Chicago Dermatological Society

PROTOCOL BOOK
October 12, 2022

Co-hosted by University of Illinois at Chicago Department of Dermatology

Guest Speaker: Faramarz H. Samie, MD, PhD

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Director Micrographic Surgery and Dermatologic Oncology Fellowship
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Program

Co-hosted by University of Chicago
Wednesday, October 12, 2022
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 Session**
"Update on Management of Cutaneous Squamous Cell Carcinoma"
Faramarz H. Samie, 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. - 1:15 p.m. **Box Lunches & visit with exhibitors**

1:15 p.m. - 2:15 p.m. **CDS Business Meeting**

Program adjourns

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Case Presented by Victoria Kuritza, MD
Maria M. Tsoukas, MD PhD and Wenhua Liu, MD

History of Present Illness:
A 38-year-old female presented to clinic with a several-year history of slowly enlarging nodules on her scalp and left leg. These nodules were occasionally tender and red but otherwise not bothersome. The patient recalled having similar nodules on her left knee surgically removed and thought they contained "calcium deposits" but could not remember further details. She also noted the leg nodules were present overlying a rash on her left leg present since birth.

Past Medical History:
Unremarkable

Medications:
Levonorgestrel (Mirena) IUD

Allergies:
No known drug allergies

Social History:
Social alcohol use, no history of tobacco or drug use

Review of Systems:
On review of systems, she denied fevers, chills, headaches, joint pains, or muscle aches.

Physical Examination:
There were 2 flesh colored 5cm soft nontender mobile nodules on the bilateral parietal scalp. Involving the left posterior upper and lower leg was a linear thin scaly confluent plaque in a blaschkoid distribution along with scattered erythematous firm nodules and hyperkeratotic papules.

Histopathology:
Proximal left leg, skin: Filiform hyperkeratosis. Sections of skin show compact orthokeratosis, mild papillomatosis, and epidermal hyperplasia. In one area, there is a hyperparakeratotic plug in a dilated follicle, which shows trichilemmal differentiation. There is a mild superficial perivascular lymphocytic infiltrate.
Distal left leg, skin: Trichilemmal cyst (pilar cyst). Sections show a squamous-lined cyst with abrupt trichilemmal type keratinization. A granular cell layer is not seen within the cyst lining.

Diagnosis:
Nevus Trichilemmocysticus

Treatment and Course:
The patient underwent excision of 2 leg nodules. She was lost to follow-up due to a change in insurance.

Discussion:
Nevus trichilemmocysticus (NTC) falls within the larger spectrum of epidermal nevi, which are cutaneous hamartomas typically present at birth or in early childhood. They are characterized by

keratinocytic or epidermal appendage cell hyperplasia. Epidermal nevi often initially present as a linear tan patch or thin plaque, though there can be exceptions. They can be isolated or part of a syndrome, with neurological and musculoskeletal symptoms being common systemic findings. Epidermal nevi are a rapidly evolving research area, and new research highlights the complexities impeding the simple “genotype to phenotype” correlation.

In general, pathogenesis of epidermal nevi is known to occur through genetic mutations and epigenetic transformation. Mutations are seen in multiple pathways, especially those involved in cell proliferation and differentiation. Ultimately, cell expression during post-zygotic embryologic development in utero occurs, leading to 2+ genetically different cell populations at birth, known as mosaicism. Typically, earlier timing of post-zygotic mutations leads to more extensive cutaneous or extracutaneous involvement.

Epidermal nevi are historically classified based on the predominant components of the hamartoma. Divisions include organoid, with predominantly adnexal components, and non-organoid or keratinocytic, with predominantly epidermal components. Examples of organoid nevi include nevus sebaceus, nevus comedonicus, and NTC. Examples of keratinocytic nevi include verrucous or classic epidermal nevi and linear porokeratosis, among others.

NTC is a type of organoid nevus first named in 2007, though there are potential earlier reports. Classically, there is extensive skin involvement in a blaschkoid distribution with multiple verrucous papules and plaques with overlying spiny projections, along with nodulocystic and comedo-like lesions. Classic histologic findings of the hyperkeratotic lesions include epidermal acanthosis, deep invaginations with orthokeratosis and parakeratotic columns, an absent granular layer, and keratosis in sebaceous ducts and acrosyringia. The cystic lesions are characterized by a wall with flat stratified epithelium and abrupt keratinization, along with an absent granular layer, indicative of trichilemmal differentiation. Comedo-like lesions also can have deep keratin-filled invaginations without a parakeratotic column.

