PROTOCOL BOOK • SEPTEMBER 13, 2023

CHICAGO DERMATOLOGICAL SOCIETY 2023

Monthly Meeting

Co-hosted by Loyola University Medical Center Division of Dermatology

Chicago Dermatological Society

PROTOCOL BOOK
September 13, 2023

Co-hosted by
Loyola University Medical Center Division of Dermatology

Guest Speaker: Margo Reeder, MD
Associate Professor
Department of Dermatology
University of Wisconsin
School of Medicine and Public Health in Madison

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INVITED GUEST LECTURER

Margo Reeder, MD

Margo Reeder, MD is an Associate Professor in the Department of Dermatology at the University of Wisconsin School of Medicine and Public Health in Madison. She received her medical degree from Mayo Clinic School of Medicine and completed her residency at University of Wisconsin School of Medicine and Public Health. She is the Medical Director of General Dermatology at UW and also a Physician Informaticist.

Dr. Reeder specializes in allergic contact dermatitis and patch testing. She is a member of the North American Contact Dermatitis Group and studies the epidemiology of allergic contact dermatitis. Dr. Reeder is a previous board member for the American Contact Dermatitis Society (ACDS) and is the current ACDS Contact Allergy Management Program (CAMP) Director.

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PROGRAM

Co-hosted by
Loyola University Medical Center Division of Dermatology

September 13, 2023
Donald E. Stephens Convention Center – Rosemont, IL

8:00 a.m.	**Registration & Continental Breakfast with Exhibitors**
8:30 a.m. - 10:15 a.m.	**Clinical Rounds** Slide viewing/posters – ongoing through the early morning
9:00 a.m.	**Welcome and Opening Comments** *Morayo Adisa, MD- CDS President*
9:00 a.m. - 10:00 a.m.	**Morning Lecture** **"Contact Dermatitis and Patch Testing: Pearls and Pitfall"** **Margo Reeder, MD**
10:00 a.m. - 10:30 a.m.	**Break and Visit with Exhibitors**
10:30 a.m. - 12:00 p.m.	**Resident Case Presentations & Discussion**
12:00 p.m. - 12:30 p.m.	**Box Lunches & Visit with Exhibitors**
12:30 p.m. - 1:00 p.m.	**CDS Business Meeting**
1:00 p.m. - 2:00 p.m.	**Afternoon Lecture** **"Updates in Allergic Contact Dermatitis"** **Margo Reeder, MD**
2:00 p.m.	***Program Adjourn***

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Loyola University Medical Center
Division of Dermatology

Chicago Dermatological Society Meeting
September 13, 2023

Dermatology Residents

Third Year
Kyle Bhatia, MD
Blanca Estupiñan, MD
Adam Souchik, MD
Zisansha Zahirsha, MD

Second Year
Adnan Ahmed, MD
Rachit Gupta, MD
Vik Patel, MD

First Year
Sarah Benton, MD
Robin Wang, MD
Lauren Watchmaker, MD

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10:30 a.m. - 12:00 p.m

Resident Case Presentations & Discussion

Chicago Dermatologic Society **Case #1**

[1]Viki Patel, MD, [2]Orr Meltzer, BS, [1]Wendy Kim, DO, [3]Mitul Modi, MD, [3]Jodi Speiser, MD
[1]Division of Dermatology, Loyola University Medical Center
[2]Stritch School of Medicine, Loyola University Medical Center
[3]Department of Pathology, Loyola University Medical Center

HISTORY OF PRESENT ILLNESS

An 11-year-old female with a past medical history of rolandic epilepsy was admitted to the burn intensive care unit with a 1-day history of a blistering, pruritic rash that initially started periorally and then spread to her trunk and extremities with subsequent facial swelling. Her mother reported that they had traveled to Florida for a family vacation and for the three days prior to onset of the rash, the patient had spent considerable time in the sun, sunbathing and swimming without any form of photoprotection. She denied any new food allergies, new medications during the trip, or any family members with similar symptoms. She was diagnosed with rolandic seizures two years prior, which were previously well-controlled on levetiracetam. She later developed tongue tingling episodes four weeks prior to presentation and was started on oxcarbazepine. Given persistent tongue paresthesias, she was in the process of titrating oxcarbazepine and recently increased to 300mg twice daily four days prior to the onset of the rash.

PAST MEDICAL HISTORY

Rolandic epilepsy

MEDICATIONS

Levetiracetam, oxcarbazepine

ALLERGIES

No known drug allergies

FAMILY HISTORY

No pertinent family history

SOCIAL HISTORY

No alcohol, smoking, or illicit drug use

PHYSICAL EXAMINATION

On physical exam, a diffuse, vesicular, nontender rash on a background of sharply demarcated dusky, erythematous plaques was present in a strongly photodistributed pattern, including the malar cheeks, arms, thighs, upper chest, and abdomen. She also had labial edema with mild crusting, but no erosions or bullae were present as well as an absence of anogenital mucosal lesions. Notably, the rash was absent on the philtrum, nasal base, chin, and other areas typically protected from direct exposure to UVR when wearing a swimsuit. Nikolsky sign was negative.

DERMATOPATHOLOGY

Histologic sections were consistent with full thickness epidermal necrolysis with serum deposition and underlying re-epithelialization. There was underlying mild predominantly lymphocytic inflammation. These changes could represent an older area of SJS/TEN spectrum disease or other bullous disease, which was favored, or, less likely a robust phototoxic drug eruption. DIF studies were negative.

ADDITIONAL STUDIES

Complete blood count, complete metabolic profile, and liver function tests were unremarkable.

DIAGNOSIS

Photodistributed Stevens-Johnson Syndrome

TREATMENT AND COURSE

Our patient was started on topical triamcinolone 0.1% ointment to affected areas on the face and lips and topical clobetasol 0.05% ointment on affected areas from the neck down with hydralazine as needed for pruritus. Three days later, she noted new dysuria but improvement of pruritus and appearance of cutaneous lesions. On physical exam, there were new punctate erosions on her vulvar mucosa. Given these new mucosal findings, a shave biopsy was obtained from an arm lesion and demonstrated full thickness epidermal necrolysis with serum deposition, underlying re-epithelialization, and underlying mild predominantly lymphocytic inflammation, in concordance with SJS/TEN. Significant improvement was noted after two weeks with continued topical therapy and only post-inflammatory hypopigmentation remained. At the most recent follow-up, our patient had no residual skin lesions and no associated sequalae.

DISCUSSION

Photodistributed SJS/TEN is an underrepresented topic in the literature. To date, there are nine reported cases of photodistributed SJS/TEN with the first reported case in 1989 and most recently in 2022. Of the nine cases, the only pediatric patient was a 12-year-old male with the inciting medication being chloroquine/sulfadoxine-pyrimethamine. Eight cases occurred in women between the ages of 19 and 48. On average, the time of ultraviolet radiation (UVR) exposure to onset of rash was between 24 to 72 hours with the majority (seven cases) being secondary to intense UVR exposure such as tanning bed use.

In our patient, the timing of the onset of rash, significant UVR exposure, mucosal involvement and histopathologic evidence strongly suggested photodistributed SJS. Previous studies have suggested that the role of UVR may provide a “second-hit” to keratinocytes that have endured cytotoxic damage from the offending agent, resulting in further cytokine activation at the epidermis and subsequent epidermal damage, producing the vesicular lesions in areas particularly exposed to the UVR. It is also possible that this initial robust local reaction evolves into a systemic response leading to more classic SJS/TEN manifestations, particularly mucositis. Our case further supports this theory.

Prior studies have also demonstrated photodistributed SJS in adult patients on antiepileptics, DMARDs, antibiotics, antifungal, antimalarials and immunosuppressives. Our case highlights the importance of assessing social history when evaluating a new onset rash in the setting of extensive UVR exposure, particularly in patients initiating or changing their antiepileptic regimen. Further exploration is needed to further delineate the etiology and pathogenesis behind the “second-hit” hypothesis of photodistrbuted SJS/TEN.

