Chicago Dermatological Society

PROTOCOL BOOK
April 12, 2023

Co-hosted by Stroger/Cook County Hospital
Department of Dermatology

Guest Speaker: Desmond Shipp, MD MSBS
Ohio State University Wexner Medical Center

Chicago Dermatological Society
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Program

Co-hosted by Stroger/Cook County Hospital - Department of Dermatology

Wednesday, April 12, 2023
University of Chicago Gleacher Center
Chicago, 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 Lecture**

"Men's Cosmetics"

Desmond M. Shipp, MD MSBS

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**

1:15 p.m. - 2:15 p.m. **Afternoon Lecture**

"Cosmetics in Men of Color"

Desmond M. Shipp, MD MSBS

Program adjourns

Key location(s): Various **CASE 1**

Immune Checkpoint Inhibitor-associated Psoriasiform Dermatitis

Presented by Jacob Dudzinski MD and Benjamin Falck MD

History of Present Illness

A 63 year-old-man with a history of plaque psoriasis and stage IIc colon adenocarcinoma on FOLFIRI and nivolumab presented with a generalized psoriasiform rash.

Past Medical History

Psoriasis, stage IIc colon adenocarcinoma

Medications

FOLFIRI, nivolumab

Review of Systems

Negative for fever, chills, malaise, pharyngitis, arthralgias, and myalgias

Physical Exam

Skin: Scaly pink to red papules and plaques scattered across his torso and extremities. Desquamative erythema and collarettes of scale were present on his hands and feet. Confluent involvement of the buttocks and low back in addition to intertriginous sites including the axillae, inguinal folds, and gluteal cleft. BSA was estimated at 15%.

Laboratory Data

Labs were unremarkable

Histopathology

LEFT THIGH, PUNCH BIOPSY:
Sections are of skin with scale crust containing neutrophils, hypogranulosis and irregular acanthosis with spongiosis and focal lymphocyte exocytosis. The dermis has tortuous, dilated blood vessels and a superficial perivascular lymphohistiocytic infiltrate with eosinophils. The GMS stain is negative for fungi.

Diagnosis

Immunotherapy-Associated Psoriasiform Dermatitis

Treatment and Course

The patient was able to achieve complete resolution of the rash with topical triamcinolone and did not experience recurrence despite rechallenge in the form of additional cycles of immunotherapy.

Discussion

Immune checkpoint inhibitors (ICIs) are a newer class of targeted chemotherapeutics being used with increasing frequency to treat various malignancies. These monoclonal antibodies target negative regulators of T-cell activation including cytotoxic T-lymphocyte-associated protein-4 (CTLA-4), programmed cell death protein 1 (PD-1), and programmed cell death ligand 1 (PD-L1), leading to T-cell activation and anti-tumor response. This heightened immunologic state is also responsible for cutaneous immune-related adverse events (irAEs), occurring in 30-60% of patients treated with ICIs.[1] They can present as aggravation of a pre-existing dermatosis or as de novo dermatoses, the most common being lichenoid, maculopapular, psoriasiform, eczematous, and immunobullous.[2] Although distressing for both patients and clinicians, the majority of cutaneous irAEs (80-87%) are mild (grade 1 to 2 based on the National Cancer Institute's Common Terminology Criteria for Adverse Events [NCI CTCAE]) and respond well to topical therapies and supportive care.[1,3] For the minority that do require systemic treatment, corticosteroids, methotrexate, mycophenalate mofetil, calcineurin

inhibitors, and tumor necrosis factor inhibitors, have been used successfully despite limited evidence regarding their impact on ICI therapy.[3]

Oncologists often base treatment of cutaneous irAEs on the NCI CTCAE, which grades cutaneous eruptions on a scale of 1-4 (4 being most severe) primarily on the amount of body surface area (BSA) involved.[1,4] While useful, a grading system based on BSA involvement fails to account for the phenotypic differences amongst cutaneous irAEs (eg an eczematous eruption involving 50% BSA is managed differently and is much less worrisome than an SJS-like eruption involving 20% BSA).[1] It also introduces a high degree of subjectivity given the variability in BSA calculations reported between dermatologists and non-dermatologists.[5,6] In addition, these guidelines often recommend discontinuation of ICI therapy for more severe grades despite increasing evidence that supports cutaneous irAEs representing a robust anti-tumor response and being associated with prolonged overall survival.[4] Thus, utilization of these guidelines can lead to premature discontinuation of ICI therapy in patients who would benefit from them the most.

With a critical BSA of 30% in mind, early intervention is paramount to prevent a stepwise progression of rash requiring interruption of immunotherapy by a guideline-compliant oncologist. To accomplish this, our supportive oncodermatology service implemented a clinic workflow that allows oncologists to select same day, urgent one week, and routine appointments for any suspected immunotherapy-associated cutaneous eruption. This case was impactful for our service because it highlighted the need for additional proactive, rather than solely reactive measures. Delayed intervention not only relates to the time it takes to see a dermatologist once a referral is placed by oncology, but also to the time interval between rash onset and first recognition. Earlier identification can be accomplished by leveraging patient participation. With that in mind, both an intake questionnaire detailing past dermatologic history as well as written and recorded patient educational materials stressing the importance of self-examination are now provided by infusion staff during the initial infusion appointment. We hope that a similar initiative to identify high risk patients can be adopted outside of academia by community dermatologists and oncologists.

We present this case of immunotherapy-associated psoriasiform dermatitis not only for clinical interest, but to highlight limitations of current guidelines and the importance of proactive and reactive dermatologist participation in academic and community settings.

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Key locations: Various **CASE 2**

Disseminated Gouty Tophi

Presented by Brigitte Frett Utter MD MPH MSW and David Othman MD MHSA

History of Present Illness

A 40-year-old man with inconsistent access to healthcare initially presented to rheumatology clinic in July 2022 endorsing a five-year history of joint swelling and polyarthralgia affecting the hands, elbows, knees, and feet for which he had been taking doses of naproxen exceeding the daily maximum dose. He was diagnosed with an unspecified inflammatory arthritis. On physical exam in rheumatology clinic, the patient was noted to have multiple raised erythematous rashes and subcutaneous nodules on his elbows, extensor arms, shins, abdomen, and glans penis. He was referred to the dermatology clinic for evaluation.