Clinical and histopathologic findings suggest that NTC is related to a mutation in follicular development and differentiation. A 2005 report of 38 family members revealed the mutation of gene TRICY1 on chromosome band 3p24-p21.2 is related to trichilemmal cyst development as an autosomal dominant trait. However, it did not explain the other clinical NTC findings. Nevertheless, it was an important discovery as a starting point to better understand the origins of NTC. Since epidermal nevi can present within a larger syndrome, the question remains whether the same can be presumed for NTC. Case reports have described patients with severe osteomalacia, frontal bossing, and bilateral arthralgias along with NTC. Parallels were drawn in all cases to the variety of epidermal nevus syndromes. As more cases of NTC are reported the association may be further elucidated.

In the literature reported for NTC, definitive treatment via excision was the mainstay of treatment. In general, treatment of epidermal nevi may be difficult. Management must be individualized and should always include a thorough history, physical examination, and genetic testing where appropriate. Topical therapies such as topical retinoid and destructive modalities such as electrodessication or cryotherapy may temporarily improve lesion appearance, but recurrence is common. Carbon dioxide laser is an alternative option; however, scarring and pigmentary alteration are potential permanent complications, especially in patients with darker skin types. We present this case of a patient with nevus trichilemmocysticus, a rare epidermal nevus, for clinical interest and to bring awareness to the possibility of systemic findings related to those found in epidermal nevus syndromes.

Essential Lesson:

- Nevus Trichilemmocysticus is an uncommon distinctive type of epidermal nevus composed of verrucous plaques with filiform projections, comedo-like lesions, and trichilemmal cysts present in a Blaschkoid distribution.
- Clinicians should be aware that NTC may be accompanied by systemic findings related to those found in epidermal nevus syndromes.

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Case Presented by Jane Zhang, MD
Wenhua Liu, MD and Roger Haber, MD

History of Present Illness:
A 71-year-old female presented to UIC Dermatology with a chief concern of oral ulcers and gum bleeding that began a year ago. Her periodontist had clinically diagnosed her with erosive lichen planus (LP) and prescribed topical and oral steroids as well as magic mouthwash, none of which she reported significantly helped. A year ago, she was also clinically diagnosed with vulvar LP by her OB/GYN after she presented with vaginal irritation, which resolved with triamcinolone ointment. Multiple oral and vaginal biopsies were inconclusive.

Past Medical History:
Gastroesophageal reflux disease and irritable bowel syndrome

Medications:
Pantoprazole and triamcinolone 0.1 % paste

Allergies:
None

Family History:
No family history of skin diseases or autoimmune diseases

Review of Systems:
Negative for fevers, chills, weakness, fatigue, vision changes, eye pain, and sore throat

Physical Examination:
Edematous and erythematous upper and lower gingivae with mild erosions. Gluteal cleft with thin eroded erythematous plaques surrounded by a white border.

Laboratory Data / Diagnostic Procedures and Tests:
Histopathology, H&E:
Upper gluteal cleft, skin:
Subepidermal cleft formation with ulceration and features of a lichenoid dermatitis. The dermis contains a dense, band-like lymphohistiocytic infiltrate at the dermal-epidermal junction. Scattered eosinophils and numerous plasma cells are noted in the dermis. Sections of skin show compact orthokeratosis, wedge-shaped hypergranulosis, and saw-toothing of rete ridges. There is subtle squamatization of the basal layer of keratinocytes and rare dyskeratotic cells.

Pemphigoid Antibody Panel:
Indirect immunofluorescence (IIF): IgG with epidermal localization in human split-skin substrate.
Enzyme-linked immunosorbent assay (ELISA): Positive IgG to BP180. Negative IgG to BP230.

Diagnosis:
Lichen Planus Pemphigoides (LP Pemphigoides)

Treatment and Course:
A prednisone taper was started along with topical steroids and Cellcept. Two months later, she reported an oral flare for which dexamethasone mouthwash was added and the dose of Cellcept

was increased. After a period of improvement, due to medication noncompliance, she experienced a second flare resulting in mouth pain and bleeding from her gums. Another prednisone taper was started, and the dose of her dexamethasone mouthwash was increased. At her last visit, she had no new lesions, and her prior lesions were improving. Her treatment regimen of Cellcept, dexamethasone mouthwash, and topical steroids was continued.