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Chicago Dermatologic Society **Case #2**

[1]Kyle Bhatia, MD, [1]Adnan Ahmed, MD, [1]Laryn Steadman, MD, [2]Jodi Speiser, MD, [1]Wendy Kim, DO
[1]Division of Dermatology, Loyola University Medical Center
[2]Department of Pathology, Loyola University Medical Center

HISTORY OF PRESENT ILLNESS

Patient 1:
A 34-year-old male presented to an outside hospital with erythroderma present for 1 week associated with leukocytosis and fever. The patient had been following with an outside dermatology provider and carried a diagnosis of psoriasis that failed to improve on methotrexate and topical steroids. He had recently been started on adalimumab and a 2-week prednisone taper, with erythroderma developing after completion of the taper. He was started on intravenous fluids and cefazolin at an outside hospital due to concern for left leg cellulitis. Skin biopsy of the left thigh was performed by general surgery, and results were pending when he was transferred to Loyola University Medical Center for further evaluation and management.

Patient 2:
A 62-year-old female was transferred to Loyola University Medical Center for liver transplant evaluation. Dermatology was consulted for a diffuse pruritic rash present for several months. She had been following with an outside dermatology provider and had been started on dupilumab for a suspected diagnosis of eczematous dermatitis. She noted improvement of her pruritus while on dupilumab but experienced no improvement of her rash.

PAST MEDICAL HISTORY

Patient 1: Suspected psoriasis, trisomy 21 (Down syndrome)

Patient 2: Suspected eczematous dermatitis, cirrhosis secondary to nonalcoholic steatohepatitis, type II diabetes mellitus, hypertension

MEDICATIONS

Patient 1: Adalimumab, recent 2-week prednisone taper, triamcinolone 0.1% ointment

Patient 2: Dupilumab, lactulose, rifaximin, insulin, metoprolol

ALLERGIES

Patient 1 and 2: No known drug allergies

FAMILY HISTORY

Patient 1 and 2: No pertinent family history

SOCIAL HISTORY

Patient 1 and 2: No pertinent social history

PHYSICAL EXAMINATION

Patient 1: The patient was erythrodermic, with thick, crusted plaques present over large areas of his scalp, face, trunk, extremities, hands, and feet.

Patient 2: The patient was well-appearing. Crusted plaques were present on the interdigital web spaces of both hands. Erythematous to hyperpigmented papules and plaques with faint scale were present diffusely on the trunk.

DERMATOPATHOLOGY

Patient 1: Histologic sections from the outside hospital biopsy demonstrated numerous mites, ova, and scybala in the stratum corneum and a diffuse dermal lymphocytic infiltrate with eosinophils.

Patient 2: Histologic sections from shave biopsies of a web space and of a papule on the back both demonstrated mites in the stratum corneum. Notably, the biopsy had only a mild inflammatory infiltrate with few eosinophils.

ADDITIONAL STUDIES

Patient 1: A complete blood count demonstrated a mildly elevated white blood cell count at 10.9 (3.5 - 10.5 K/μL), without eosinophilia.

Patient 2: A complete blood count had no relevant findings.

DIAGNOSIS

Patient 1: Erythroderma secondary to crusted scabies

Patient 2: Crusted scabies

TREATMENT AND COURSE

Patient 1 was treated with full-body application (left on overnight) of permethrin 5% cream every other day for two weeks. Additionally, he was treated with oral ivermectin 200 μg/kg on days 1, 2, 8, 9, 15, 22, and 29. His erythroderma improved within days of starting treatment. He was maintained on contact isolation until discharge. Thorough cleaning of the patient's room, bedding, and clothing was performed. Household cleaning recommendations were reviewed with the patient's family, and his household contacts were simultaneously treated with two doses of topical 5% permethrin cream spaced one week apart. Hospital staff members were monitored closely, with some opting for empiric treatment with permethrin. His therapies for psoriasis were discontinued, and he has followed up outpatient without signs of psoriatic flare.

Patient 2 was treated with full-body application (left on overnight) of permethrin 5% cream every third day for approximately one week. Treatment with oral ivermectin 200 μg/kg on days 1, 2, 8, 9, and 15 was also planned, but the patient expired from unrelated reasons midway through the course. Her symptoms had been improving at the time of her death.

DISCUSSION

Crusted scabies, formerly Norwegian scabies, is a severe form of infestation with the mite *Sarcoptes scabiei var hominis*. This infestation typically arises in patients that are unable to mount a normal immune response to mites or who have reduced ability to mechanically debride mites. Specific risk factors include human immunodeficiency virus (HIV) infection, leukemia, lymphoma, systemic lupus erythematosus, long-term corticosteroid or other immunosuppressant use, institutionalized status, dementia, and Down syndrome. The condition is also particularly prevalent in remote Aboriginal communities of Northern Australia. Of note, silent infestations in HIV patients can be unmasked with initiation of antiretroviral therapy, which is thought to be a manifestation of immune reconstitution inflammatory syndrome.

This severe form of infestation is highly contagious. A typical scabies infestation has fewer than 20 mites present, while crusted scabies infestations can have thousands to millions of mites. Spread of the infestation can occur via skin-to-skin contact or fomites, and the high mite load of the crusted variant accelerates the incubation period in a new human host to as short as 4-5 days. Additionally, shed crusts can serve as a food supply and protection for mites, allowing mites to live off human hosts for up to a week in crusted scabies infestations.

Crusted scabies infestations classically present with thick, crusted plaques either in a generalized distribution or localized to the hands, feet, periungual areas, scalp, face, trunk, or extremities. The condition can have variable presentations, including psoriasis-like plaques, which can create a diagnostic challenge. Pruritus, normally a cardinal feature of scabies infestation, can be absent in crusted scabies infestations. Severe crusted scabies infestations can present with erythroderma, and patients with crusted scabies are at risk of secondary bacterial infections and sepsis.

Diagnosis of crusted scabies infestations can be made by skin scraping with mineral oil preparation to evaluate for mites, ova, and scybala. Skin biopsy can be helpful if the diagnosis is uncertain.

The US Centers for Disease Control and Prevention (CDC) recommends treatment with both a topical scabicide and oral ivermectin for adult crusted scabies infestations. Topical permethrin 5% cream is the most commonly used topical scabicide and is applied to the entire body, left on overnight, and then washed off in the morning. Topical permethrin should be used every 2-3 days for 1-2 weeks (or until cured) for crusted scabies infestations. Oral ivermectin 200 μg/kg is administered, depending on infection severity, in three doses (days 1, 2, and 8), five doses (days 1, 2, 8, 9, and 15), or seven doses (days 1, 2, 8, 9, 15, 22, and 29). Keratolytic agents can be helpful in removing thick crusts and can help to improve the efficacy of topical scabicides.

Strict infection control measures including contact isolation, laundering of linens, and thorough room cleansing are necessary. Treatment of the patient's household members should be performed simultaneously to prevent ongoing transmission and repeat infestations. All exposed patients, visitors, and staff should also be treated. Detailed

guidelines can be found on the CDC website, and consultation with infection control in the inpatient setting is essential.

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Chicago Dermatologic Society **Case #3**

[1]Adnan Ahmed, MD, [1]Zisansha Zahirsha, MD, [1]Sacharitha Bowers, MD
[1]Division of Dermatology, Loyola University Medical Center

HISTORY OF PRESENT ILLNESS

A one-day-old male born at 39 weeks via home birth presented to the Loyola University Medical Center emergency department with his parents for evaluation of two open wounds on his scalp. The parents reported that the wounds were present at birth. The mother had reportedly received prenatal care, but records were not available. The mother expressed that the patient had some difficulty latching during breast feeding but otherwise had no concerns. The parents denied any consanguinity and reported they had an older son without any medical problems.

