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**

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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

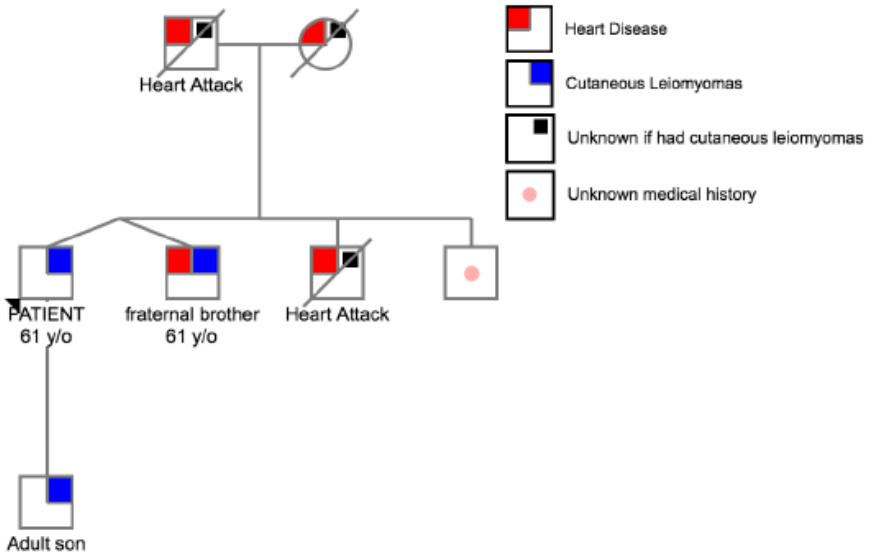
MEDICATIONS

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
and Maria M. Tsoukas, MD, PhD

UPDATE

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

CHICAGO DERMATOLOGICAL SOCIETY **Case #1**

Presented by Sreya Talasila, MD and Joaquin Brieva, MD
Department of Dermatology, Feinberg School of Medicine, Northwestern University

HISTORY OF PRESENT ILLNESS

A 50-year-old previously healthy Caucasian female was referred to dermatology for evaluation of a pruritic, faintly erythematous truncal eruption present for 4 months. Concurrently, she had been following with hepatology for work-up of incidentally noted transaminitis on routine blood work, the etiology of which was suspected to be autoimmune hepatitis and for which she was being treated with a prednisone taper.

On review of systems, she reported previous development of painful vaginal lesions several months prior. She had been diagnosed with candidal vaginitis and treated with an oral antifungal without improvement. She was eventually prescribed valacyclovir, and the lesions resolved.

PAST MEDICAL HISTORY

Degenerative joint disease

SOCIAL HISTORY

Married, reports being in a monogamous relationship with her husband

MEDICATIONS

Multivitamin

PHYSICAL EXAM

Upper extremities and trunk with faintly erythematous, monomorphic, vaguely annular macules and patches. Palms and soles clear. Oral cavity clear.

LABS/IMAGING

Abnormal:

Labs: ALT 101 (ref. 8-40), AST 67 (ref. 8-40), alkaline phosphatase 611 (ref. 33-115), GGT 196 (ref. 3-55), anti-treponemal antibody positive, RPR 1:1024

Ultrasound abdomen: The liver demonstrates heterogeneous echotexture with a focal area of decreased echogenicity within the posterior segment of the right lobe measuring 2.8 cm.

MRCP: Multiple lesions with a "target" appearance are present throughout both lobes of the liver. The diagnostic considerations include metastatic lesions.

CT abdomen: Multiple heterogeneously enhancing hepatic masses representing metastases until proven otherwise. A less likely diagnosis is hepatic vasculitis.

PET/CT: There are multiple hypermetabolic lesions scattered throughout the liver, most numerous in the right lobe. These have very increased metabolic activity consistent with multiple hepatic metastases. There is no definite localization of a primary malignancy.

Normal/Negative: CBC, BMP, total bilirubin, direct bilirubin, total protein, CRP, ESR, ANA, hepatitis A/B/C serologies, HIV Ag/Ab, leptospira IgM, Lyme DNA, *Borrelia burgdorferi* IgM and IgG

HISTOPATHOLOGY

Skin biopsy: Mild interface and perivascular dermatitis. Immunohistochemistry for anti-treponemal antibody is negative.

Liver biopsy: Liver parenchyma with necrotizing scarring nodules, acute inflammation characterized by a lymphoplasmacytic infiltrate and focal necrosis, consistent with inflammatory pseudotumor-gummatous lesions. *Treponema pallidum* immunostaining was positive for spirochetal bacteria, supporting the diagnosis of spirochetal bacteria-associated gumma.

DIAGNOSIS

Tertiary hepatic syphilis overlapping with secondary cutaneous syphilis

TREATMENT AND COURSE

The patient was treated with 14 days of IV penicillin G followed by 7 days of IM penicillin G given concern for neurosyphilis (due to patient's report of vision changes). Her cutaneous findings quickly resolved. There was significant interval resolution of hepatic lesions on follow-up imaging.

DISCUSSION

Syphilis is a sexually transmitted disease caused by the spirochete *Treponema pallidum*. Syphilis progresses through four stages, which represent a continuum, and symptoms of different stages may overlap.

Primary syphilis typically presents as a painless solitary chancre at the site of inoculation 10-90 days after exposure. The chancre resolves spontaneously in one to four months. Without treatment, blood-borne spread of *T. pallidum* results in secondary syphilis, which presents weeks to months after the chancre appears. The skin is most frequently affected with a symmetric erythematous macular and papular rash on the trunk and proximal extremities, including the palms and soles. Condylomata lata are also associated with secondary syphilis, which presents as soft, verrucous plaques on mucosal surfaces. During the latent stage, skin lesions resolve, however serologic tests remain positive. Tertiary or late syphilis develops years after the initial infection and can involve any organ system. Cutaneous tertiary syphilis manifests with gummatous lesions (papules, nodules, and papulonodules that commonly ulcerate). Gummas, which histologically are seen as granulomas, result from a delayed hypersensitivity reaction to the spirochete.

CNS involvement can occur during any stage of syphilis. If clinical evidence of neurologic involvement is present, a CSF examination should be performed. Syphilitic uveitis is common, and an ophthalmologic evaluation should be performed for any ocular complaints. Hepatic involvement is rare in tertiary syphilis. The clinical picture can be mistaken for hepatic metastasis, as in this case.

The clinical conundrum with this patient is the timing of her infection. There are cases reported of late syphilis presenting only 1 year after infection. This patient may have had accelerated tertiary syphilis due to immunosuppression secondary to her treatment with prednisone. This has not been previously reported in the literature. However, syphilis is known to progress rapidly in patients with HIV, so it is conceivable that other means of immunosuppression would result in more rapid progression to tertiary syphilis.

KEY POINTS

1. Syphilis is a "great mimicker" with protean cutaneous manifestations.
2. Syphilis may progress rapidly through its four stages, which overlap, in immunosuppressed patients.

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CHICAGO DERMATOLOGICAL SOCIETY **Case #2**

Presented by Brittany Dulmage, MD and Ahmad Amin, MD
Department of Dermatology, Feinberg School of Medicine, Northwestern University

HISTORY OF PRESENT ILLNESS

A 29-year-old African American female presented with a 1-month history of pruritic papules that started on her arms and spread to her face and legs, which were pronounced within her tattoos. She also endorsed nausea, hot flashes, fatigue, and mild shortness of breath.

PAST MEDICAL HISTORY

None

MEDICATIONS

None

PHYSICAL EXAM

Bilateral eyebrows and glabella have prominent, deeply indurated skin folds leading to a leonine appearance. Prominent madarosis of the bilateral lateral eyebrows. Innumerable tightly clustered 1-3 mm skin-colored to pink, indurated, firm, monomorphic papules over the arms, legs, and back.

LABS/IMAGING

Abnormal: SPEP and immunofixation showed monoclonal protein IgG lambda
Normal/Negative: CBC with differential, CMP, CPK, UPEP, hepatitis panel, ANA, TSH, HSV serologies, echocardiogram, bone marrow biopsy, bone survey

HISTOPATHOLOGY

The epidermis is unremarkable. Within the reticular dermis, there is a proliferation of haphazardly arranged prominent fibroblasts embedded in a myxoid stroma. Colloidal iron stain demonstrates dermal deposits of acid mucopolysaccharides.

DIAGNOSIS

Scleromyxedema

TREATMENT AND COURSE

The patient was started on bortezomib and methylprednisolone therapy with improvement in her skin and stabilization of immunoglobulin levels. To ensure durable disease control, she plans to undergo autologous hematopoietic stem cell transplantation.

DISCUSSION

Scleromyxedema is a cutaneous mucinosis that is characterized clinically by a generalized papular and sclerodermoid eruption in the setting of a monoclonal gammopathy. Histopathological features of scleromyxedema include mucin deposition, increased spindle-like fibroblast proliferation, and fibrosis. Additionally, diagnosis of scleromyxedema requires the absence of thyroid dysfunction. Middle-aged adults are most commonly affected, and the disease does not have a predilection for either gender.

Patients with scleromyxedema almost universally present with 2-3 mm, tightly spaced papules involving the hands, neck, and head, particularly the glabella and post-auricular areas. Without

treatment, papules will continue to appear and may coalesce. Unlike scleroderma and scleredema, there are no focal areas of sparing in advanced disease. Involved skin in scleromyxedema may be indurated leading to additional typical clinical features of leonine facies, microstomia, and the "donut sign" over affected proximal interphalangeal joints. Affected skin may be, but is not always, intensely pruritic.

Paraproteinemia, typically IgG lambda, is observed in more than 80% of patients with scleromyxedema. When features of scleromyxedema are present but a monoclonal protein is not detected, localized papular mucinosis should be considered. An atypical variant of scleromyxedema lacking a detectable monoclonal protein has also been proposed. A case of scleromyxedema with monoclonal protein detection in lesional skin but not peripheral blood has also been reported.

Dysphagia with reduced proximal esophageal motility or aperistalsis as well as myopathy are commonly reported systemic manifestations of scleromyxedema. Fatal cases of scleromyxedema due to systemic involvement have also been reported including cardiopulmonary failure in the setting of mucin deposition in coronary and pulmonary vessels and myocardium. Fatal central nervous system (CNS) involvement including encephalopathy, seizures, and coma has been reported with unknown etiology and no mucin deposition identified in CNS tissues.

Historically suggested first-line treatments include melphalan, systemic corticosteroids, and plasmapheresis. More recently, reported cases have been treated with thalidomide, lenalidomide, bortezomib, IVIG, and autologous stem cell transplantation. Bortezomib is a proteasome inhibitor which induces cell-cycle arrest and apoptosis of plasma cells. In a case series of 13 patients treated with IVIG, all showed complete or partial response; however, the effect of IVIG is temporary with return of disease in the absence of maintenance therapy.

KEY POINTS

1. Diagnosis of scleromyxedema is made in patients with a papular cutaneous eruption, monoclonal gammopathy, and no thyroid dysfunction who have a skin biopsy showing mucin deposition, increased collagen and spindle-like fibroblasts.
2. Subsets of patients with scleromyxedema will develop systemic symptoms including possibly fatal cardiopulmonary or CNS involvement.
3. Treatment options for scleromyxedema include bortezomib, thalidomide, lenalidomide, IVIG or autologous stem cell transplantation.

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CHICAGO DERMATOLOGICAL SOCIETY **Case #3**

Presented by Amin Esfahani, MD[1], Cristina Isales, MD[2], Lacey Kruse, MD,[3] and Pedram Gerami, MD[1]
[1]Department of Dermatology, Feinberg School of Medicine, Northwestern University
[2]Department of Pathology, Feinberg School of Medicine, Northwestern University
[3]Division of Dermatology, Ann & Robert H. Lurie Children's Hospital of Chicago, Feinberg School of Medicine, Northwestern University

HISTORY OF PRESENT ILLNESS

A full-term 3-month-old African American girl presented with a growth on the scalp. The lesion was first noted at birth and was initially thought to be a keloid. Her parents noted that the growth had gradually enlarged over the past three months of life. The patient was otherwise healthy.

PAST MEDICAL HISTORY

Born at 39 weeks via Cesarean section for transverse lie

MEDICATIONS

None

FAMILY HISTORY

No family history of skin cancer

PHYSICAL EXAM

13 cm hyperpigmented, hypertrichotic thin plaque on the left temporal, parietal, and occipital scalp. Within this plaque, on the left parietal scalp, there was a 4.8 cm x 2.5 cm firm, hyperpigmented lobulated exophytic nodule.

HISTOPATHOLOGY

Left parietal scalp: malignant melanoma, Breslow depth 2.75 mm, Clark's level IV, without ulceration, mitotic count of 12/mm^2

- Fluorescence *in situ* hybridization (FISH) showed segmental chromosomal aberrations in 6p25 in greater than 80% of enumerated cells
- Genetic testing significant for an activating mutation in pathogenic variant of *NRAS*

Left scalp: intradermal nevus, congenital type

PRELIMINARY DIAGNOSIS

Malignant melanoma arising within a large congenital melanocytic nevus

TREATMENT AND COURSE

The patient underwent a wide local excision (WLE), repaired with a split-thickness skin graft, and sentinel lymph node biopsy. Histopathology of the WLE revealed a Breslow depth of 8mm. A proliferative nodule was also noted in this specimen. Two out of five sentinel lymph nodes were positive for malignant melanoma (largest deposit 1.3 mm x 0.2 mm). PET-CT demonstrated increased metabolic activity in the left posterior cervical lymph node basin concerning for metastatic lymphadenopathy, with no other metabolically active foci. Lymph node dissection was performed, with two out of twenty-eight lymph nodes showing melanoma micrometastases. On follow-up exams, a mobile <1cm lymph node was noted on the left occipital scalp, which has been clinically stable. The patient's current staging is T4aN2bM0 (Stage III). However, repeat PET-CT from late October 2016 was concerning for progressing metastatic disease. Currently, various treatment options including chemotherapy and immunotherapy, in addition to excision of the remainder of the congenital melanocytic nevus, are in consideration.

