rare condition

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Case 6

Case Presented by Kimberly Jerdan, MD
and Michelle Bain, MD

History of Present Illness:
Four year old identical triplets were referred from general pediatrics for concern for molluscum contagiosum. These papules were present for four months and were limited to the chest. Per the father, there was no history of trauma, irritation, or manipulation to the affected areas.

Past Medical History:
Prematurity (born at 32 weeks) and congenital dermal melanocytosis.

Medications:
None

Allergies:
No known drug allergies

Family History:
The father reports he had similar papules on his chest during adolescence that resolved with isotretinoin.

Review of Systems:
The patients' father denied fevers, chills, night sweats, or weight loss on their behalf.

Physical Examination:
Erythematous to maroon papules are scattered on the central chest of all three patients. On dermoscopy, homogenous white macules were surrounded by light brown to erythematous halos.

Laboratory Data/Diagnostic Procedures and Tests:
None

Histopathology:
None

Diagnosis:
Eruptive vellus hair cysts in identical triplets

Treatment Course:
The family elected to defer treatment at this time.

Discussion:
Eruptive vellus hair cysts (EVHCs) were first described by Esterly, Fretzin, and Pinkus in 1977. EVHCs are red or brown monomorphous papules overlapping with pilosebaceous and apocrine units. EVHCs are typically found on the chest and extremities, although some have been reported on the face, abdomen, axilla, buttocks or genital area as well.

It has been suggested that most cases of EVHCs are the result of a de novo mutation. However, in the literature, 20 families are affected by autosomal dominant EVHCs based on

phylogeny. In 2015, EVHCs were reported in identical twins further supporting the case for a genetic mutation. Today we augment that by presenting an occurrence of triplets with EVHCs. Interestingly, the patients' father reports similar lesions in his own childhood, further underscoring a genetic basis.

The de novo form is noted to be more common and clinically presents later, with average onset at 16 years old and an average age of diagnosis of 24 years old. This form occurs without preceding trauma or manipulation.

Other variants of EVHCs have been described. Late Onset EVHC occurs age 35 or older, with 57 as the average age of reported lesions, and a female to male predominance of 2.5 to 1. This may be attributed to proliferation of ductal follicular keratinocytes or loss of perifollicular elastic fibers exacerbated by exogenous factors such as manipulation, UV rays, or trauma. Unilesional EVHC is reported with an average age of diagnosis of 27 years old. Some of these lesions may be pedunculated at greater than eight millimeters. There is also a female to male predominance of 2 to 1. EVHCs with steatocystoma multiplex can be seen with an average age of onset 18.7 years old and a female to male predominance of 0.2 to 1. There may be a family history of this subset as reported in three patients with this pattern.

There are two theories to explain the pathogenesis of eruptive vellus hair cysts. The first theory proposes retention of vellus hair and keratin in a cavity formed by an abnormal vellus hair follicle causing infundibular occlusion. The second theory proposes the growth of benign, follicular hamartomas that differentiate to become vellus hairs.

The recommended work up for EVHCs varies by patient and age. EVHCs present an opportunity to employ non-invasive diagnostic procedures, especially for the pediatric population, to avoid scarring and pain from manipulation or biopsy. Although many clinicians may comfortably diagnose EVHCs clinically, one paper suggested six cases with a diagnosis of steatocystoma multiplex, KP or milia prior to histopathology revealing vellus hair cysts.

Dermoscopy presents as a possible diagnostic aid for EVHCs. EVHCs exhibit yellowish-white homogenous circular structures with a maroon or erythematous halo. One may see a central gray-blue color point due to melanin in the pigmented hair shaft. One dermoscopy review of EVHCs also reports radiating capillaries. Occasionally non-follicular homogenous blue pigmentation may be seen due to a connection to atrophic hair follicles in the mid-dermis and no normal hair follicle around the cysts.