PAST MEDICAL HISTORY

None

MEDICATIONS

None

ALLERGIES

No known drug allergies

FAMILY HISTORY

No pertinent family history

SOCIAL HISTORY

Home birth at 39 weeks

PHYSICAL EXAMINATION

Jaundice was noted. The vertex scalp demonstrated two well-demarcated ulcers, each measuring approximately 1.5 cm, with overlying heme crust, without membrane or bone visualized. There was increased surrounding terminal hair density consistent with a subtle hair collar sign. The soft palate had a palpable cleft. The right hand had a supernumerary digit extending from the fifth finger. The left hand had underdevelopment of the fifth digit. On the midline lumbosacral back there was a 0.5 x 1.0 cm pink vascular patch extending across the midline with overlying hypertrichosis. There also was 0.5 cm sacral dimple noted. Testicles were not palpable, and hypospadias was noted. The patient was unable to open his eyes and the bilateral eyelids had yellow discharge.

ADDITIONAL STUDIES

Initial lab work was significant for elevated total bilirubin of 11.4 mg/dL (<8.0 mg/dL) and low glucose level of 11 mg/dL (40-80 mg/dL). A basic metabolic panel was significant for a sodium level of 149 mmol/L (133-142 mmol/L) and creatinine of 1.28 mg/dL (0.2-0.7 mg/dL). A renal ultrasound demonstrated bilateral hydronephrosis. Ultrasound of the head showed a possible malformation or agenesis of the corpus callosum. Follow up magnetic resonance imaging of head was limited by motion and was unable to further evaluate the

corpus callosum. Spinal ultrasound demonstrated low-lying conus medullaris at level of L3-4 with a heterogenous mass at the level of the sacral dimple. Pelvic ultrasound demonstrated ectopic testicles at the lower poles of the kidneys. Karyotype testing revealed three copies of chromosome 13.

DIAGNOSIS

Trisomy 13 (Patau Syndrome)

TREATMENT AND COURSE

The patient was started on local wound care with petrolatum jelly and Xeroform gauze for his aplasia cutis congenita. Initially, the patient had difficulty breathing requiring blow-by oxygen in the emergency department but tolerated room air for the remainder of his admission. Given his cleft palate, he was started on feeds via a nasogastric tube and was noted by speech therapy to be at high risk for aspiration from oral feedings.

Multiple specialties were consulted during the patient's admission. Neurosurgery evaluation recommended further imaging and no surgical intervention. Orthopedic surgery also recommended against any surgical intervention for the supernumerary digit. Endocrinology was consulted due to the patient's hypernatremia and hypoglycemia and recommended intravenous dextrose fluids. His hypoglycemia resolved by discharge. Urology recommended straight catheterization for the patient given the concern for possible tethered spinal cord. Ophthalmology was also consulted.

After diagnosis of trisomy 13, a multidisciplinary meeting was held with the family. The family elected for discharge with home hospice care.

DISCUSSION

Trisomy 13 (Patau Syndrome) is a chromosomal aneuploidy that occurs due to a nondisjunction event during gametogenesis resulting in three copies of chromosome 13. The expression of trisomy 13 can be complete, mosaic or partial (Robertsonian translocation). The majority of cases are due to maternal nondisjunction, but paternal cases have also been noted. It is the third most common trisomy with an incidence rate of 1 in 10,000 to 16,000 cases. Mortality rates within the first year are approximately 90%.

Fetal ultrasound screenings evaluating for fetal nuchal translucency during pregnancy can assist in determining the diagnosis. Amniocentesis during early second trimester can also be helpful. However, confirmatory diagnosis can only be made by karyotyping or fluorescence in situ hybridization analysis (FISH) after birth.

The clinical phenotype of trisomy 13 is wide-ranging. Presentations can include but are not limited to aplasia cutis, polydactyly, cleft lip or palate, cardiac deformities, microcephaly, and spina bifida. Patients with the disorder will typically have midline defects. Additionally, patients may have liver abnormalities, seizure disorders, and are at elevated risk of developing cancer

There is no cure for trisomy 13 and care is directed at the needs of the patient. Patients diagnosed with trisomy 13 require multidisciplinary care, often including dermatology, neurosurgery, urology, ophthalmology, and cardiology. Treatment is mostly supportive. Interventions for cardiac and neurologic abnormalities are not typically offered due to the unknown long-term benefits for patients. Most treatment regimens for patients are targeted at supporting nutrition and hydration. Currently, it is recommended to engage in a discussion with parents regarding all available treatment options, and many researchers recommend multidisciplinary meetings within hospitals to generate uniform management guidelines for the condition.

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Chicago Dermatologic Society **Case #4**

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[1]Division of Dermatology, Loyola University Medical Center
[2]Section of Dermatology, Edward Hines Jr. VA Hospital

HISTORY OF PRESENT ILLNESS

Patient 1 (update):
A 60-year-old female patient with a history of spinal arthritis and anxiety presented with scattered erythematous, heme-crusted papules and intense pruritus of the posterior neck and bilateral upper extremities, with the right side substantially worse than the left. The patient was sleeping only three to four hours a night due to her symptoms. Prior cervical spine plain radiographs showed degenerative changes most prominent at C5-6. Failed treatments included topical steroids, pramoxine 1% lotion, capsaicin 0.025% cream, calcipotriene 0.005% cream, gabapentin, topiramate, amitriptyline, propranolol, N-acetyl cysteine, and hydroxyzine without relief. Last year, she underwent successful treatment with onabotulinum toxin 100 units injected into the right posterior neck and arm with subsequent resolution of symptoms for one year.

Patient 2:
A 75-year-old male with a history of prurigo nodularis for six years presented with excoriated pink papules and hyperpigmented macules spanning the right posterior neck down the lateral right arm. He was determined to have brachioradial pruritus. Failed treatments included topical steroids, tacrolimus 0.1% ointment, capsaicin 0.025% cream, pramoxine 1% lotion, intralesional triamcinolone, N-acetyl cysteine, gabapentin, quetiapine, sertraline, and neck stretching exercises.

Patient 3:
A 67-year-old male presented with longstanding burning, flushing, and needle-like sensations of the scalp without cutaneous changes. Previous MRI of the cervical spine revealed multilevel disc degeneration, osteophytes, and stenosis spanning the C4-C7 levels. He was diagnosed with scalp dysesthesia. Failed treatments included topical steroids, camphor/menthol lotion, pregabalin, and duloxetine.

PAST MEDICAL HISTORY

Patient 1: Anxiety, arthritis, hyperlipidemia
Patient 2: PTSD, hyperlipidemia, essential thrombocytopenia
Patient 3: Arthritis, gout, diabetes

MEDICATIONS

Patient 1: Diclofenac gel, rosuvastatin, topiramate
Patient 2: Hydroxyurea, N-acetyl cysteine, pravastatin, sertraline, quetiapine,
Patient 3: Allopurinol, diclofenac gel, duloxetine, metformin, pregabalin

ALLERGIES

All: No known drug allergies

FAMILY HISTORY
All: No pertinent family history

SOCIAL HISTORY
All: No tobacco, alcohol or illicit drug use

ADDITIONAL STUDIES
Labs including a complete blood count, comprehensive metabolic panel, and thyroid stimulating hormone were unremarkable for all patients.

DIAGNOSIS
Patients 1 and 2: Brachioradial pruritus
Patient 3: Scalp dysesthesia

TREATMENT AND COURSE
Patient 1: One year after her initial treatment, she returned for repeat injections and noted that the right forearm was the most pruritic area. A total of 100 units were administered in the same fashion, but 50 units were injected distal to the elbow to address increased pruritus in this region. The patient initially tolerated the procedure well, but two weeks later developed weakness with handgrip, specifically with flexion of the right thumb and index finger. Nonetheless, she was pleased with the treatment results, as her pruritus has been in remission for the last six months.