Past Medical History

Prediabetes, hypovitaminosis D, latent tuberculosis

Medications

Naproxen, vitamin D, rifampin

Social History

Alcohol: 4-5 beers/day

Review of Systems

Negative for systemic symptoms
Positive for skin lesions and polyarthralgias

Physical Exam

Non-skin:	Joint swelling and tenderness of hands, wrists, knees, and feet
Skin:	Clusters of soft yellow papules, in some areas coalescing into plaques on R and L extensor arms, bilateral legs, across the central abdomen, and circumferentially around the glans penis

Laboratory Data

ESR	37 mm/h	[0-20 mm/h]
Uric acid	10.6 mg/dL	[3-7 mg/dL]
Creatinine	0.7 mg/dL	[0.6-1.4 mg/dL]
Quantiferon gold	Positive	[Negative]
Total cholesterol	157 mg/dL	[130-240 mg/dL]
Fasting triglycerides	171 mg/dL	[30-150 mg/dL]

Histopathology

RIGHT EXTENSOR ARM, SHAVE BIOPSY:
Nodular aggregates of acellular, amorphous, pale eosinophilic material surrounded by palisading arrangement of histiocytes and multinucleated giant cells are seen. These findings are consistent with gouty tophi.

Procedures

Arthrocentesis, right olecranon bursa: 0mL of fluid aspirated

Radiology

Ultrasound, right second PIP, left third MCP, and right olecranon bursa: double contour sign of right second and left third MCP suggestive of MSU deposition; multiple tophi in the right olecranon bursa.

Diagnosis

Disseminated gouty tophi

Treatment and Course

The patient was started on prednisone 10mg PO daily and allopurinol 100mg PO daily. Over the next several visits with rheumatology, prednisone was tapered to 5mg daily and allopurinol was increased to 300mg daily. He was also started on colchicine 0.6mg twice daily. On follow up, his uric acid level was noted to have decreased from 10.6 to 8.0 mg/dL with significant improvement in arthritic pain. He continues to follow with the rheumatology service for medical management of gout.

At his initial dermatology appointment, the patient indicated that the most bothersome cutaneous lesions were those on the glans penis as they made foreskin retraction and urination difficult and were greatly impacting his sexual health. The case was discussed with the urology service, and the patient was scheduled for definitive surgical management of the penile lesions. He opted not to pursue surgical excision of existing non-penile lesions due to their extent, as well as risk of scarring and other complications.

Discussion

Gout, also known as monosodium urate crystal deposition disease, is an inflammatory metabolic disease where plasma urate concentrations exceed urate solubility.[4,11] This leads to extracellular fluid urate saturation and results in monosodium urate crystal deposition in a range of body tissues. Commonly affected areas include the joints manifesting as gouty arthritis, the soft tissues leading to tophi, and the urogenital system causing urolithiasis. Gouty nephropathy and panniculitis can also rarely occur.[11]

Gout is estimated to affect about 3% of the US adult population.[4] Serum urate concentrations exceeding 7-8 mg/dL are necessary but not sufficient for the development of gout. Indeed, approximately 2/3 of people with longstanding hyperuricemia do not clinically experience monosodium urate crystal deposition disease.[9] Clinically apparent gout is multifactorial, with uric acid levels playing a role in conjunction with other genetic, nutritional, inflammatory, and medical comorbid factors. Identified risk factors for gout include impaired renal function, obesity, alcohol use, lead exposure, diuretic use, and hypertension. Elevated uric acid levels may be secondary to overproduction, reduced excretion, or both. Diseases in which there is high turnover of nucleic acids, such as psoriasis and lymphoproliferative disorders, are also associated with hyperuricemia.[3,11,12]

In males, adult serum urate levels of 5-6 mg/dL are reached around puberty but in females, serum urate concentrations are lower than in age-matched males due to estrogen-mediated increases in urinary excretion of urate. After menopause, the urate concentrations in females begin to rise to levels comparable to males. These sex differences in urate concentration result in epidemiological differences between males and females in the age of onset of gout: men become affected by the fourth or fifth decades and women by the sixth or seventh decades. There appears to be an average period of asymptomatic hyperuricemia of at least 10 years or more in both males and females prior to clinical manifestations of gout.[4]

Gouty tophi occur when urate crystals precipitate out from supersaturated fluids and deposit into cutaneous structures. The presence of these crystals leads to interleukin-1 production causing inflammation and pyrexia. IL-1 is postulated to play a critical role in both acute and chronic gout by activating both neutrophils and complement. As neutrophils ingest crystals, lysosome rupture is triggered leading to leakage of lysozymes, triggering subsequent cellular and tissue damage.[11]

Gout involves four clinical stages: (i) asymptomatic hyperuricemia, (ii) acute arthritis, (iii) periods between attacks known as intercritical gout, and finally (iv) chronic tophaceous gout.[9] Tophi usually appear 10 or more years after the clinical onset of the disease. Chronic tophaceous gout usually occurs in the subcutaneous tissues overlaying joints, tendons, and cartilage, and manifests as firm pink nodules or swellings. The overlying skin can be yellow, erythematous, or ulcerated, and can drain clear fluid or reveal white flakes of urate. The differential diagnosis includes rheumatoid nodules, xanthomas, and calcinosis cutis. Rarely, gout can present as disseminated cutaneous papules, nodules,

or ulcerations as in our patient's case. In these cases, tophi can involve atypical extra-auricular sites including the trunk, extremities, and genitalia. Risk factors for the development of disseminated gout include renal insufficiency, hypertension, chronic use of diuretic medications, longer duration of gout, and lack of adherence to medical management of gout.[10]

