Chicago Dermatological Society

PROTOCOL BOOK
September 21, 2022

Co-hosted by Loyola University
Division of Dermatology

Guest Speaker: Dr. Donna Culton
University of North Carolina School of Medicine

Program

Co-hosted by Loyola University Division of Dermatology
Wednesday, September 21, 2022
Stephens Convention Center
Rosemont, Illinois

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**
Joerg Albrecht, MD PhD - CDS President

9:00 a.m. - 10:00 a.m. **Morning Session**
"Conquering the Oral Cavity - An approach to oral anatomy, exam, biopsy pearls and common conditions"
Donna Aline Culton, MD PhD

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. - 1:15 p.m. **CDS Business Meeting**

Business meeting adjourns and clinical session resumes

1:15 p.m. - 2:15 p.m. **Afternoon Lecture**
"Diagnosis and management of inflammatory diseases of the oral mucosa" - Case-based tips and tricks
Donna Aline Culton, MD PhD

2:15 p.m. **Meeting adjourns**

Chicago Dermatologic Society **Case #1**

[1]Kyle Bhatia, MD, [2]David Eilers, MD
[1]Division of Dermatology, Loyola University Medical Center
[2]Section of Dermatology, Edward Hines Jr. VA Hospital

HISTORY OF PRESENT ILLNESS

A 35-year-old male patient presented to the Hines VA Medical Center with a 3-day history of fevers, rectal ulcerations and pain, and a rash present on his face, abdomen, dorsal and palmar hands, and dorsal feet. The patient endorsed recent travel to New York City and multiple new male sexual partners.

PAST MEDICAL HISTORY

HIV

MEDICATIONS

Dolutegravir/lamivudine

ALLERGIES

No known drug allergies.

FAMILY HISTORY

No pertinent family history.

SOCIAL HISTORY

Sexual history notable for being a male who has sex with males (MSM). Endorsed occasional alcohol use. No smoking or illicit drug use.

PHYSICAL EXAMINATION

The patient was well-appearing. Cutaneous examination revealed seven umbilicated vesicles scattered on the nose, cheeks, chin, and the vermilion border of the lower lip. There were a few similar vesicles present on the abdomen, palmar and dorsal hands, and dorsal feet. Two perianal ulcerations and bilateral tender inguinal lymphadenopathy were also present.

ADDITIONAL STUDIES

The patient was swabbed for monkeypox, with initial testing positive for “non-variola Orthopox DNA” by PCR. The swab was subsequently sent to the CDC where further PCR testing confirmed monkeypox infection. Viral swabs for HSV and VZV were negative. The patient also tested negative for gonorrhea, chlamydia, syphilis, and Covid-19. His HIV viral load was undetectable (<20 copies) and CD4 count was 412 (500 – 1400 cells/microL).

DIAGNOSIS

Monkeypox infection, Clade IIb (formerly West African clade)

TREATMENT AND COURSE

The patient was maintained on contact and airborne isolation precautions throughout his hospital stay. His fevers resolved within his first day of admission. He developed few new papulovesicles, and his initial lesions were stable throughout his stay. He remained well-appearing and hemodynamically stable, with his only bothersome symptom being rectal pain. He was ultimately started on a 14-day course of oral tecovirimat per the infectious disease department. He was discharged to home isolation with clearance from the local public health department after a 4-day hospital stay. His rash and other symptoms resolved within 4 weeks.

DISCUSSION

**Last updated August 28, 2022*

Monkeypox is a rare zoonotic *Orthopoxvirus* infection, with the *Orthopoxvirus* genus also including variola (smallpox), vaccinia (used in smallpox vaccines), and cowpox, among others. Monkeypox is clinically similar to smallpox, though it is less contagious and causes less severe illness. The infection was first discovered in 1958 in colonies of monkeys kept for research. The true source of the virus is unknown, though African rodents and non-human primates can harbor the virus. The first human case of monkeypox was diagnosed in 1970, and the virus is considered endemic to certain regions of West and Central Africa. Occasional outbreaks outside Africa, including a midwestern US outbreak in 2003, have occurred prior to 2022. These outbreaks have been linked to exposure to imported animals or international travel.

In May 2022, case clusters of monkeypox were reported in North America and Europe. Over the following several months, case numbers rose dramatically. As of August 28, 2022, cases have been reported in over 90 countries that have not historically reported monkeypox, with US case counts exceeding 17,000. The virus has been declared a public health emergency in the US, and the World Health Organization has declared the outbreak a public health emergency of international concern.

There are two clades of monkeypox, Clade I (formerly known as the Congo Basin clade) and Clade II (formerly known as the West African clade). Clade II is further subdivided into Clade IIa and Clade IIb, with Clade IIb referring to the group of variants driving the 2022 outbreak. Historical data has demonstrated that Clade I is more infectious and carries a mortality rate of approximately 10%, while Clade II is less infectious and carries a mortality rate of approximately 3%.

Monkeypox infection has an incubation period of 3-17 days. The infection may or may not be associated with a prodrome of fever, headache, malaise, lymphadenopathy, and/or myalgias. Skin lesions typically occur within the first several days and progress through a macular and papular stage, before evolving into vesicles and pustules which eventually crust over. These pustules are often umbilicated. The face, palms, soles, and oral mucous membranes are commonly affected areas. In the 2022 outbreak, increased rates of genital and anorectal involvement are being seen. On any given part of the body, lesions typically develop simultaneously and evolve together through the aforementioned stages.

The illness typically lasts 2-4 weeks and is most often transmitted through direct contact with the rash or bodily fluids or through respiratory secretions during face-to-face contact. It can also be transmitted through fomites, from placenta to fetus, or by contact with, preparation, or consumption of an infected animal. The 2022 outbreak has disproportionally affected males aged 18-44, with MSM and recent travel being major risk factors for infection.

For many patients with monkeypox, the virus is self-limiting, and therapy is supportive. In certain populations, including those with severe disease or those at risk of severe disease (immunocompromised patients, pregnant patients, pediatric patients below 8 years of age, patients with atopic dermatitis or other cutaneous conditions, among others), certain smallpox treatments may be considered. These include tecovirimat, an oral or intravenous FDA-approved smallpox antiviral, for which the FDA holds a non-research expanded access Investigational New Drug protocol that allows for use in monkeypox infections in adults and children of all ages.

Other options include vaccinia immune globulin, brincidofovir, and cidofovir. There are two smallpox vaccines available, JYNNEOS and ACAM2000, which have demonstrated efficacy in preventing monkeypox infection. Efforts have begun to vaccinate those in at-risk networks and those who have had high risk exposures.

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Chicago Dermatologic Society **Case #2**

[1]Laryn Steadman, MD, [2]Jodi Speiser, MD, [1]Wendy Kim, DO, [1]Eden Lake, MD
[1]Division of Dermatology, Loyola University Medical Center
[2]Department of Pathology, Loyola University Medical Center

HISTORY OF PRESENT ILLNESS

A seven-year-old female patient presented via the emergency department with ten days of fever, facial swelling, cracked lips, and waxing and waning morbilliform rash affecting the face, trunk, and extremities. She had previously been hospitalized overnight at the onset of illness at an outside hospital with adenovirus and coronavirus NL63; her symptoms were presumed due to viral insult. After discharge, her fever rose to 105.9°F and the rash persisted despite treatment with acetaminophen, ibuprofen, and diphenhydramine. On admission, the patient complained of continued pruritic rash, chills, abdominal pain, decreased appetite, sore throat, myalgias, arthralgias, and lethargy.

The patient had been started on levetiracetam, lamotrigine, and oxcarbazepine for focal seizure disorder diagnosed at an outside institution approximately three months prior to presentation. The patient suffered from one year of staring spells increasing in frequency with deteriorating school performance. Electroencephalogram (EEG) at the time of epilepsy diagnosis showed frequent focal epileptiform discharges consistent with benign rolandic epilepsy.

PAST MEDICAL HISTORY

Asthma, seasonal allergies, focal epilepsy

MEDICATIONS

Albuterol inhaler, famotidine, fluticasone propionate inhaler, lamotrigine 25 mg twice daily, levetiracetam 400 mg twice daily, loratadine, montelukast, oxcarbazepine 240 mg twice daily

ALLERGIES

No known drug allergies.