Treatment for EVHCs is usually for aesthetic discomfort. Twenty-five percent of EVHCS resolve spontaneously with transepidermal hair elimination or a granulomatous reaction. A case report of four siblings with congenital EVHCs also described a mother with similar lesions that resolved spontaneously in early adulthood, just as our patients' father noted. Otherwise, the treatments listed above have been tried with minimal improvement. Of note, one paper demonstrated that 0.1% tazarotene cream yielded better results than erbium:YAG or incision and drainage of EVHCs. One report demonstrated partial improvement with calcipotriene within two months with some lesions completely resolved and others with flattening. This may be attributed to the antiproliferative and prodifferentiating effects on the ductal follicular keratinocytes by calcipotriene. Another report stated that isotretinoin and Vitamin A derivatives were not effective for clearing EVHCs.

Essential Lesson:

- A subset of eruptive vellus hair cysts are genetic, with a likely autosomal dominant inheritance.
- Dermoscopy can aid in the diagnosis of eruptive vellus hair cysts, which is of particular use in the pediatric population.

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Case Presented by Stephanie Wang, MD, Benjamin Garden, MD
Iris K. Aronson, MD and Michelle Bain, MD

FAST BREAK

This 63-year-old Mexican male with a history of renal transplantation presented for evaluation of a non-healing ulcer on the right ear.

Case 8

Case Presented by Huayi Zhang, MD
and Carlotta Hill, MD

History of Present Illness:
A 63 year old Caucasian male with a past medical history of psoriasis was referred for evaluation of grey, hyperpigmented skin patches and numbness of extremities. The patient was initially diagnosed with psoriasis on skin biopsy in 2004, for which he received topical steroids, narrow band ultraviolet B phototherapy and cyclosporine from 2005-2010. The patient recalled visiting southern Florida and Mexico on numerous occasions during those years. As his psoriasis improved in 2010, he began to feel numbness in his feet which gradually spread to his hands and face. In 2013, the patient underwent electromyography and a positron emission tomography scan, and was diagnosed with small fiber neuropathy. Finally, in March 2016, because of progressive hypoesthesia, the patient underwent left superficial peroneal nerve biopsy at the Mayo clinic which showed acid fast bacilli concerning for leprosy. Four skin biopsies were performed and sent to the National Hansen's Disease Clinic for further evaluation.

Past Medical and Surgical History:
1. Psoriasis
2. Coronary artery disease, status post coronary artery bypass grafting in 2013
3. Aortic regurgitation (status post aortic valve replacement)
4. Hypertension
5. Hyperlipidemia
6. History of nicotine abuse, last use 2011

Medications:
Metoprolol, aspirin, gabapentin, tramadol, and acetaminophen

Allergies:
No known drug allergies

Family History:
Father with psoriasis. No family member with Hansen's disease. No family history of malignancy

Social History:
The patient does not use tobacco (last use 2011), drinks alcohol socially and does not use illicit drugs. He is divorced but is currently engaged. He has several grandchildren that he visits often.

Review of Systems:
The patient confirmed numbness of the cheeks, and numbness and tingling of the hands and feet bilaterally. The patient denied nausea, vomiting, shortness of breath, chest pain, depression, oral pain, or difficulty swallowing.

Physical Examination:
The patient's abdomen and trunk show scattered large erythematous plaques with overlying silvery scales. On the upper and lower back are large grey, hyperpigmented annular patches with mild scaling. Scattered erythematous plaques with silvery scale are also noted on the

patient's elbows, and upper and lower legs bilaterally. A neurological exam shows decreased tactile sensitivity in a stocking and glove distribution.

Laboratory Data:
The following were negative or within normal limits:
Complete blood count with differentials, basic metabolic panel and liver function test, serum angiotensin converting enzyme level, Glucose-6-phosphate dehydrogenase level, urinalysis, and Quantiferon gold

Histopathology:
05/16: Left superficial peroneal nerve – National Hansen's Disease Clinic: Hansen's disease, lepromatous (lepromatous leprosy-borderline lepromatous), active. Polymerase chain reaction assay for *Mycobacterium leprae* DNA is positive

06/16: Left scapula skin – National Hansen's Disease Clinic: Chronic inflammatory infiltrates replace approximately 15% of the dermis. These are composed of disorganized aggregates of lymphocytes and histiocytes at all levels of the dermis. Fite stains reveal small numbers of acid fast organisms consistent with tuberculoid leprosy.