DISCUSSION

Congenital melanocytic nevi (CMN) are present in 1-6% of neonates. They are more common in individuals with skin phototypes III-VI. CMN are commonly categorized according to size. The current classification system divides CMN into four categories based on the largest predicted diameter in adulthood. In this classification system, small CMN are defined as less than 1.5 cm in largest diameter; medium as 1.5-20 cm; large as 20-40 cm and giant as > 40 cm in diameter. Since CMN enlarge proportionally to a child's growth, a good rule of thumb for estimating the increase in diameter from infancy to adulthood is to multiply the size of lesions on the head of a newborn by a factor of two and those on other anatomic sites by a factor of three. Genetically, large and giant CMN exclusively harbor somatic gain-of-function mutations in *NRAS*, and the proportion of *BRAF* mutations increases with reduction in size of the CMN. On histopathology, when compared to acquired nevi, CMN demonstrate nevomelanocytes that tend to extend deeper into the dermis and subcutaneous tissue. These melanocytes often track along or within neurovascular and adnexal structures. The three major complications of CMN include melanoma, proliferative nodules and neurocutaneous melanosis (NCM). All three complications are most commonly associated with large and giant CMN.

NCM is a rare complication of CMN related to leptomeningeal and CNS melanosis. The risk of NCM is highest in those with CMN larger than 40 cm in final size, CMN located in the posterior axial position, patients with multiple satellite nevi, or individuals with numerous medium-sized CMN. Limited evidence suggests that approximately 1-10% of patients with evidence of NCM on imaging develop neurological symptoms such as developmental delay, seizures and hydrocephalus. Symptoms present at a median age of 2 years. The preferred imaging modality is MRI with gadolinium. The age at which imaging should be performed is controversial, but the traditional recommendation is six months of age. Prognosis in symptomatic patients is poor.

The lifetime risk of melanoma in small and medium-sized CMN is considered to be less than 1%. When melanoma does occur, it tends to present after puberty within the dermal-epidermal junction. For patients with large and giant CMN, the lifetime risk of developing cutaneous or extracutaneous melanoma is estimated to be between 2 and 5%, with greater than 50% of cases occurring within the first five years of life. Less than thirty cases of infantile (defined as diagnosed before the age of one) or congenital melanoma have been reported since 1925. Fifteen of these cases have been associated with CMN with the remainder classified as either *de novo* or from transplacental metastases. Given the high mortality associated with melanoma, it is critical to differentiate between malignant melanoma and proliferative nodules. Proliferative nodules are benign melanocytic proliferations, arising in congenital nevi in the newborn population with histologic and clinical appearance similar to that of a melanoma. Current evidence suggests that proliferative nodules are at least ten times more common than melanoma. As such, adjunctive studies including array comparative genomic hybridization (CGH) and FISH have been utilized to assist in differentiation. In general, segmental chromosomal aberrations have been observed in congenital melanomas.

There is limited evidence on the management of melanoma in the pediatric population. The majority of guidelines are derived from the adult literature. Generally, wide local excision is performed. As in adults, it is recommended that sentinel lymph node biopsy be performed in lesions with Breslow depth greater than 1 mm. There is very limited evidence on the use of adjuvant therapy in pediatric patients with stage III melanoma. The most commonly cited adjuvant therapy is Interferon-α2b. Options for children with distant metastases include enrollment in clinical trials and palliative radiation. Given the association with melanoma, close clinical follow-up of patients with large and giant CMN is recommended.

KEY POINTS

1. The three major complications of CMN are proliferative nodules, melanoma and neurocutaneous melanosis. All of these entities are most commonly seen with large and giant CMN.
2. Current evidence suggests that the lifetime risk of cutaneous or extracutaneous melanoma developing in association with a large or giant CMN is approximately 2-5%.
3. Three types of congenital melanoma exist: those associated with a congenital melanocytic nevus, *de novo* congenital melanoma, and transplacental metastasis. Less than 30 cases have been reported in the literature to date.
4. Differentiating between malignant melanoma and proliferative nodules arising in CMN in the newborn population is challenging and may require adjunctive modalities such as comparative genomic hybridization (CGH) and fluorescence *in situ* hybridization (FISH) to aid in diagnosis.

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CHICAGO DERMATOLOGICAL SOCIETY **Case #4**

Presented by Kassandra Holzem, MD, Lauren Guggina, MD, and Jennifer Choi, MD
Department of Dermatology, Feinberg School of Medicine, Northwestern University

HISTORY OF PRESENT ILLNESS

A 77-year-old Caucasian male with chronic lymphocytic leukemia presented with a 3-month history of scattered cutaneous ulcerations. The lesions initially developed as multiple erythematous papules and nodules that subsequently ulcerated with purulent drainage. The patient reported mild associated pain without pruritus. Multiple skin biopsies and tissue cultures performed by outside providers were unrevealing. He had previously failed treatment with systemic corticosteroids, itraconazole, metronidazole, and piperacillin-tazobactam. He was subsequently transferred to Northwestern Memorial Hospital for further evaluation due to a 5-day history of declining mental status.

PAST MEDICAL HISTORY

Chronic lymphocytic leukemia, depression, gout, hyperlipidemia, hypertension, paroxysmal atrial fibrillation

MEDICATIONS

Allopurinol, colchicine, digoxin, escitalopram, ibrutinib

PHYSICAL EXAM

On the patient's face, trunk, and extremities, there were several scattered erythematous to violaceous fluctuant papulonodules and plaques ranging in size from 0.2 to 3 cm, as well as several eroded and verrucous erythematous to violaceous plaques.

LABS/IMAGING

Abnormal:

Labs: albumin 3.2 (ref. 3.5-5.7), quantitative IgG 388 (ref. 700-1600), quantitative IgA 58 (ref. 70-400)

MRI brain: well-circumscribed T1 hypointense and T2 isointense lesion in the posteromedial occipital lobe with peripheral enhancement and associated edema concerning for a cerebral abscess

Normal/Negative: CBC, BMP, AST, ALT, LDH, TSH, ACE, ANCA, quantitative IgM, T-cell monitoring panel, syphilis antibody, fungal blood culture, cutaneous gram stain, cutaneous bacterial culture, cutaneous fungal culture, cutaneous mycobacterial culture, EEG, and video EEG

HISTOPATHOLOGY

Outside surgical pathology interpretation: skin with suppurative periseptal and lobular panniculitis with scattered large cells with smudgy nuclei. Special stains, including DPAS, PAS, Giemsa, GMS, Gram, and AFB, were negative for microorganisms.

Dermatopathology interpretation: dermal abscess with tissue necrosis and large cells with smudgy nuclei and prominent nucleoli. Focal erythrophagocytosis was noted within these large cells. Special stains, including DPAS, PAS, Giemsa, GMS, Gram, and AFB, were negative for microorganisms.

Tissue PCR: *Acanthamoeba* spp.

DIAGNOSIS

Disseminated acanthamoebiasis

TREATMENT AND COURSE

Shortly after admission, tissue PCR results from a previously performed biopsy demonstrated *Acanthamoeba* spp. Empiric broad-spectrum antimicrobial therapy was initiated with clarithromycin, fluconazole, flucytosine, pentamidine, and sulfadiazine. The Centers for Disease Control and Prevention (CDC) was contacted, and miltefosine was added to the regimen. Despite aggressive management, the patient's mental status failed to improve, and he was ultimately discharged with hospice care.

DISCUSSION

Acanthamoeba is a free-living amoeba that is found worldwide in water and soil. It is a rare human pathogen and is one of only four such amoebae with the ability to cause disease. Infection with this organism typically affects the eye, nervous system, or skin and can lead to three main forms of illness, including *Acanthamoeba* keratitis, granulomatous amoebic encephalitis, and disseminated acanthamoebiasis.

Acanthamoeba keratitis most commonly occurs in healthy contact lens wearers due to poor contact lens hygiene. Though localized to the eyes, this form of disease can result in serious complications, including blindness. Granulomatous amoebic encephalitis (GAE) and disseminated acanthamoebiasis occur due to hematogenous spread following direct inoculation into broken skin or inhalation in an immunocompromised host. Mortality risk is high with disseminated disease and GAE.

Cutaneous disease can occur with disseminated acanthamoebiasis and GAE. Lesions are typically nonspecific, ulceronecrotic or verrucous plaques that may be painful or asymptomatic. The differential diagnosis is broad, and biopsy with tissue culture is essential to the diagnosis. Histopathologic evaluation reveals dense dermal histiocytic inflammation. Careful examination may reveal amoebic trophozoites within the infiltrate; however, these are frequently mistaken for histiocytes. Advanced techniques, such as PCR, should be employed if available.

No established treatment regimen for disseminated acanthamoebiasis exists. Miltefosine is a phosphocholine analogue that is available as an investigational drug from the CDC for treatment of infections due to free-living amoebae. Though the number of cases treated with a miltefosine-containing regimen is small, case series suggest a survival advantage. Clinicians caring for patients with suspected acanthamoebiasis should contact the CDC for guidance on diagnosis and management.

KEY POINTS

1. Disseminated acanthamoebiasis should be considered in the differential diagnosis of widespread cutaneous lesions that fail to respond to broad-spectrum antimicrobial agents.
2. Histopathologic diagnosis of *Acanthamoeba* infection is often difficult as amoebae are frequently misidentified as histiocytes. Tissue PCR should be employed if available.

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CHICAGO DERMATOLOGICAL SOCIETY **Case #5**

Presented by Steve Xu, MD, MSc (Lond.), Michael W Pelster, MD, and Anne Laumann, MBChB/MRCP (UK)
Department of Dermatology, Feinberg School of Medicine, Northwestern University

UNKNOWN

A 58-year-old female presented with skin changes of the left breast present since her 20s that worsened after a lumpectomy 4 years prior.

CHICAGO DERMATOLOGICAL SOCIETY **Case #6**

Presented by Lida Zheng, MD[1] and Anthony J Mancini, MD[2]
[1]Department of Dermatology, Feinberg School of Medicine, Northwestern University
[2]Division of Dermatology, Ann & Robert H. Lurie Children's Hospital of Chicago, Feinberg School of Medicine, Northwestern University

HISTORY OF PRESENT ILLNESS

A 3-day-old female was born at 38 weeks gestation with a large facial mass and disseminated deep cutaneous red to blue nodules. There was no history of maternal infection, and routine prenatal serologies for infection were unremarkable. The infant was diagnosed prenatally with a facial mass. Fetal MRI revealed that the mass seemed to arise from the left frontal lobe through a defect in the cribriform plate. Apgar scores were 8 and 9 at one and five minutes, respectively.

PHYSICAL EXAM

Vitals: afebrile, weight 3.7 kg (8 lbs 2.5 oz), head circumference 42 cm (including head mass)
HEENT: see skin exam below, no corneal opacities, normal ears
Cardiovascular: regular rate and rhythm, no murmurs
Abdominal: soft, no masses, no appreciable hepatosplenomegaly
Neurological: alert, normal tone
Lymph nodes: no lymphadenopathy
Skin: On the superior half of the forehead was a large, firm, multilobulated, exophytic, erythematous tumor with foci of necrosis. Over the scalp, face, trunk and extremities were numerous, deep red to blue, infiltrative papules and papulonodules, several with central necrosis and crusting.

LABORATORY

Abnormal: PTT 48 (ref. 31.1-38.6)
Normal/Negative: CBC, PT/INR, BMP, LFTs. Blood cultures negative. Mother and infant both A+ blood type. Maternal prenatal serologies/testing reported negative (varicella, rubella, CMV, and toxoplasmosis).

IMAGING

MRI Head/Brain: 4.5 x 7.0 x 10.3 cm facial mass with a thick peripheral-enhancing nodular component and central cystic necrosis without evidence of intracranial extension. Numerous enhancing nodules throughout the scalp, superficial and deep neck and visualized chest wall, mediastinum and upper extremities. Unremarkable MRI appearance of the brain, with no evidence of intracranial extension.

HISTOPATHOLOGY

Proliferation of undifferentiated small round blue cells with scant cytoplasm, hyperchromatic nuclei and prominent eosinophilic nucleoli infiltrating through the dermis and subcutaneous tissue. Mild pleomorphism was noted. Rare multinucleated giant tumor cells were noted as well as numerous apoptotic bodies and mitotic figures. Tumor cells stained strongly positive for desmin, myogenin, and myoD1. Sampled specimen was negative for PAX3-FOXO1 and PAX7-FOXO1 fusion transcripts by RT-PCR.

DIAGNOSIS

Congenital metastatic rhabdomyosarcoma, suspect alveolar subtype

TREATMENT AND COURSE

The patient's lesions rapidly enlarged in size and number. Further imaging also showed suspicious lesions of the paraspinal muscles, retroperitoneum, pancreas, splenic hilum, and hepatorenal fossa. She developed significant respiratory distress related to airway obstruction and was treated with non-invasive ventilatory support. Given the poorly differentiated nature of her tumor, limited reported responses of metastatic disease to chemotherapy, poor candidacy for surgical intervention, and multiple discussions with the family, the decision was made to pursue palliative care. The patient died at 17 days of age.