When cutaneous gouty tophi are suspected, a biopsy is recommended for definitive diagnosis. With hematoxylin-eosin preparations, tophi in subcutaneous tissue are made-up of an amorphous, amphophilic material with stellate empty spaces surrounded by giant cells, lymphocytes, and plasma cells. These spaces are areas of dissolved uric acid crystals. If fixed with alcohol and polarized, tophi reveal brightly refractile brown sheaths of needle-like crystals.[11]

Gout is treated acutely with colchicine, NSAIDs, and corticosteroids. Colchicine can be helpful in gout due to its ability to inhibit neutrophil phagocytosis of urate crystals and alter transport of phagocytosed crystals into lysosomes. It can treat both gout flares and reduce recurrent or rebound attacks. Indomethacin and other NSAIDs decrease both local inflammation and pain.[11]

Drugs to lower the uric acid level are generally not initiated until the acute flare has resolved. These include febuxostat, probenecid, and allopurinol. Allopurinol is a xanthine oxidase inhibitor that decreases uric acid production and is indicated in cases of severe tophaceous deposits, such as in our patient's case. Serum urate lowering agents are taken indefinitely. While a target uric acid level of 6 mg/dL is generally recommended, some authors advocate for a target of 5 mg/dL for patients with severe or widespread gout such as our case. A more aggressive target level is intended to aid in crystal dissolution and prevention of additional flares and deposition.[9] Tophi may dissolve 6-12 months after the uric acid level normalizes though extended courses of 2-3 years are often needed for clearance in patients with miliarial gout. Surgery is rarely indicated, though in the case of our patient, given the location of the tophi on the glans penis and their interference with his activities of daily living, acute intervention is warranted.[3,4] We present this case of disseminated gout as a rare presentation of monosodium urate crystal deposition disease highlighting medical and surgical management needs.

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Key location(s): Shoulders and Upper Back **CASE 3**

Intravascular Large B-Cell Lymphoma

Presented by Kumar Nadhan MD, Vesna Petronic-Rosic MD MSc MBA and Shiraz Fidai MD

History of Present Illness

A 57-year-old man presented with an asymptomatic truncal rash that began one month prior and was spreading. Associated symptoms included fevers, chills, and unspecified, unintentional weight loss over the past four years. The patient did not try any treatments prior to presentation.

Past Medical History

None

Medications

None

Social History

None

Review of Systems

Negative for headaches, vision changes, shortness of breath, nausea, vomiting, diarrhea
Positive for fever, chills, weight loss, fatigue, chronic hyperhidrosis, right-sided chest pain, left upper quadrant abdominal pain, anorexia

Physical Exam

Non-skin:	Splenomegaly. No hepatomegaly. No cervical, supraclavicular, axillary or inguinal lymphadenopathy present
Skin:	Anterior shoulders and central back with finely reticulated non-blanching purpura

Laboratory Data

Uric Acid	7.7 mg/dL	3.0-7.0 mg/dL
Total Bilirubin	1.1 mg/dL	0.2-1.2 mg/dL
Direct Bilirubin	0.4 mg/dL	0.0-0.2 mg/dL
Alkaline Phosphatase	481 U/L	20-120 U/L
GGT	640 U/L	3-60 U/L
AST	170 U/L	0-40 U/L
ALT	29 U/L	5-35 U/L
LDH	1,714 U/L	85-201 U/L
WBC	13.4 k/uL	4.4-10.6 k/uL
HGB	9.2 g/dL	12.8-16.8 g/dL
MCV	78.5 fL	82-98 fL
Neutrophil	44%	45-75%
Bands	20%	0-9%
Lymphocyte	14%	18-43%
Atypical Lymphocyte	11%	0%
Metamyelocyte	3%	0%
Myelocyte	1%	0%
Monocyte	7%	4-11%
Basophil	1.0%	0.2-1.0%
Syphilis Screen	Non-reactive	Non-reactive

Reflexive flow cytometry:
16% circulating mature large B-cells with pleomorphic/blastoid features. Cell populations showed lymphocytes: 94%, dim CD45/blasts: 2%, monocytes: 2%, and granulocytes: 1%. Further analysis showed that T-cells expressed all pan-T-cell antigens tested (CD2, CD3, CD5 and CD7) with a CD4/CD8 ratio of 4:1. There was no increase in NK cells and G/D T-cells. The B-cells were few and polyclonal.

Bone marrow core biopsy, left posterior iliac crest:
Hypercellular bone marrow (80-90% cellularity; 47% lymphoma cells) composed of intrasinusoidal and interstitial nodular lymphoma involvement with background hematopoiesis. Markedly increased marrow iron; sideroblastic iron present and no ringed sideroblasts identified. Diffuse 1+ marrow reticulin fibrosis.

Peripheral smear:
26% abnormal blastoid pleomorphic cells with irregular nuclear membranes, open chromatin with prominent (often multiple) nucleoli, high nuclear to cytoplasmic ratio and modest agranular deeply basophilic cytoplasm. 100 cell differential shows 51% segmented neutrophils, 9% lymphocytes, 14% monocytes and 26% lymphoma cells. There are many smudge cells.

Histopathology
RIGHT ANTERIOR SHOULDER, PUNCH BIOPSY:
There is a malignant large cell lymphoid infiltrate involving small and medium sized vessels (luminal and full-thickness vessel wall involvement). Immunohistochemistry (CD3, CD20, PAX5, and CD34) highlights CD20/PAX5 positive large lymphoma cells and CD34 positive endothelial cells. CD3 highlights background T cells.

Radiology
CT, chest: No acute cardiopulmonary process. No lymphadenopathy.
MRI with/without contrast, abdomen: Small bilateral pleural effusions. Trace upper abdominal ascites. Severe splenomegaly with geographic and wedge-shaped areas of nonenhancement, most suggestive of splenic infarcts. No hepatomegaly, biliary ductal dilatation, or choledocholithiasis. No lymphadenopathy.

Diagnosis
Intravascular Large B-cell Lymphoma (IVLBCL)

Treatment and Course
The patient was treated with R-CHOP: rituximab, cyclophosphamide, doxorubicin hydrochloride, vincristine sulfate, and prednisone. He was recently seen at his two month follow up and has completed three cycles of chemotherapy with full resolution of his skin lesions and significant improvement of B-symptoms.