06/16: Right trunk skin – University of Illinois at Chicago: Lesion shows psoriasiform dermatitis without granulomas. Fite stain shows no microorganisms, periodic acid–Schiff and Gomori methenamine silver stain do not show definitive fungal elements.

Diagnosis:
Hansen's disease – lepromatous leprosy

Treatment Course:
The patient was started on minocycline 100 milligrams once daily, rifampin 600 milligrams once a month, dapsone 100 milligrams daily, and prednisone 60 milligrams tapered every two weeks by 10 milligrams. He noted improvement of the numbness in his feet bilaterally.

Discussion:
Leprosy, also known as Hansen's disease, is a chronic infection of the skin and peripheral nerves caused by *Mycobacterium leprae*. Although its coexistence with psoriasis is extremely rare, the two diseases shared a similar classification in ancient times. Recent publications suggest that genetic factors, reinforced innate immunity and the role of neuropeptides and apoptosis may have an impact on the rarity of this coexistence. In a global survey conducted by Kumar et al of 145,661 cases of leprosy, only 20 individuals had psoriasis. This corresponds to a psoriasis prevalence of 0.014%, two orders of magnitude lower than the expected for the world population.

Several findings serve to illustrate the seemingly disparate nature of the two diseases. *Mycobacterium leprae* invades nerves, causing nerve damage, which results in neuritis and hypoesthesia of the skin. Psoriasis on the other hand, requires intact nerves, with studies showing the functional role of cutaneous nerves and their neuropeptides in the pathogenesis of psoriasis. Previous nerve damage decreases neurogenic inflammation, which can inhibit psoriatic plaque formation. Genetic studies have shown the association of HLA-DR2 and HLA-DQW1 with leprosy, but HLA-B13 and HLA-B17 with psoriasis. It has also been noted that thick psoriatic plaques may be the result of decreased apoptosis, whereas in leprosy an increase in spontaneous apoptosis is often seen. All above findings support the hypothesis that psoriasis and leprosy are almost mutually exclusive.

However, our patient presents with this rare coexistence. Recent studies published by Bassukas et al pose a new hypothesis that psoriasis may have the propensity to protect against the development of clinical leprosy through an overstimulation of the innate immunity and an amplification of the antibacterial defense mechanisms. The Th1 response is heightened in the skin of psoriasis patients, which may be responsible for local control of *M. Leprae.* Even though our patient travelled frequently to areas where leprosy is endemic and may have contracted the disease early on, the signs and symptoms of leprosy were not present while he had more aggressive psoriasis. He manifested with leprosy only after undergoing treatment for psoriasis. However, to completely support the hypothesis, one will need to pursue genetic and additional testing for confirmation.

Essential Lesson:

- Leprosy and psoriasis are almost mutually exclusive diseases due to genetic, immune and cell mediated factors.
- Leprosy is associated with HLA-DR2 and HLA-DQW1, psoriasis is associated with HLA-Cw6, HLA-B13, and HLA-B17.
- Psoriasis may protect against the development of clinical leprosy through overstimulation of the innate immunity, amplification of the antibacterial defense mechanisms, and a heightened Th1 response.

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Case 9

Case Presented by Mark Juhl, MD, Michael Sotiriou, MD and Maria M. Tsoukas, MD, PhD

History of Present Illness:
A 35 year old male presented for a facial rash of six months duration. He described several small papules, initially on the left chin, which progressively enlarged. He subsequently developed similar lesions on the scalp and cheek. The lesions were mildly pruritic but otherwise asymptomatic. He reported shaving, but denied other forms of trauma, sick contacts, or recent travel.