FAMILY HISTORY

Mother with Raynaud disease, history of febrile seizures and migraine headaches. Sibling with partial epilepsy and migraine headaches. Additional sibling with migraine headaches. Paternal aunt with epilepsy.

SOCIAL HISTORY

Second grader

PHYSICAL EXAMINATION

The patient was ill-appearing and minimally interactive on exam. She had shoddy cervical lymphadenopathy bilaterally. Her face was notable for diffuse edema (right worse than left) with overlying pink patches on the bilateral cheeks. The vermillion lips were noted to have erythema, fissuring, and minimal heme-crusting without vesicles or oral mucosal involvement. Ocular mucosa was clear. On the chest, abdomen, back, upper and lower extremities were many pink, non-scaly papules coalescing into plaques. The palms and soles were spared.

DERMATOPATHOLOGY

Histologic sections from a punch biopsy demonstrated orthokeratosis with apoptotic keratinocytes in all levels of the epidermis and in the acrosyringium. There were interface changes with blurring of the dermo-epidermal junction by lymphocytes with vacuolization of the

basal cell keratinocytes. There was a moderate superficial dermal chronic inflammatory cell infiltrate with eosinophils.

ADDITIONAL STUDIES

A complete blood count demonstrated an elevated white blood count at 18 (4.0-11.0 K/μL) and elevated eosinophils at 5.2 (0.0-0.7 K/mm^2). A complete metabolic panel was notable for elevated alanine aminotransferase at 119 (5-15 U/L) and elevated aspartate aminotransferase at 147 (7-34 U/L). SARS-CoV2 testing was negative. Group A Strep PCR was negative.

DIAGNOSIS

Drug reaction with eosinophilia and systemic symptoms (DRESS) in a pediatric patient

TREATMENT AND COURSE

The patient's oxcarbazepine and lamotrigine were discontinued upon admission due to concern for DRESS. Neurology was consulted and recommended continuing but tapering levetiracetam until completion of 24-hour video EEG. She was started on 1 mg/kg per day intravenous methylprednisolone with continued clinical worsening, necessitating an increase to 2 mg/kg per day. For symptomatic treatment of rash, she was given triamcinolone 0.1% ointment to use twice daily to affected areas on the body and hydrocortisone 2.5% ointment to use twice daily to the face and groin. The patient was transferred to the pediatric intensive care unit for closer monitoring given continued high fevers, rising liver function tests, and rising white blood cell count which peaked at 67.4 (4.0-11.0 K/μL).

Cytomegalovirus (CMV) PCR was positive, but CMV IgM antibody was negative. Rhino-enterovirus was positive via respiratory viral PCR panel. Karius testing was positive for HHV6 and human adenovirus C, but HHV6 PCR was negative. Cold hemagglutinins, ANCA, ANA, and double stranded DNA antibody were all negative. Additionally, rheumatoid factor, anti-cyclic citrullinated peptide antibody, Smith antibody, SSA/SSB antibodies, Scl-70 antibody, and Jo-1 IgG antibody were negative. Complement 3 and 4 were within normal limits.

The patient was started on supplemental oxygen and chest x-ray demonstrated small bilateral pleural effusions. On hospital day five, pediatric allergy recommended a trial of cyclosporine 2 mg/kg per day as an adjunct to corticosteroids. Six days after admission and after negative EEG, levetiracetam was discontinued. By hospital day eight, the patient was requiring 14L supplemental oxygen at 50% FiO_2. A chest tube was placed which drained exudative fluid demonstrating no growth on culture. Transthoracic echocardiogram was within normal limits. She completed a five-day course of cefepime and a four-day course of cyclosporine. Despite cyclosporine, her liver function worsened: alanine aminotransferase rose to 1865 (5-15 U/L) and aspartate aminotransferase rose to 1947 (7-34 U/L). She was continued on high-dose methylprednisolone. Her ferritin was 8134 (13-58 ng/mL) and D-dimer was 13,569 (<500 mg/mL feu). Both hematology and hepatology were consulted due to concern for hemophagocytic lymphohistiocytosis and liver injury, respectively.

Flow cytometry of peripheral blood revealed no monoclonal T or B lymphocyte populations. Blood cultures were negative. HIV testing was negative. Acute hepatitis panel, ceruloplasmin, alpha-1 antitrypsin, smooth muscle antibody, anti-mitochondrial antibody, and liver-kidney microsome antibody were all unremarkable.

She was then given a trial of intravenous immunoglobulin at 2g/kg over two doses and improved dramatically within 24 hours. Liver function tests were nearly normal at the time of discharge. She continued to have waxing and waning rash with variable morphology. At one point, she had

severe erythema and pruritus on the palms and soles as well as new edematous pink papules on the forearms and dorsal hands. Clobetasol 0.05% ointment was added for symptomatic relief. Parvovirus B19 testing and repeat Group A strep testing were negative at that time. The patient was seen in follow-up after a twenty-two-day hospitalization with complete clearance of rash and normalization of all lab values.

DISCUSSION

Drug reaction with eosinophilia and systemic symptoms (DRESS) is a severe cutaneous adverse reaction seen in the setting of medication use, often aromatic anti-epileptic drugs. Overall mortality approaches 10% in adults, but is, fortunately, estimated to be much lower in children (from 1-4%). Common clinical findings include fever, morbilliform rash, lymphadenopathy, peripheral eosinophilia, and involvement of one or more organ systems. The liver is the most commonly affected organ with cases of fulminant liver failure leading to death or necessitating transplant. The kidneys, lungs, and heart can be involved as well. Symptoms develop approximately 2-6 weeks after initiation of the culprit drug, but may appear sooner in pediatric patients.

The pathogenesis of DRESS is unknown; however, it is typically regarded as a T-cell mediated delayed hypersensitivity reaction. Reactivation of human herpesviruses is commonly seen in DRESS patients and may play a role in pathogenesis as well. HHV-6 is most common followed by CMV, EBV, and HHV-7. Serial viral reactivation may explain the often prolonged, waxing and waning course of disease.

Treatment in both children and adults involves prompt cessation of the suspected culprit drug followed by initiation of high dose oral or intravenous corticosteroids. In patients who fail to respond to steroids, additional treatment options include intravenous immunoglobulin (IVIG) and cyclosporine, amongst others. These additional treatments have limited evidence. IVIG has shown a decrease in time to improvement in pediatric patients when combined with systemic corticosteroids. However, trials of IVIG involving adult patients have demonstrated a high rate of serious adverse events suggesting it may be better reserved for children. In our patient, dermatology favored a trial of IVIG over cyclosporine given her positivity for multiple viruses and the potential for further immunosuppression with cyclosporine. However, there was reluctance amongst other specialists given reports of adverse events with IVIG in adults. Thus, cyclosporine was used first with failure to improve.

Identifying the culprit drug in DRESS is a key step in treatment. For some patients, the culprit may be obvious based on timeline, but in others, adjunctive methods may be needed to determine the causative drug. These methods include patch testing, intradermal tests, and prick tests. It is also crucial to exclude other potential causes of a patient's symptoms. In our patient's case, multiple specialists were consulted and extensive testing was done without any other clear etiology. Specific consideration was given to hemophagocytic lymphohistiocytosis (HLH) given the patient's exceptionally high ferritin. Recent literature has suggested significant overlap between HLH and DRESS.

Resolution of symptoms may be protracted and patients often require oral prednisone tapers of weeks to months with a risk of relapse upon discontinuation. Taper should not be attempted until after normalization of lab values. Long-term sequelae are frequent and include hypothyroidism, diabetes mellitus, and liver failure. Autoimmune sequelae may be more common in children after recovery from DRESS and may include vitiligo, alopecia areata, and systemic lupus erythematosus. Patients may also experience recurrence with exposure to other

drugs unrelated to the initial insult. DRESS is a rare but potentially life-threatening, adverse reaction requiring multidisciplinary care and long-term follow-up.

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Chicago Dermatologic Society **Case #3**

[1]Joy Tao, MD, [1]Marisa Luck, PhD, [2]David Eilers, MD
[1]Division of Dermatology, Loyola University Medical Center
[2]Stritch School of Medicine, Loyola University Chicago
[3]Section of Dermatology, Edward Hines Jr. VA Hospital

HISTORY OF PRESENT ILLNESS

A 60-year-old female patient 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. Biopsy performed by an outside dermatologist was consistent with prurigo nodularis. The patient was then referred to psychiatry, diagnosed with anxiety, and started on oral topiramate and hydroxyzine without relief. She was also using ammonium lactate cream and topical mometasone cream five times daily, also without improvement. The patient was sleeping only three to four hours a night, waking up every couple of hours to apply cold compresses and topicals to her arms. Pertinent past medical history included arthritis of the neck and back. Prior cervical spine plain radiographs showed degenerative changes most prominent at C5-6 with moderate right foramen and mild left foramen stenosis.