Discussion:

LP pemphigoides is a very rare, acquired, autoimmune blistering disorder. Available data estimates the worldwide prevalence to be about 1 out of 1,000,000 people. It often manifests with overlapping features of both LP and bullous pemphigoid (BP). The condition usually presents in the fifth decade of life with a slight female predominance. Interestingly, there is a male predominance in children, who can be affected. Though primarily idiopathic, it has been associated with angiotensin-converting enzyme inhibitors, PD-1 inhibitors, PD-L1 inhibitors, labetalol, narrowband UVB, and psoralen plus UVA (PUVA).

Initially, patients typically present with lesions of classic LP: pink-to-purple, flat-topped, pruritic, polygonal papules and plaques. After weeks to months, tense vesicles and bullae usually develop. They can arise on the sites of LP as well as on uninvolved skin. While one study found a mean lag time of about 8.3 months for blistering to present after LP, concurrent presentations of both have been reported. Oral mucosal involvement is seen in 36% of cases. The most-commonly affected sites are the extremities. However, involvement can be widespread.

The pathogenesis of LP pemphigoides is not known. The proposed mechanism is that LP injury of basal keratinocytes exposes hidden basement membrane (BM) and hemidesmosome antigens including BP180, also known as BPAG2, a 180 kDa transmembrane protein of the BM zone (BMZ) with collagen-like domains. This triggers a Th1 and Th2 response where T-cells recognize the extracellular portion of BP180. Antibodies are then formed against the likely autoantigen, which studies have suggested is the MCW-4 epitope within the C-terminal end of the NC16A domain of BP180.

Histopathology reveals characteristics of both LP (lichenoid lymphocytic interface inflammation, saw-toothing of rete ridges, wedge-shaped hypergranulosis, and colloid bodies) as well as BP (subepidermal separation with presence of eosinophils). Direct immunofluorescence (DIF) shows linear deposits of IgG and/or C3 along the BM. IIF often reveals IgG against the roof of the BMZ in human split skin substrate.

The primary differential diagnosis includes bullous LP and BP. Clinically, however, the bullae in bullous LP only arise within LP lesions. Furthermore, bullous LP would not have positive direct immunofluorescence (DIF) for IgG and/or C3, IIF, or ELISA for BP180 autoantibody because the mechanism does not involve autoantibody production. Instead, for bullous LP, it is hypothesized that the severe interface dermatitis of LP causes the epidermis to separate from the dermis. BP, on the other hand, lacks lichenoid lesions clinically and thus would present differently on histology. Another difference is that BP can be associated with additional autoantibodies against BP230 also known as BPAG1, a 230 kDa intracellular noncollagenous glycoprotein. Lastly, in BP, the NC16A epitopes of BP180 that are targeted are MCW-0-3.

In terms of treatment, topical steroids are often used for localized disease and can be used concomitantly with systemic agents. Oral prednisone may be given for widespread LP pemphigoides or disease unresponsive to topical steroids. Other treatments that have been used as monotherapy or in adjunct with oral corticosteroids include azathioprine, mycophenolate mofetil, hydroxychloroquine, dapsone, tetracycline in combination with

nicotinamide, acitretin, ustekinumab, baricitinib, and rituximab with IVIG. In children, dapsone and/or topical steroids are generally recommended as first-line due to the side effects of systemic steroids, which are considered second-line in cases of treatment failure.

For additional management, potential medication culprits should be discontinued. Secondary infections should be treated with appropriate systemic antibiotics. Mechanical skin trauma should be avoided. Patients with oral involvement may require a modified diet of soft foods to avoid further mucosal insult. Dentistry, ophthalmology, and/or otolaryngology may need to be consulted depending on disease extent and severity.

We highlight a case of lichen planus pemphigoides with atypical clinical presentation to emphasize the importance of the biopsy in conjunction with the pemphigoid panel for accurate diagnosis and optimal treatment.

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Case Presented by Carolina Puyana MD
Marylee Braniecki MD, Vassilios Dimitropoulos MD, and Roger Haber MD

History of Present Illness:
A 67-year-old male presented to dermatology clinic for evaluation of a raised lesion of his right forearm for 5 years. The patient described his lesion as a non-healing sore with a "lump" under the skin. The lesion had slowly increased in size, it easily bled upon minor trauma, and it was often tender to palpation.

Past Medical History:
Diabetes mellitus, hypertension, hyperlipidemia, peripheral neuropathy, gastroesophageal reflux disease. No personal or family history of skin cancer.