Past Medical History:
Asthma and hypertension

Medications:
Albuterol and furosemide

Allergies:
No known drug allergies

Family History:
No history of skin cancer

Social History:
The patient smoked cigarettes daily with a ten pack-year history. He drank a quart of vodka weekly, smoked marijuana occasionally, and reported unprotected sex with multiple partners, both male and female.

Review of Systems:
The patient denied fevers, chills, weight loss, diarrhea, headaches, stiff neck, abnormal gait, and numbness.

Physical Examination:
The mentum and submentum has a large, crusted, eroded, and indurated verrucous plaque with a raised border and draining purulent material. Similar boggy plaques are noted on the left cheek and left scalp. There is no regional lymphadenopathy.

Laboratory Data:
The following were positive or abnormal:
Human immunodeficiency virus antibody screen: reactive
Human immunodeficiency virus, quantitative: 910 copies/ml
Rapid plasma reagin, qualitative: reactive
Rapid plasma regain, quantitative: 1:128 dilutions
Tissue culture for aerobic bacteria: Methicillin-resistant *Staphylococcus aureus* and *Citrobacter koseri*

The following were negative or normal:
CD4 Count: 607 cells/µl (normal 500-1500 cells/µl)
Quantiferon gold
Tissue culture for anaerobic bacteria, fungal, viral, and atypical mycobacteria

Histopathology:
Chin, skin: Pseudoepitheliomatous hyperplasia with dense dermal acute and chronic inflammation, composed of neutrophils, lymphocytes, and prominent plasma cells. Gomori methenamine silver, Fite, and treponemal immunostaining were negative. A gram stain showed gram-positive cocci in clusters.

Diagnosis:
Blastomycosis-like pyoderma

Treatment Course:
Based on sensitivities, a 14 day course of doxycycline was initiated. Simultaneously, he was referred to infectious disease for treatment of concurrent syphilis with benzathine penicillin G and human immunodeficiency virus with antiretroviral therapy. Skin lesions completely resolved after five weeks.

Discussion:
First described in 1903 as “pseudoepiteliomas cutanés,” blastomycosis-like pyoderma (BLP) is a chronic pyoderma that presents similarly to vegetating deep fungal infections. It typically presents as one or multiple vegetating nodules and/or plaques on the extremities of middle aged to elderly adults. Necrosis, pustules, fistulae, and abscesses may also be present. Minor trauma and sun-damaged skin are thought to increase the likelihood of BLP. This entity potentially represents an exaggerated inflammatory reaction due to immune dysregulation and an underlying, prolonged pyogenic bacterial infection. The most commonly reported pathogen is *Staphylococcus aureus*; additionally, β-hemolytic streptococci, certain gram-negative bacteria including *Pseudomonas aeruginosa,* and members of the enterobacteriaceae family, notably citrobacter species, have been reported. Mixed bacterial infections have rarely been reported in BLP.

Proposed diagnostic criteria in recent literature for the diagnosis of BLP include: (1) large verrucous plaques with multiple pustules and an elevated border, (2) typical histologic findings of psudoepitheliomatous hyperplasia with abscesses on biopsy, (3) growth of one or more pathogenic bacteria, and (4) negative cultures for other infectious etiologies.

Many patients with this entity have decreased immunologic resistance to bacterial infections due to diagnoses including human immunodeficiency virus, as seen in our patient, malnutrition, alcoholism, leukemia, immunosuppressant use, and/or radiation therapy. Monotherapy with systemic antibiotics requires long-term treatment and often fails. Our patient’s immune status was not only compromised by an untreated human immunodeficiency virus (HIV) infection, but also by a concurrent syphilitic infection. Syphilis has been reported to cause immune dysregulation including, but not limited to, altered cell surface markers and increased likelihood of HIV co-infection. Our patient’s rapid and complete response to doxycycline and penicillin is unusual for BLP. This raises the hypothesis that the concurrent syphilitic infection may have contributed to immune evasion by these bacteria. Treatment of the concurrent syphilis may have hastened the resolution of his BLP.