PAST MEDICAL HISTORY

Anxiety, arthritis, hyperlipidemia

MEDICATIONS

Diclofenac gel, rosuvastatin, topiramate

ALLERGIES

No known drug allergies.

FAMILY HISTORY

Brother with melanoma.

SOCIAL HISTORY

Nonsmoker, no alcohol use, no illicit drug use.

PHYSICAL EXAMINATION

The patient appeared mildly uncomfortable and was actively scratching at the lesions. The posterior neck, bilateral shoulders and upper extremities had scattered erythematous heme-crusted papules, with the right side worse than the left.

DERMATOPATHOLOGY

Biopsy performed by an outside provider showed findings consistent with prurigo nodularis.

ADDITIONAL STUDIES

A complete blood count, comprehensive metabolic panel, thyroid stimulating hormone, ferritin, and vitamin D levels were unremarkable.

DIAGNOSIS

Brachioradial pruritus

TREATMENT AND COURSE

Over the course of five months, the patient failed multiple topical and oral medications including camphor and menthol lotion, capsaicin cream, mometasone cream, clobetasol ointment,

calcipotriene cream, N-acetyl cysteine 1200 mg twice daily, propranolol 10 mg twice daily, amitriptyline 10 mg daily, and gabapentin 300 mg three times daily. Additionally, the patient was referred to neurology and physical medicine and rehabilitation who both recommended conservative physical therapy; however, the patient lived far away and was unable to attend multiple sessions per week.

The patient elected to treat with onabotulinumtoxinA injections, which were used off-label for brachioradial pruritus. A total of 100 units were administered intradermally to the right upper arm and right posterior neck, with two units per injection site spaced two centimeters apart. The patient tolerated the treatment without any adverse effects. At follow-up three months later, she reported disappearance of her pruritus and gradual resolution of the prurigo nodules as well as improved sleep quality. One year later, the pruritus continued to be well-controlled with only mild intermittent symptoms. She declined repeat botulinum toxin injections at that time.

DISCUSSION

Brachioradial pruritus is a chronic disorder of intractable, intense pruritus that leads to significantly diminished quality of life. It mainly affects the proximal dorsolateral forearms and upper arms with occasional involvement of the shoulders, upper back, and cervical area. The etiology of brachioradial pruritus is thought to be due to cervical radiculopathy with possible exacerbation by ultraviolet light radiation exposure. Studies also suggest that chronic scratching itself leads to dysregulation of the dermal immune system and neural networks, including the release of prostaglandins, activation of eosinophils and mast cells, and then decreased density of dermal nerve fibers. Treatment focuses on symptomatic relief and includes sun protection, topical capsaicin, ice packs, gabapentin, amitriptyline, doxepin, antipsychotics, and investigational therapies, such as dupilumab or combination topical amitriptyline and ketamine.

Botulinum toxin has been used in numerous pruritic conditions refractory to traditional treatments. It has reportedly shown efficacy in reducing perceived itch in subjects affected by, but not limited to, lichen simplex chronicus, psoriasis, burn scars, atopic dermatitis, lichen planus, post-herpetic itch, notalgia paresthetica, Fox-Fordyce disease, and Hailey-Hailey. 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) and transient receptor potential ankyrin 1 (TRPA1) in the dorsal root ganglia, which are considered responsible for histamine-dependent and histamine-independent itch respectively. Another animal model of psoriasis demonstrated reduced blood vessel and adjacent nerve infiltration with improved inflammation and epidermal hyperplasia with botulinum toxin administration compared to saline-injected controls. Together, these results show promise for the use of botulinum toxin in the treatment of pruritus.

We report a case of treatment-refractory brachioradial pruritus with associated prurigo nodularis successfully treated with botulinum toxin A injections. Our patient had failed multiple conservative treatments including topical and oral therapies prior to receiving onabotulinumtoxinA injections. While further studies must be performed to understand itch relief mechanisms, botulinum toxin may be a potential therapeutic avenue for those with refractory brachioradial pruritus and other pruritic dermatoses.

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[1]Erin Garfield, 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

A male neonate born at 39 weeks 6 days gestation presented at the time of birth with a diffuse eruption of pink to red macules and thin papules on the face, trunk, and extremities, resembling a “blueberry muffin rash.” The pregnancy was complicated by a history of maternal human papilloma virus (HPV) and gestational diabetes. The mother and father were otherwise healthy with no consanguinity, and no family history of autoimmune disease or immunodeficiencies. The patient was born by vaginal delivery with birthweight of 6 pounds, 5 ounces. The birth was complicated by meconium-stained fluid, but APGAR scores were 9 and 9 at 1 and 5 minutes after birth. The patient continued to feed well, void and have bowel movements, and remained hemodynamically stable on room air. Based on the appearance of the cutaneous eruption, there was concern for extramedullary hematopoiesis and infection. Given the concern for TORCH infection, the patient was started on ampicillin/gentamicin empirically while undergoing further work-up.

PAST MEDICAL HISTORY

No past medical history.

MEDICATIONS

No medications. No known exposures to maternal medications in utero.

ALLERGIES

No known drug allergies.

FAMILY HISTORY

Mother and father were otherwise healthy without any personal or family history of autoimmune disease or immunodeficiency. Mother received regular prenatal care and had presented for induction at 39 weeks, 6 days gestation. The pregnancy was complicated by maternal HPV infection and gestational diabetes.

SOCIAL HISTORY

No relevant social history.

PHYSICAL EXAMINATION

There was a diffuse eruption of pink to red non-blanching macules and occasional thin papules over the face, scalp, chest, abdomen, back, and upper and lower extremities. The palms and soles were spared. Darier’s sign was negative. There was no axillary or cervical lymphadenopathy.

DERMATOPATHOLOGY

Histologic sections from a punch biopsy from the right leg showed a mild perivascular and peri-eccrine infiltrate of crushed inflammatory cells that were focally positive for CD117 by immunohistochemistry, and negative for E-cadherin and CD61. There was no evidence of extramedullary hematopoiesis, leukemia cutis, or mastocytosis. Findings were overall non-specific. The specimen was sent for intradepartmental review at Lurie Children’s hospital with concurrence.

ADDITIONAL STUDIES

The patient was blood type O+, and the mother was B+. Metabolic newborn screen was negative. A complete blood cell count demonstrated thrombocytopenia with platelets of 38 (150-400K/uL) that improved to 86 after a platelet transfusion. Blood cultures were negative. Tissue culture of a skin lesion was also negative. CMV, parvovirus, and HSV 1&2 blood PCRs were negative. CMV urine PCR was also negative. Flow cytometry showed no evidence of monoclonal B cell population or T cell abnormalities. Maternal labs showed HIV non-reactivity, rubella immunity, RPR non-reactivity, and Hepatitis B negativity. Abdominal ultrasound showed no organomegaly. Head ultrasound was unremarkable. Dilated eye exam and hearing tests were all normal. Diagnostic bone marrow aspirate showed a low-normal number of megakaryocytes, and a cellular bone marrow with trilineage hematopoiesis and left shifted granulopoiesis. There was no evidence of leukemia.