Patient 2: After treatment failure of multiple topical and oral therapies, the patient elected to undergo onabotulinumtoxinA injections for his brachioradial pruritus. Following the same protocol as the previous case, 100 units were injected intradermally into the right posterior neck, shoulder and upper arm. The patient tolerated the procedure well and reported significant improvement in pruritus. Three months later, he returned for repeat injections and noted residual pruritus of the posterior neck, thus more botulinum toxin was concentrated in this area. The patient tolerated the procedure well and is satisfied with his treatment results.

Patient 3: After failure of multiple modalities including topical, oral and physical therapies, the patient elected to undergo off-label incobotulinumtoxinA injections for scalp dysesthesia. A total of 100 units were injected into the scalp. Two weeks later, the patient reported resolution of his symptoms and has not had recurrence for three months.

DISCUSSION
Botulinum toxin has been used in numerous neuropathic conditions refractory to traditional treatments. In regards to pruritus, it can reduce acetylcholine, histamine and histamine-related vasomotor responses. While the exact mechanism is still unclear, animal models investigating the antipruritic effects of botulinum toxin have demonstrated downregulation of transient receptor potential cation channel subfamily V member 1 (TRPV1) in the dorsal root ganglia, which is considered responsible for histamine-dependent itch. This same channel is abundant in the outer root sheath of hair follicles, and therefore may be implicated in scalp dysesthesia as well. Other studies have

demonstrated the analgesic properties of botulinum toxin via inhibition of substance P, glutamate, and calcitonin gene-related peptide release. Several recent publications have reported successful treatment of scalp dysesthesia with botulinum toxin as well. Together, these results show promise for the use of botulinum toxin in the treatment of neuropathic pruritus and pain.

When using botulinum toxin for neuropathic dysesthesias, we recommend initially evenly distributing injection points and later tailoring injections according to the patient's response. We use a dilution of 100 units with 4-6 mL saline, resulting in about 2 units per 0.1 mL. Injections are superficial, in the intradermal plane. Caution should be taken when injecting the distal extremities. Remission of symptoms varies widely, but typically lasts between three months and one year. While further studies are needed to understand itch relief mechanisms, botulinum toxin may inhibit local chemical mediators, disrupt the itch-scratch cycle, and be a potential therapeutic avenue for those with refractory neuropathic pain and pruritus.

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Chicago Dermatologic Society **Case #5**

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HISTORY OF PRESENT ILLNESS

A 46-year-old male with a history of diabetes and hyperlipidemia presented to our dermatology clinic for a rash on his face and trunk that was slowly progressing over eight months. The lesions were not painful or pruritic. The patient was previously treated with over-the-counter acne products and a course of trimethoprim/sulfamethoxazole per his primary care provider with no improvement. The patient otherwise felt well, with no notable systemic symptoms.

PAST MEDICAL HISTORY

Diabetes mellitus, hyperlipidemia

MEDICATIONS

Atorvastatin, empagliflozin, linagliptin, lisinopril, metformin

ALLERGIES

No known drug allergies

FAMILY HISTORY

Multiple family members with lung cancer

SOCIAL HISTORY

Non-smoker

PHYSICAL EXAMINATION

The patient was well-appearing. On the forehead, cheeks, chest, abdomen, and back there were numerous scattered red papules, many in a grouped distribution. The lesions were soft on palpation. No cervical, submental, submandibular, occipital, axillary, or inguinal lymphadenopathy was appreciated.

DERMATOPATHOLOGY

Histologic sections from a tangential shave biopsy of a lesion on the chest demonstrated a dense, nodular histiocyte-rich infiltrate in the dermis demonstrating focal emperipolesis. The histiocytes were positive for S100 and CD68 and negative for CD1a. There was an associated mixed infiltrate composed of lymphocytes, plasma cells, neutrophils, and eosinophils. The T-cells demonstrated a CD4:CD8 ratio of 4:1.

ADDITIONAL STUDIES

Erythrocyte sedimentation rate was elevated at 37 (0 – 15 mm/hr). C-reactive protein was elevated at 11.4 (<8.1 mg/L). Serum protein electrophoresis demonstrated increased alpha 2 globulin at 0.8 (0.1 - 0.4 g/dL), increased beta globulin at 1.6 (0.6 - 1.3 g/dL), increased gamma globulin at 1.9 (0.7 - 1.5 g/dL), and decreased albumin/globulin ratio at

0.8 (1.0 - 2.4). No monoclonal spikes were seen. Immunoglobulins demonstrated increased IgA at 665 (66 - 143 mg/dL). Complete blood count, complete metabolic panel, lactate dehydrogenase, and uric acid were unremarkable.

DIAGNOSIS
Rosai-Dorfman disease

TREATMENT AND COURSE
A diagnosis of cutaneous limited Rosai-Dorfman disease was favored given the patient's negative review of symptoms and lymph node exam. However, considering the patient's abnormal serum protein electrophoresis and elevated inflammatory markers, the patient was referred to hematology/oncology for further imaging to rule out systemic involvement. A whole-body PET-CT was ordered, though the patient never completed the scan and was subsequently lost to follow-up.

For the patient's cutaneous lesions, treatment with topical or intralesional corticosteroids was discussed. As the lesions were asymptomatic, the patient elected to monitor. At the patient's dermatology follow-up appointment 3 months later, his cutaneous lesions were noted to be improved, becoming flatter, smaller, and less erythematous. The patient denied any new skin lesions.

DISCUSSION
Rosai-Dorfman disease (RDD), also known as sinus histiocytosis with massive lymphadenopathy, is a rare, non-malignant, histiocytic proliferative disorder affecting lymph nodes and extra-nodal tissues. RDD is a heterogenous entity with a range of clinical phenotypes, first described by Rosai and Dorfman in 1969. RDD tends to affect children and young adults, with a male predominance. Clinical features include bilateral massive cervical lymphadenopathy, fever, elevated ESR and CRP, anemia, leukocytosis, and polyclonal hypergammaglobulinemia.

Around 40% of RDD cases involve extra-nodal tissues, including the skin and soft tissues, orbit and eyelid, upper respiratory tract, central nervous system, and gastrointestinal tract. The skin is the most frequently involved extra-nodal site, with cutaneous lesions presenting as slow-growing, painless, red to brown nodules, papules, or plaques. The head and neck region is the most frequently involved followed by the trunk and extremities. Cutaneous limited RDD without extra-nodal involvement is rare, comprising just 3% of RDD cases. Of note, there are reports of initially cutaneous limited RDD that preceded systemic involvement, thus clinical follow up to exclude systemic involvement is recommended. Unlike systemic RDD, cutaneous limited RDD tends to affect middle-aged females of Asian or Caucasian origin, and patients are typically healthy and lack prodromal symptoms and laboratory abnormalities. Due to the rarity and non-specific clinical presentation of cutaneous limited RRD compared to other histiocytic, inflammatory, and neoplastic processes, diagnosis is difficult and often delayed.

The etiology of RDD remains unclear. Human herpesvirus and Epstein-Barr virus viral components have been identified in involved tissues, however they are not present in

every case. RDD has been associated with IgG4-related disease, however this is controversial. Most cases of RDD are sporadic, but a familial form of RDD due to mutations in SLC29A3 has been recognized. SLC29A3 encodes a nucleoside transporter, and mutations in this gene are also associated with H syndrome, pigmented hypertrichosis, insulin-dependent diabetes mellitus, and Faisalabad histiocytosis syndrome. More recently, studies have demonstrated the presence of MAP2K1, KRAS, NRAS, and ARAF mutations in involved tissues. These genes encode kinases in the MAPK/ERK pathway, a key regulator of cellular survival and proliferation, raising the possibility of a clonal origin.