DISCUSSION

Rhabdomyosarcomas (RMS) are primitive mesenchymal cell-derived tumors of striated muscle origin which represent approximately 3-4% of all childhood cancers. Although uncommon, they make up half of all pediatric soft tissue sarcomas. The majority of RMS present in childhood, typically between the ages of 2-6 years. Only 1-2% of RMS are congenital, and 5-10% occur prior to age 1. The most common primary sites are the head and neck, genitourinary tract, and the extremities. The primary symptoms usually relate to mass effect on the affected region. There are several subtypes of RMS: alveolar (the suspected subtype in this case), embryonic (including the botryoid variant), and anaplastic (formerly called pleomorphic). RMS may occasionally be associated with neurofibromatosis type 1, Li-Fraumeni syndrome, Noonan syndrome, Beckwith-Wiedemann syndrome and Costello syndrome. Notably, patients with neurofibromatosis type 1 have a 20-fold increased risk of RMS.

Histologic evaluation is required for diagnosis. Pathology reveals small, round, blue cells that stain positively for desmin, myogenin, and/or myoD1. Of the histological subtypes, the alveolar subtype shows stronger myogenin and myoD1 staining. The alveolar subtype represents 20-30% of RMS, and a substantial proportion (25-30%) present with metastatic disease. Alveolar subtype RMS also characteristically exhibit a chromosomal translocation of t(2;13) or t(1;13) to generate a fusion gene of PAX3 or PAX7 and FOXO1; however, 20% are fusion gene negative.

Multidisciplinary treatment protocols (surgery, radiation, and chemotherapy) have improved the outcome of children with RMS over the last 30 years. The 5-year survival rate has improved from 53% in 1975 to 67% in 2010. Patients are stratified into risk groups to guide treatment, which is determined by stage, site, size, the age of the patient, and histology.

Neonatal RMS is particularly challenging, especially if local control via surgical resection is not feasible. Both ages <1 year and > 10 years have been independently associated with a poorer prognosis. Metastasis, alveolar subtype, and ulceration of lesions (indicating rapid growth) are also associated with a worse prognosis. Favored sites of metastatic spread are the lungs, followed by the bone marrow, lymph node and bones. The 5-year event-free survival of patients with alveolar subtype is 40%, compared to 70% for the embryonic subtype. Increased rate of metastases is thought to contribute to the worse prognosis seen with alveolar subtype RMS.

The differential diagnosis of congenital RMS with cutaneous metastases mirrors that of a "blueberry muffin" baby, the description classically applied to newborns presenting with diffuse violaceous to blue, non-blanching papules and nodules secondary to extramedullary hematopoiesis or a diffusely metastatic malignancy. Infectious etiologies include neonatal toxoplasmosis, rubella, cytomegalovirus, herpes simplex virus, and Epstein Barr virus. Malignancies that may present in this fashion include cutaneous metastases from neuroblastoma, leukemia, and sarcomas like RMS. Blueberry muffin lesions can also be seen in primary disorders of red blood cells, including erythroblastosis fetalis and in patients with Langerhans cell histiocytosis. Additional diagnostic considerations include multifocal lymphoangioendotheliomatosis with thrombocytopenia and blue rubber bleb nevus syndrome. In a study examining post-mortem

cutaneous metastases of non-hematopoietic cancers, the most likely pediatric tumors to metastasize to the skin were RMS and neuroblastoma, both of which are more likely than their adult counterparts to disseminate to multiple cutaneous sites.

KEY POINTS

1. Pediatric rhabdomyosarcoma is an aggressive soft tissue sarcoma that can rarely present with localized skin involvement or disseminated cutaneous metastases.
2. The congenital alveolar subtype of pediatric RMS is an extremely aggressive form of this tumor, with few long-term survivors.
3. The newborn baby presenting with multiple red or blue cutaneous nodules ("blueberry muffin" baby) merits prompt evaluation with skin biopsy and consideration of a variety of infectious and neoplastic disorders.

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CHICAGO DERMATOLOGICAL SOCIETY **Case #7**

Presented by Elisha Singer, MD, Sarah Adams, MD, and Jennifer Choi, MD
Department of Dermatology, Feinberg School of Medicine, Northwestern University

HISTORY OF PRESENT ILLNESS

A 60-year-old female with a history of a malignant islet cell tumor of the pancreas was referred for evaluation of a cutaneous eruption of eight months duration. She described the eruption as pruritic, inflamed, and at times oozing and painful. Initially located on her bilateral legs, the eruption subsequently spread to her bilateral thighs, elbows, and ultimately the perianal and genital skin. She also complained of dry, cracked lips at the corners of her mouth. Previous transiently successful treatments included intramuscular triamcinolone acetonide and a methylprednisolone dose pack. On review of systems, the patient noted a six-pound weight loss over the preceding four months; she denied fevers, fatigue, drenching night sweats, diarrhea or joint pains.

PAST MEDICAL HISTORY

Malignant islet cell tumor of the tail of the pancreas s/p distal pancreatectomy and splenectomy, followed by recurrent metastatic disease to liver and peri-aortic lymph nodes
Ductal carcinoma in situ of the right breast s/p right mastectomy and tamoxifen therapy
DVT/PE
Supraventricular tachycardia
Type 2 diabetes mellitus
Hypothyroidism

MEDICATIONS

Enoxaparin, diltiazem, levothyroxine, insulin glargine, glipizide, prochlorperazine

SOCIAL HISTORY

Married with two children. Denied tobacco, alcohol or drug use.

PHYSICAL EXAM

The patient was a well-appearing female in no acute distress. The extensor surfaces of the thighs and legs, as well as the perianal and genital region were noted to have erythematous patches and thin plaques with overlying exfoliative, "flaky-paint" scale. There were thin fissures at the lateral commissures of the mouth. No cervical, axillary or inguinal lymphadenopathy was palpable.

LABS

Abnormal: glucose 329, chromogranin A 119 (ref. <15), glucagon 618 (ref. <134)
Normal/Negative: vitamin B1, vitamin B6, vitamin B12

HISTOPATHOLOGY

The epidermal surface revealed a layer of epidermal necrosis with parakeratotic strands. Beneath this, there was underlying orthokeratosis, a reactive epidermis, and scattered necrotic cells.

DIAGNOSIS

Necrolytic migratory erythema

TREATMENT AND COURSE

The patient's necrolytic migratory erythema was successfully controlled with 20 mg of prednisone daily for two weeks. However, upon discontinuation, she developed recrudescence of her cutaneous eruption necessitating chronic, low-dose steroid therapy with prednisone 10 mg daily, which led to significant control of her skin disease. Her malignant islet cell tumor was initially treated with long-acting octreotide followed by radioembolization therapy to her liver metastases; however, given progression of her disease, she was transitioned to everolimus. She subsequently developed new metastatic disease to her T9 vertebral body and was therefore started on sunitinib malate, but given intolerance to this, she was switched to capecitabine and temozolomide chemotherapy.

DISCUSSION

Necrolytic migratory erythema (NME) is a rare paraneoplastic condition that is the presenting manifestation of glucagonoma syndrome in 70% of affected patients. Becker et al. first reported this condition in 1942 in a patient with pancreatic cancer that developed an erythematous vesicular eruption. In 1973, Wilkinson et al. named this condition necrolytic migratory erythema.

Glucagonomas are rare neuroendocrine pancreatic tumors with an estimated incidence of one in 20 million. They most often occur in individuals 40 to 70 years old and are primarily located in the body or tail of the pancreas. Glucagonoma syndrome, in addition to NME, also includes glucose intolerance, weight loss, anemia, aminoaciduria, venous thromboembolic disease, psychiatric disturbances, and increased glucagon levels.

NME is characterized by a pruritic and recalcitrant dermatitis. The lesions consist of erythematous, crusted plaques most often located in the genital and perianal region, lower extremities, and at times the trunk or upper extremities. Additionally, there may be associated angular stomatitis and glossitis. NME is characterized by periods of spontaneous exacerbation and remission.

There are several theories regarding the underlying pathophysiology of NME. Reports indicate that hyperglucagonemia causes increased hepatocyte gluconeogenesis and lipolysis, ultimately leading to hypoaminoacidemia. Elevated glucagon levels also stimulate the production of arachidonic acid, prostaglandins, and leukotrienes, which are thought to contribute to the inflammatory reaction in NME. The fact that NME often clears with medications that suppress glucagon levels supports the central role of hyperglucagonemia. In addition to glucagon's role, many patients with NME have underlying deficiencies of zinc, protein, amino acids, and essential fatty acids, and reports indicate that supplementation of these nutrients may lead to clearance of NME.

Diagnosis of NME is often challenging, as the skin lesions often mimic other dermatoses including atopic dermatitis, seborrheic dermatitis, psoriasis, pemphigus vulgaris, candidiasis, and nutritional deficiencies. Histological analysis characteristically reveals epidermal pallor, spongiosis, and necrotic keratinoctyes. A perivascular infiltrate of lymphocytes and histiocytes may also be seen. Laboratory analysis reveals elevated serum glucose, glucagon, and chromogranin, as well as a normochromic normocytic anemia. The serum zinc level is often decreased as well. Pancreatic tumors can be visualized with computer tomography (CT), positron emission tomography (PET), magnetic resonance imaging (MRI), or pancreatic arterial angiography.

Surgical removal of the pancreatic tumor is the definitive treatment for glucagonoma syndrome. However, surgical removal is not always feasible given that at least 50% of well-differentiated glucagonomas have metastasized at the time of diagnosis. Medical therapies include octreotide (a somatostatin analogue), everolimus (an mTOR inhibitor), sunitinib (a tyrosine kinase

inhibitor), and standard chemotherapeutic agents. Recently, reports indicate that repletion of amino acids, essential fatty acids, and zinc also may also be effective treatment modalities.

To date, there are no reports of systemic corticosteroid therapy as an effective treatment for NME. Though use of topical clobetasol propionate 0.05% for NME has been reported in the literature, the case report was confounded by the concomitant use of systemic octreotide. Furthermore, our patient did not respond to topical treatment with halobetasol propionate 0.05% ointment alone, suggesting that systemic steroid therapy may be more effective than topical therapy. As corticosteroids are known to inhibit production of phospholipase A2 and thus epidermal arachidonic acid, there is pathophysiological rationale for the efficacy of corticosteroid therapy in NME. This case supports the use of systemic corticosteroids as an adjunctive therapy in patients with treatment-refractory NME.

KEY POINTS

1. NME is characterized by a pruritic and recalcitrant dermatitis with lesions most often located in the genital and perianal region, lower extremities, and at times the trunk or upper extremities, with periods of spontaneous exacerbation and remission.
2. Diagnosis of NME is challenging as skin lesions often mimic other dermatoses including atopic dermatitis, seborrheic dermatitis, psoriasis, pemphigus vulgaris, candidiasis, and nutritional deficiencies.
3. Laboratory analysis commonly reveals elevated serum glucose, glucagon, and chromogranin, as well as a normochromic normocytic anemia.

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CHICAGO DERMATOLOGICAL SOCIETY **Case #8**

Presented by Joshua Owen, MD, PhD[1] and Anthony J Mancini, MD[2]
[1]Department of Dermatology, Feinberg School of Medicine, Northwestern University
[2]Division of Dermatology, Ann & Robert H. Lurie Children's Hospital of Chicago, Feinberg School of Medicine, Northwestern University

UNKNOWN

A 28-day-old infant presented with a spreading bullous skin eruption, tachycardia, and low-grade fever.

CHICAGO DERMATOLOGICAL SOCIETY **Case #9**

Presented by Betty Kong, MD, PhD, Kassandra Holzem, MD and Emily Keimig, MD
Department of Dermatology, Feinberg School of Medicine, Northwestern University

HISTORY OF PRESENT ILLNESS
A 42-year-old male presented with a several month history of erythematous scaling plaques on the lower extremities. He was initially diagnosed with asteatotic eczema and was given instructions for dry skin care. He returned two months later with a worsening ichthyosiform eruption and significant lower extremity edema. At that time, he also endorsed fatigue, weight loss, fevers, and night sweats.

One year prior, the patient had developed erythema nodosum-like lesions following an episode of streptococcal pharyngitis confirmed by elevated anti-streptolysin O (ASO) titers. These lesions spontaneously resolved.

PAST MEDICAL HISTORY
None

MEDICATIONS
None

SOCIAL HISTORY
Works as a firefighter

PHYSICAL EXAM
Upper extremities with scaly, erythematous, annular thin plaques. Lower extremities with non-pitting edema extending to the mid thighs with overlying ill-defined erythematous scaly patches, some of which had scattered heme-crusted erosions and ulcerations.

LABS/IMAGING
Abnormal:
Labs: WBC 1.5 (absolute neutrophil count: 0.8, absolute lymphocyte count: 0.7), Hgb 13.0, platelets 116 (ref. 150-400), ALT 114 (ref. 8-40), AST 129 (ref. 8-40), ferritin 2945 (ref. 24-336), LDH 654 (ref.140-280), angiotensin-converting enzyme (ACE) 169 (ref. 9-67)
CT chest/abdomen/pelvis: mild diffuse bronchial wall thickening; non-calcified pulmonary nodules in the right lower lobe; mild hepatosplenomegaly; mildly enlarged lymph nodes in the axillary and external iliac chains
Bone marrow biopsy: hypercellular bone marrow with granulocytic hyperplasia and scattered non-caseating granulomas; fungal and AFB stains negative; CMV PCR negative

Normal/Negative: calcium, HIV, parvovirus IgM, CMV IgM, EBV IgM, hepatitis serologies, QuantiFERON gold, blood cultures, *Histoplasma* urine antigen, *Blastomyces* urine antigen, ANA, anti-mitochondria antibody (AMA), ANCA, alpha-fetoprotein (AFP), peripheral flow cytometry, transthoracic echocardiogram

HISTOPATHOLOGY
Granulomatous lobular panniculitis. Stains for fungi, bacteria, and acid fast bacilli were negative.