DIAGNOSIS

Neonatal lupus erythematosus

TREATMENT AND COURSE

The patient was discharged from the hospital after infection was ruled out and platelet counts stabilized, though there was still no clear etiology for the diffuse cutaneous eruption. Hematology followed the patient closely in the outpatient setting due to thrombocytopenia, and the patient was readmitted to the hospital 9 days later due to a platelet count of 28 requiring a platelet transfusion. He was discharged shortly after the transfusion, but readmitted again 7 days later for platelet count of 14 and worsening neutropenia. At that time, IVIG 1 gram/kg was administered with only mild improvement in thrombocytopenia and absolute neutrophil count. The patient underwent a bone marrow aspirate which showed a left shift with few megakaryocytes and no evidence of leukemia. Two months after birth, the patient presented for outpatient dermatology follow-up with new annular plaques on the temples and pre-auricular cheeks, periorbital edema with erythematous scaly plaques, and reticulated erythematous thin plaques on the forehead, temple, and scalp. Based on this new cutaneous presentation as well as concurrent persistent cytopenias, there was concern for neonatal lupus. The patient was sent for EKG and echocardiogram to evaluate for heart block which were both normal. The patient's mother was sent for ENA profile, ANA, and antiphospholipid antibodies. The mother's ENA was positive for anti-RNP, anti-SSA, and anti-SSB antibodies as well as a high titer ANA. The patient also underwent ENA profile which was similarly positive for anti-RNP at 23 (<20), anti-SSA at 74 (<20), and anti-SSB at 86 (<20). The patient started diligent sun protection with the plan to repeat EKG at 6 and 12 months. The cutaneous eruption continues to improve with diligent sun protection alone.

DISCUSSION

Neonatal lupus can occur in neonates born to mothers with seropositivity for anti-Sjogren syndrome A (anti-SS-A) antibodies, anti-Sjogren syndrome B (anti-SS-B) antibodies, and sometimes anti-ribonucleoprotein (anti-RNP) antibodies. Mothers that are seropositive for these antibodies may be symptomatic at the time of birth or have a known prior connective tissue disease diagnosis, but about 50% of the mothers may be completely asymptomatic at the time of delivery, as seen in our patient's case. Maternal antibodies can enter the fetal blood stream through the transplacental route at as early as 12 weeks' gestation and may cause inflammation that affects the skin, hepatobiliary, hematological, neurological, and cardiac systems of the neonate. Systemic and cutaneous manifestations are typically evident by 1 month of age, but only about 18% of patients show cutaneous manifestations at the time of birth.

Cutaneous manifestations of neonatal lupus most commonly occur in sun-exposed areas including the head, neck, and extremities. Annular, scaly plaques with periocular involvement

and periorbital edema are classic cutaneous presentations, but more rare morphologies include atrophic, bullous, and papulosquamous lesions. More generalized eruptions have also been described. Skin biopsies from patients with neonatal lupus characteristically show destruction of the basal layer of skin, epidermal atrophy, and a perivascular infiltrate. Cutaneous lesions typically spontaneously clear by 6-12 months of age, coinciding with the disappearance of maternal IgG antibodies in the patient's serum. Some studies have described sequelae of cutaneous lesions in up to 34% of patients including telangiectasia, hypopigmentation, hyperpigmentation, and atrophic scarring. The presence of cutaneous lesions at the time of birth is associated with an increased risk of atrophic scarring. Effective treatments include avoidance of sun exposure, low to mid potency topical steroids or topical calcineurin inhibitors, and systemic corticosteroid therapy. For telangiectasias that persists after the cutaneous eruption resolves, pulsed dye laser has been used successfully.

While cutaneous, hepatobiliary, and hematologic manifestations of neonatal lupus are typically reversible, congenital heart block is not. Congenital heart block is the most serious complication of neonatal lupus and may occur in 15-30% of patients. The risk of congenital heart block is highest in patients of mothers with anti-SSA antibodies. Other cardiac complications in newborns of anti-SSA seropositive mothers includes endocardial fibroelastosis, which can lead to a dilated cardiomyopathy. Mothers who have a child with neonatal lupus have a 35% risk of having a second affected child. In these at-risk mothers, it is important to perform fetal echocardiograms weekly during the peak period of cardiac injury between 16- and 26-weeks gestation.

Neonatal lupus is commonly misdiagnosed as eczema or a fungal infection, and may present with non-classic cutaneous manifestations. It is imperative for dermatologists to recognize the variety of cutaneous presentations of neonatal lupus in order to perform appropriate screening, particularly for congenital heart block. It is also important to note that while rare, cutaneous manifestations of neonatal lupus can appear at the time of birth as well. Here we present a case of neonatal lupus that presented at the time of birth as a "blueberry muffin-like" eruption to highlight an atypical cutaneous manifestation that may lead to a delay in diagnosis.

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[1]Viki Patel, MD, [1]Mathew Joseph, MD, [1]Monika Kaniszewska, MD, [2]Jodi Speiser, MD, [3]David Eilers, MD
[1]Division of Dermatology, Loyola University Medical Center
[2]Department of Pathology, Loyola University Medical Center
[3]Section of Dermatology, Edward Hines Jr. VA Hospital

HISTORY OF PRESENT ILLNESS

A 75-year-old male presented to our Hines VA dermatology clinic in January of 2022 for a persistent rash on the left upper extremity believed to be secondary to hogweed exposure.

The patient noted that he received the COVID-19 vaccine on May 4, 2021 and then tested positive for COVID-19 on June 1, 2021. On June 4, 2021, the patient developed the "hogweed rash" and was referred to neurosurgery after he lost of ability to clench his left fist.

Three days after he was diagnosed with COVID, the patient developed "blisters" that resolved within a week of onset. He subsequently developed a pruritic scaly rash two weeks later in the same location. Since that time, the patient noted that he was unable to fully close his open hand and endorsed swelling of the left forearm, hands, and fingers. The patient did not recall any hogweed exposure but believed it was the inciting factor after searching Google for similar-appearing rashes. After discussion, it was determined that the "blisters" that the patient developed corresponded to shingles.

PAST MEDICAL HISTORY

Type 2 diabetes mellitus, primary varicella infection as a child

MEDICATIONS

Glipizide

ALLERGIES

No known drug allergies.

FAMILY HISTORY

No pertinent family history.

SOCIAL HISTORY

No alcohol, smoking, or illicit drug use.

PHYSICAL EXAMINATION

The patient was well-appearing. He had a papulosquamous rash on the left dorsolateral forearm, upper arm, and ventral wrist that extended to fingers, primarily on digits 4 and 5. The lesions were well-demarcated with scaly pink to red papules and plaques, some with infiltrative yellow to red dermal appearance and many with atrophic centers. Others were more polygonal, flat, scaly and violaceous. Significant withdrawal to pain was elicited by palpation of the left 4th and 5th digit and of the ulnar nerve at the proximal ventral forearm. There was also muscular atrophy of left hand in an ulnar distribution. Overall, there was an apparent C8 dermatomal pattern of the lesions.

DERMATOPATHOLOGY

Histologic sections from the initial punch biopsy were consistent with suppurative, necrotizing granulomatous dermatitis. AFB, PAS, Gram, and GMS stains were negative. A repeat punch biopsy one month later demonstrated the same findings.

ADDITIONAL STUDIES
No additional relevant studies.

DIAGNOSIS
Wolf's isotopic response

TREATMENT AND COURSE
The patient was initially started on Hydrocortisone 2.5% cream without improvement. He was then switched to Fluocinonide 0.05% ointment twice daily with moderate improvement in pruritus. Also, given the concerning features of apparent muscular atrophy in the ulnar distribution, the patient was subsequently referred to neurology for further management.

DISCUSSION
Wolf's isotopic response is a dermatological sign that is characterized by the occurrence of a new dermatosis at the site of a previous unrelated and already resolved dermatosis. This phenomenon was first coined in 1995 when *Wolf et al.* described a case of new-onset psoriasis within the dermatome of previously healed herpes zoster. Interestingly, the mechanism of action is largely unknown with various theories proposed to explain this phenomenon. These include the viral hypothesis, vascular hypothesis, immunologic hypothesis, and neural hypothesis.

Of note, prior varicella zoster viral (VZV) infection is noted to be the primary dermatosis in greater than 95% of reported cases, as seen in our patient. The secondary dermatoses that may occur can vary widely. Reported secondary dermatoses include acneiform eruptions, localized chronic urticaria, granulomatous dermotoses, pseudolymphoma, xanthomatous eruptions, papulosquamous eruptions, morphea, keloids, and even malignancies such as leukemia cutis and Kaposi sarcoma.

In our patient, the secondary dermatosis was a granulomatous dermatitis in a C8 dermatomal distribution at the site of previous shingles infection. Of note, the shingles in our patient was presumed to be secondary to re-activation following COVID-19 infection or vaccination. There are multiple case studies in which patients developed herpes zoster following the inactivated COVID-19 vaccine. It is proposed that the mechanism of this reaction is a transient lymphocytopenia that occurs after vaccination, subsequently paving a path for the dormant virus to become re-activated. COVID-19 infection itself can cause a similar reaction. One retrospective cohort study revealed that individuals diagnosed with COVID-19 had a 15% higher risk of developing herpes zoster than those without COVID-19. In our case, it is likely that our patient developed herpes zoster following the infection itself (three days prior to the onset of the rash) rather than the vaccine (which he received one month prior).