Discussion
Intravascular large B-cell lymphoma (IVLBCL) is a rare and aggressive type of non-Hodgkin lymphoma that affects both cutaneous and systemic vasculature. IVLBCL is characterized by the proliferation of malignant B lymphocytes within small and medium-sized blood vessels, leading to obstruction of blood flow and end-organ damage. IVLBCL typically affects older adults (median age at diagnosis: 60-70) and is often diagnosed in advanced stages due to its nonspecific presentation, earning the nickname, "The Oncologist's Great Imitator."[10]

Although highly variable, the clinical presentation of IVLBCL includes B-symptoms (up to 75% of patients), cutaneous (40%) and neurologic (30%) findings.[1,4] Interestingly, lymphadenopathy and hepatosplenomegaly are not common clinical features as is seen in other hematopoietic malignancies. Cutaneous eruptions, when present, include painful indurated violaceous plaques, ulcerated nodules, red papules, and/or 'peau d'orange' lesions.[3] Lesions are classically found on the trunk and

extremities. Our patient presented with reticulated, nonblanching purpura on the trunk, which correlates with an obstruction in blood flow.

IVLBCL can be further subclassified into three variants – two systemic and one cutaneous. The two systemic variants are (1) a classic form characterized by symptoms relating to the main organ involved i.e. CNS, and (2) a hemophagocytic variant heralded by multiorgan failure, hepatosplenomegaly, and pancytopenia.[7,9] The classic form predominates in Western countries while the latter has been described in reports from Asia. Finally, there is a (3) primary cutaneous variant which has histologic features of IVLBCL but is limited to skin-only. The primary cutaneous form represents up to 25% of IVLBCL cases within Western countries (only 3% in Asian countries) and is associated with a favorable prognosis.[6]

The diagnosis of IVLBCL is largely made on bone marrow as peripheral blood smears and complete blood count are often non-specific. In up to two-thirds of cases, bone marrow biopsy is insufficient, at which point skin biopsy will play a supportive role in the diagnosis. Histopathology reveals lymphoma cells within vessels, which stain with CD20 and PAX5 markers. A deep biopsy is crucial for obtaining an adequate sample as the median depth to tumor cells is 3.64mm from the top of the epidermis. Most experts advocate for three punch biopsies down to subcutaneous fat from sites such as the thighs and the abdomen to increase diagnostic yield.[5]

Treatment options for IVLBCL include chemotherapy, radiation therapy, or a combination of both. High-dose chemotherapy with autologous stem cell transplantation is often used in advanced cases. The prognosis of IVLBCL is poor, and median survival time is 6-12 months.[8] Multiorgan failure can develop rapidly and is a frequent cause of death. Early diagnosis and prompt treatment administration are crucial in improving outcomes for patients. However, even with treatment, the disease can recur. The most common site is the CNS and occurs in up to 25% of patients within the first three years post-diagnosis.[2]

We present this rare entity to highlight the importance of considering IVLBCL in the differential diagnosis for patients with non-specific B-symptoms and cutaneous findings suggestive of vessel obstruction.

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Key location(s): Left lower leg **CASE 4**

Pretibial Mucinosis in a Euthyroid Patient

Presented by Elena Gonzalez MD, Vesna Petronic-Rosic MD MSc MBA and Shilpa Mehta MD

History of Present Illness

A 62-year-old woman presented with pain and swelling of the left leg for one week. The patient was previously evaluated in the dermatology clinic, and a clinical diagnosis of elephantiasis nostras verrucosa (ENV) was made. At the time, leg elevation and compression were recommended, after which the patient was lost to follow up.

Past Medical History

Morbid obesity (BMI 35), diabetes, hypertension, stroke

Medications

Glipizide, nifedipine, atorvastatin, aspirin

Review of Systems

Negative for fever, fatigue, changes in bowel habits, abdominal or chest pain, weight change, difficulty concentrating, anxiety, or hyperhidrosis

Physical Exam

Non-skin:	No palpable inguinal lymphadenopathy
Skin:	Left lower leg with numerous skin-colored firm nodules confluent into a large plaque that involves the entire anterior aspect of the leg. Right lower leg with diffuse induration and hyperpigmentation

Laboratory Data

WBC	8.6 k/uL	[4.4-10.6 k/uL]
Hb	13.3 g/dL	[11.7-14.9g/dL]
Plt	360 k/uL	[161-369 g/uL]
TSH	1.044 uIU/mL	[0.34-5.6 uIU/mL]
T4 free	0.89 ng/dL	[0.61-1.64 ng/dL]
Serum electrophoresis	Polyclonal immunoglobulins	
Serum immunofixation	No M protein	

Histopathology

LEFT ANTERIOR LEG, SHAVE BIOPSY:
There is an atrophic epidermis with effacement of the rete ridges. Angioplasia with vertically oriented vessels and horizontal fibrosis is present. There is significant dermal edema with basophilic threads and granular material separating the collagen bundles. Colloidal iron shows increased mucin deposition extending from the papillary to the reticular dermis.

Microbiology

Blood culture: no growth of bacteria.

Radiology

Xray, tibia and fibula: Marked soft tissue thickening and no bony abnormalities.

Venous duplex ultrasound, lower extremities: Negative for deep vein thrombosis.

Diagnosis

Pretibial mucinosis in a euthyroid patient, complicated by cellulitis.

Treatment and Course

The patient was treated with a short course of antibiotics resulting in resolution of the cellulitis. She was referred to a lifestyle center for weight loss. Compression and leg elevation were recommended for management of the chronic skin changes. Detailed vascular studies to assess the degree of venous insufficiency and to explain the asymmetry were planned. However, she was lost to follow up from our clinic after multiple hospital admissions for her underlying medical conditions.