DIAGNOSIS
Subcutaneous sarcoidosis, Darier-Roussy subtype

TREATMENT AND COURSE

The patient was started on prednisone 20 mg daily. This was increased to 40 mg daily due to worsening swelling and evolving lesions on the arms and legs. Methotrexate has been considered as a steroid-sparing agent; however, it has been deferred given his elevated transaminases pending further evaluation by hepatology. He is also being evaluated by pulmonology, rheumatology, and hematology/oncology.

DISCUSSION

Sarcoidosis is a systemic granulomatous disorder of unknown etiology. It most commonly involves the lungs but can involve essentially every organ system, including the skin. Its cutaneous manifestations can be diverse, nonspecific, and protean. Therefore, it is a diagnosis of exclusion requiring negative workup for autoimmune, infectious, and neoplastic etiologies.

Cutaneous manifestations are seen in up to one third of patients and may be the first presentation of the disease. A variety of morphologies have been described, including papular (most common), annular, hypopigmented, plaque, erythrodermic, ichthyosiform, morpheaform, lupus pernio, and subcutaneous (Darier-Roussy) variants. Additionally, erythema nodosum is the most common nonspecific cutaneous finding in sarcoidosis and is associated with a good prognosis.

The classic presentation of subcutaneous sarcoidosis includes painless, firm, mobile nodules, representing disease infiltration of the subcutaneous tissue. The overlying epidermis may be normal, erythematous, or violaceous. The upper extremity is the most frequently affected area, and facial involvement is rare. About 90% of patients will have systemic involvement, but the overall prognosis is good.

Of note, our patient is a firefighter, one of several occupations in which environmental exposures have been implicated in the pathogenesis of sarcoidosis. Indeed, several studies have reported an increased incidence of sarcoidosis among first responders after the World Trade Center attacks on September 11, 2001. Other occupational risks associated with the development of sarcoidosis include employment in the agriculture sector and/or exposures to insecticides and microbial bioaerosols.

KEY POINTS

1. Sarcoidosis is a granulomatous condition of unknown etiology that can present with a myriad of systemic findings. Diagnosis requires exclusion of infectious and autoimmune etiologies.
2. Darier-Roussy sarcoidosis is a rare variant of sarcoidosis that presents with subcutaneous nodules.
3. An erythema nodosum-like eruption should prompt a workup for associated conditions, including sarcoidosis.

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CHICAGO DERMATOLOGICAL SOCIETY **Case #10**

Presented by Joel Sunshine, MD, PhD and Ahmad Amin, MD
Department of Dermatology, Feinberg School of Medicine, Northwestern University

HISTORY OF PRESENT ILLNESS
A 53-year-old Caucasian male presented with a mass on the left upper arm. He had first noted the mass one month prior to presentation and reported a relatively stable appearance outside of it becoming more "bruised" over time. He denied any associated pain, pruritus, preceding trauma, recent illnesses, fevers, chills, weight loss, or night sweats.

PAST MEDICAL HISTORY
GERD, scoliosis, hyperlipidemia

MEDICATIONS
Pantoprazole

FAMILY HISTORY
Father with melanoma

PHYSICAL EXAM
Left upper arm: A 3 x 2 cm firm, mobile, subcutaneous mass that was warm to touch with overlying erythema and fine vessels.

LABS/IMAGING
Ultrasound of the left upper extremity showed a 3.1 x 1.0 x 2.5 cm lobulated hypoechoic mass in the subcutaneous fat with multiple internal septations and prominent vascularity.

HISTOPATHOLOGY
Incisional biopsy showed a deep dermal tumor arranged in a trabecular pattern with no connection to the dermoepidermal junction. The tumor was composed of sheets of uniform small cells with high nuclear to cytoplasmic ratio, nuclei with dense chromatin and small nucleoli, numerous mitotic figures, and apoptotic cells. Focal areas of necrosis and pseudorosette formation were noted. The dermis also showed a variable, mostly perivascular, lymphohistiocytic infiltrate. Immunohistochemistry was positive for polyomavirus, synaptophysin, and cytokeratin (AE1/3, with a dot-like pattern) and was negative for vimentin and chromogranin.

DIAGNOSIS
Merkel cell carcinoma (MCC)

TREATMENT AND COURSE
The patient was referred to surgical oncology for wide local excision and sentinel lymph node biopsy. Preoperative MRI of the humerus showed the tumor abutting the fascia of the triceps, but there was no abnormality or enhancement within the muscle. PET/CT showed no evidence of metastatic disease. Merkel cell polyomavirus antibody titer was 1330. The re-excision specimen was clear of any involvement, and sentinel lymph node biopsy was negative for carcinoma. The patient will be followed closely at 3-month intervals with plans to monitor the Merkel cell polyomavirus titer and to perform surveillance chest X-ray and ultrasound of the left upper extremity.

DISCUSSION
MCC predominantly affects older patients with lower Fitzpatrick phototypes, most often on sun-exposed areas of the head, neck, and extremities. It carries a disease-related mortality of 30% at 2

CHICAGO DERMATOLOGICAL SOCIETY **Case #1**

Presented by Olga Radkevich-Brown, MD, PhD, Sarah Stein, MD
Section of Dermatology, Department of Medicine, University of Chicago

HISTORY OF PRESENT ILLNESS

A 4-month-old African American male infant was transferred from an outside hospital to the pediatric intensive care unit with lethargy, hypothermia, profound hypoglycemia, and hypotension. On day 5 of admission, Pediatric Dermatology was consulted for evaluation of a scaly rash on the forehead, lips, neck and upper chest, noticed after the patient was extubated. Nutritional history was notable for the finding that since about 2 weeks of age, the parents had been overdiluting the powdered formula. One month prior to admission, when the family noticed that the infant appeared underweight, he was switched to goats' milk formula, which was also inappropriately diluted.

PAST MEDICAL HISTORY

Born at full term via spontaneous vaginal delivery, with no maternal or fetal complications during pregnancy, labor or delivery

FAMILY HISTORY

Mother and maternal grandmother with sickle cell trait

MEDICATIONS

Ceftazidime, metronidazole, vancomycin, levocarnitine, thiamine, parenteral nutrition, fat emulsion, dextrose 20% in water, esomeprazole, topical zinc oxide paste

ALLERGIES

None

PHYSICAL EXAMINATION

Weight 3.5 kg (7 lbs 11.5 oz, below 1st percentile weight-for-age and weight-for-height)
Height 56.5 cm (22 inches, below 1st percentile stature-for-age)
Head circumference 36.5 cm (14.4 inches, below 1st percentile head circumference-for-age)
Body mass index 11.4 (normalized BMI values are only available for ages 2 to 20 years)
On upper chest, extending into the neck fold, there were brown adherent scales similar in appearance to flaky paint. Similar scaling was noted on the forehead and around the eyes and nose. There were focal areas of desquamation revealing pink patches, but no erosions or ulcerations. Lips were dry and peeling, with fissuring and crusting at bilateral oral commissures. Buccal mucosa, gingiva and tongue were unremarkable; hard palate had a focal petechial plaque, consistent with intubation trauma. There was pronounced scrotal edema. Skin of the buttocks was erythematous, without desquamation or erosions. Nails were normal.

LABORATORY DATA

Comprehensive metabolic panel on initial presentation:

- ↓ glucose 10 mg/dL (reference range 60-109)
- ↓ Na, K, Cl, CO_2, Ca, creatinine
- ↑ blood urea nitrogen (BUN), alanine aminotransferase (ALT), aspartate aminotransferase (AST)
- ↓ alkaline phosphatase
- ↓ total protein 4.6 g/dL (6-8.3), albumin 3.4 g/dL (3.5-5.0), and pre-albumin 9 mg/dL (21-41)
- ↑ ammonia 77 μg/dL (20-70)
- Normal venous lactate 1.14 mmol/L (0.56-2.20), anion gap 15 mmol/L (6-15)

Complete blood count on initial presentation:

↓ hemoglobin 7.8 g/dL (9.3-13.2)

↓ mean corpuscular volume (MCV) 60.4 fL (73-107)

Normal leukocytes, platelets

Vitamin and micronutrient levels measured prior to supplementation:

Normal serum folate, vitamin B12 (cyanocobalamin), iron, zinc. 25-hydroxy vitamin D

Inborn errors of metabolism markers measured prior to supplementation:

↓ Amino acids, quantitative, blood: multiple amino acids were reduced, not indicative of specific disorder, but a dietary artifact secondary to low protein diet

↓ Carnitine: reduced total, free and acylcarnitine, no accumulation of esterified species

Normal urinary organic acids

Normal newborn screen

Vitamin and micronutrient levels measured after supplementation was initiated:

↓Vitamin B6 (pyridoxal 5 phosphate), vitamin C (ascorbic acid), vitamin E (α-tocopherol), selenium

Normal vitamin A (free retinol), vitamin B3 (niacin), copper, free fatty acids, triglycerides, free fatty acids

IMAGING

Abdominal ultrasound demonstrated moderate amount of ascites

DIAGNOSIS

"Flaky paint" dermatosis associated with kwashiorkor

TREATMENT AND COURSE

The patient required intensive care for hypovolemic shock, multiple electrolyte disturbances, and intubation for airway protection. His infectious workup was negative, but he received a course of vancomycin, ceftazidime and metronidazole for presumed gut bacterial translocation. Based on history of inappropriate formula mixing, very low weight and height for patient's age, and low albumin and pre-albumin, he was diagnosed with severe malnutrition. He was started empirically on carnitine supplementation, multivitamins and total parenteral nutrition with lipid supplementation. He had persistent hypoglycemia requiring high glucose infusion rates. Extensive metabolic workup demonstrated reduced levels of all carnitine species and reduced levels of multiple amino acids, consistent with severe malnutrition rather than an inborn error of metabolism, particularly in the setting of a normal newborn screen evaluation. Workup for specific vitamin and trace element deficiencies revealed low selenium and vitamin C, and borderline levels of vitamin B6 and E. He was eventually transitioned to oral amino acid-based formula and finally milk protein-based formula, and maintained appropriate glucose levels. After a three-week hospital stay, he was discharged to foster care. Petroleum jelly was recommended for the care of the nutritional dermatosis.

DISCUSSION

Protein-energy malnutrition describes a spectrum of malnutrition disorders, including marasmus, kwashiorkor, and an intermediate state between the two. Marasmus is an adaptation to chronic and global nutrient deficiency, while kwashiorkor is due to disproportionately increased carbohydrate intake or decreased protein intake, particularly seen during periods of stress. In marasmus, weight is usually less than 60% of ideal body weight, with no edema, while kwashiorkor has been traditionally characterized by less dramatic weight loss (60-80% of ideal body weight) due to edema in the setting of hypoproteinemia and hypoalbuminemia. These conditions are predominantly seen in developing countries, however, cases are reported in the US and developed countries as well.

Marasmus is rare in the US, except in cases of extreme malnutrition such as neglect. Patients demonstrate dry and wrinkled skin, with generalized loss of subcutaneous fat and muscle. Kwashiorkor has been reported more commonly and is attributable to nutritional ignorance, food faddism, presumed food allergy and/or specific food avoidance. The classic cutaneous findings of kwashiorkor are fine reddish-brown scales resembling flakes of peeling paint, and termed "flaky paint" dermatosis. Other cutaneous manifestations include erosions in the areas of friction, focal hyper- and hypopigmentation, and lightening of the hair, with alternating lighter and darker areas of hair pigmentation known as the "flag sign", which reflects states of inconsistent nutritional intake. Hair is dry, brittle and lusterless, and nails become thin, soft and separate easily from the nail bed.

The clinical picture of kwashiorkor is not always uniform, and differentiation from other nutritional dermatoses is not always straight-forward. In fact, dietary intake of several micronutrients, as well as macronutrients, can be absent at the same time. Acquired zinc deficiency, essential fatty acid, riboflavin (vitamin B2), niacin (vitamin B3) and pyridoxine (vitamin B6) deficiencies, cystic fibrosis, certain inherited immunodeficiencies, Langerhans cell histiocytosis, and inborn errors of metabolism, including hereditary acrodermatitis enteropathica, Hartnup's disease and multiple carboxylase deficiency, as well as atopic dermatitis, should be considered in the differential diagnosis of protein-energy malnutrition and generalized eczematous dermatitides.

Other etiologic considerations in kwashiorkor should include, but are not limited to, social and economic factors (lack of income, education, or access to healthcare), deliberate restriction of dietary intake (anorexia nervosa, perceived allergy, or medically indicated dietary restrictions), catabolic states (malignancy, liver disease), malabsorption (cystic fibrosis, celiac disease, inflammatory bowel disease), psychologic/neurologic diseases (food aversion, psychosocial deprivation), or acute decompensation in chronic borderline malnutrition, for example due to infection.

Initial diagnostic evaluation recommended by the World Health Organization consists of screening for hypoglycemia and anemia, and a comprehensive workup to rule out coexisting infectious disease. Additional laboratory testing includes a complete blood count, measurement of levels of total protein, albumin, zinc, sweat chloride, and biotinidase, and evaluation for HIV infection. Biopsy will demonstrate the histological features of malnutrition: epidermal pallor with overlying confluent parakeratosis. These findings are not specific for kwashiorkor, but will differentiate nutritional dermatosis from other dermatoses such as atopic dermatitis and Langerhans cell histiocytosis. Treatment of protein-energy malnutrition requires aggressive nutritional support, as well as management of concomitant conditions such as dehydration and infection. Oral refeeding is preferred over intravenous hyperalimentation, but the potential complications of rapid refeeding must be carefully managed.