As the clinical presentation of RDD is often non-specific, histopathologic and immunohistochemical findings are key to diagnosis. Lesions show a dense dermal infiltrate of histocytes admixed with scattered lymphocytes, plasma cells, and neutrophils. Emperipolesis is a hallmark, showing intact cells such as lymphocytes, plasma cells, and erythrocytes engulfed in the cytoplasm of histiocytes. The histiocytes stain positive for S100, CD68, CD163, and negative for Langerhans cell markers CD1a, CD34, and langerin.

RDD is commonly self-limited, with spontaneous regression of the masses. Therefore, observation is recommended for asymptomatic RDD. In cases of disseminated or refractory RDD, treatments such as systemic corticosteroids, immunomodulators, chemotherapy, and radiotherapy have been used with success. For a solitary or small number of cutaneous lesions, surgical excision is highly effective. Topical or intralesional corticosteroids and cryotherapy are additional options.

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Chicago Dermatologic Society **Case #6**

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HISTORY OF PRESENT ILLNESS

A 75-year-old female presented to our dermatology clinic for routine screening examination, during which two erythematous lesions on the left cheek were noted and biopsied. Thirteen months prior, the patient had presented to plastic surgery clinic for a non-healing wound on the left eyebrow. Shave biopsy at that time revealed a moderate to poorly differentiated squamous cell carcinoma. A wide local excision utilizing intraoperative frozen sections (IFS) was completed by the plastic surgery service. IFS demonstrated residual moderate to poorly differentiated squamous cell carcinoma (SCC), 5.2 cm in the greatest dimension, invading to a depth of 1 cm. Multifocal perineural invasion was present. Although margins were clear, the tumor was noted to be less than 1mm from the peripheral and deep margins.

PAST MEDICAL HISTORY

Cerebrovascular accident with residual aphasia
Infective endocarditis with septic emboli
Bovine aortic valve replacement
Paroxysmal atrial fibrillation
Heart failure with preserved ejection fraction
Chronic thrombocytopenia
Coronary artery disease
Obstructive sleep apnea
Hypertension
Hyperlipidemia

MEDICATIONS

Amiodarone, amlodipine, atorvastatin, bumetanide, donepezil, gabapentin, hydrocodone-acetaminophen, levetiracetam, levothyroxine, loperamide, loratadine, nystatin powder, omeprazole, ondansetron, potassium Chloride, sertraline, trazodone

ALLERGIES

Tramadol

FAMILY HISTORY

No pertinent family history

SOCIAL HISTORY

This patient was residing in an assisted living facility due to medical comorbidities. She was a former smoker.

PHYSICAL EXAMINATION
On examination, the medial left cheek had a 0.5 x 0.5 cm erythematous papule, while the lateral aspect of the left cheek had a 0.8 x 0.5 cm erythematous papule.

DERMATOPATHOLOGY
Both biopsies demonstrated moderately differentiated squamous cell carcinoma, with no connection to the epidermis. These findings were felt to likely represent metastasis from another location.

ADDITIONAL STUDIES
PET/CT scan was negative for distant metastasis

DIAGNOSIS
Moderate to poorly differentiated squamous cell carcinoma with regional metastasis

TREATMENT AND COURSE
Our patient's two new biopsy-proven SCCs were both considered to be possible regional metastases. The risk of regional metastases was felt to be relatively high, given the limitations of using intraoperative frozen section during a wide local excision and narrow margins of excision.

During her initial visit with dermatology, adjuvant radiation was recommended given the high-risk features of the initial moderate to poorly differentiated SCC and narrow margins of excision. During her consult with radiation oncology, adjuvant radiation therapy with curative intent was again recommended due to the depth of invasion and risk of drainage through lymphatic channels, but this was declined due to difficulty with transportation.

A PET/CT scan was done and did not find any further metastasis. Given no identification of further disease, patient and family were given options including systemic therapy and local treatment, ultimately opting for Mohs surgery.

Mohs surgery was completed for both SCCs and repair method utilized a full thickness skin graft for one lesion and a unilateral rotation flap for the other. The patient had excellent healing of both sites, and to date has not had a recurrence of her SCC.

DISCUSSION
Cutaneous squamous cell carcinoma (cSCC) is one of the most common types of cancers worldwide, and the incidence is continuing to increase worldwide. Though most cSCCs are indolent and treated with excision, high-risk lesions (about 4% of all cSCCs) do have metastatic potential. cSCCs are categorized into low- and high-risk tumors based on tumor diameter, tumor thickness, poor differentiation, invasion to/beyond the subcutaneous fat, perineural/lymphatic invasion, male sex, or location on the face. High-risk tumors, especially poorly differentiated cSCCs, require larger margins for clearance.

Though no consensus guidelines for the use of imaging in high-risk cSCC of the head/neck exist, imaging can change management in nearly a third of cases. Imaging

should be considered for all tumors T2b/T3 (per the Brigham and Women's Hospital staging criteria) and may also be considered for T2a tumors in the setting of immunosuppression or other risk factors. CT scan tends to be a quick, relatively less expensive initial imaging modality that is useful if bony or soft tissue invasion or spread to cervical lymph nodes is suspected. MRI scan is useful for perineural invasion and orbital/intracranial extension. High frequency ultrasound (HFUS) can be used for smaller or thinner lesions less than 10 mm, mainly to evaluate thickness of the lesion. Lastly, PET scan is the preferred imaging modality to rule out distant metastatic disease.

Treatment options include surgical modalities, including wide local excision, Mohs micrographic surgery, curettage and electrodessication, and nonsurgical modalities including photodynamic therapy, topical therapies, radiation, and cryosurgery. For high-risk tumors or metastatic cSCC, a combination of surgical treatments with chemotherapy, lymph node dissection, and/or adjuvant radiation therapy is often needed.

Mohs micrographic surgery is the gold standard of treatment for cSCC, especially in tumors with high-risk features. Patients who underwent Mohs surgery experienced an overall 5-year survival of approximately 96%, with significantly lower rates of local recurrence, nodal metastasis, and disease-specific death compared to standard wide local excision.

This patient had many high-risk SCC features: >2cm diameter, poor differentiation, perineural invasion, tumor thickness >6mm, and location on the face. Instead of Mohs surgery, a traditional wide local excision with intraoperative frozen section (IFS) was performed by plastic surgery. Excision with IFS has been touted to have similar effectiveness and low recurrence rates without the high expense of Mohs surgery, though at the cost of increased operative times. Though literature comparing excision with IFS to Mohs surgery is sparse, studies examining intraoperative frozen section find a significant false negative rate of clear margins, nearly 30% in some studies. In contrast, Mohs surgery is able to evaluate 100% of surgical margins. If there was remaining cSCC in this case, it would likely have been evident during Mohs surgery. Additionally, this tumor was deemed fully excised, though many academic centers do not consider a tumor <1mm from the margin to be a complete excision and require presentation at a multidisciplinary tumor board, re-excision, or adjuvant radiation therapy.

Risk factors for recurrence of cSCC include incompletely excised tumor, immunosuppression, asymmetrical growth, invasion beyond the subcutaneous fat, and poorly differentiated features. Implications of a falsely-negative operative margin are significant, as patients with untreated or incompletely treated high-grade poorly differentiated cSCCs can suffer from increased clinically relevant growth of the tumor within a year. Given the high-risk features, it was felt that Mohs surgery would have presented a more effective option for treatment of the original moderate squamous cell carcinoma, and could have potentially reduced the risk of regional metastasis as compared to wide local excision with IFS. This case is intended to highlight the importance of Mohs micrographic surgery in treatment of high-risk non-melanoma skin cancers of the head and neck.