Medications:
Lantus, ozempic, metformin, lisinopril, atorvastatin, aspirin, gabapentin, duloxetine, famotidine

Allergies:
Erythromycin

Social History:
Works as a mechanic. Denied tobacco or drug use and endorsed occasional alcohol use.

Review of Systems:
The patient denied any fevers, chills, night sweats, or weight loss.

Physical Examination:
The right distal forearm on the dorso-radial side had a 12 mm x 10 mm gritty plaque with a 7 mm x 6 mm central light tan papule adjacent to a 4 cm linear scar. There is no axillary or cervical lymphadenopathy.

Histopathology:
Right Forearm, tangential biopsy, skin: Well differentiated porocarcinoma extending into the dermis and approaching the inked base. Intraepidermal and dermal neoplastic proliferation of atypical poroid cells, which show uptake for CAM5.2 and CK7.

Diagnosis:
Porocarcinoma

Treatment and Course:
The patient underwent Mohs surgery, requiring a total of one stage to completely clear the tumor of any atypical cells. The surgical defect was reconstructed with a complex linear closure. Sutures were removed two weeks later as the site was healing well. The patient was then scheduled for a total body skin exam in three months, with no evidence of recurrence.

Discussion:
Porocarcinoma, also referred to as an eccrine porocarcinoma, malignant eccrine poroma, or malignant hidroacanthoma simplex, is a rare malignant adnexal tumor of eccrine differentiation.[1] However, from a theoretical point of view, it is possible that sometimes these may exhibit apocrine differentiation. Porocarcinomas are thought to develop de-novo or arise within a pre-existing

poroma, studies show this transformation may take from 6 to 8.5 years.[2] Clinical signs that should make one suspect malignant transformation of a poroma include ulceration, bleeding, and rapid growth of a previously long-standing lesion. Porocarcinomas and eccrine poromas share oncogenic gene fusions, such as the YAP1- gene fusions.[3]

Most epidemiological data on porocarcinomas stem from case studies and few national database studies, such as the National Cancer Institute Surveillance, Epidemiology, and End Results database. Porocarcinomas are estimated to account for 0.005% to 0.01% of malignant cutaneous neoplasms, with an age-adjusted incidence rate of 0.04 per 100 000 person-years in the United States.[4-7] Porocarcinomas arise most commonly in the seventh and eight decades of life.[8] While the most common site remains unclear, these have been reported on the head, neck, and extremities. There is no clear preference in sex, ethnicity, or skin type.[8] Risk factors include chronic immunosuppression, chronic ultraviolet light exposure, pesticides among others.[9,10]

Lesions lack a distinctive clinical appearance, mimicking a variety of lesions. Porocarcinomas commonly present as an individual, firm erythematous, violaceous, or skin colored ulcerated papule, plaque, or nodule. It may be asymptomatic or associated with pruritus, tenderness, or bleeding.[11] Invasive porocarcinomas are aggressive tumors because they frequently metastasize to the skin, lymph nodes, lung, and bone. Clinically, the differential diagnosis includes basal cell carcinoma and squamous cell carcinoma (SCC), less commonly hidradenoma, melanoma, Merkel cell carcinoma, pyogenic granuloma, and Paget's disease, among others. [8,12]

Definite diagnosis is made through histopathology. The degree of cytologic atypia on porocarcinomas is variable, therefore attention should be paid to other markers of malignancy.[5,13] Porocarcinoma is composed of poroid cells that infiltrate the dermis or subjacent deeper tissues and ductal differentiation is usually clearly visible. Lesions arising from a pre-existing poroma commonly have two distinct areas, a benign poroma associated and an area of pleiomorphic cells and duct formation, either confined to the poroma (in situ) or invading the surrounding stroma (invasive). Porocarcinomas without a precursor lesion show features of a poroma with an infiltrative growth pattern, variable degree of atypia, mitotic figures, necrosis, and ulceration. Squamous metaplasia is also common resulting in a histologic appearance in-foci indistinguishable from SCC. These can also show pagetoid growth within the epidermis leading to epidermotropic cutaneous metastases[5,14] Although immunohistochemistry is not necessary to make a diagnosis of porocarcinoma, uptake for CK7, Cam5.2, CEA, or EMA can help highlight ductal differentiation. Porocarcinoma may also express D2-40, calretinin, and p63, distinguishing from most adenocarcinomas metastasizing to skin.