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CHICAGO DERMATOLOGICAL SOCIETY **Case #2**

Presented by Carly Roman, MD, Haider Bangash, MD, Farah Abdulla, MD, Keyoumars Soltani, MD
Section of Dermatology, Department of Medicine, University of Chicago

HISTORY OF PRESENT ILLNESS

A 52-year-old Caucasian man presented for dermatologic evaluation of multiple facial papules. These lesions had been present for 15 years and were asymptomatic. Prior treatment by an outside dermatologist included electrodessication and curettage, which led to transient improvement, but the lesions eventually recurred. A prior biopsy was reportedly consistent with a benign "hair follicle growth". He was otherwise in good health with no systemic complaints.

PAST MEDICAL HISTORY

None

FAMILY HISTORY

Unknown; patient was adopted.

MEDICATIONS

None

ALLERGIES

None

PHYSICAL EXAMINATION

Numerous, monomorphic, 2-3 mm skin colored to slightly hypopigmented papules clustered on the face and superior chest.

HISTOPATHOLOGY

A 3mm punch biopsy of a representative lesion of the right mandible was taken. Histopathologic analysis showed thin epithelial strands emanating from follicular structures and from the overlying epithelium. Around the cords was a proliferation of loose connective tissue consistent with a fibrofolliculoma.

TREATMENT AND COURSE

Based on the clinical and histopathologic data, there was suspicion for Birt-Hogg-Dubé syndrome. Evaluation for visceral manifestations with a CT chest/abdomen/pelvis was recommended. The imaging revealed multiple bilateral pulmonary cysts, but was negative for pneumothoraces. Kidneys were grossly unremarkable.

Regular imaging to monitor for the development of renal neoplasms was recommended. Avoidance of high atmospheric pressure such as air travel and scuba diving was encouraged. Cosmetic treatment of the fibrofolliculomas was discussed but deferred.

DIAGNOSIS

Birt-Hogg-Dubé syndrome

DISCUSSION

Birt-Hogg-Dubé syndrome (BHDS) is an autosomal dominant disorder characterized by multiple fibrofolliculomas, trichodiscomas and acrochordon-like lesions as well as visceral manifestations. It is a rare syndrome occurring in approximately 1/200,000 people. It is caused by a mutation in the tumor suppressor gene FLCN (folliculin). The diagnostic criteria are as follows: Major criteria, 1) At least five

fibrofolliculomas or trichodiscomas with at least one of them confirmed histologically and occurring in adult onset, 2) Pathogenic FLCN germline mutation; Minor criteria, 1) Multiple bilateral and basilar lung cysts with no other apparent cause, with or without spontaneous primary pneumothorax, 2) Renal cancer, early onset (<50 years) or multifocal or bilateral renal cancer, or renal tumor composed of mixed chromophobe and oncocytic morphology, 3) A first-degree relative with BHDS. The diagnosis of BHDS is feasible when a patient meets one major or two minor criteria.

BHDS is characterized by the cutaneous triad of fibrofolliculomas, trichodiscomas, and acrochordons. Fibrofolliculomas and trichodiscomas are thought to be part of a morphological spectrum. These lesions typically appear after the age of 20 and present as numerous, small, dome-shaped whitish papules on the face, neck and upper torso. These lesions are benign and require no treatment. If treatment is desired for cosmesis, options include carbon dioxide laser ablation, superficial electrodessication or dermabrasion. Recurrence is likely following any of these therapies.

Pulmonary involvement is common in BHDS, manifesting as multiple basilar pulmonary cysts and the development of pneumothoraces. Pulmonary cysts are seen in >80% of patients and most commonly occur in the fourth to fifth decades. The cysts are typically asymptomatic until the development of a pneumothorax, which has an estimated incidence of 33-38%. The odds of this complication are 50 times more likely than in an unaffected individual and is correlated to the number, diameter and volume of the lung cysts. The surrounding lung parenchyma is largely normal, thus pulmonary function is only minimally impaired or normal. There has been no established lung cancer association. Baseline high-resolution chest CT is recommended to better characterize the extent of disease and facilitate patient education. Although no disease specific data exists, patients are advised to not smoke and avoid scuba diving as the change in ambient atmospheric pressure could predispose to development of a pneumothorax. There is a theoretical risk of air travel as the pressurized cabin may result in gas expansion within the pulmonary cysts and lead to the development of a pneumothorax, though in general air travel is thought to be safe. Pleurodesis is recommended after the first episode of pneumothorax.

The presence of renal tumors varies between 25% to 35% with a mean age at diagnosis of 50 years and a male predominance. They are frequently multiple, bilateral and slow growing. A variety of histological subtypes have been observed including hybrid oncocytic tumor, chromophobe RCC, oncocytoma, papillary RCC and clear cell RCC. Benign renal cysts have also been documented in patients with BHDS, but their exact prevalence compared to the general population is unknown. Renal tumors associated with BHDS generally follow a favorable clinical course as the clinical behavior of the hybrid oncocytic tumor, chromophobe RCC and oncocytoma are not usually aggressive. Regular screening is essential, although the optimal mode, timing and duration of surveillance are unclear. CT and MRI are more sensitive than ultrasound in detecting smaller lesions. There are no established guidelines, but the general recommendations include screening around age 20 with repeat imaging every 36 to 48 months. Other less common associations include colonic adenomas, medullary thyroid carcinoma, and tissue nevi.

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CHICAGO DERMATOLOGICAL SOCIETY **Case #3**

Presented by Ashley Jenkins, MD, Aisha Sethi, MD, and Vesna Petronic-Rosic, MD
Section of Dermatology, Department of Medicine, University of Chicago

UNKNOWN

A 32-year-old male presented with a new rash, eye redness, retro-orbital pain, fatigue, and generalized muscle aches.

CHICAGO DERMATOLOGICAL SOCIETY **Case #4**

Presented by Stephanie M. Kazantsev, MD, Ashley Jenkins, MD, Farah R. Abdulla, MD, Sarah L. Stein, MD
Section of Dermatology, Department of Medicine, University of Chicago

HISTORY OF PRESENT ILLNESS

Dermatology was consulted to evaluate a hospitalized five-week-old full term girl for "worsening diffuse mucosal and cutaneous hemangiomas." At birth, the infant was reported to have several tiny red spots on her skin that gradually enlarged. At 3 weeks of age, a red bump in the diaper region and one on the right cheek had developed surface breakdown. She was evaluated by hematology/oncology and topical timolol gel was initiated. Evaluations prior to admission included an abdominal ultrasound that showed multiple hypervascular hepatic lesions, consistent with hemangiomas, a chest x-ray that showed "large cardiac size", and a transthoracic echocardiogram (TTE) demonstrating hypofunction and mitral insufficiency.

PAST MEDICAL HISTORY

Born at 39 weeks via repeat c-section following an uncomplicated pregnancy with normal prenatal ultrasounds.

FAMILY HISTORY

Non-contributory

MEDICATIONS

Timolol 0.5% gel

ALLERGIES

NKDA

PHYSICAL EXAM

Well appearing, well developed five-week-old female. Pulse tachycardic with rate of 155. Cardiac exam demonstrated Grade II/VI systolic ejection murmur. Respiratory exam demonstrated normal effort and normal breath sounds. Abdominal exam notable for hepatomegaly with liver edge palpable 5cm below costal margin. Numerous (>50), red dome-shaped vascular papules scattered densely over the entire body, ranging in size from about 0.5 to 2cm. In the oropharynx, several red 1-2mm macules noted on the gingivae and floor of the mouth. No papules were ulcerated or eroded.

LABORATORY DATA

Complete blood count: within normal limits
Basic Metabolic panel: within normal limits
Liver Function test: notable for total bilirubin 1.9 mg/dL (0.1-1.0), AST 182 U/L (8-37), ALT 39 U/L (8-35)
Thyroid function tests: normal including TSH, T3 and free T4
N-terminal pro-brain natriuretic peptide (NT-proBNP): 657 pg/mL (<125)
Troponin: within normal limits
Coagulation studies: notable for PTT 38.3 s (24.0-34.0)

IMAGING

Abdominal Ultrasound: Multiple hypervascular hepatic lesions, consistent with hemangiomas.
MRI Liver: Innumerable T2 hyperintense enhacing hepatic high flow lesions, compatible with hemangiomas. Cardiomegaly, secondary to high flow.
Electrocardiogram: Normal sinus rhythm, right atrial enlargement, right axis deviation, right ventricular

hypertrophy, possible biventricular hypertrophy.
Transthoracic echocardiogram (TTE): Mild concentric left ventricular hypertrophy, mild left ventricular dilation. Left ventricular wall motion is mildly, globally reduced. Shortening fraction 30%. There is mild mitral regurgitation. Mild left atrial dilation. Single mitral regurgitation jet directed posteriorly. Patent foramen ovale. Left to right atrial shunt, small.
MRA brain, MRI brain and soft tissue neck: Several subcentimeter posterior fossa lesions likely represent a manifestation of diffuse hemangiomatosis.

DIAGNOSIS
Multifocal infantile hemangiomas with extracutaneous disease

TREATMENT AND COURSE
The patient was started on propranolol 0.65 mg/kg/day divided three times per day, with stepwise increase to 4.0 mg/kg/day divided three times per day. She was also started on furosemide at 3mg twice per day, with increase to 6mg twice per day. She has tolerated the medications and dosing changes well. Direct laryngoscopy and broncoscopy showed no airway involvement. Ophthalmologic exam revealed normal fundus and ocular exam.

Since discharge, NT-proBNP has continued to decrease (657 at 7-weeks-old, 108 at 12-weeks-old) and repeat echocardiogram demonstrated improved cardiac output with left ventricular shortening fraction ~36%. Repeat abdominal ultrasounds at 7-weeks-old, 9-weeks-old, and 14-weeks-old demonstrated stable hepatic hemangiomas.The cutaneous hemangiomas are overall stable with some becoming lighter in color and flatter. No bleeding or ulceration has occurred.

Multidisciplinary care has included pediatric specialists from dermatology, hematology/oncology, surgery, cardiology, otolaryngology, ophthalmology, and neurology.

DISCUSSION
Infantile hemangiomas (IH) are estimated to affect 4-10% of all neonates and infants. They occur more frequently in girls, caucasians, premature or low birthweight infants, multiple gestation pregnancy, and infants born to older mothers. These lesions can be further classified as focal, multifocal, segmental, and indeterminate, affecting the skin in a superficial, deep or mixed manner.

Among affected infants, an estimated 15-30% have multiple hemangiomas. The presence of five or more cutaneous hemangiomas is associated with a higher incidence of extracutaneous hemangiomas, most commonly hepatic hemangiomas. The presence of multiple cutaneous hemangiomas without visceral involvement has been categorized as multifocal infantile hemangiomas without extracutaneous disease (previously benign neonatal hemangiomatosis). The presence of multiple hemangiomas affecting the skin and visceral organs has been termed multifocal infantile hemangiomas with extracutaneous disease (multifocal IH; previously diffuse neonatal hemangiomatosis). Complications of multifocal IH are often a result of hepatic hemangiomas (HH). A classification for HH has been proposed, including solitary, multifocal, and diffuse. Multifocal HH usually occur in the setting of multiple small skin hemangiomas. The HHs may be asymptomatic, but if they contain arteriovenous shunts then congestive heart failure can ensue. Diffuse HH is associated with massive hepatomegaly and hypothyroidism. The hypothyroidism is the result of type 3 iodothyronine deiodinase produced by the hemangioma.

Accurately differentiating multifocal IH from other multifocal vasular anomalies is vital for treatment and prognostic purposes. Other diagnoses to consider include multifocal lymphangioendotheliomatosis with thrombocytopenia (MLT), pyogenic granuloma, tufted angioma, Kaposiform hemangioendothelioma, glomuvenous malformation, mucocutaneus venous malformations, blue rubber bleb syndrome, and capillary malformation-arteriovenous malformation. Differentiating IH from other possible diagnoses can

usually be done clinically, however occasionally can be challenging. IH typically appear within a few weeks of birth, followed by a period of rapid growth over months, followed by gradual involution. Other organ systems may be involved, most commonly the liver, and rarely the gastrointestinal tract. IH demonstrate glucose transporter-1 (GLUT-1) positivity on immunohistochemical staining. Furthermore, while thrombocytopenia is associated with other diagnoses like MLT, tufted angioma, and Kaposiform hemangioendothelioma, it is not associated with IH. In contrast to IH, MLT is GLUT-1 negative, associated with severe thrombocytopenia, severe gastrointestial bleeding, and commonly involves the lungs and bone/synovium.

Treatments for complicated solitary and multifocal IH include beta blockers, systemic corticosteroids, interferon-alpha-2a, vincristine, cyclophosphamide, and carbon dioxide laser. Propranolol was first reported as an effective treatment for IH in 2008, and has since become the preferred systemic therapy for slowing or even stopping the growth of hemangiomas and promoting more rapid involution. It was approved by the US Food and Drug Administration for the treatment of IH in 2014. Multiple case studies have reported a rapid response of multifocal IH to propranolol therapy, including cases complicated by high-output cardiac failure.

This case highlights the clinical presentation, diagnosis and treatment of an infant with multifocal IH with extracutaneous disease.

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CHICAGO DERMATOLOGICAL SOCIETY **Case #5**

Presented by Kathleen Kelley, MD, Diana Bolotin, MD, PhD, Christopher R. Shea, MD, Keyoumars Soltani, MD, Farah Abdulla, MD, Arlene Ruiz De Luzuriaga, MD, MPH, Vesna Petronic-Rosic, MD, MSc
Section of Dermatology, Department of Medicine, University of Chicago

HISTORY OF PRESENT ILLNESS

In July 2015, a 69-year-old woman presented to the University of Chicago Dermatology Clinic with a lesion on the helix of her left ear that had been present for roughly 3 weeks. On exam, an 8 mm light brown, scaly, thin papule with a 2mm black macule within it was noted on the patient's superior helical rim (primary lesion). The lesion was biopsied, and revealed an invasive malignant melanoma with ulceration, 2 mitotic figures per millimeter squared, and a Breslow depth of 1.6mm (Clark level IV). Ten days after the initial biopsy, the patient was treated with a wide resection and sentinel lymph node biopsy. The excised tissue showed no residual melanoma, and the margins were clear. A sentinel lymph node biopsy was performed of four sentinel nodes in the left tail of the parotid gland and was negative. A CT head and soft tissue neck were negative for discrete neck mass or significant cervical lymphadenopathy. Her staging at that time was T2bN0M0, corresponding to Stage IIA by the current American Joint Committee on Cancer (AJCC) staging criteria. She underwent a delayed reconstruction of the auricle in October 2015. The patient was subsequently followed with clinical exams every three months in Dermatology Clinic.