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Chicago Dermatologic Society **Case #7**

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HISTORY OF PRESENT ILLNESS

A 40-year-old female patient presented to our dermatology clinic for near total hair loss over a span of six months. Hair loss included the scalp, eyebrows, eyelashes, and axillae. She denied pain, pruritus, or burning of the scalp. Upon review of systems, she denied fevers, chills, night sweats, weight changes, or heat or cold intolerance. She denied recent surgery, stressful life events, or infections. She reported taking biotin supplements.

PAST MEDICAL HISTORY

Benign thyroid nodule

MEDICATIONS

Biotin supplement, multivitamin

ALLERGIES

No known drug allergies

FAMILY HISTORY

No pertinent family history

SOCIAL HISTORY

No tobacco, alcohol, or illicit drug use

PHYSICAL EXAMINATION

The patient was well-appearing. There were alopecic patches spanning >90% of the scalp with scattered exclamation point hairs and preserved follicular ostia. The eyebrows, eyelashes, and axillae had decreased hair density. No nail pitting was observed.

ADDITIONAL STUDIES

Complete blood count, comprehensive metabolic panel, lipid profile, free and total testosterone, dehydroepiandrosterone sulfate (DHEA-S), HIV 1/2 antibodies and antigen, quantiferon tuberculosis gold plus, and acute hepatitis panel were unremarkable.

DIAGNOSIS

Alopecia totalis

TREATMENT AND COURSE

After discussion of the patient's treatment goals, near total (>90%) hair loss and rapid progression, oral JAK inhibitor baricitinib was recommended. The decision was made to start baricitinib at 4 mg daily.

She was seen for follow-up ten days after medication initiation and endorsed increased frequency of headaches and increased hair loss of the eyebrows. The patient was

motivated to continue the treatment trial, and at 3-month follow-up, she had significant regrowth of scalp, eyebrow, and eyelash hair. Some alopecic patches were still present on the occipital and temporal scalp bilaterally. She reported intermittent mild abdominal pain, however liver function tests were normal. Therapy was continued.

At 6-month follow-up, the patient continued to have significant regrowth of hair, with clearing of all alopecic patches. She continued to endorse mild, diffuse abdominal pain, however she was not interested in discontinuing treatment. We discussed decreasing the dose of baricitinib to 2 mg daily, and the patient opted to continue at 4 mg daily to reduce the risk of disease recurrence.

DISCUSSION

Baricitinib is a selective, reversible Janus kinase (JAK) 1 and 2 inhibitor approved by the FDA in June 2022 for severe alopecia areata, an immune-mediated nonscarring hair loss disease, marking the first biologic approved for the disease. The JAK family of protein tyrosine kinases are thought to affect the cytokine signaling involved in the pathogenesis of alopecia areata. Phase 3 studies found oral baricitinib to be superior to placebo in both 4 mg and 2 mg daily doses. In the two trials, 38.8% and 35.9% of patients, respectively, treated with 4 mg baricitinib daily were found to have SALT scores of 20 or less (roughly 80% or more scalp hair coverage) at 36 weeks, which were higher than placebo by 32.6 percentage points. For patients treated with 2 mg baricitinib daily, 22.8% and 19.4% of patients were found to have SALT scores of 20 or less at 36 weeks, which were 16.6 and 16.1 percentage points higher than placebo.

Black Box Warnings for baricitinib and other JAK inhibitors include serious infection, malignancy, and thrombosis. However, these risks are based on data that may not be generalizable, as the warnings were applied to all JAK inhibitors based on tofacitinib in rheumatoid arthritis trials. This patient population often takes concomitant immunosuppressants and is at an increased risk of coronary artery disease due to their disease. Pooled data from industry trials showed no cases of major adverse cardiovascular events, malignancy, venous thromboembolism, or mortality in patients on baricitinib who were under 65 years old with no specified risk factors. For the 659 patients 65 years or older or with identifiable risk factors, there was one patient with history of multiple cardiovascular risk factors who experienced a major adverse cardiovascular event, one patient with BMI ≥ 30 kg/m^2 who experienced a pulmonary embolism during COVID infection, and three patients who developed malignancy. The rates of these adverse events were at or below the expected population range for patients at age 65 years or older.

There are three recommended doses of baricitinib for alopecia areata. Though the standard dosing is 2 mg once daily, 4 mg once daily can be considered for patients with near complete or complete scalp hair loss, or after initial 2 mg dosing if treatment response is not adequate. The medication is also available in 1 mg doses for patients with renal impairment or those taking probenecid, as it inhibits OAT3 which is a transporter used for the excretion of baricitinib. To decrease the risk of serious infection, it is important to test for latent tuberculosis and screen for viral hepatitis prior to initiating

treatment, and to pause treatment during a herpes zoster infection. In addition, a CBC, CMP, and lipid panel should be checked prior to institution, and a lipid panel should be checked at roughly 12 weeks. Routine lab monitoring is recommended.

Our patient's short duration of disease may have improved her outcome, however near total hair loss is typically associated with slower and less robust responses. This case serves as attestation of the efficacy of the novel treatment baricitinib for alopecia areata. Offering patients this systemic option when indicated is an important consideration, as scalp hair regrowth is associated with increase in quality of life. It should be considered as a first-line therapy for patients with >50% hair loss or as second-line for those with <50% hair loss who fail intralesional or topical corticosteroids.

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Chicago Dermatologic Society **Case #8**

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HISTORY OF PRESENT ILLNESS

A 57-year-old male presented for evaluation of tender, pink lesions on the bilateral shoulders that had been present for several years.

PAST MEDICAL HISTORY

Clear cell renal cell carcinoma of the left kidney status post partial nephrectomy, hypertension, generalized anxiety disorder, gastroesophageal reflux disorder

MEDICATIONS

Amitriptyline, diclofenac, famotidine, losartan, tadalafil, tamsulosin

ALLERGIES

Cefepime

FAMILY HISTORY

Sister with cutaneous and uterine leiomyomas

SOCIAL HISTORY

Remote history of polysubstance abuse including tobacco, cocaine, and alcohol

PHYSICAL EXAMINATION

The patient was well-appearing. Scattered pink, firm, tender papules coalescing into plaques were present on the bilateral shoulders.

DERMATOPATHOLOGY

A shave biopsy of a lesion on the right shoulder demonstrated a well-demarcated dermal proliferation of cytologically bland smooth muscle cells consistent with leiomyoma.

ADDITIONAL STUDIES

Genetic testing was positive for a pathogenic variant in *FH* (fumarate hydratase gene): c. 1189G>A (p. Gly397Arg)

DIAGNOSIS

Hereditary leiomyomatosis and renal cell cancer (HLRCC) or Reed's Syndrome

TREATMENT AND COURSE

The patient had multidisciplinary outpatient follow up with dermatology, urology, oncology, and genetics. He successfully underwent surgical excision of symptomatic cutaneous leiomyomas without recurrence. His immediate family awaits further genetic testing.

DISCUSSION

Hereditary leiomyomatosis and renal cell cancer **(**HLRCC) syndrome, also known as Reed's syndrome, is an autosomal dominant condition that has been reported in approximately 300 families worldwide, with a higher incidence in Eastern Europeans. A mutation in the tumor suppressor gene fumarate hydratase (*FH*) is present in 76-93% of families. Other cases are suspected to be sporadic, mosaic, or due to an unidentified mutation.

The definitive diagnosis of HLRCC is through genetic testing. A clinician should be suspicious for HLRCC if a patient has 2 or more minor criteria for HLRCC, including: 1) solitary cutaneous leiomyoma and family history of HLRCC, 2) early onset renal tumors of type 2 papillary histology 3) multiple early onset (<40 years old) symptomatic uterine fibroids.