Furthermore, the phenomenon "reverse isotopic response" or "isotopic nonresponse" has also been described in the literature. This term refers to the sparing of skin previously affected by a primary dermatosis followed by a second generalized dermatosis. Again, this is most commonly due to herpes zoster. There is one case report of a patient with cutaneous T-cell lymphoma who had prominent skin-sparing only at the site of resolving dermatomal shingles.

In conclusion, our case of Wolf's isotopic response highlights the importance of considering the wide range of secondary dermatoses that may follow varicella zoster infection. Also, this case demonstrates that herpes zoster can be induced by COVID infection. Finally, we highlight the need to evaluate for possible extracutaneous manifestations, such as ulnar nerve motor neuropathy in this case.

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[1]Division of Dermatology, Loyola University Medical Center
[2]Department of Pathology, Loyola University Medical Center

HISTORY OF PRESENT ILLNESS

A 19-year-old female with past medical history of Hashimoto's thyroiditis and clinically diagnosed Crohn's disease (CD) presented to Loyola University Medical Center as a direct admit from the gastroenterology clinic due to severe perianal pain. She had a history of perianal irritation beginning in February 2021 leading to a diagnosis of a perianal fistula. In October 2021, upper and lower endoscopy, as well as MRI imaging of the abdomen failed to demonstrated definitive clinical or pathologic evidence of CD on multiple histologic samples of the stomach and large intestine. However, given the clinical findings of perianal fistula, iron deficiency anemia, and elevations of CRP, a clinical diagnosis of CD was made, and treatment with infliximab 10 mg/kg intravenous infusion every 8 weeks was instituted with improvement in perianal irritation. However, upon follow-up, the patient was found to have severe perianal pain which precluded a clinical exam, prompting admission. During her admission, the patient had an exam under anesthesia with colorectal surgery. With dermatology guidance, biopsies were taken of both ulcerations.

PAST MEDICAL HISTORY

Crohn's disease, Hashimoto's thyroiditis, acne vulgaris, anxiety, depression

MEDICATIONS

Infliximab 10mg/kq intravenous infusion every 8 weeks, ondansetron, vitamin B12

ALLERGIES

No known drug allergies.

FAMILY HISTORY

Multiple family members with ulcerative colitis.

SOCIAL HISTORY

Student, never smoker, denied alcohol or illicit drug use.

PHYSICAL EXAMINATION

Exam under anesthesia revealed a 10 x 6 cm ulceration with serpiginous borders of the superior gluteal cleft and a 3.5 x 3 cm ulceration of the perineum. Both ulcerations were down to muscle.

DERMATOPATHOLOGY

Histologic sections from incisional biopsies performed under anesthesia showed findings of acute and chronic neutrophilic, T cell, B cell, and plasma cell inflammation, fibrosis, microabscess formation, and IgG4 positive plasma cells of up to 150/HPF. Immunostains for HSV I&II, CMV, and adenovirus, as well as GMS, AFB, PAS, and mucicarmine stains were negative. S100 IHC, kappa and lambda ISH were both reviewed and non-contributory to the diagnosis.

ADDITIONAL STUDIES

Testing for HLA-B51, HLA-B27, fungal, anaerobic, and aerobic tissue cultures, HIV, and multiple HSV PCR tests throughout the disease course were all negative. Immunoglobulin studies revealed normal total immunoglobulin and IgM, IgG, and IgA levels. They did however show elevated IgG4 of 133 (4-86mg/dL). C reactive protein was elevated to 72.7 (<8.1 mg/dL).

Complete metabolic panel, complete blood count with differential, and thyroid stimulating hormone were all within normal limits. Blood cultures were negative.

Magnetic resonance imaging of the pelvis with and without contrast revealed a large skin ulceration of the anal canal extending to the left para midline gluteal cleft, with intersphincteric fistula and without abscess. It also demonstrated inflammatory changes along the left perineum, though these were not completely visualized on the study.

DIAGNOSIS

Cutaneous Crohn's disease with incidental elevations in IgG4

TREATMENT AND COURSE

The patient followed up within one week of discharge with Loyola dermatology and was started on clobetasol 0.05% ointment and oral prednisone 40 mg daily (1 mg/kg) for 2 weeks with a 4-week taper. Infliximab treatments were continued through gastroenterology at the same dosage.

The patient ultimately sought a second opinion from the Mayo Clinic Rochester dermatology, dermatopathology, and gastroenterology departments. Dermatology favored cutaneous CD versus pyoderma gangrenosum. Dermatopathology believed the biopsy findings were non-specific but could be compatible with CD in the right clinical setting. IgG4 positive plasma cells were thought to be incidental and non-contributory. Gastroenterology also favored CD. No changes to the treatment plan were recommended, with the exception of a repeat oral prednisone taper for 2 weeks.

Over the next several months, the patient continued to improve with a decrease in size of gluteal cleft ulceration to 2 x 1.5 cm and resolution of the perineal ulceration. Attempts were made to stop clobetasol and start tacrolimus 0.1% ointment BID, however the patient could not tolerate tacrolimus ointment due to intense burning discomfort. In May 2022 the patient had a significant infusion reaction prompting a switch to ustekinumab 90 mg subcutaneous injection every 12 weeks, which was begun in June 2022. She developed striae at the site of the gluteal cleft ulceration, prompting a re-trial of tacrolimus ointment, which the patient was able to tolerate without discomfort given overall improvement in ulceration.

DISCUSSION

Crohn's disease is a chronic and progressive inflammatory disorder classified under the umbrella term inflammatory bowel disease (IBD) along with ulcerative colitis. It has a complex etiology that is not completely elucidated, but has been shown to have genetic, environmental, microbial, and immune components.

Genetic susceptibility loci including NOD2, ATG16L1, IRGM involved in autophagy pathways, as well as IL23R, IL12B, and IL10 defects have been implicated in CD pathogenesis. Heritability studies have shown that this accounts for 20-25% of the genetic link with IBD. These are more common in those of Northern European and Ashkenazi Jewish ancestry. Environmental factors including smoking, frequent ASA and NSAID usage, stress, higher latitudes, colder climates, and high air pollution have also been linked to IBD. Affected patients have alterations in gut microbiota, including a decrease in *Bacteroidetes* and *Firmicutes* species and increase in *Enterobacteracea*. Mucosa-adherent and invasive *E*. coli is also increased in CD, which has been shown to induce granuloma formation in Boxer dogs. Defects in innate immunity through TLR and NOD alterations, mucosal barrier function, and adaptive immunity in the Th1 and Th17 cell populations have all also been implicated in CD.

Cutaneous manifestations of CD are numerous and include contiguous cutaneous disease seen in roughly 50% of patients. This presents as perianal erythema, abscess, or fistula. Less commonly, CD may appear at distant sites with the same histology, a phenomenon known as metastatic CD, with nearly 100 reported cases. Other commonly seen cutaneous sequelae include erythema nodosum, pyoderma gangrenosum, sweet syndrome, bowel associated dermatosis-arthritis syndrome, pyodermatitis-pyostomatitis vegetans, SAPHO syndrome, and PAPA syndrome.

Perianal fistulizing disease is a common complication of CD, with roughly 20% of patients experiencing a perianal fistula during their disease course. Of these patients, 40% will have a perianal fistula as their presenting sign, prior to the onset of GI symptoms. Fistulizing patients tend to have an earlier onset, higher rate of recurrence, and worse prognosis overall.

The cutaneous course often follows that of the GI tract. Treatment is aimed at rapid remission with corticosteroids, biologics, and disease-modifying antirheumatic drugs (DMARDs), followed by maintenance with biologic and DMARD combination therapy. Infliximab is first line for fistulizing disease as it is the only biologic studied with randomized controlled trials for this presentation, however other biologics have been noted to be effective clinically. Antibiotics have not shown efficacy as monotherapy, but are synergistic with biologics and DMARDs in inducing remission of fistulas. Local treatments include topical or intralesional corticosteroids, topical calcineurin inhibitors, and mainstays of chronic wound care.