In late May 2016, the patient returned to clinic with a new 2mm dark brown papule (lesion A) on the left posterior auricle that she had noticed the previous morning. Biopsy of this lesion revealed an invasive malignant melanoma with Breslow depth of 0.93mm and Clark Level IV. One week later, the patient had another brown papule (lesion B) on the helix of the left ear biopsied. This lesion was within 2cm of the primary melanoma but outside the original scar, and biopsy was consistent with another invasive malignant melanoma.

PAST MEDICAL HISTORY

Actinic keratoses
Severely atypical compound nevus treated with complete excision on 9/23/2015
Psoriasis as a teenager
Osteoarthritis
Glaucoma
No prior history of skin cancers

FAMILY HISTORY

Negative for skin cancer

MEDICATIONS

Calcium citrate/vitamin D3 supplement daily
Nabumetone 750 mg PO BID

ALLERGIES

Sulfonamides

PHYSICAL EXAMINATION

Primary lesion, 7/20/15: 8mm light brown, scaly, thin papule with an eccentric 2mm black macule within it on the upper helical rim of the left ear (shave biopsy)

Lesion A, 5/24/16: 2mm dark brown papule on the left posterior auricle (4mm punch biopsy)

Lesion B, 6/1/16: 3mm brown, variegated macule on the helix of the left ear (4mm punch biopsy)

HISTOPATHOLOGY

Biopsy – primary lesion – 7/20/15
Left ear helix biopsy: Invasive malignant melanoma with nevoid features and Breslow depth of 1.6mm, Clark level IV. Ulceration was present, and 2 mitotic figures per millimeter squared were identified. Both radial and vertical growth phases were present.
Excision of primary melanoma – 7/30/15
Left ear helix excision: Auricular skin with solar damage and with no residual melanoma.
Sentinel Lymph Node pathology – 7/30/15
Four sentinel lymph nodes and nine non-sentinel lymph nodes were excised. All were negative for tumor.
Biopsy – lesion A – 5/24/16
Left posterior auricle biopsy: Invasive malignant melanoma with a Breslow depth of 0.93mm, Clark level IV. Three mitotic figures per millimeter squared were present. No ulceration was identified, and only vertical growth was present.
Biopsy – lesion B – 6/1/16
Left ear helix biopsy: Invasive malignant melanoma with a Breslow depth of 1.01mm. Fewer than 1 mitotic figure per millimeter squared was present. No ulceration was identified, and both radial and vertical growth phases were present.
Excision of lesion A and lesion B – 6/27/16
Left posterior auricle excision: Scarred skin with no residual melanoma. S-100 staining was negative.
Left ear helix excision: Scarred skin with no residual melanoma.

IMAGING

3 month Surveillance CT Head and Soft Tissue Neck with IV contrast – 9/29/15
Evidence of postsurgical changes in the left neck, with no discrete neck mass or significant cervical lymphadenopathy. There was no evidence of intracranial metastatic disease.
CT Soft Tissue Neck with IV contrast – 6/23/16
Evidence of postoperative findings in the left neck, with no significant cervical lymphadenopathy based on size criteria.
CT Chest, Abdomen, and Pelvis with IV contrast – 6/23/16
No specific evidence of metastatic disease in the chest, abdomen, or pelvis.

DIAGNOSIS

Epidermotropic metastatic malignant melanoma

TREATMENT AND COURSE

This patient was determined to have regional metastatic disease based on the current AJCC guidelines. These guidelines define melanomas that occur within 2cm of an original melanoma as satellite metastases, and those that are more than 2cm from the primary lesion but within the same nodal draining basin as in-transit. Based on these criteria, lesion A and lesion B are an in-transit and satellite metastasis, respectively. This highlights the important clarification that metastatic disease in this patient refers to in-transit and satellite lesions, which are regional metastases and not distant, widespread metastasis.

In late June 2016, the patient underwent wide local excision of metastatic malignant melanomas (lesions A and B). The margins on these excisions were clear. She has been seen by Hematology-Oncology and discussed at Melanoma Tumor Board; the recommendations from this conference were to pursue imaging studies, which were negative for discrete mass or lymphadenopathy. These recommendations were based on repeat clinical staging done after metastatic melanoma occurred that put her at Stage IIIC disease

(T2bN2cM0) based on AJCC guidelines. The presence of in-transit and satellite metastases automatically elevates her nodal staging to N2c. She does not have distant systemic metastases, which limits her M staging to M0. Current National Comprehensive Cancer Network (NCCN) guidelines recommend imaging work up and allow for close observation of patients with Stage IIIC disease that has been completely resected and who have negative imaging. Adjuvant therapy is a suggested consideration in these patients. Our patient and her multidisciplinary care team had a conversation regarding the risks and benefits of adjuvant therapy compared to the risks and benefits of local resection with close observation, and the latter was the preferred treatment route. She continues to be followed closely in Dermatology Clinic with complete skin and clinical lymph node exams every 3 months.

DISCUSSION

This patient was diagnosed with epidermotropic metastatic malignant melanoma (EMMM) of the left ear, and is considered to have Stage IIIC disease. EMMM is a type of malignant melanoma in which the invasive metastatic malignant cells involve the epidermis. Typically, metastatic melanoma to the skin involves the subcutis and the dermis, and spares the epidermis. In rare cases, metastatic melanoma involves the epidermis, resulting in the histopathological feature of epidermotropism, as is demonstrated in this case. In cases with EMMM, epidermotropic metastases tend to closely mimic primary malignant melanoma (MM), making the diagnostic distinction challenging. Staging and subsequent treatment for these two types of melanoma are different, so making this distinction is crucial.

There are three potential ways to consider this case. The first is that the patient developed three independent, primary malignant melanomas in close proximity to each other. Multiple localized primary melanomas have been described, but these are typically associated with trauma, irritation, immunodeficiency, or other predisposing factors, and our patient had no known risk for developing multiple primary melanomas in one location. The second possibility is that this patient experienced numerous local, non-metastatic recurrences of her malignant melanoma. We feel this is unlikely given that the margins were clear on the excised cutaneous lesions, the sentinel lymph nodes were negative, and the patient's recurrences were outside of her original scar. The third option is that the two subsequent lesions represent cutaneous epidermotropic metastases of the original invasive melanoma of the helical rim.

We feel that the third option, EMMM, is the most clinically and pathologically consistent scenario in this patient's case. Historically, the distinction between EMMM and primary MM has been established by a set of criteria outlined by Kornberg et al in 1978. These authors found that certain cases of clinically metastatic melanoma show histopathologic features such as involvement of the epidermis that until then were attributed to primary melanoma. Classic criteria for EMMM include dermal involvement greater than or equal to epidermal involvement, junctional epidermal involvement not extending beyond the edge of the dermal component, atypical melanocytes filling the papillary dermis with thinning of the epidermis, widening of the papillae with formation of an epithelial collarette, and identification of atypical melanocytes in vascular lymphatic spaces. Until recently, these criteria were widely accepted; however subsequent reports have described cases of EMMM that do not fit into this definition, calling these criteria into question. For example, the findings of small size, extensive pagetoid scatter, symmetry, extension of the intraepidermal component beyond the dermal component, epidermal-only involvement, and involvement of adnexal epithelium have been described in EMMM.

Our own case exhibits the classic findings of EMMM, as well as features more recently described in the primary literature. For example, lesion A demonstrated effacement of the epidermis and inward turning of the rete ridges surrounding the dermal melanocytic proliferation, which are classic features of EMMM. Some more recently described findings were appreciated in this melanoma as well, such as involvement of the adnexal epithelium and epidermal involvement that is greater than the dermal component.

Clearly, malignant melanoma with involvement of the epidermis creates an extremely challenging diagnostic puzzle. In this case, identifying her disease as EMMM rather than multiple primary lesions elevates her staging to IIIC. The 5-year survival rate for Stage IIIC melanoma is estimated at roughly 40%. The overall incidence of in-transit metastases in melanoma is 4%, and in-transit metastases are seen more often in tumors >1mm thick. It is well known that in-transit lesions are likely to recur, but currently, the consensus is that the morbidity associated with multiple resections of individual in-transit lesions is more desirable than the morbidity associated with adjuvant therapies. The utility of repeating a SLN biopsy in patients with multiple in-transit disease is not known. For such cases, the standard of care is a multidisciplinary approach to consider whether a difference in staging that could occur based on SLN results, would potentially change management. Presently, no randomized controlled trials exist to study the value of adjuvant therapy in patients with in-transit disease who are declared disease-free following surgical treatment. A recent randomized, double-blind, phase III clinical trial showed statistically significant higher rates of recurrence-free, overall, and distant metastasis-free survival in patients with Stage III melanoma treated with ipilimumab, compared to placebo. Notably, this study excluded patients with in-transit disease.

Patients diagnosed with EMMM are expected to have a poor prognosis due to the nature of metastatic disease, and case reports describe distant metastatic disease at the time of diagnosis, or within one year; however there appears to be a subset of patients who have slow expansion of their disease burden and do much better than anticipated. Given the rare occurrence of EMMM, no large studies have been done to evaluate this possibility.

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CHICAGO DERMATOLOGICAL SOCIETY **Case #6**

Presented by Laura Buford, MD, Christopher R. Shea, MD
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HISTORY OF PRESENT ILLNESS

A 37-year-old Caucasian female presented to clinic complaining of excessive sweating of the face and scalp. This condition began approximately 15 years prior and has been progressively worsening for the past two years. Initially, she experienced flushing and mild sweating of the face occurring while eating. Over time, the condition progressed from seemingly inconsequential prandial perspiration to life-altering drenching sweating of the face and scalp in response to any gustatory stimuli such as going to the grocery store, seeing food on television, or making lunch for her kids. Her attempts to avoid triggers are interfering with all aspects of her life. She is unable to complete basic activities of daily living, and personal and professional relationships are affected. She sought help specifically from a dermatologist at the urging of her family.

PAST MEDICAL HISTORY

Type I diabetes mellitus (DM) complicated by diabetic retinopathy, neuropathy, and nephropathy; cholelithiasis, and thyroid goiter

PAST SURGICAL HISTORY

Wisdom tooth extraction, cholecystectomy, and thyroidectomy

FAMILY HISTORY

There is no family history of hyperhidrosis or autonomic dysfunction.

SOCIAL HISTORY

The patient lives at home with her family. She is a current tobacco user. She denies past or current recreational drug use.

MEDICATIONS

Insulin

ALLERGIES

No known medical allergies

REVIEW OF SYSTEMS

HEENT: blurry vision
GI: inadequate food intake
GU: diabetic nephropathy
Neuro: diabetic neuropathy
Endocrine: DM, weight loss
Skin: dryness in distal lower extremities
Psychiatric: significant impairment of quality of life and inability to carry out activities of daily living

PHYSICAL EXAMINATION

Physical examination revealed an underweight woman. The hair of the scalp was slightly damp and of normal density. A transverse surgical scar was present on the anterior neck just cranial to the sternal notch, but no other primary skin findings of the affected area were appreciated. The bilateral lower extremities were dry with slightly decreased hair density in a stocking distribution. Sensory deficits to soft touch and temperature discrimination were noted in the same distribution.

DIAGNOSIS
Diabetic gustatory hyperhidrosis

TREATMENT AND COURSE
The patient was started on glycopyrrolate 1 mg by mouth twice daily with excellent results at one month follow up. She had resumed all activities of daily living, and her quality of life has been restored. She experienced mild xerostomia, which is reportedly well-controlled with gum or sugar-free candy. She has maintained regular follow up with ophthalmology as recommended, and no changes in vision have been noted.

DISCUSSION
Secondary hyperhidrosis is defined as excessive sweating due to or associated with an underlying systemic disorder. It is not as common as primary hyperhidrosis and can be caused by a variety of conditions. The diagnosis of secondary hyperhidrosis is typically clinical, so a detailed history and physical exam are paramount in making the correct diagnosis. Past medical history, surgical history, and medication history must be thoroughly evaluated, and a complete review of systems is imperative in identifying secondary causes. Laboratory testing and radiographic imaging are occasionally necessary.

Secondary hyperhidroses are subcategorized into five groups based on the source of aberrant neural impulse: cortical, hypothalamic, medullary (or gustatory), spinal cord, and local. Medullary or gustatory hyperhidrosis results from afferent nerve impulses to the nuclei in the medulla oblongata, and can be further classified as physiologic or pathologic. In physiologic gustatory hyperhidrosis, taste receptors provide afferent stimuli that travel through the glossopharyngeal nerve to the medullary nuclei resulting in erythema of the cheeks and sweating on the upper cutaneous lip. This is common after ingestion of spicy foods. Pathologic gustatory hyperhidrosis results when disrupted parasympathetic secretomotor fibers heal with aberrant nerve connections to adjacent sympathetic sudomotor fibers as seen in auriculotemporal syndrome (Frey syndrome) and chorda tympani syndrome.