Discussion

Cutaneous mucinoses are a diverse group of conditions characterized by the deposition of glycosaminoglycans (mucin) in the dermis and adnexal structures. This deposition can be localized or generalized. The diseases can be divided into two groups: primary cutaneous mucinoses, in which mucin deposition is the main histological feature, and secondary mucinosis, which refers to those conditions in which mucin can be an additional histologic finding.[1]

Classically, accumulation of mucin on the shins is associated with pretibial myxedema and prompts thyroid function testing. However, in a small percentage of patients with pretibial mucinosis, thyroid dysfunction is not identified.[2] Pretibial mucinosis in euthyroid patients has been described in states of venous insufficiency and obesity.[2–4] The terms pretibial stasis mucinosis and obesity-associated lymphedematous mucinosis (OALM) have been introduced to describe such patients. It has been postulated that the hypoxia induced by chronic venous insufficiency and/or obesity-associated lymphedema induces angiogenesis and plasma protein extravasation, eventuating in increased production and deposition of mucopolysaccharides.[5] However, Moshin *et al* reported a case of pretibial mucinosis without any apparent cause, suggesting there may be other, not yet identified, causes.[6]

Pretibial mucinosis typically presents with skin-colored to yellow-red, semi-translucent papules, plaques, and/or nodules. It is often bilateral but can present asymmetrically with involvement of one extremity, as seen in our patient. Key differential diagnoses include pretibial myxedema and elephantiasis nostras verrucosa (ENV). It is important to note that in most cases of pretibial myxedema, thyroid disease precedes the development of cutaneous findings. Additionally, most patients with Graves' disease and pretibial myxedema will have orbitopathy.[7,8] Lack of known thyroid dysfunction and orbitopathy on presentation should raise suspicion for another disease entity. ENV may be distinguished clinically from pretibial mucinosis by its predilection to develop on the dorsa of the feet and extend proximally over time.

The histopathologic findings of pretibial mucinosis are distinct from classical pretibial myxedema and assist in confirming the diagnosis. Important clues include epidermal atrophy, angioplasia with vertically-oriented capillaries in the mid to upper dermis, increased stellate fibroblasts, and hemosiderin deposition.[8] These features are not observed in pretibial myxedema, which typically has an acanthotic epidermis and lacks angioplasia, fibrosis, and hemosiderin deposition. ENV is easily distinguished on histopathology by the absence of mucin deposition.

Treatment options for pretibial mucinoses are limited and entail weight loss and modalities that improve lymphatic and venous blood flow, such as compression stockings or pneumatic compression. Second- and third-line therapeutic options include topical steroids or intralesional steroids, pentoxifylline, octreotide, plasmapheresis, and intravenous immunoglobulins. More recently, Castineiras *et al* reported the successful use of fractional CO2 laser in a patient with nodular pretibial mucinosis.[9]

Our patient had an atypical presentation, as pretibial mucinosis was isolated to one leg. Thyroid studies were unrevealing, and evaluation for plasma cell dyscrasia was negative. We concluded that she developed pretibial mucinosis due to a combination of obesity and venous stasis. The absence of thyroid disease and histological findings can differentiate between the two conditions. We present this

case to raise awareness of pretibial mucinosis in euthyroid patients. Given the prevalence of obesity and venous insufficiency, we believe this entity may be underdiagnosed.

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Key location(s): Left Lower Extremity **CASE 5**

A 20-Year History of Leg Ulceration: Cutaneous Blastomycosis and Candida Albicans

Presented by Hiren Kolli MD, Vera Tesic MD, MS and Vesna Petronic-Rosic MD, MSc, MBA

History of Present Illness

A 58-year-old man with a twenty-year history of a non-healing ulcer on his left lower leg presented for further evaluation and management. He initially visited the vascular clinic in 2017 with a 16-year history of non-healing leg ulcers. At the time, the patient denied any pain and endorsed a history of leg swelling and varicose veins. Their physical exam was notable for ulcers on the left medial shin and malleolus with normal pulses. Venous duplex ultrasound in 2017 revealed reflux throughout the left great saphenous vein. He was diagnosed with venous insufficiency and given wound care instructions, but then lost to follow up. The patient returned to the vascular clinic in 2022 with a single large ulcer and was referred to the dermatology service for further evaluation.

Past Medical History

Deep venous thrombosis, hepatitis B, varicose veins

Medications

Amlodipine, tenofovir, aspirin

Social History

Tobacco (pack/day): 0.1 pack/day

Review of Systems

Negative for fevers, chills, dyspnea, productive cough, myalgia, arthralgia, pleuritic chest pain
Positive for focal pain, pruritus

Physical Exam

Skin: The left lower extremity had a draining 8 x 7 cm ulcer with yellow fibrinous exudate at the base, heaped up erythematous to violaceous border, and focal keratotic scale-crust. The surrounding skin of the lower leg had erythema, hypopigmented macules, a lack of hair and induration up to level of knee.

Laboratory Data

Hepatitis B Surface Antigen	Reactive	[Negative]
Hepatitis Be Antigen	Reactive	[Negative]
Hepatitis B Core Total Antibody	Reactive	[Negative]
Hepatitis A IgG	Reactive	[Negative]
Blastomyces Antigen	0.36	[Not Detected]

Histopathology

LEFT DISTAL ANTERIOR LEG, PUNCH BIOPSY:
Sections are of skin with hyperplasia of the epidermis. The underlying dermis has pronounced neovascularization and a dense diffuse mixed inflammatory cell infiltrate with lymphocytes, histiocytes, plasma cells, neutrophils, eosinophils, and extensive hemorrhage. The PAS and GMS stains highlight numerous hyphae within the stratum corneum as well as broad budding large yeast deep in the dermis. The AFB and Gram stains are negative for microorganisms. Tissue culture is recommended for definitive diagnosis.

Microbiology

Fungal Culture: Candida albicans, 4+ growth, Blastomyces dermitiditis, 2+ growth

Radiology
Xray, chest: Lung volumes are within normal limits. Lung fields bilaterally are clear. No focal airspace consolidations, no pulmonary masses or nodules are demonstrated.