Our patient did show elevated IgG4 on both histology and serology, raising initial concerns for IgG4 related disease (IgG4-RD). IgG4-RD is a heterogenous group of disorders characterized by fibrotic mass formation in a variety of organ systems that is progressive and can be fatal. It is sub-categorized into four distinct types: pancreato-biliary, retroperitoneal/aortitis, head and neck limited, and Mikulicz/systemic, each with its own prognosis and treatment intricacies. Hallmarks of the disorder histologically include lymphoplasmacytic infiltrate, “storiform” tissue fibrosis, obliterative phlebitis, elevated tissue IgG4+ plasma cells, and tissue IgG4 positive/IgG positive plasma cell ratio exceeding 40%. The first 3 criteria are deemed essential and the last 2 are supportive, as tissue elevations in IgG4 can be seen in a variety of neoplastic and inflammatory processes.

Although our patient did have an increased IgG4 plasma cell number and IgG4/IgG ratio on histology, she did not show storiform fibrosis or obliterative phlebitis. Other emerging markers for IgG4-RD include serum IgG4/total IgG ratio with IgG4/IgG >10% indicating possible IgG4-RD. Our patient had a percentage of 8.4, indicating low likelihood of disease. In addition, American College of Rheumatism and European League Against Rheumatism IgG4 related disease classification criteria also did not support a diagnosis of IgG4-RD in this case.

Our patient had an atypical case of histology negative CD presenting with perianal disease with severe ulceration. Biopsies showed elevated IgG4 raising the possibility of IgG4-RD, although further investigation did not support this diagnosis. This case allowed an opportunity to highlight an uncommon presentation of CD, and an uncommon systemic dermatologic diagnosis.

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Mafee, MD
[1]Division of Dermatology, Loyola University Medical Center
[2]Department of Pathology, Loyola University Medical Center

HISTORY OF PRESENT ILLNESS
An 84-year male presented for Mohs micrographic surgery for a biopsy-proven basal cell carcinoma on the right superior helix. The lesion was present for approximately 1 year.

PAST MEDICAL HISTORY
Atrial fibrillation, Parkinson's disease, prostate cancer (cT1c)

MEDICATIONS
Carbidopa, sinemet CR, flecainide, pantoprazole, rasagiline mesylate

ALLERGIES
No known drug allergies.

FAMILY HISTORY
No pertinent family history.

SOCIAL HISTORY
No pertinent social history.

PHYSICAL EXAMINATION
The patient was overall well-appearing. The helix of the right ear demonstrated a 1.0 x 1.3 cm ulcerated, indurated plaque with rolled borders and central hyperkeratotic crust.

DERMATOPATHOLOGY
Initial shave biopsy revealed a basal cell carcinoma, with nodular and infiltrative subtypes. Frozen sections from the first Mohs stage demonstrated residual superficial, infiltrative, and basosquamous basal cell carcinoma. In addition, there was a brisk inflammatory infiltrate throughout the deep margins. The second stage was negative for any residual basal cell carcinoma, but there was still a brisk atypical lymphocytic infiltrate, with some areas showing lymphocytes almost in a linear cord-like distribution. Because of these findings, the tissue was sent for permanent sections, which demonstrated infiltration of small to medium sized lymphoid cells. Immunohistochemistry stains (CD20, CD3, CD5, CD10, BCL-2, BCL-6, CD43 and Ki-67) were performed and reviewed. The lymphoid cells stained positive with CD20, BCL-2 and negative with CD5, CD10, BCL6 and CD43. Ki-67 stain showed a proliferation fraction of less than 5%. B cell clonality studies and PCR demonstrated positive IGH and positive IGK suggestive of clonal rearrangement of the immunoglobulin heavy chain IGH and immunoglobulin kappa light chain IGK genes.

ADDITIONAL STUDIES
The patient underwent PET scan which demonstrated no definite areas of intense metabolic activity suggestive of malignancy.

DIAGNOSIS
Primary cutaneous marginal zone B-cell lymphoma

TREATMENT AND COURSE

Mohs micrographic surgery was completed for the concomitant basal cell carcinoma on the patient's right helix lesion, after which tissue samples were sent for permanent processing and resulted in a diagnosis of primary cutaneous marginal zone B-cell lymphoma. The patient was referred to medical oncology. PET scan did not demonstrate any evidence of systemic disease, and therefore the oncology team recommended a watch and wait approach for the patient's newly diagnosed cutaneous B cell lymphoma with the plan for close lab-follow-up.

DISCUSSION

Primary cutaneous B-cell lymphomas are a type of Non-Hodgkin's lymphoma that have been increasing in incidence, diagnosed at a current rate of approximately 4 cases per million individuals. Of all the primary cutaneous lymphomas, primary cutaneous B-cell lymphomas (PCBCL) comprise about 25%. PCBCL's are divided into three main types: primary cutaneous marginal zone lymphoma (PCMZL), primary cutaneous diffuse large B-cell lymphoma, leg type, and primary cutaneous follicle-center lymphoma.

Diagnosis of PCBCL can be difficult, and requires biopsy that should include subcutaneous fat. Staging is crucial to rule out systemic lymphoma. The National Comprehensive Cancer Network also recommends the use of immunohistochemistry stains including CD3, CD5, CD10, CD20, BCL2, BCL6, MUM1 for all samples as well as CD21, CD23, CD43, Cyclin-D1, Ki-67, IgM, IgD, and kappa/lambda light chain analysis to assist with diagnosis. PCMZL typically stains positive for BCL-2 and sometimes CD43, and is usually negative for BCL-6, CD10 and CD23. Initial laboratory workup should include basic studies such as complete blood count with differential, complete metabolic panel and LDH. In addition, imaging should be performed in all patients with suspected PCBCL with CT scan of the chest, abdomen, and pelvis or a whole-body PET scan to evaluate for systemic disease.

There is some evidence to suggest that dermoscopy can be useful in diagnosis of PCBCL. Navarrete-Dechent et al. in 2019 described key dermoscopic findings of primary cutaneous lymphomas (B and T-cell), including an orange discoloration (71.4%), organized geographical presentation (85%), and involvement by follicular plugs (85%) in comparison to controls. Geller et al, in 2019 reported that a salmon color (79.3%) and presence of serpentine vessels (77.6%) were also frequently present.

Treatment of PCMZL depends on the extent of disease. For patients with a single or small number of lesions, local therapy can be attempted with surgical excision or radiation therapy. Other therapies may include topical corticosteroids, intralesional corticosteroids, topical nitrogen mustard, or bexarotene, but there is limited data available on the effectiveness of these options. For multifocal disease, intralesional or systemic rituximab is the most effective treatment. Observation is also reasonable because PCMZL tends to be indolent. Overall prognosis is excellent, with 5-year survival rates estimated at greater than 95%. However, relapse can occur in approximately one-third of patients.

There are numerous prior reports in the literature of PCBCL imitating the cutaneous findings of basal cell carcinomas (BCC), where histology demonstrates evidence of lymphoma but does not demonstrate any basaloid tumor. Additionally, Chambers et al. report a case of a patient who was found to have cutaneous lymphoma in an area on the face that was previously treated for a BCC. To our knowledge, this is the first reported case of a patient who demonstrated histological features of both BCC and PCBCL in the same lesion, which was discovered during Mohs micrographic surgery. This case also highlights the importance of further evaluation with permanent sections when an atypical finding is seen on Mohs sections.

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Chicago Dermatologic Society **Case #8**

[1]Blanca Estupiñan MD, [1]Wendy Kim DO
[1]Division of Dermatology, Loyola University Medical Center

HISTORY OF PRESENT ILLNESS

A 37-year-old non-verbal Caucasian male with severe developmental delay presented with diffuse blanching erythema and superficial desquamation of the trunk, bilateral upper and lower extremities, which then progressed to painful erosions on the trunk, upper extremities, inguinal folds, palms, soles, and genitals.

PAST MEDICAL HISTORY

Seborrheic dermatitis, severe developmental delay, non-verbal at baseline, bipolar disorder, constipation complicated by megacolon, GERD, intermittent post-prandial emesis, hypothyroidism

MEDICATIONS

Omeprazole, polyethylene glycol 3350, levothyroxine, vitamin D3, ketoconazole 2% and T-gel shampoos, diphenhydramine

ALLERGIES

Amoxicilin, amphetamines, clozapine, methylphenidate, quetiapine, risperidone, valproic acid

FAMILY HISTORY

No pertinent family history.