Diabetic gustatory hyperhidrosis is highly characteristic of diabetic autonomic neuropathy, but the pathophysiology is not completely understood. It has been hypothesized to be either a compensatory response to anhidrosis or hypohidrosis of the bilateral lower extremities or a pathologic medullary hyperhidrosis caused by aberrant connection of sympathetic sudomotor afferent fibers and parasympathetic secretomotor fibers. The gustatory nature and characteristic distribution on the head, face, and scalp suggest that both physiologic and pathologic mechanisms play a role in the genesis of this condition.

Sweating abnormalities are common in poorly-controlled DM and are thought to arise as a consequence of autonomic dysfunction, microangiopathy, and neuropathy. Diabetic gustatory sweating typically occurs in patients with diabetic nephropathy, and the onset may be sudden. It typically persists indefinitely; although, unexplained resolution after renal transplantation has been described. The severity ranges from mild to debilitating. Anticholinergic drugs are highly effective if tolerated. Glycopyrrolate is available in both systemic and topical preparations. Care should be taken to counsel patients on side effects and regular follow up with ophthalmology should be emphasized. Case reports of successful treatment with botulinum toxin as well as the topical application of aluminum chloride 20% solution have been reported. While mild cases often do not require treatment, treatment of severe cases can be life changing.

This case of diabetic gustatory hyperhidrosis was presented for clinical interest.

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CHICAGO DERMATOLOGICAL SOCIETY **Case #7**

Presented by Rebecca Kaiser, MD, Keyoumars Soltani, MD, Vesna Petronic-Rosic, MD, MSc, Christopher R. Shea, MD
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PATIENT A

HISTORY OF PRESENT ILLNESS
A 43-year-old, African American female presented for evaluation of exquisitely painful, expanding, lesions of the bilateral thighs and buttocks. She reported onset two weeks previously with bullae, which rapidly evolved to retiform, purpuric plaques. She endorsed nausea and fatigue but denied fever and chills.

PAST MEDICAL HISTORY
Alcoholic cirrhosis, complicated by renal failure (hemodialysis initiated one month earlier), chronic anemia, neuropathy, and protein-calorie malnutrition

FAMILY HISTORY
Non-contributory

MEDICATIONS
Lactulose, rifaximin, sulfamethoxazole-trimethoprim, sevelamer carbonate, midodrine, pantoprazole, zinc sulfate

ALLERGIES
Ceftriazone, ciprofloxacin

PHYSICAL EXAMINATION
Examination revealed a well-nourished, tearful African American woman. On the bilateral thighs and buttocks were retiform purpuric plaques with surrounding, indurated rims of erythema that were exquisitely tender to touch. Flaccid bullae and serous drainage were located at the periphery of select purpuric plaques, and one plaque was centrally ulcerated. Her lower extremities were grossly edematous. No lymphadenopathy was appreciated.

HISTOPATHOLOGY
Punch biopsy of the left thigh was obtained for histopathologic analysis, which demonstrated amphophilic granular deposits in the blood vessel walls and free in the subcutaneous adipose tissue. These deposits were highlighted by the von Kossa stain. There were additional areas of vessel wall necrosis with leukocytoclasis, and extravasated red blood cells. Staining with periodic acid-Schiff and Gram stains was negative for organisms.

LABORATORY DATA
Complete Blood Count: Grossly abnormal with leukocyte count of 13.7x10^3/μL (3.5 – 11.0), hemoglobin of 7.0 g/dL (11.4 – 14.4), and platelet count of 130x10^3/μL (150 – 450)
Comprehensive metabolic panel: within normal limits except for elevated creatinine of 2.9 mg/dL (0.5 – 1.4), albumin of 3.3 g/dL (3.5 – 5.0), total bilirubin of 4.5 mg/dL (0.1 – 1.0), unconjugated bilirubin of 2.2 mg/dL (0.1 – 1.0), and serum alkaline phosphatase of 141 U/L (30 – 120)
Mineral Balance: Calcium (corrected for albumin), inorganic phosphate, and magnesium were within normal limits.
Parathyroid Hormone: 39 pg/mL (15 – 75)

Coagulation Studies: PT 21.8 s (12.0 – 14.7), INR 1.9 (0.9 – 1.1), and PTT 47.6 s (24.0 – 34.0)

DIAGNOSIS
Calciphylaxis with concurrent leukocytoclastic vasculitis

CLINICAL COURSE
The patient was admitted for pain control and shortly thereafter discharged to a subacute rehabilitation center. Sodium thiosulfate was started after histologic-confirmation of calciphylaxis diagnosis. She was readmitted two weeks later with profound anemia, leukocytosis, progression of ulcerations, and worsening pain. Plastic surgery recommended against debridement. Wound cultures grew Pseudomonas aeruginosa and Enterococcus faecalis. After initial treatment with vancomycin and piperacillin/tazobactam, infectious disease specialists recommended the discontinuation of antibiotics, attributing bacterial growth to colonization rather than acute infection. The patient was maintained on sodium thiosulfate and discharged to a subacute rehabilitation center. She died soon thereafter—six weeks following her tissue diagnosis of calciphylaxis and leukocytoclastic vasculitis.

PATIENT B

HISTORY OF PRESENT ILLNESS
A 50-year-old Caucasian female was admitted to the hospital from an outpatient hepatology visit with erythematous to violaceous, exquisitely painful lesions on her thighs. The patient stated that she developed nodules on her thighs three weeks previously, which subsequently became erythematous, warm, and tender. She reported two admissions at an outside hospital for pain control.

PAST MEDICAL HISTORY
Alcoholic cirrhosis complicated by end-stage renal disease (hemodialysis initiated three months earlier), type 2 diabetes mellitus, and depression

PAST SURGICAL HISTORY
Transjugular intrahepatic portosystemic shunt placement with multiple revisions

FAMILY HISTORY
Non-contributory

MEDICATIONS
Insulin (regular human; glargine), lactulose, rifaximin, midodrine, sodium bicarbonate, zinc sulfate, ferrous sulfate, alprazolam, doxepin, duloxetine, gabapentin, famotidine

ALLERGIES
No known drug allergies

PHYSICAL EXAMINATION
Examination revealed a well-nourished, comfortable-appearing, Caucasian female. On the right buttock and bilateral thighs were large, 10 – 30 cm erythematous to violaceous, indurated, retiform plaques, some with central duskiness, ulceration, and black eschar.

HISTOPATHOLOGY
Punch biopsy of the right thigh was obtained for histopathologic analysis, which demonstrated amphophilic granular deposits in the blood vessel walls and free in the subcutaneous adipose tissue. The von Kossa stain confirmed calcium in the vessels and soft tissue. A deep blood vessel demonstrated focal

fibrinoid necrosis of its wall and karyorrhexis of neutrophils, as well as focal thrombosis. Staining with periodic acid-Schiff, methenamine silver, and Fite stains were negative for organisms.

LABORATORY DATA

Complete Blood Count: notable for leukocyte count of 11.9*10^3/μL (3.5 – 11.0), hemoglobin of 7.3 g/dL (11.4 – 14.4)
Comprehensive metabolic panel: within normal limits except for elevated creatinine of 5.2 mg/dL (0.5 – 1.4), albumin of 2.2 g/dL (3.5 – 5.0), conjugated bilirubin of 0.5 mg/dL (0.0 – 0.3), and serum alkaline phosphatase of 240 U/L (30 – 120)
Mineral Balance: calcium (corrected for albumin) and magnesium were within normal limits. Inorganic phosphate 5.5 mg/dL (2.5 – 4.4 mg/dL), 15-Hydroxy-Vitamin D < 7 ng/mL (10 – 52)
Parathyroid Hormone: 255 pg/mL (15 – 75)
Coagulation Studies: PT 15.8 s (12.0 – 14.7), INR 1.3 (0.9 – 1.1), and PTT 47.6 s (24.0 – 34.0)
Auto-antibodies/Serology: ANA, C3, C4, cryoglobulin, anti-dsDNA, and RF all within normal limits

DIAGNOSIS

Calciphylaxis with concurrent leukocytoclastic vasculitis

CLINICAL COURSE

The patient was started on sodium thiosulfate by nephrology. Her hospital course was complicated by the development of acute abdominal pain, with CT scan revealing pneumoperitoneum. Exploratory laparotomy revealed a gastric perforation. The patient was transferred to the surgical ICU, where her postoperative course was complicated by persistent hypotension (requiring vasopressor support), pain, and clotting of multiple central lines. Her condition stabilized prior to development of a rectovaginal fistula, which was repaired surgically. She decompensated shortly following this surgical procedure with respiratory failure and profound hypotension requiring ventilation and vasopressor support. Her family decided to withdraw care, and she died thirteen weeks following her tissue diagnosis of calciphylaxis and leukocytoclastic vasculitis.

DISCUSSION

Calciphylaxis, also known as calcific uremic arteriopathy, is a devastating and uncommon disease, causing significant morbidity and associated with a one-year mortality rate of 45 – 80%. Calciphylaxis predominantly affects patients with chronic kidney failure treated with dialysis. It has also been described in patients with normal kidney function, most commonly those with primary hyperparathyroidism, malignancy, alcoholic liver disease, coagulopathies, and connective tissue diseases. Incidence peaks in the fifth decade of life. Caucasian patients are more commonly affected, as are females. Among patients on hemodialysis, high-risk comorbid conditions include diabetes mellitus, obesity, autoimmune conditions, hypercoagulable states, prolonged treatment with dialysis, and hypoalbuminemia.

The first clinical diagnosis of calciphylaxis was by Bryant and White in 1898, who described it in a six-month-old child with hydronephrosis. The term “calciphylaxis” was coined by Selye, *et al.* in 1961 to describe an induced systemic hypersensitivity reaction producing cutaneous calcinosis in rats. This inducible calcification resulted from exposure of rats to calcifying “sensitizers,” such as vitamin D compounds, parathyroid hormones, and sodium sulfathiazole, and subsequent “challengers,” such as metallic salts and albumin. Although an imperfect recapitulation of human disease, this rat model shaped the conception of calciphylaxis as resulting from dysregulation of calcium, phosphate, and parathyroid hormone levels. Subsequent research has begun to unravel the complex nature of this disease, but the exact pathogenesis remains elusive.

The lesions of calciphylaxis start out as livedoid erythema and subsequently evolve to retiform purpura, indurated plaques, nodules, and ulcerations, all of which are extremely painful. Palpable calcification and

bullae have been noted. A distal pattern of involvement is associated with favorable outcomes whereas involvement of the thighs, buttocks, or abdomen portends a grave prognosis . Involvement of the face and upper extremities is rare. Although cutaneous lesions are most common, vascular calcification within internal organs has been reported. Sepsis is the most common cause of death.

Biopsy is required to definitively diagnosis calciphylaxis. The hallmark histopathologic feature is intravascular calcium deposition in the media of dermal and subcutaneous arterioles. Calcium deposition can be highlighted with von Kossa or Alizarin red stains. Thrombi, fibrointimal hyperplasia, panniculitis, and cutaneous necrosis can also be seen. Multiple sources note a characteristic absence of vasculitis.

The treatment of calciphylaxis requires a multi-disciplinary approach. Wound care, including use of hyperbaric oxygen and sterile maggot therapy, aims to facilitate wound healing, avoid buildup of devitalized tissue, and prevent infection . Surgical debridement remains controversial due to the risk of infection. Regulation of calcium, phosphate, and parathyroid hormone levels is recommended. Multiple systemic treatment options exist, the mainstay of which is intravenous sodium thiosulfate. Its exact mechanism of action is unknown, but it is thought to act as an antioxidant, vasodilator, and chelator of calcium salts. Small studies have shown potential benefits of bisphosphonates as well as cinacalcet (a calcimimetic suppressor of parathyroid hormone secretion). The use of systemic corticosteroids remains controversial although growing evidence suggests inferior outcomes in patients treated with corticosteroids and other immuno-suppressants due to an increased risk of sepsis. Nutritional optimization, pain management, and aggressive dialysis are also important.

The implications of the histopathologic findings of leukocytoclastic vasculitis with calciphylaxis are unclear and, to our knowledge, have not been described previously. Leukocytoclastic vasculitis (LCV) is an immune complex-mediated, small vessel vasculitis with characteristic histopathologic features of vessel wall neutrophilic infiltration with leukocytoclasis, endothelial cell damage, fibrinoid necrosis, and extravasation of red blood cells. Infectious, autoimmune, drug, and malignant etiologies have been described, though the majority of LCV cases are idiopathic. LCV is often isolated to cutaneous vasculature but also can be seen with systemic vasculitis.

Incidental vasculitis, resulting from vascular injury in areas of trauma or ulceration, has been described. Though both of our patients had ulcers, incidental vasculitis is focally restricted to areas of ulceration and necrosis, the features of which were not noted in our tissue cuts. Alternatively, these histopathologic findings could demonstrate a previously undescribed population of calciphylaxis patients. Both patients described in this series shared certain clinical features - hepatorenal syndrome, calciphylaxis diagnosis rapidly following initiation of dialysis, and precipitous clinical decline. More cases and research will be required to determine what, if any, implications—prognostic, therapeutic, or otherwise--these concurrent histopathologic features possess.

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CHICAGO DERMATOLOGICAL SOCIETY **Case #8**

Presented by Larry A Napolitano Jr, MD, Christopher R. Shea MD, Arlene Ruiz de Luzuriaga MD,MPH
Section of Dermatology, Department of Medicine, University of Chicago

HISTORY OF PRESENT ILLNESS

A 47-year-old Caucasian male, recently diagnosed with HLA-DQ2 and anti-tissue transglutaminase antibody-positive celiac disease was referred to dermatology by his gastroenterologist for evaluation and treatment of a pruritic blistering rash of the extensor elbows, knees, and buttocks. The gastrointestinal symptoms, abdominal pain and diarrhea, and cutaneous symptoms started two years prior to presentation and had taken a waxing and waning course. The rash initially improved with a gluten-free diet, but subsequent flares led the patient to present to an outside dermatologist, who obtained biopsies, which led to the diagnosis of dermatitis herpetiformis. He was prescribed mometasone 0.1% ointment for use twice daily during flares, but with inadequate response.