Traditionally, porocarcinoma has been managed with wide local excision with recurrence and metastatic rates of up to 35%.[14,15] Metastatic disease most commonly develops in regional lymph nodes followed by lungs.[8] No consensus on recommended excision margin exists, historically these range from 3mm to greater than 2 cm. More recently, Mohs surgery is advocated to be the preferred treatment following reports of decreased regional recurrences compared with wide local excision.[11] The American Academy of Dermatology Mohs surgery appropriate use criteria rate the use of Mohs as appropriate for the treatment of apocrine/ eccrine carcinomas. There is little evidence on treatments such as radiotherapy for unresectable tumors, or adjuvant radiotherapy.[11,15,16] The utility of sentinel lymph node biopsy remains the subject of debate.[17] The efficacy of chemotherapy has not been demonstrated widely but it plays a role in the metastatic setting. Agents reported in the literature include 5-fluorouracil or docetaxel. Additionally, treatment with isotretinoin and interferon alpha has been reported with partial remission.[18] Further studies into the YAP-NUTM1 fusions involved in oncogenesis of poromas could explore their potential role as therapeutic target. In our patient, there was no clinical lymphadenopathy and tumor

margins were cleared with surgery, thus adjuvant therapies were not pursued. Herein, we present a patient with porocarcinoma, a rare adnexal tumor, to highlight its unique clinical and histopathological findings.

Essential Lesson:

- Porocarcinomas are rare malignant adnexal neoplasms, thought to develop de-novo or arise within a pre-existing poroma. Signs that should make one suspect malignant transformation of a poroma include ulceration, bleeding, and rapid growth of a previously long-standing lesion.
- Mohs surgery is the preferred treatment for porocarcinoma because it allows for systematic evaluation of 100% of the tumor margin leading to lower recurrence rates.

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Case Presented by Christine Pak, MD
Marylee Braniecki, MD and Michelle Bain, MD

History of Present Illness:
A nine-year-old African American boy presented for evaluation of a mole on his left posterior ankle that was present since birth and proportionally grew with the patient. The lesion became firm during the past 3 years and the mother endorsed that patient had intermittent pressure-like pain around the mole and left foot for the past year. Each episode lasted about 30 minutes, and symptoms were worse with walking and better at rest. The lesion was also sometimes pruritic. The patient did not have any personal or family history of similar lesions. His growth and development were normal.

Past Medical History:
None

Medications:
None

Allergies:
No known drug allergies

Family History:
No history of skin conditions or autoimmune conditions

Review of Systems:
The patient denied any fevers, chills, night sweats, weight loss, or joint pains.

Physical Examination:
There was a 3.1 by 4.3 cm well-demarcated, round, firm hyperpigmented hyperkeratotic plaque with few excoriations on the left posterior ankle. There was no surrounding erythema. The left lower extremity had sensation intact distal to the lesion and distal pulses were palpable. The remaining skin exam was unremarkable. Grossly, there was no limb-length or leg circumference discrepancy of the lower extremities on visual evaluation.

Laboratory Data/Diagnostic Procedures and Tests:
Soft tissue cutaneous ultrasound of the left lower extremity is pending

Histopathology:
Left posterior ankle, skin: The epidermis showed papillated reactive verrucoid acanthosis and hyperkeratosis with subepidermal capillary ectasia and evidence of underlying diffuse dermal stromal hemosiderin deposition. There was a modest vascular proliferation in the deep dermis and fat but no conspicuous vascular proliferation or evidence of thickened capillary sized vessels in the subcutis.

The deep stromal hemosiderin deposition suggested that there may be adjacent deep seated vascular proliferation that was not visible in this current biopsy. There was also a single multinucleated giant cell detected in the stroma, amid the hemosiderin, raising the possibility of prior trauma at this site. There was no melanocytic proliferation.

Immunohistochemistry with CD31 highlighted the endothelial lining of the cystically dilated vessels in the papillary dermis and modest vascular proliferation in the deep dermis and fat. Immunostains of WT-1 (Wilms tumor 1 protein) and GLUT-1(Glucose transporter-1 protein) were negative. D2-40 (podoplanin) lymphocytic immunostain highlighted the dilated subepidermal endothelial lined channels and few scattered small superficial dilated vessels throughout the stroma. Iron highlighted diffuse stromal hemosiderin deposition.