SOCIAL HISTORY

No alcohol, tobacco or drug use.

PHYSICAL EXAMINATION

On the trunk, bilateral upper and lower extremities the patient had diffuse blanching erythematous patches. The patient later developed erythematous, eroded plaques with scattered areas of superficial desquamation on the trunk, thighs, inguinal folds, genitals, palms, and soles.

DERMATOPATHOLOGY

Initially, punch biopsies for H&E and DIF were obtained from the back. Findings included mild interface dermatitis with many dyskeratotic keratinocytes throughout the epidermis with overlying basket-weave orthokeratosis. No significant acanthosis was present. DIF was negative.

A second punch biopsy was obtained from the left shoulder, which revealed acanthosis with pallor of the upper epidermis, confluent parakeratosis and mild superficial perivascular lymphocytic inflammation. Rare dyskeratotic keratinocytes were noted.

ADDITIONAL STUDIES

Laboratory studies were significant for low zinc 52 (60-130 ug/dL), magnesium 1.6 (1.8-2.5 mg/dL), calcium 8.5 (8.9-10.3 mg/dL), low normal alkaline phosphatase 32 (30-110 U/L), and glucagon 11 (8-57 pg/mL).

DIAGNOSIS

Acquired zinc-deficiency dermatitis in an adult patient

TREATMENT AND COURSE:

Our patient was treated with triamcinolone 0.1% ointment BID and zinc oxide 20% cream to all eroded areas. Daily zinc sulfate 220 mg (containing 50 mg of elemental zinc) supplementation was initiated as well as a multivitamin and Ensure nutritional drinks. At clinic follow up 1 month later, his skin had re-epithelialized and only residual superficial desquamation on the palms and soles remained. Zinc supplementation was discontinued after his zinc levels normalized a few months later. He continued to follow with dermatology and has not had recurrence of his condition.

DISCUSSION

Zinc is an essential nutrient for skin function, wound healing, and immune function. Zinc can be found in breast milk, animal-based foods, shellfish, legumes, and green leafy vegetables. Deficiency can be acquired or inherited as acrodermatitis enteropathica, an autosomal recessive disorder due to a zinc transporter gene mutation. Risk factors for developing zinc deficiency include alcoholism, anorexia nervosa, diets high in mineral-binding phytate (i.e. Middle Eastern diets), vegan diets, and intenstinal malabsorption. It is also associated with HIV, chronic renal insufficiency, medications, and pregnancy. It is estimated that 17% of the global population is at risk for zinc deficiency. This prevalence increases to nearly one-third in developing regions such as South Asia and sub-Saharan Africa. A population study using the National Health and Nutrition Examination Survey from 2011-2014 reported a zinc deficiency prevalence of 8% in U.S. citizens aged 10 and older.

Clinically, zinc deficiency favors the perioral, acral, and anogenital regions and presents with erythematous plaques with scale and erosions. Occasionally, vesicles, bullae, or psoriasiform plaques develop. The zinc deficiency triad of depression, diarrhea, and dermatitis is present in only 20% of patients. Other associated findings include alopecia, paronychia, onychodystrophy, conjunctivitis, stomatitis, and angular chelitis.

Histopathologic findings may be relatively non-specific, depending on when a biopsy is obtained. To identify acquired zinc deficiency, a helpful finding is necrosis of the upper one-third of the epidermis, which has also been reported in acrodermatitis enteropathica and pellagra. Early histopathologic findings include pallor and ballooning of the upper half of the epidermis. As the lesions progress, acanthosis with confluent parakeratosis and degenerative changes of the upper epidermis can be seen. The papillary dermis may show dilated, tortuous vessels and a mild perivascular lymphocytic infiltrate. In later stages, pallor of the upper epidermis is usually missing.

Cutaneous and systemic manifestations of zinc deficiency rapidly respond to zinc sulfate or zinc gluconate supplementation. Recommended dosing is 1-2 mg/kg/day or 3 mg/kg/day of elemental zinc for acquired zinc deficiency and acrodermatitis enteropathica, respectively. Of note, commercially available 220 mg zinc sulfate tablets contain 50 mg of elemental zinc. With the COVID pandemic and resultant economic hardships and financial strains, as clinicians we may encounter more cases of nutritional deficiency dermatitis, thus a detailed history of dietary habits and recognition of key clinical findings is essential.

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Chicago Dermatologic Society **Case #9**

[1]Adnan Ahmed MD, [2]Jodi Speiser MD, [1]Mariam Mafee MD, [1]Wendy Kim DO[1], Eden Lake MD,
[1]Division of Dermatology, Loyola University Medical Center
[2]Department of Pathology, Loyola University Medical Center

HISTORY OF PRESENT ILLNESS

A 15-year-old female with no significant past medical history presented as a transfer from an outside hospital due to concern for Stevens-Johnson syndrome. Four days prior, the patient developed gingival irritation and swelling. Due to concern for a metal allergy, her braces were removed by her orthodontist at that time. One day later, the patient reported development of "hives" on her bilateral hands and feet. The rash continued to worsen and began to involve her legs, buttocks and elbows. She described the rash as raised and purple in color. At the outside hospital, she received prednisone and diphenhydramine without improvement.

Associated with this rash were arthralgias of her hands and feet causing difficulty with mobility. She denied any ocular pain, urinary symptoms, recent colds, or gastrointestinal illnesses. The patient did not start any new medications prior to the onset of this rash. She tested positive for COVID-19 at the outside hospital.

PAST MEDICAL HISTORY

No pertinent past medical history.

MEDICATIONS

No medications.

ALLERGIES

No known drug allergies.

FAMILY HISTORY

No pertinent family history.

SOCIAL HISTORY

No known alcohol, tobacco, or illicit drug use.

PHYSICAL EXAMINATION

Many purpuric papules were seen on the bilateral buttocks, elbows, dorsal hands, dorsal feet, ankles, lower legs, and thighs. There were numerous variably sized hemorrhagic bullae on the lower legs, feet and ankles. The oral and ocular mucosae were clear.

DERMATOPATHOLOGY

Histologic sections from a punch biopsy of the right thigh showed subepidermal bullae formation with underlying perivascular and interstitial neutrophilic inflammation. There were scattered fibrin thrombi in vessels as well as red blood cell extravasation. Immunofluorescence studies for IgG, IgA, IgM, C3 and fibrinogen revealed a non-diagnostic staining pattern.

ADDITIONAL STUDIES

A complete blood count demonstrated an elevated white blood count at 32.7 (3.5 - 10.5 K/μL) and increased platelet count of 458 (150-400 K/UL). Complete metabolic panel was significant for a sodium of 129 (136-144 mmol/L), albumin of 3.1 (3.6-5.0 gm/dl), protein of 6.4 (6.5-8.3 gm/dl) and calcium of 7.8 (9.0-11.5 mg/dl). Urinalysis was significant for small amount of blood, but no protein was found.

DIAGNOSIS
Bullous leukocytoclastic vasculitis in the setting of COVID-19 Infection

TREATMENT AND COURSE
Given the patient's extensive skin involvement and arthralgias, she was started on 50 mg oral prednisone daily (1mg/kg). Additionally, she was started on topical clobetasol 0.05% twice daily. She was discharged from the hospital 9 days after her presentation with some improvement in her symptoms. She completed a one-month prednisone taper. Three weeks after her discharge, some of her lower extremity bullae had begun to ulcerate and she was prescribed a seven-day course of amoxicillin/clavulanate potassium 500-125 mg by the general surgery team for possible wound infection.

Aerobic culture done by dermatology revealed few colonies of Staphylococcus aureus, few colonies of Pseudomonas aeruginosa, and very few colonies of Escherichia coli. She was then hospitalized for IV antibiotics and started on IV cefepime and clindamycin. Bedside debridement was performed by dermatology. The patient was discharged on a 10-day course of levofloxacin and amoxicillin/clavulanate potassium per infectious disease recommendations after bacterial sensitivities resulted.

After her second hospitalization, the patient had two more outpatient debridements by dermatology. She continued to slowly improve with topical clobetasol 0.05% ointment and zinc oxide barrier cream to hypergranulated areas. She was advised to also apply petrolatum ointment to any remaining open wounds and apply nonstick dressings.