The pathogenesis of HLRCC is poorly understood. Overall, it is thought that the mutation in *FH* leads to an accumulation of fumarate and a shift towards anaerobic metabolism. This potentially leads to downstream cellular proliferation and resistance to apoptosis, leading to formation of leiomyomas and renal cell cancer.

HLRCC syndrome has three primary clinical manifestations: cutaneous leiomyomas, uterine leiomyomas, and renal tumors. Cutaneous leiomyomas appear at an average age of 25-years-old and are usually the earliest presenting sign of the syndrome. They can present with a pseudo-Darier sign in which there is transient piloerection or elevation of the nodule when rubbed. Upwards of 90% of HLRCC patients report associated pain and discomfort, with over 20% experiencing a significant decrease in quality of life secondary to cutaneous leiomyomas. On histopathology, leiomyomas are characterized by whirls of elongated smooth muscle cells. Treatments vary depending on the degree of pain and extent of leiomyomas, including surgical excision, CO_2 laser, and medical management of pain. Medications that block smooth muscle contraction and treat neuropathic pain have been shown to be effective, such as gabapentin, nifedipine, and botulinum toxin. Transformation of leiomyoma to leiomyosarcoma has rarely been reported – currently in the literature there are four unrelated individuals with reported transformation.

Uterine leiomyomas typically present at an average age of 30 in HLRCC syndrome patients, which is 10 years earlier than the general population. Most women with HLRCC develop uterine leiomyomas. Treatment includes surgery, such as myomectomy and uterine artery embolization, and medical options such as IUD placement. Renal cell carcinomas are typically present in only 20-34% of families but are notably aggressive with upwards of 70% mortality within 5 years due to metastasis. Thus, if identified, treatment of renal cell tumors is recommended rather than surveillance. Recent trials have demonstrated promise with bevacizumab, a VEGF inhibitor, plus erlotinib, an EGFR inhibitor, for advanced HLRCC renal tumors.

After diagnosis, it is recommended the patient receive a yearly skin check, gynecologic exam if applicable, and MRI of the kidneys. As an autosomal dominant disease, first-degree relatives have a 50% chance of inheriting the gene and should be screened. If a

patient has biological children with a partner who also carries a mutated *FH* gene, it can result in fumarate hydratase deficiency leading to early onset encephalopathy and seizures. This case of HLRCC highlights the dermatologist's crucial role in identifying patients with genodermatoses via the cutaneous manifestations and promptly referring these patients for genetic testing.

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Chicago Dermatologic Society **Case #9**

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HISTORY OF PRESENT ILLNESS

A 79-year-old male presented to the Edward Hines Jr. VA dermatology clinic for a new, changing pigmented lesion of the right nipple present for less than 1 year. The lesion was asymptomatic. Due to high clinical suspicion of malignancy, a saucerization biopsy was performed.

PAST MEDICAL HISTORY

Type 2 diabetes mellitus, hypertension, hyperlipidemia, renal cell cancer s/p left total nephrectomy/adrenalectomy and adjuvant radiation in 1990, chronic kidney disease stage III, benign prostatic hypertrophy, hiatal hernia, hyperthyroidism, osteoporosis

MEDICATIONS

Amlodipine, ammonium lactate cream, cholecalciferol, cyanocobalamin, finasteride, methimazole, midodrine, risedronate

ALLERGIES

No known drug allergies

FAMILY HISTORY

No relevant family history

SOCIAL HISTORY

Former smoker with 5-year pack history, social alcohol use

PHYSICAL EXAMINATION

The patient was well appearing. A 3 cm brown, pink, and blue indurated plaque was noted on the right nipple and surrounding areola. There was no nipple discharge, ulceration, or underlying mass noted. Right axillary lymph nodes were not palpable. The contralateral side was unaffected without skin changes or palpable masses. Dermoscopy revealed irregular pigmentation, blue-white veil, and atypical vessels.

DERMATOPATHOLOGY

Saucerization revealed atypical intraepidermal melanocytic proliferation with pagetoid spread, marked subjacent dermal fibrosis, and pigment incontinence with dermal melanophages. The fibrosis measured to a depth of 0.6 mm. This was consistent with melanoma-in-situ with follicular extension and possible regression of a dermal component.

Similarly, mastectomy histopathology showed nests of large atypical intraepidermal pagetoid cells that extended down to hair follicles. The cells were pigmented, had nuclear atypia and scattered prominent nucleoli. Immunohistochemistry showed intraepidermal lesional cells with strong staining for cytokeratin (CK) AE1/AE3, CK8-18, GATA3, and ER. Additionally, there was focal positivity for PR and HER2 was equivocal. The cells were negative for tyrosinase, Melan-A, SOX10, CK7, CK20, keratin 903, and epithelial membrane antigen. This staining pattern is somewhat unusual, however, the histologic findings and immunohistochemical staining pattern supported the diagnosis of pigmented Paget's disease of the breast. Sentinel lymph node biopsy was negative.

ADDITIONAL STUDIES

None relevant

DIAGNOSIS

Pigmented mammary Paget's disease

TREATMENT AND COURSE

The patient underwent right total mastectomy and sentinel lymph node biopsy in early October 2023. Histopathology samples suggested a true diagnosis of pigmented mammary Paget's disease and underlying ductal carcinoma in-situ, nuclear grade 3. Sentinel lymph node biopsy was negative. 3 weeks later, the patient presented to an outside hospital with altered mental status and passed away after a rapid deterioration. The cause of death is unknown.

DISCUSSION

Male breast cancer is very rare, consisting of less than 1 in 100 breast cancer cases. Most male patients are diagnosed in the 7^{th} and 8^{th} decades of life. Mammary Paget's disease (MPD) was first described by Sir James Paget in 1874 when he noticed women with chronic, diffuse eczema of the nipple and areola associated with ulceration, discharge, itching, and burning sensation who subsequently developed invasive breast cancer within 2 years. Among the presenting symptoms, MPD garners clinical attention due to its unique association with breast cancer. 93-100% of MPD cases were associated with underlying invasive breast tumors. Although MPD is prevalent in women, it comprised 1.45% of all male breast cancer, while comprising 0.68% of all female breast cancer. The diagnosis of MPD is often delayed or missed due to its similar presentations with other diseases, including dermatitis, psoriasis, Bowen's disease, and basal cell carcinoma.

As seen in our case, pigmented mammary Paget's disease (PMPD) can be difficult to diagnosis because it can mimic malignant melanoma both clinically and histopathologically. Dermoscopy is often non-informative of the diagnosis, as both melanoma and PMPD can display irregular vessels, blue grey dots, chrysalis-like structures, irregular pigment networks, and regression like structures. Rare cases of PMPD have been reported in males, with seven of these cases mimicking melanoma clinically and six mimicking melanoma histologically. Because of the similarities on routine

hematoxylin and eosin staining, immunohistochemistry is the key differentiator between melanoma and PMPD.

As individual stains vary, immunohistochemical panels are recommended for accurate diagnosis. For MPD, CK 7 and HER-2-neu are effective diagnostic markers, with studies showing 95-100% and 91-95% sensitivity, respectively. Our case was negative for CK7, which although uncommon, is not unheard of, with a study done by Lundquist et al. showing negative CK7 staining in 1 out of 22 cases. CAM5.2, which contains CKs 7 and 8, is also a reliable study for detecting MPD, staining positive in 100% of cases. However, a study done by Smith et al. reported diffuse CAM5.2 staining in only 4 out of 9 cases, and therefore, it has been determined to not be as sensitive as CK7 alone. S-100 has a sensitivity of 97-100% in malignant melanoma cases, but up to 60% of MPD cases also stain positive for S-100. Furthermore, HMB-45 showed 77-100% sensitivity in primary melanoma, while two studies encompassing 24 cases of MPD were all HMB-45 negative. These findings emphasize the importance of careful immunohistochemical stain selection to delineate a diagnosis of PMPD from malignant melanoma.