Venous duplex ultrasound, left lower extremity: In the left great saphenous vein, there is abnormal venous reflux seen throughout the thigh and leg and at the saphenofemoral junction. The vein measures between 8.2 and 9 mm in the thigh. This vein measures 9.2 mm in the leg. A large tributary branch is noted at the level of the calf measuring 7.8 mm.

Diagnosis
Ulcerative primary cutaneous blastomycosis

Treatment and Course
The patient was treated with a loading dose of itraconazole 200mg PO TID for 3 days and then instructed to take 200mg PO BID for the following 6-12 months. Considerable improvement with near healing of the ulcer as well as resolution of symptoms was observed after 3 months of therapy.

Discussion
In North America, blastomycosis is primarily found in the regions near the Great Lakes and the St. Lawrence, Ohio and Mississippi River valleys with cases having been described in other parts of the world including South America, Africa and India. Infection has been associated with outdoor occupations or recreational activities, given that the thermally dimorphic fungus *B. dermatitidis* typically resides in decaying wood and soil. Most infections start with primary pulmonary involvement through inhalation of spores. It has been widely accepted that cases of cutaneous blastomycosis most commonly occur after lymphohematogenous spread from a primary pulmonary infection, even in the absence of overt pulmonary disease. Primary cutaneous blastomycosis, which is caused by direct, traumatic inoculation of the organism, is fairly rare, but has been reported as a result of laboratory or autopsy exposure, animal bites or scratches, infection of open wounds, and outdoor trauma.[5,6]

The skin manifestations of cutaneous blastomycosis can range from papulopustular and nodular lesions to verrucous and ulcerative lesions. The ulcerative form, which is less common, begins as erythematous nodules or pustules which ulcerate in an asymmetric, spreading pattern. This form may be associated with miliary abscesses in the ulcer periphery which ultimately communicate with the ulcer via sinuses.[7] Cutaneous inoculation blastomycosis has been described as a chancre at the trauma site. A review of published inoculation cases established that physical examination of lesions cannot differentiate cutaneous inoculation blastomycosis from secondary cutaneous blastomycosis.[3] It can be associated with lymphangitis and lymphadenitis, which are typically absent in cases of secondary cutaneous blastomycosis. In a review of inoculation blastomycosis cases, only two patients were documented as having ulcerated lesions.[1]

We report a case of cutaneous blastomycosis that was initially misdiagnosed as a venous stasis ulcer. Our patient originally presented to the vascular clinic in 2017 with a 16-year history of non-healing ulcers on the left lower extremity. At that time, the patient denied any pain and endorsed a history of leg swelling and varicose veins. Their physical exam revealed a 3 x 3.5 cm ulcer on the medial shin, a 1 x 1.5 cm ulcer on the medial malleolus, excoriated and thickened skin changes from the foot to the mid-calf with normal pulses. Venous duplex ultrasound in 2017 was notable for reflux throughout the left great saphenous vein. The clinical features and diagnostic exams led the providers to a diagnosis of venous insufficiency, but the patient was lost to follow up after being given wound care instructions. The patient returned to the vascular clinic in 2022 with a singular, large 8 x 4 cm ulcer and was referred to the dermatology service for further evaluation.

Tissue culture demonstrated a concurrent infection with *C. albicans*, a fungus that affects all ages with the most frequent presentations being intertrigo, cheilitis, diaper dermatitis, and interdigital candidiasis. In the commensal, noninvasive state, *C. albicans* exists in the yeast form on the tissue

surface and it is the hyphal form, which was present in this case, that penetrates epithelia and endothelia, causing tissue damage and allowing access to the bloodstream.[4] The question was raised whether the hyphal forms could have belonged to B. *dermatitidis*, however this species only exists in this form at 22-25^{0}C.[6] This yeast infection may be explained in part by long wrapping of the wound and the application of antibiotics during treatment but may also have led to the atypical clinical presentation and the primary complaint of pruritus. Furthermore, we found one case report of a nonhealing ulceration on the left leg of twenty-five years duration that was given the preliminary diagnosis of pyoderma gangrenosum (PG) and determined to be cutaneous blastomycosis.[2] On histopathological examination, PG usually shows ulceration, pseudoepitheliomatous hyperplasia, and neutrophil rich dermal inflammatory infiltration, which can also be seen in cutaneous blastomycosis. This demonstrates that skin involvement in cutaneous blastomycosis has a wide variety of manifestations, making clinical diagnosis challenging. Thus, we report this case as a unique presentation of cutaneous blastomycosis as well as a reminder to be vigilant when examining ulcers, and that biopsies should be done for recalcitrant ulcerations.

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Key location(s): Groin, left forearm **CASE 6**

Vagisil Dermatitis

Presented by Lindsay Sklover MD and Vesna Petronic-Rosic MD, MSc, MBA

History of Present Illness

A 68-year-old woman with a 2-year history of gluteal and genital papules and plaques was admitted for acute worsening of her disease. She had shallow ulcers and lakes of pus in the genital region as well as a new-onset rash of the left forearm. The patient was treating her symptoms with over-the-counter anti-itch creams, Vagisil Maximum Strength Anti-Itch Creme and Vagicaine, with recently increased usage due to progression of her symptoms.