Diagnosis:
Angiokeratoma circumscriptum neviforme versus verrucous hemangioma

Treatment and Course:
The patient was initially treated with topical clobetasol 0.05 % ointment twice daily to the affected area on the body. It was also recommended that the patient follow up in 1 month for monitoring. Instead, the patient returned 3 months after the initial encounter for a punch biopsy. During this visit, mother reported that the lesion was stable in size and pruritus continued despite applying topical clobetasol. Patient was then lost to follow-up.

Discussion:
Verrucous hemangioma (VH) is a rare form of non-hereditary, congenital, localized, vascular malformation usually involving the unilateral lower extremity in approximately 95% of cases. The diameter of verrucous hemangioma can range from 4 mm to as large as 5 cm to 7 cm.

Its principal differential diagnosis, angiokeratoma circumscriptum neviforme (ACN), is a rare subtype of vascular ectasias. Classically ACN presents as red-colored macules at birth that transform into well circumscribed bluish-black plaques with hyperkeratotic surface. Most commonly the lesion affects lower extremities, thighs, and gluteal region unilaterally, but other sites have been reported in literature. It remains unclear if the lesion progresses proportionally to the child's growth. The worldwide prevalence is estimated to be about 0.16% with a female predominance (3:1).

The International Society for the Study of Vascular Anomalies (ISSVA) classification of 2018 considered VH, now called verrucous venous malformation, as simple vascular malformation III associated with somatic mutation of MAP3K3 gene. On the other hand, ACN still remains under the category of “provisionally unclassified vascular anomalies” as the pathogenesis is yet to be elucidated. However, it is known that ACN is caused by telangiectasia of preexisting veins and capillaries in the papillary dermis.

Both entities can share similar clinical history and presentation involving a birthmark that gradually enlarges during childhood to become wart-like later in life, usually after trauma to the lesion. Initially they appear as erythematous patches that evolve to violaceous plaques with verrucous and hyperkeratotic surfaces. These lesions can also appear later in life during adulthood. In both cases, spontaneous regression is not expected. Despite these similarities in the initial clinical appearance of VH and ACN, it is imperative to differentiate the two lesions as they have different histologic features and clinical behaviors. A correct clinical suspicion is necessary to obtain an adequate deep biopsy specimen.

Histopathology is crucial for making the correct diagnosis. Since the first characteristic descriptions of VH and angiokeratoma and its subvariants were published in 1967 to distinguish these identities, many histopathologic and immunochemical stains have been utilized. Histopathologic characteristics of VH and ACN have overlapping features including marked hyperkeratosis, irregular acanthosis, and papillomatosis. VH is characterized by an underlying

mixed capillary and cavernous hemangioma in the dermis and subcutaneous fat. One study noted that 60% of the samples exhibit many inflammatory cells and that hemosiderin pigment was frequently seen in the upper dermis. On the other hand, vascular ectasia in ACN is confined to papillary dermis and not present in subcutaneous tissue, distinguishing it from VH.

Immunostaining of VH typically expresses markers for vascular neoplasms, such as WT-1 and GLUT-1, and lacks D2-40 immunostaining. Contrary to VH, immunohistochemical findings of ACN reveal negative endothelial expressions of WT-1 and GLUT-1 along with positive expression of D2-40. The vascular markers like CD31 can highlight the extent of lesion, but CD31 stains weakly positive or negative in angiokeratoma, whereas staining VH highlights endothelial cells lining the vascular channel.

An MRI of the lesion can reveal local vascular infiltration of the deeper dermis and subcutaneous fat, but it is typically not used for evaluation of ACN. Identifying the depth of lesion can guide biopsy and surgical management of VH. Alternatively, one could utilize cutaneous ultrasound to identify the differences in the depth of vessel involvement. For this patient we planned for cutaneous ultrasound to offer a minimally invasive option.

Rarely, ACN has been reported to co-exist with other vascular malformations. For example, Cobb syndrome or Klippel-Trenaunay syndrome (KTS). Clinicians should order a computed tomography (CT) scanogram, which measures the limb symmetry and lengths radiographically.

Treatment options of VH and ACN are similar, including surgical excision, electrocautery, and/or laser ablation. Recently topical sirolimus was suggested to be effective and safe for treating both entities. Ideally, VH should be excised while still small as it enlarges and spreads with body growth. Smaller lesions can be locally excised or with electrocautery, whereas larger lesions are better treated by wide excision or even deeper excisions followed by skin grafts. VH has a tendency for recurrence, especially when subjected to trauma, secondary infection, or size greater than 2 cm in diameter. Currently combined therapy of laser and surgery is considered a first-line treatment for VH. For small ACN, cryotherapy, electrocoagulation, and curettage are effective. Large lesions are better treated with complete surgical excision and laser ablation. Recurrence of ACN is uncommon after the surgical excision. To provide most effective care for the patient with either VH or ACN, the patient would likely need a well-coordinated medical team from multiple specialties for diagnosis, treatment, and follow up. We present this case of a violaceous hyperkeratotic plaque on an African American patient with a possible diagnosis of VH or ACN to highlight the unique presentation, importance of recognition, and current research on work-up and management of these two rare entities.