DISCUSSION
Leukocytoclastic vasculitis (LCV) is a small vessel vasculitis that primarily affects the post capillary venules and can be triggered by a wide variety of conditions. It can be idiopathic or induced by certain medications, malignancies, autoimmune conditions or even infections. With an overall incidence of 45 cases per million individuals per year, the epidemiology of LCV varies based on the underlying cause. The pathogenesis of LCV involves immune complex deposition from immunoglobulins or complement proteins in blood vessel walls leading to neutrophil recruitment. This results in fibrinoid necrosis, and recruitment of additional cytokines such as IL-1, IL-6, IL-8 and tumor necrosis factor.

The main clinical findings of LCV are palpable purpura, most often on the lower extremities. It is hypothesized that this is due to increased venous pressure in the lower extremities. Findings are typically bilateral and widespread. Papules typically develop over a few hours. Hemorrhagic bullae, vesicles, ulcerations and nodules may also be seen, such as in our patient. Additionally, a phenomenon known as reverse koebnerization has been seen, where lesions tend to disappear with pressure bandages. While extracutaneous manifestations are not seen in most patients (<30% in reported cases of LCV), fevers, myalgias, and arthralgias can be seen.

Biopsy is key for diagnosing LCV and it is recommended that a punch biopsy be taken within the first 24 hours of the lesion onset. Histopathology for LCV usually exhibits neutrophils in the blood vessels of the superficial dermis, fibrinoid necrosis, and leukocytoclasia. Extravasation of red blood cells can also be seen. Presence of eosinophils has been noted as well and may indicate medication-induced LCV. In addition to histopathology, a separate punch biopsy should be taken for direct immunofluorescence (DIF). DIF positive for IgA is diagnostic for IgA vasculitis. Whereas, IgG or IgM may be suggestive of lupus or other autoimmune conditions. For DIF, biopsies done after 48 hours may be falsely negative.

Treatment for LCV depends on its severity. Mild cases of LCV can be treated with supportive measures such as compression stockings, elevation, and rest; these cases typically spontaneously resolve within 3-4 weeks. More severe cases may require a prolonged steroid taper of 3-5 weeks. A small case series also found some utility with oral dapsone. If LCV is due to a systemic illness or is resistant to corticosteroids, then immunosuppressive agents such as azathioprine or methotrexate can be considered.

Infection has been a known trigger for LCV and there have been a variety of case studies that have shown both the COVID-19 vaccine and infection as triggers in LCV. While the mechanism behind how COVID-19 infection can lead to LCV has not been completely elucidated, it is hypothesized that immune system cross reactivity or molecular mimicry with viral particles may lead to immune complex deposition. A recent study found that, of cutaneous manifestations from COVID-19 infection, LCV made up approximately 2% of findings. A leading theory for how COVID-19 can cause LCV involves the Angiotensin Converting Enzyme 2 (ACE2) mechanism. It is well documented that COVID-19 viral particles target the vascular endothelium through ACE2. This causes enhancement of the cytokine storm and recruitment of complement proteins and interleukins, specifically IL- 6. This leads to overall perivascular inflammation and recruitment of neutrophils causing LCV. Given the lack of systemic symptoms and medication trigger in our patient's case, we strongly suspect COVID-19 as the inciting factor for her extensive LCV.

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Chicago Dermatologic Society **Case #10**

[1]Zisansha Zahirsha, MD, [1]Wendy Kim, DO
[1]Division of Dermatology, Loyola University Medical Center

HISTORY OF PRESENT ILLNESS

A 2-month-old Caucasian female born full term presented to dermatology for a bleeding red perianal rash noticed at 3 weeks of age that was initially treated with topical emollients as a presumed diaper dermatitis without improvement. She was otherwise well appearing without changes in feeding, urination, or stooling.

PAST MEDICAL HISTORY

No pertinent past medical history.

MEDICATIONS

No medications.

ALLERGIES

No known drug allergies.

FAMILY HISTORY

No pertinent family history.

SOCIAL HISTORY

No known alcohol, tobacco, or illicit drug use.

PHYSICAL EXAMINATION

The patient was well-appearing. A 5.0 x 4.0 cm bright red-violaceous plaque with local maceration and ulceration was seen from the skin superior to the anus and extending to the superior gluteal cleft. In addition, a 0.6-centimeter skin colored papule was located off-center at the right medial gluteal cheek approximately 2 centimeters from the anal verge.

DERMATOPATHOLOGY

No dermatopathology available.

ADDITIONAL STUDIES

Abdominal, pelvic, and renal ultrasounds were unremarkable. MRI abdomen and pelvis with and without contrast did not note extracutaneous involvement of the hemangioma or other internal organ abnormalities. Lumbar spine ultrasound demonstrated the spinal cord extending to at least the L4 level and a sinus tract extending from the sacral dimple. MRI lumbar spine with and without contrast demonstrated tethering of the spinal cord extending to approximately the S2 level. The tethered cord was associated with an intradural lipoma extending from L4 through the sacrum and a probable mild hydrosyringomyelia of the lower lumbosacral cord. In addition, a right para-midline sacral sinus tract at the level of the coccyx extended through the subcutaneous fat with possible spinal canal communication. These findings were consistent with spinal dysraphism.

DIAGNOSIS

Lower body hemangioma, urogenital anomalies, myelopathy, bony deformities, anorectal malformations, renal anomalies (LUMBAR) syndrome

TREATMENT AND COURSE

After diagnosing the patient with LUMBAR syndrome and associated closed spinal dysraphism, the patient was started on oral propranolol 1 mg/kg/day divided into 3 doses after cardiac evaluation. She had rapid clinical improvement of her perianal hemangioma and associated ulceration within nine days of oral propranolol initiation. The patient had urology, neurosurgery, and orthopedic evaluation with scheduled outpatient follow up in a multidisciplinary spina bifida clinic to determine the best treatment approach for her structural abnormalities.

DISCUSSION

LUMBAR syndrome is a collective term to describe lower body hemangioma syndromes, taking the place of previous nomenclature including PELVIS and SACRAL syndrome. LUMBAR syndrome has a prevalence of less than 1 in a million, and there are no standardized diagnostic criteria currently. However, all reported cases involve a lower body segmental hemangioma overlying congenital anomalies. Lipomas and cutaneous defects, such as a sacral dimple in our patient, can be found in 50% of cases and ulceration is present in a variable number of cases. Myelopathy is the most common extracutaneous anomaly, with other congenital defects being reported as well. Among a study of 20 children with lumbosacral hemangiomas and spinal cord dysraphism, 60% had tethered cord, 50% had a spinal lipoma or lipomyelomeningocele, and 40% had sinus tracts.

For detecting spinal anomalies in these cases, ultrasound has a sensitivity of 50% and specificity of 78%, but studies have reported 15-42% of patients with normal ultrasound findings were found to have spinal dysraphism on MRI. Hence, MRI is considered the gold standard for neuroimaging in cases of lumbosacral hemangiomas despite the additional risks of sedation in infants. The MRI can be delayed until 4 to 6 months of age assuming there are no cutaneous markers of dysraphism, neurological signs, or ulceration. Other high-risk cutaneous lesions for closed spinal dysraphism besides hemangiomas include atypical dimples greater than 5 millimeters in diameter or greater than 2.5 centimeters from the anal verge, cutis aplasia, or elevated lesions.

Tethered cord syndrome involves attachment of the spinal cord to abnormally inelastic structures, such as the intradural lipoma in our case, leading to the conus medullaris being lower than the anatomical L2 to L3 level and subsequent stretch-induced neurologic dysfunction. When patients are diagnosed with tethered cord syndrome, upwards of 60% have dermatologic lesions suggestive of a diagnosis, with younger children being more likely to have dermatologic manifestations be the presenting sign. As progression of closed spinal dysraphism is highly variable, surgery is controversial in asymptomatic patients with radiographic evidence of tethered cord. Indications for surgery include neurologic symptoms, internal exposure of the spinal cord, and pain relief. In addition, the presence of a syrinx should not be a consideration for surgery.

Many cases of closed spinal dysraphism initially present with dermatologic manifestations, and segmental lumbosacral hemangiomas are high risk for ulceration and structural abnormalities. Abdominopelvic and neurologic imaging is crucial in these cases with MRI being the gold standard for spinal imaging. Management of LUMBAR syndrome requires a multidisciplinary approach to optimize patient outcomes.

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