Past Medical History

Psoriasis vulgaris, alpha-1-antitrypsin deficiency, hypertension, hypothyroidism

Medications

Acyclovir, albuterol, alendronate, hydrochorothiazide, levothyroxine, lovastatin, mirabegon, paroxetine, verapamil

Allergies

Latex

Review of Systems

Negative for fevers, chills, diarrhea, constipation, or hematuria
Positive for pruritus

Physical Exam

Skin: Left forearm and wrist with lichenified, fissured pink plaques, and overlying scale-crust
Mons pubis and buttocks with numerous irregularly shaped ulcers, copious thick yellow-green discharge, and a rim of erythema
Glutes and posterior and lateral thighs with hyperpigmentation, lichenified plaques, and numerous ulcers. Perianal sparing was noted
Foley catheter in place

Laboratory Data

WBC	14.4 x 10^3 cells/μL	[4.4-10.6 x 10^3 cells/μL]
Urinalysis	Cloudy	[Clear]
Hemoglobin	8.6 g/dL	[11.7-14.9 g/dL]
Neutrophil %	76.5%	[45.5-74.5%]

Histopathology

N/A

Microbiology

Urine culture: +*Escherichia coli*, >100,000 cfu/ml
Wound culture: +1 *Staphylococcus aureus*
HSV1/HSV2/VZV PCR DNA: Not detected

Radiology

N/A

Diagnosis

Ulcerative allergic contact dermatitis

Treatment and Course

Vagisil Maximum Strength Anti-Itch Creme and Vagicaine were immediately stopped, and the affected areas were thoroughly cleansed. The ulcers were covered with petroleum jelly, non-adherent gauze, and paper tape. By hospital day three, the ulcers were significantly improved, and drainage had resolved. The patient was discharged on topical triamcinolone 0.025% cream twice daily.

Discussion

Allergic contact dermatitis (ACD) is one of the most common diseases worldwide, encompassing about 20% of all causes of contact dermatitis. Significant overlap exists with irritant contact dermatitis, contact urticaria, and endogenous forms of eczema which can complicate establishing an accurate diagnosis. Common allergens include nickel, chromium, cobalt, fragrances, rubber, plastics, preservatives, dyes, neomycin, benzocaine, sulfonamides, quinidine, wool wax, Balsam of Peru, eye therapeutics, light filter substances, disinfectants, pesticides, technical oils, and plants. Many new culprits are being discovered as formulations and ingredients continue to change.[5] ACD presents as a delayed-type hypersensitivity reaction. In the initial phase, the patient is exposed to a chemical that penetrates the skin, leading to a cascade of events that results in the creation of primed T-cells. Upon re-exposure to the offending chemical, the primed T-cells are activated and promote the release of multiple cytokine and chemokine factors resulting in an eczematous reaction.

Vagisil Maximum Strength Anti-Itch Creme (CVS Equate Vagicaine) is a topical antipruritic specifically designed for the vulvovaginal area.[4] Directions on the package insert recommend using a cap-size amount three to four times daily and not exceeding greater than seven days of use. The two main active ingredients are 20% benzocaine and 3% resorcinol. Resorcinol is a superficial peeling agent with limited depth to the papillary dermis. It is found in many antiseptics and disinfectants and known to cause irritant contact dermatitis.[2] Benzocaine, an ester local anesthetic, is commonly found in many over-the-counter products, including sunburn remedies, throat sprays, poison ivy treatments, and dental preparations. Ester anesthetics are known to cause ACD more frequently than amides as esters are broken down into metabolites of para-aminobenzoic acid (PABA) by pseudocholinesterase in the blood.[3] Due to their similar structure, these compounds can cross-react with various other compounds, including p-phenylenediamine (PPD), methylparaben, N-iso-propyl-N′-phenyl-p-phenylenediamine (IPPD), p-aminosalicylic acid, and azo-aniline dyes. Patients with benzocaine allergies are advised to avoid PABA and PABA-based sunscreens, meta-aminobenzoic acid, or benzoic acid local anesthetics (both topical and injectable forms), PPD (which can be found in permanent hair dyes), sulfonamides, sulfonylureas, and thiazide-related diuretics. Patients with benzocaine allergies frequently test negative on patch testing.

The eczematous, lichenified left forearm of our patient was the underpinning physical finding that enabled us to diagnose an ulcerative allergic contact dermatitis.[2] The patient stated she was applying the topical vaginal anti-itch cream multiple times daily to her buttocks in a posterior-to-anterior motion with her left hand, with residual cream extending onto her forearm. She washed her hands after each use but did not wash beyond the wrist area.

The forearm illustrated the commonly observed clinical features of ACD, *i.e.,* a well-demarcated excoriated erythematous, crusted plaque. The gluteal region exhibited numerous pink papules and plaques with ulceration. We postulated the ulcers were secondary to the use of a peeling agent in combination with the acute inflammatory reaction of ACD, which was further worsened by occlusion with the diapers and undergarments she was wearing. The pain, pruritus, and burning from the lesions encouraged the patient to continue using the medication, which was in turn making the dermatitis worse. After the patient stopped both the Vagisil and Vagicaine topical creams, she began to heal rapidly, with re-epithelialization of the ulcers and almost complete resolution of the erythema within three days.

Few case reports exist discussing the implication of topical vaginal anti-itch creams in allergic contact dermatitis. One case report cites a 14-year-old transgender male who was found to have chronic vulvar inflammation and labial enlargement, as well as benzocaine-induced methemoglobinemia,

secondary to large quantities of topical vaginal anti-itch cream.[1] Both our patient and the patient described in this case report were using the medication for far longer than the recommended seven days and had rapid resolution of their lesions once the cream was stopped. Our patient was also anemic on admission, with a hemoglobin of 8.6 g/dL, which potentially may have been secondary to methemoglobinemia from repeated application of benzocaine-containing cream. Unfortunately, due to lack of follow up in the dermatology clinic, we do not know if the anemia resolved with cessation of the topical creams.

The clinical presentation of ACD is highly variable, and we report this case to illustrate the risk of ulcerative ACD from a commonly used over-the-counter medication.

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Key location(s): Trunk and limbs **CASE 7**

Corymbiform Syphilis

Presented by Subuhi Kaul MD and Shilpa Mehta MD

History of Present Illness

A 42-year-old man with a 6-month history of an itchy, painful rash presented to the dermatology clinic for evaluation. The rash began on his abdomen and later spread to his extremities. The individual lesions started as small red spots which then transformed into purple flat lesions and ulcers. Within the past one week, he developed painful lumps on the left forearm. Additionally, he complained of a self-resolving asymptomatic penile lesion prior to the onset of the current rash. He reported unprotected sexual intercourse with one female partner in the preceding year.