Due to the rarity of this entity, no controlled trials have been completed, but additional treatments with varying results have been reported including curettage, surgical excision, carbon dioxide laser, potassium iodide, permanganate soaks, radiotherapy, disodium chromoglycate, and acitretin. Effective treatment with systemic retinoids, as well as combination of trimethoprim-sulfamethoxazole and cryotherapy, have been reported.

Essential Lesson:

- Blastomycosis-like pyoderma should be included in the differential diagnosis of large verrucous plaques.
- If Blastomycosis-like pyoderma is diagnosed, an emphasis should be placed on discovering and treating any underlying immunodeficiency.

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Case 10

Case Presented By Eden Lake, MD,
Lawrence S. Chan, MD and Maria M. Tsoukas, MD, PhD

History of Present Illness:
This 24 year old female presented with several months of a progressive scalp ulcer. The scalp ulcer began in 2012 as a coin-shaped lesion, and was initially diagnosed as discoid lupus erythematosus based on biopsy results by an outside physician. She was treated with topical triamcinolone cream which was not effective. A few months prior to presentation at our hospital, the patient noted skin lesions on the back, arms and face. She presented to the emergency department due to increased pain and purulence from the scalp lesion.

Past Medical History:
Self-reported history of lupus

Medications:
None prior to the current diagnosis

Allergies:
No known drug allergy

Review of Systems:
The patient denied fevers, chills, weight loss, changes in urination, easy bruising, fatigue, but did notice intermittent left upper quadrant pain.

Physical Examination:
The patient's scalp is superficially debrided revealing an erythematous, eroded, boggy scalp that is very tender to palpation. The remaining scalp shows crusting and scale adherent to the residual hair, with yellow to brown debris. Her face has few erythematous papules and hyperpigmented macules. There is no conjunctival injection of the eyes and no erosions or erythema of the oral mucosa. The bilateral extensor arms have erythematous, hyperpigmented macules and patches as well as crusted plaques and few flaccid bullae, one which shows a positive Nikolski sign. The bilateral anterior lower extremities have erythematous crusted plaques. The lower abdomen has one large erythematous erosion as well as hyperpigmented macules and patches and one violaceous plaque with overlying crust. The upper to mid-back has erythematous, violaceous, and hyperpigmented patches and eroded plaques, some with overlying hemorrhagic crust. Some macules and patches are annular in configuration with a hyperpigmented rim and central hypopigmentation. The upper back has few flaccid, slightly erythematous bullae.

Laboratory Data:
The following were positive or abnormal:
Complement 3 elevated to 177 mg/dl (normal 79-152)
Erythrocyte sedimentation rate elevated to 55 mm/hr (normal 0-20)
Enzyme Linked Immunosorbent Assay:
IgG Desmoglein 3 antibodies: elevated to 69 units (normal <20)
IgG Desmoglein 1 antibodies: elevated to 340 units (normal <20)

The following were negative or within normal limits:
Antinuclear antibody, antibodies to dsDNA, ssDNA, Smith, SSA, SSB, RNP.
Complete blood count, basic metabolic profile, urinalysis, HIV antibody, hepatitis acute panel and Quantiferon Gold assay. Blood culture had no growth

Diagnostic Procedures and Tests:
05/16 X-ray, Skull Partial: Negative for osseous destruction to suggest osteomyelitis

Histopathology:
Right scalp, skin (hematoxylin and eosin stain): Suprabasilar and intraepidermal acantholysis with no interface or basal vacuolar changes. Herpes simplex virus and periodic acid–Schiff stains are negative.

Right forearm, skin (direct immunofluorescence): 3+ granular IgG deposition along the dermal epidermal junction; 2+ intraepidermal IgG intercellular deposition. 2+ speckled to granular deposition of C3 along the dermoepidermal junction. 1-2 + fibrinogen is seen around blood vessels.