PAST MEDICAL HISTORY

Gastroesophageal reflux disease
Celiac disease

FAMILY HISTORY

Family history of colon cancer in mother and thyroid disease in father

MEDICATIONS

Mometasone 0.1% ointment twice daily during flares, omeprasole 40 mg twice daily

ALLERGIES

No known drug allergies

PHYSICAL EXAMINATION

Clusters of well-demarcated, 3-5 mm, pink papules, a few having erosive centers, scattered over extensor knees, extensor elbows, and superior buttocks bilaterally. Intact vesicles were not observed.

LABORATORY DATA

Thyroid-stimulating hormone 2.08 (0.3-4.00 mcU/mL)
HLA-DQ2-positive, HLA DQ8-negative
Anti-tissue transglutaminase IgA antibody 21 Units (negative= <20 U, weak positive 20-30 U, positive =>30 U)
Anti-gliadin IgG antibody 18 U (negative <20 U, weak positive 20-30 U, positive =>30 U)
Glucose-6-phosphate dehydrogenase (G6PD) 10.0 U/g Hb (8.8-13.4)

HISTOPATHOLOGY

Slides from punch biopsy of the left buttock were reviewed at the University of Chicago. There were microabscesses in the dermal papillae, composed mainly of neutrophils and a few eosinophils. Subepidermal vesicles were noted. The dermis had a superficial and deep perivascular infiltrate of lymphocytes and eosinophils.

DIAGNOSIS

Dermatitis herpetiformis

TREATMENT AND COURSE

Upon presentation to the University of Chicago dermatology practice, his gluten free diet was continued, and he was started on dapsone 50 mg by mouth daily for one month with good control. This dose was subsequently decreased to 25 mg by mouth daily without recurrence of the rash for two months. Due to patient's concerns about recent increase in headaches and relationship to medications, dapsone was subsequently discontinued. Pruritic vesicles occurred within 48 hours. Dapsone was restarted at 25 mg by mouth daily with stable control of dermatitis herpetiformis for six months. While on 25 mg of dapsone, the patient developed nausea, right upper quadrant abdominal pain, and headaches. Gastrointestinal work-up was negative and gastroenterology attributed symptoms to dapsone. The patient discontinued his oral dapsone with subsequent cutaneous DH flare within three days. However, his gastrointestinal symptoms resolved within five days of stopping oral dapsone. A trial of triamcinolone 0.1% ointment and flurandrenolide 0.05% lotion did not improve his cutaneous symptoms. The patient restarted dapsone at his maximum tolerated dose of 6.75 to 12.5mg by mouth three times a week with persistent, but stable, cutaneous manifestations. Given poor tolerance of oral dapsone, this medication was discontinued and topical dapsone 5% gel initiated with twice daily application to affected areas. The patient reported initial resolution and subsequent stable control with topical-only regimen. The patient restarted pral dapsone (12.5 mg by mouth three times a week) of his own volition, without gastrointestinal upset. Patient is now 6months out, with well controlled DH, and intermittent diarrhea.

DISCUSSION

Dermatitis herpetiformis (DH) was initially described by Louis Duhring in 1884. It is a rare dermatologic condition with an estimated prevalence of 11.2 per 100,000 people, affecting mostly patients of Northern European descent and with a male to female ration ranging from 1.5:1 to 2:1. DH is multifactorial disease with strong genetic and autoimmune influences, including a clear immunologic relationship to celiac disease. DH is a polymorphic pruritic skin disease typically characterized by grouped, 1-to 3-mm papules, seropapules, vesicles, crusted erosions, and/or excoriations. Diagnosis of DH can be done via serologic testing, genetic testing or direct immunofluorescence studies. Anti-endomysial and anti-tissue transglutaminase antibodies can be detected through serology, each found to be highly specific with moderate sensitivity for DH. The absence of human leukocyte antigen (HLA) DQ2 or DQ8 has high negative predictive value for DH, such that patients lacking these alleles are very unlikely to have the disease. On direct immunofluorescence, granular deposits of IgA at the tips of dermal papillae are pathognomonic of DH. Proper management of DH includes a strict gluten-free diet (GFD). A consultation with a dietician can be helpful, as a GFD can be difficult to maintain. Sulfone medications, such as dapsone, are often necessary for rapid control of symptoms. Oral dapsone is usually well tolerated, with hematologic abnormalities being the most notable side effect. However, neurological and GI symptoms, including headaches, neuropathy, abdominal pain, nausea, vomiting, and pancreatitis are not uncommon. Prior to starting oral dapsone a screening of glucose-6-phosphate dehydrogenase deficiency is warranted to prevent severe dapsone-mediated hemolysis.

Topical dapsone is a well-tolerated medication with mild side effects including local dryness, rash and sunburn. Topical dapsone was initially introduced in 2004 for the topical treatment of acne vulgaris. It is considered safe to use in patients with glucose-6-phosphate dehydrogenase deficiency and those with sulfonamide allergies, giving a possible treatment option for those with contraindication to oral dapsone. A review of the literature revealed two case reports of methemoglobinemia due to topical dapsone.

There have been two reports in the literature of successful treatment of DH with topical dapsone 5% gel. The first was in a 14 year old male with direct immunofluorescence confirmed DH, with recalcitrant disease on oral dapsone at 25mg daily. A split-body trial of topical dapsone was performed for four weeks with subsequent blinded examination by two dermatologists finding relative improvement of the skin treated with topical dapsone. The second case involved a 66-year-old female, who was started on topical dapsone while awaiting lab work to start oral dapsone. She experienced dramatic improvement in her DH

within two weeks of starting therapy and had lasting control at one year of follow up on GFD and topical dapsone only. Our case demonstrates short term disease control with twice daily topical dapsone 5% gel and a typically subtherapeutic dose of oral dapsone (12.5 mg three times weekly) in a patient unable to tolerate therapeutic doses of oral dapsone.

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CHICAGO DERMATOLOGICAL SOCIETY **Case #9**

Presented by Haider K. Bangash, MD, Vesna Petronic-Rosic, MD, MSc, Arlene Ruiz de Luzuriaga, MD, MPH
Section of Dermatology, Department of Medicine, University of Chicago

UNKNOWN

A 51-year-old African American male presented with a 3-year history of recurrent pruritic nodule on right cheek.

CHICAGO DERMATOLOGICAL SOCIETY **Case #10**

Presented by Juliana Gao, MD[1], Vera Tesic, MD[2], Vesna Petronic-Rosic, MD, MSc[1]
[1]Section of Dermatology, Department of Medicine, University of Chicago
[2]Department of Pathology, University of Chicago

HISTORY OF PRESENT ILLNESS

An 85-year-old Caucasian female presented to dermatology clinic for evaluation of a growing painful nodule on the scalp. It had recently become crusted. She also complained of intermittent associated stabbing and shooting pain. The lesion was thought to be a cyst, and she was scheduled for excision.

Prior to the onset of symptoms, the patient had traveled to India and Belize, returning to the United States just a few weeks prior to presentation.

PAST MEDICAL HISTORY

Squamous cell carcinoma in-situ
Basal cell carcinoma

FAMILY HISTORY

Non-contributory

MEDICATIONS

Atovaquone-proguanil
Calcium carbonate
Econazole cream

ALLERGIES

No known drug allergies

PHYSICAL EXAMINATION

Initial examination in clinic showed a 1 cm subcutaneous nodule with overlying linear erosion and hemorrhagic crust. Examination in procedure clinic 4 weeks later showed a 2.5 cm subcutaneous nodule with central 1 mm “punched-out” opening.

INTRAOPERATIVE FINDINGS

After the area was prepped and anesthetized, a standard fusiform incision was made over the subcutaneous nodule. Upon removal of the overlying skin, a 1.2 cm yellow striated larva was identified. The larva was alive and moving at the time. The specimen was then sent to microbiology for further identification.

HISTOPATHOLOGY

Histopathology of the overlying skin showed dense, chronic inflammation, with neovascularization and edema associated with tunneling epithelium, consistent with granulation tissue and overlying fistula tract.

LABORATORY DATA

The larva was identified as *Dermatobia hominis*

DIAGNOSIS

Furuncular botfly myiasis

TREATMENT AND COURSE

The patient was empirically started on cephalexin 500 mg twice a day for a total of ten days. A head CT was obtained and did not show evidence of skull or sinus involvement. At one week follow up, she was healing well and reported resolution of the stabbing and shooting pain over the area.

DISCUSSION

Geographic locations of cutaneous myiasis are usually limited to the tropical and subtropical areas, including countries in Central America, South America, Africa and the Caribbean Islands. It is very uncommon within the United States, and the majority of patients had recent travel to topical areas. Most commonly, the botfly causes furuncular myiasis, but patients with open wounds can also develop wound myiasis. Cavitary myiasis occurs when the botfly larva is deposited near facial orifices, where it can then burrow deeper to involve the nearby sinuses.

Dermatobia hominis (human botfly) is one of the most common flies that cause human infestation worldwide, and one of the two frequent causes of furuncular myiasis. The life cycle of a botfly involves a blood-sucking arthropod as well as a warm-blooded host (mammal or avian). The adults of *D. hominis* are free living. During breeding, they lay eggs on the bodies of mosquitos, where they are cemented via a glue-like substance. Larvae develop within the eggs and remain there until the arthropod comes in contact with a warm-blooded host during feeding. Once in contact with the host, the larva penetrates into the skin and remains in a subdermal cavity for the next 5 to 10 weeks where it feeds on the host as it matures. Typically, these present as boil-like lesions with a central punctum which functions as a breathing hole for the larva. Once the larva matures, it burrows through the breathing hole and drops to the ground where it pupates and becomes a free-living botfly.

During their course of maturation, botfly myiasis usually does not pose any danger to the host. Patients may experience pruritus, sensations of movement and lancinating pain, which may be explained by rotational movement of the larvae and its rows of hooklets. Secondary bacterial infections with *Staphylococcus* and Group B S*treptococcus* have been reported. Overall, furuncular myiasis is a self-limited infestation as the larvae will eventually leave the host; however, leaving the parasite to perform its natural cycle is generally not recommended.

There are several methods used for the extractions of the botfly larvae. Traditional folk remedy calls for a strip of bacon over the central punctum to suffocate the larvae, which forces it to surface for air over the course of several hours, at which point the larva can then be gently extracted with a forceps. This can also be accomplished using petroleum jelly, liquid paraffin, beeswax, or even nail polish. Other authors have advocated the use of 1% lidocaine to paralyze the parasite, and liquid nitrogen to stiffen the larvae for easier extraction. In most cases, surgical excisions and extractions are unnecessary, but can be done under local anesthesia if other methods of extractions are unsuccessful. Antibiotics are recommended if there are signs or symptoms of secondary bacterial infection.

We present this case of furuncular myiasis for clinical interest, and to highlight the importance of travel history in the diagnosis of cutaneous parasitic infections.

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years and 50% at 5 years after diagnosis. MCC usually presents as a rapidly growing, asymptomatic, reddish-blue dermal papule or nodule that develops over the course of weeks to months. Many patients present with metastatic disease, and there is a high risk of local, regional, and distant recurrences despite treatment.

There are three main risk factors associated with the development of MCC – ultraviolet radiation, immunosuppression, and the Merkel cell polyomavirus (MCPyV). Approximately 80% of all MCCs are associated with MCPyV, whose large T antigen inactivates p53 and retinoblastoma (Rb) proteins. Patients with MCPyV-positive tumors often produce virus-specific T cells and antibodies, which can be monitored during the disease course. MCPyV-positive tumors show strikingly low mutational burdens, especially when compared to UV-induced, MCPyV-negative MCCs, which are characterized by a greater than 100-fold higher mutational burden. Immunosuppressed patients, particularly solid organ transplant recipients and patients with B-cell lymphoma, show increased MCC incidence.

Patients who present with localized disease are staged using PET/CT and MRI. They are treated with complete resection of the primary tumor and SLN biopsy. They are also considered for adjuvant radiation therapy to the local lymph node basin, which is associated with improved overall survival in stage I or II MCC (localized, clinically node-negative disease, with primary tumor size < 2 cm or > 2cm, respectively).

Until recently, options for treatment of advanced MCC (stage III/IV) were limited. Cytotoxic chemotherapy, while frequently inducing temporary responses, offers a median progression-free survival of only 3 months and is not associated with an improved overall survival compared to surgical resection alone. Several recent trials using programmed cell death protein 1 (PD-1)-directed immune checkpoint inhibitors have shown substantial promise. A recent phase II study of pembrolizumab, an anti-PD-1 antibody, in 26 patients with advanced MCC showed objective responses in 14/25 (56%) patients, with 4 complete responders (CRs) and 10 partial responders (PRs). With a median follow-up of 33 weeks, only 2 of 14 patients had relapsed. Six-month progression-free survival was 67%. Importantly, both MCPyV-positive and negative patients showed responses to pembrolizumab, with 62% and 50% response rates, respectively. Another phase II trial with avelumab, an anti-programmed death ligand (PD-L1) antibody, in patients with MCC refractory to chemotherapy, showed objective responses in 28/88 (31.8%) patients, including 8 CRs and 20 PRs, with maintenance of response in the majority (23/28 or 82%) of patients.

KEY POINTS

1. MCC is a rare but aggressive skin cancer. Localized disease is treated with surgical resection and/or radiation but has a high rate of local, regional, and distant recurrences.
2. PD-1 pathway checkpoint inhibitors have shown substantial promise for patients with advanced MCC.

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