Past Medical History

Tuberculosis (2005, treated), latent syphilis (2014, treated), trichomoniasis (2018, treated)

Medications

None

Review of Systems

Negative for fever, weight loss, swelling in axillae or groin, headache, ocular complaints, myalgia
Positive for a history of dry cough, rhinorrhea, and nasal congestion for the past 5 months

Physical Exam

Non Skin:	Congested nasal mucosae with obscured nasal cavity Examination of the palms, soles and other mucosae was unremarkable Discrete non tender left axillary and bilateral inguinal lymphadenopathy
Skin:	Several violaceous ovoid patches, depressed plaques, and a few crusted ulcers, surrounded by multiple discrete pink scaly papules coalescing into plaques, on the trunk, left lateral neck, arms, and legs. Some papules appeared edematous. Multiple discrete 5mm skin-colored nodules present on the left volar forearm and dorsal hand. Tenderness was appreciated in some lesions

Laboratory Data

Syphilis Enzyme Immunoassay (EIA)	Reactive	[Non-reactive]
Rapid Plasma Reagin (RPR)	1:64	[Non-reactive]
HIV 1 and 2 screen	Non-reactive	[Non-reactive]
Hepatitis B surface antigen	Non-reactive	[Non-reactive]
Hepatitis C antibody	Non-reactive	[Non-reactive]
Antinuclear antibody	Negative	[Negative]
Myeloperoxidase (MPO)	<0.02	[0-0.9]
Proteinase 3 (PR3)	<0.02	[0-0.9]

Histopathology

LEFT LATERAL TRUNK, PUNCH BIOPSY:
Left lateral trunk: The epidermis has vacuolization of the basal layer and exocytosis of lymphocytes. There is a band-like as well as superficial and deep perivascular and periadnexal mixed inflammatory cell infiltrate with histiocytes, multinucleate giant cells (with elastophagocytosis), lymphocytes, neutrophils, and eosinophils. Poorly formed granulomas are present. The infiltrate also extends interstitially all the way to the subcutaneous fat. Even though blood vessels and adnexal structures are surrounded by these dense infiltrates, there is no evidence of vasculitis. AFB, GMS, PAS, and Gram stains are negative for microorganisms. Immunohistochemical staining for *Treponema pallidum* is positive. Therefore, the diagnosis is granulomatous dermatitis due to syphilis.

LEFT VOLAR FOREARM, PUNCH BIOPSY:

The epidermis has vacuolization of the basal layer and exocytosis of lymphocytes. The papillary dermis is slightly edematous and there is hemorrhage right underneath the dermal epidermal junction. There is a superficial and deep perivascular and periadnexal mixed inflammatory cell infiltrate with histiocytes, multinucleate giant cells, lymphocytes, neutrophils, and eosinophils. Loosely formed granulomas are present. The infiltrate also extends interstitially all the way to the subcutaneous fat. Blood vessels appear obliterated by the dense infiltrate in the deep dermis and subcutaneous fat. There are small foci of necrosis and fibrinoid degeneration with neutrophils and nuclear dusting without vascular participation. A large blood vessel at the base of the specimen is unaffected. The AFB, GMS, PAS, and Gram stains are negative for microorganisms. Immunohistochemical staining for *Treponema pallidum* is positive. Therefore, the final diagnosis is granulomatous vasculitis due to syphilis.

Microbiology
N/A

Radiology
N/A

Diagnosis
Secondary syphilis with corymbiform configuration

Treatment and Course
The patient received two intramuscular injections of 2.4 million units of benzathine penicillin at 1-week intervals. After the first dose of penicillin, lymphadenopathy resolved, all lesions flattened, and upper respiratory symptoms improved. Per the patient, his partner received treatment as well. However, he was lost to follow-up after the 2nd injection.

Discussion
Secondary syphilis, a sexually transmitted infection caused by the spirochete Treponema pallidum, can present with myriad morphologies, and is thus considered "the great imitator". The various presentations include macular, papular, nodular, pustular, psoriasiform, lichenoid, frambesiform, leukoderma, lues maligna, clavi syphillitici, and acral pebbles.[1] The lesions are most often asymptomatic but can be itchy in up to 41% of the patients[1,2] A rare pattern known as corymbiform or corymbose is a distinctive configuration of secondary syphilis.[3]

The word *Korymbos* is of Greek origin and is used in botany for a clustered appearance of multiple flowers arising from a single main pedicle. In dermatology, the terms corymbiform or corymbose refer to a large central lesion surrounded by multiple smaller satellite lesions akin to an explosion.[4] This pattern is thought to be highly specific for a form of secondary syphilis that represents a late manifestation, reinfection or relapse.[5] Other morphologically and pathologically distinct cutaneous conditions that may demonstrate a similar configuration are nodular amyloidosis, collagenoma, melanoma with satellitosis, linear IgA disease, IgA pemphigus, and Sweet syndrome and can be considered in the differential diagnosis in the appropriate clinical context.[4,6,7] Additionally, patients may have lesions with different morphologies as in lues maligna, where lesions representative of various stages are concurrently present.[8]

The histopathology of corymbiform syphilis can vary widely; it can present as a dense dermal plasma cell infiltrate, a diffuse CD8+ atypical lymphocytic dermal infiltrate with sparse plasma cells, or a chronic granulomatous dermatitis. In addition, histopathology can vary depending on the lesion biopsied.[3,5,9] This explains the histology from the papule in our patient, which demonstrated a mixed infiltrate and poorly formed granulomas without vasculitis, whereas the nodular lesion showed the presence of granulomatous vasculitis.

The treatment of secondary syphilis with a corymbiform clinical presentation is a single dose of intramuscular benzathine penicillin. A response to therapy is determined by a four-fold decrease in

Rapid Plasma Reagin (RPR) or Venereal Disease Research Laboratory (VDRL) titers within 6 to 12 months of appropriate therapy.[10]

We present this case as a rare manifestation of secondary syphilis. As in all cases of secondary syphilis, lesions may spontaneously resolve and progress to late-stage syphilis, which is associated with life-threatening complications. Keeping in mind the recent rise in the number of syphilis cases nationally, prompt identification and treatment by dermatologists and other physicians is essential to prevent such complications.

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