Essential Lesson:

- Angiokeratoma circumscriptum neviforme (ACN), a rare subtype of angiokeratoma, and verrucous hemangioma (VH) both have similarities in clinical and histological presentation. Therefore, both should be considered in the differential diagnosis of hyperkeratotic vascular lesions of the lower extremity.
- VH and ACN are usually distinguished by dilation of vessels in the superficial dermis versus deeper layer. However, further stains and/or imaging may be required for lesions with overlapping clinical and histological features.
- When VH or ACN is suspected, it is imperative to build a well-coordinated multispecialty team to provide effective care for the patient.

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Case Presented by Ryan Bunney, MD
Marylee Braniecki, MD and Roger Haber, MD

History of Present Illness:
A 49-year-old female presented for evaluation of “itchy red bumps” on her arms and legs. The rash had been present for multiple years and was most bothersome when it would flare in the summertime, especially with exposure to sunlight and heat. When flaring, she reported new lesions and intense pruritus on her extremities. The patient had prior oral ivermectin treatment without resolution. The patient also followed with rheumatology for nonspecific joint pain.

Past Medical History:
Chronic obstructive pulmonary disease, hypertension, hyperlipidemia, diastolic congestive heart failure, obesity, non-alcoholic steatohepatitis, hypothyroidism, depression

Past Surgical History:
Appendectomy, cholecystectomy, hysterectomy

Medications:
Albuterol, fluticasone-salmeterol, mometasone/formoterol, aspirin, atorvastatin, furosemide, metoprolol tartrate, levothyroxine, bupropion, paroxetine

Allergies:
No known allergies.

Family History:
No family history of skin conditions or autoimmune conditions.

Review of Systems:
No fevers or chills. Endorsed shortness of breath, joint pain, and weight loss.

Physical Examination:
Arms and legs with pink excoriated macules and papules with peripheral ridges of scale. There is sparing of the palmoplantar surfaces, face, trunk, and genitals.

Laboratory Data/ Diagnostic Procedures and Tests:
Elevated: ALT 45
The following were negative or within normal limits: CBC with differential, ESR, CPK, CRP, alpha-1-antitrypsin, anti-SCL-70 Ab, anti-thyroid peroxidase Ab, anti-thyroglobulin Ab, anti-CCP Ab, anti-smith Ab, anti-DsDNA Ab, anti-smooth muscle Ab, anti-JO-1 Ab, anti-Mitochondrial Ab, IgG, C3, C4, and Rh factor.

Histopathology:
Right upper shin, skin: Central epidermal thinning with focal loss of granular cell associated with microfocal keratinocytic dyskeratosis and overlying cornoid lamella.
Right lower shin, skin: Epidermal papillation with cornoid lamella formation.
Colloidal iron stain: Negative for stromal mucin.

Diagnosis:
Eruptive pruritic papular porokeratosis

Treatment and Course:
The patient underwent intentional split side treatment. The right extremities were treated with 5% imiquimod cream. The left extremities were treated with 0.1% triamcinolone ointment. The patient was extensively counseled on sun-protective measures. After one month of treatment the patient endorsed minimal improvement in her lesions and pruritis bilaterally and did not notice a significant difference between the two treatments. She self-discontinued both medications and after an additional month her pruritus spontaneously resolved. Upon follow up one year later, she had a residual presence of a few scattered violaceous and brown lesions without any pruritis and no recurrence of an eruptive episode within the year. She was encouraged to continue to follow up with her primary care physician for age-appropriate malignancy screening and to continue to follow up with her hepatologist.

Discussion:
Porokeratosis is a disorder of keratinization characterized by the histologic presence of cornoid lamellae. It is a rare disease with unknown prevalence and is typically seen in adult males, although it has been reported in the pediatric population. The most common cutaneous findings include hyperkeratotic, minimally atrophic macules, patches, papules, and/or or plaques with a peripheral ridge of scale. The lesions vary from dark brown to erythematous to skin-colored and its distribution is variable.