Commonly, there is a delay in diagnosis of PMPD in the range of four weeks to two years. Men are shown to have a worse prognosis than women when a diagnosis of breast cancer is made, with men having a five-year survival rate of 77.6% versus 86.4% in women. The prognosis of PMPD depends on the staging, which is determined by the tumor, node, metastasis staging of the underlying breast cancer. Treatment is also guided by staging of the underlying breast cancer. Mastectomy has been the treatment historically, though lumpectomy can be considered. Recent meta analyses have shown that lumpectomy and total mastectomy have similar survival rates if adjuvant whole breast radiation is undertaken after lumpectomy. Sentinel lymph node biopsy is recommended, and adjuvant therapy with chemotherapy, radiation, or hormonal therapy may be suggested in all cases.

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Chicago Dermatologic Society **Case #10**

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HISTORY OF PRESENT ILLNESS

A 60-year-old Caucasian male presented to dermatology for an asymptomatic exanthem involving the trunk and lower extremities developing two weeks after a COVID-19 infection that progressed to painful skin tightening of the bilateral upper and lower extremities. He was otherwise well without history of sclerodactyly, Raynaud's phenomenon, dysphagia, or dyspnea.

PAST MEDICAL HISTORY

No pertinent past medical history

MEDICATIONS

Omeprazole, fluticasone

ALLERGIES

Morphine, simvastatin

FAMILY HISTORY

No pertinent family history

SOCIAL HISTORY

No known tobacco or illicit drug use. Drinks 2 beers per week.

PHYSICAL EXAMINATION

The patient was well-appearing. Initial physical examination was notable for non-scaly pink erythematous patches on the trunk and reticulated purpuric patches on the lower legs. On follow up examination, there was symmetric tender induration seen on the bilateral arms, forearms, thighs, legs, trunk, and chest. Irregular cobblestoning and marked follicular orifices were present, consistent with "peau d'orange". Furrows were present along the length of superficial veins on the upper arms, consistent with a "groove sign". The hands, feet, and face were spared, and capillaroscopy was unremarkable.

DERMATOPATHOLOGY

Histologic sections from initial 4mm punch biopsies demonstrated perivascular and interstitial lymphohistiocytic infiltrate with eosinophils and involvement of the subcutis. A repeat 6mm punch biopsy upon progression of the disease demonstrated dermal sclerosis with mixed periappendageal and interstitial inflammation extending to the subcutis without fascial visualization.

ADDITIONAL STUDIES

Complete blood counts demonstrated a maximum eosinophil count of 2.09 x 10^9 (0.02-0.5 x 10^9/L) and eosinophil percentage of 29.1% (1-4%). Aldolase was elevated at 9.6 (1.0-7.5 U/L). A hypercoagulable work up was negative, including antiphospholipid panel, cryoglobulin panel, RF, and haptoglobin. A rheumatologic work up was negative, including antinuclear antibody (ANA) screen, antineutrophil cytoplasmic body (ANCA) screen (including p-ANCA and c-ANCA), and autoantibodies to dsDNA, chromatin, ribosomal P, SS-A 60, SS-A 522, SS-B, Sm, SmRNP, RNP 68, Scl-70, Jo-1, and Centromere B. An infectious work up was negative, including HIV, respiratory viral panel, mycoplasma antibodies, Quantiferon gold, and hepatitis panel. COVID-19 respiratory PCR was positive.

IMAGING

CT chest, abdomen, and pelvis with IV and oral contrast were unremarkable. MRI left femur and foot with and without contrast demonstrated nonspecific abnormal fascial enhancement.

DIAGNOSIS

Eosinophilic fasciitis

TREATMENT AND COURSE

The patient had failed trials of topical antifungals, topical steroids, oral doxycycline, and oral hydroxychloroquine prior to progression of his eosinophilic fasciitis. After diagnosing the patient with eosinophilic fasciitis, the patient was started on oral prednisone daily and oral methotrexate once weekly with folic acid on the other days of the week. The patient had dermatology, rheumatology, and physical therapy outpatient follow up. He has residual sclerosis of the skin overlying the upper and lower extremities despite dramatic improvement of his symptoms.

DISCUSSION

Eosinophilic fasciitis, originally called Shulman Syndrome, has been considered within the spectrum of deep morphea and involves diffuse inflammation of fascia and muscle leading to a cytotoxic cellular immune response. Cases present as initial symmetric edema and erythema with subsequent induration of extremities typically sparing the digits and face. Various etiologies of eosinophilic fasciitis have been reported, with upwards of 40% of cases related to intense physical exertion or trauma. Other etiologies include medications such as statins, chemical compounds such as epoxy resin, rheumatologic conditions, hematologic malignancy, and infections such as *Borrelia burgdorferi* or *Mycoplasma arginini*. When related to infections such as Borrelia or Mycoplasma, eosinophilic fasciitis has been reported to evolve over the course of 4 to 24 months. There have been three isolated case reports of COVID-19 induced sclerosing connective tissue disorders including eosinophilic fasciitis, generalized morphea, and pansclerotic morphea within weeks to four months of the infection. Our patient's disease progression over 4 months would be consistent with these reports. The condition has been reported more commonly in Caucasian adults with a mean age of onset of 40 to 50 years old.

Multiple diagnostic criteria for eosinophilic fasciitis have been proposed. Using the diagnostic criteria of Pinal-Fernandez et al., our patient meets diagnosis via one of the two major and four of the five minor criteria. The major criteria include: (1) swelling, induration, and thickening of the skin; (2) fascial thickening with lymphocytes and macrophages on wedge biopsy. Minor criteria include: (1) muscle weakness or elevated aldolase; (2) groove sign or peau d'orange; (3) hyperintense fascia on MR T2 weighted images; (4) peripheral eosinophilia > 0.5 x 10^9/L; (5) hypergammaglobulinemia > 1.5g/L. Using the diagnostic criteria of Jinnin et al., our patient meets diagnosis via one major and one minor criteria. The major criterion is: (1) symmetrical plate like sclerotic lesions on four limbs while excluding systemic sclerosis and an absence of Raynaud's phenomenon. The minor criteria are: (1) skin biopsy with fascia demonstrating fibrosis of connective tissue and cellular infiltrate of fascia; (2) thickening of fascia on imaging such as MRI.

Lab abnormalities commonly reported in eosinophilic fasciitis include peripheral blood eosinophilia in upwards of 93% of cases, hypergammaglobulinemia, elevated erythrocyte sedimentation rate, and elevated serum aldolase. Such as in our patient, peripheral blood eosinophilia and aldolase tend to improve with disease remission, and aldolase can be an indicator of disease activity and relapse. TIMP metallopeptidase inhibitor 1 (TIMP1) has also been reported as a promising serological marker of disease activity in case reports. To identify fascial inflammation, fascial biopsy or imaging studies can be performed, with fascial biopsy being considered the gold standard.

Although eosinophilic fasciitis can spontaneously resolve, most cases are treated with oral prednisone with rapid improvement. Poor outcomes including refractory disease or permanent sclerosis and joint contractures are associated with pediatric onset or the presence of morphea lesions and truncal involvement, such as our case. Concomitant morphea has been reported in upwards of 50% of cases and typically suggests more aggressive disease. In refractory or severe cases, a steroid-sparing immunosuppressant, such as methotrexate in our case, can be added to the treatment regimen. Eosinophilic fasciitis has been reported to be associated with several conditions including arthritis, carpal tunnel syndrome, and hematologic disorders in upwards of 10% of cases. COVID-19 infection could be a predisposing factor to eosinophilic fasciitis, and early diagnosis and management of the disease is required to optimize patient outcomes.

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