Diagnosis:
Pemphigus erythematosus (Senear-Usher Syndrome)

Treatment Course:
The patient was treated with systemic steroids during her hospitalization. She received intravenous vancomycin and oral clindamycin for superimposed infection of the scalp with methicillin-resistant *Staphylococcus aureus*. Upon discharge from her first hospitalization the patient was prescribed oral prednisone 60 milligrams daily, which she took for one month. She was asked to return for follow-up but could not due to lack of insurance. Instead, she presented to the emergency department after six weeks, seeking further treatment. She had improved with the prednisone but was observing recurrence. No additional medications could be started also due to lack of insurance, and the patient had not been able to return to clinic for treatment or laboratory monitoring. At her most recent visit, upon obtaining insurance coverage, the workup was initiated to start her on a steroid-sparing immunosuppressant such as azathioprine.

Discussion:
Pemphigus erythematosus (PE) was first described in 1926 by Dr. Senear and Dr. Usher in a case series of 11 patients. The case series demonstrated an overlapping clinical presentation of pemphigus foliaceus (PF) and lupus erythematosus, seen in middle-aged patients with higher prevalence in females. Clinically the patient often has malar involvement that mimics a severe seborrheic dermatitis with well-defined erythematous, scaly, crusted plaques. Non-facial lesions may begin as small, flaccid bullae with a positive Nikolsky sign, favoring the upper trunk and face, although lesions have been reported to extend to the feet. Lesions often resolve with hyperpigmentation. Consistent with the clinical findings in PF, mucosal involvement in PE is rare. Our patient has an unusual presentation with significant scalp involvement and lack of a prominent facial seborrheic or malar dermatitis.

Diagnosis of PE is made with direct immunofluorescence (DIF) demonstrating immunoglobulin G (IgG) and complement deposition both intercellularly and at the dermoepidermal junction (DEJ), along with the clinical and pathological findings of pemphigus foliaceus. This DEJ deposition (defined particularly in non-lesional skin) is occasionally referred to as a lupus band. Complement at the basement membrane may be seen in PF, however the presence of immunoglobulins at the junction is rare. While antinuclear antibody serology is positive in 30-

80% of patients, PE patients rarely meet the diagnostic criteria for systemic lupus erythematosus. Cases have been reported with normal lupus serologies, normal complement studies, and normal inflammatory markers. Enzyme Linked Immunosorbent Assay serology is also helpful, often yielding positivity for both antibodies to desmoglein 1 and desmoglein 3, as seen in our patient. Histopathology alone demonstrates acantholysis within the superficial epidermis, consistent with PF.

There is an academic debate regarding the significance and etiology of the linear deposition of IgG and complement at the DEJ. Both PE and PF have been reported to have severe exacerbations with ultraviolet (UV) exposure. It has been demonstrated that *in vivo* high doses of UV exposure can induce cleavage of the desmoglein 1 ectodomain, and in PF the auto-antibodies to desmoglein 1 can precipitate the cleaved ectodomain along the basement membrane, resulting in DEJ deposition. These findings may be present on only UV-exposed sites in a patient with PE. This same finding can be seen in other forms of cutaneous lupus, with DEJ deposition present on sun-exposed lesional skin but not on sun-exposed non-lesional skin.

PE is often easier to manage than pemphigus vulgaris. Treatments such as systemic prednisone as well as topical corticosteroids, and dapsone may be particularly effective. Other potential treatments include methotrexate, cyclophosphamide and azathioprine. Avoidance of UV exposure is critical for the overall management of both PE and PF.

Essential Lesson:

- Senear-Usher syndrome (pemphigus erythematosus) is a rare variant of pemphigus foliaceus with deposition of IgG and/or complement at the basement membrane seen on direct immunofluorescence.
- The treatment consists of systemic steroids, dapsone, and/or immunosuppressants. Ultraviolet protection is critical to management.

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Presented by Monica Boen, MD
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UPDATE

We presented a case of Acrodermatitis Continua of Hallopeau to CDS in 2014. This is a brief update on his care.