The pathogenesis of porokeratosis is hypothesized to be a combination of genetic susceptibility, ultraviolet radiation, and immune status. Mutations in the mevalonate pathway are thought to be a possible catalyst for the development of porokeratosis. Additionally, disseminated subvariants have been known to favor sun-exposed areas of the body, making ultraviolet radiation a likely trigger for the disease. Finally, immunosuppressed patients may be at increased risk for porokeratosis. Of note, malignant transformation of porokeratosis is estimated to occur in 7.5-11% of patients, with squamous cell carcinoma being the most common malignancy.

Porokeratosis is a diagnosis based on histology. The most defining feature is the presence of a cornoid lamella, a parakeratotic column within the epidermis. In addition, there is typically loss or interruption of the epidermal granular layer, as well as the presence of dyskeratotic keratinocytes. These findings are often accompanied by a lymphocytic inflammatory infiltrate within the underlying dermis.

Eruptive pruritic papular porokeratosis (EPPP), also referred to as inflammatory or eruptive disseminated porokeratosis, is a rare variant that has been infrequently described in the literature. It is a diagnosis that can be made by the presence of an acute eruptive episode, new disseminated cutaneous lesions, pruritus, and histopathology consistent with porokeratosis. These acute episodes may be a single event or may recur, such as in our patient. Many patients diagnosed with EPPP have an underlying chronic porokeratosis.

EPPP was first described by Kanaski et al. (1992) and to date there have been less than forty case reports describing this variation. Similar to other porokeratosis subvariants, EPPP is predominantly found in the adult male population with a median age of sixty-six years old. Also similarly, immunosuppression is thought to play a role in the development of EPPP as 30% of all reported patients were immunosuppressed. Notably, liver dysfunction is associated with the development of both porokeratosis and EPPP. EPPP has been reported in patients with hepatitis B, hepatitis C, hepatocellular carcinoma, and cirrhosis. Our patient had non-alcoholic steatohepatitis and was followed by hepatology at the time of her EPPP diagnosis.

Two distinctive features of EPPP compared to other variants include a lack of family history in all reported cases and a lack of malignant transformation to squamous cell carcinoma. Furthermore, EPPP has a greater relationship with non-cutaneous malignancy than other variants, with 30% of EPPP cases being associated with malignancy. The mean onset of EPPP was approximately three months either prior to or following a diagnosis of malignancy. The most common malignancies were solid tumors that involved the gastrointestinal tract, however hematologic malignancies were also reported. To account for the differing possible associations with the development of EPPP, Shoimer et al. (2014) proposed the classification of EPPP based on these categories: paraneoplastic, immunosuppressed, inflammatory, and other, which lacks any of the aforementioned associations.

Resolution of EPPP may be achieved by stopping or reducing immunosuppressive therapies if tolerated or by treating any underlying malignancy, as seen in several of the reported cases. There have been no randomized control trials conducted on the efficacy of various treatments specifically for porokeratosis or EPPP. Response to direct treatment of EPPP was inadequate in the majority of cases reported, however despite this inadequacy, 75% of patients achieved spontaneous resolution. Therefore, while treatment may not be necessary for resolution of EPPP, it should be offered based on lesion size, location, treatment availability, and patient preference. Current treatment modalities include destructive, topical, and oral therapies. Destructive therapies include cryotherapy, curettage, photodynamic therapy, laser therapy, and excision. Topical therapies include 5-fluorouricil, 5% imiquimod, corticosteroids, retinoids, diclofenac, vitamin D analogs, and over-the-counter urea or salicylic acid. Oral therapies include antihistamines and for severe cases, oral retinoids may be offered. For all patients with EPPP, it is necessary to provide sun protection counseling, as it may be a trigger for the eruption. Finally, due to the increased malignancy risk, it is important to verify the patient has received age-appropriate malignancy screening and to ensure continued follow up with both their primary care physician and the dermatology clinic. We present this case to bring to light a rare variant of porokeratosis, its association with malignancy and hepatic disease, and its typical course.

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Case 6

Case Presented by Brian Cahn, MD
Timothy Tan, DO and Sheryl Hoyer, MD

History of Present Illness:
A 46-year-old transgender woman with past medical history of a vulvoplasty (penile inversion, urethroplasty, clitoroplasty, labiaplasty and orchiectomy) in August 2021 presented with redness, irritation, itching, burning and tenderness of her vulva for the past 6 months. Additionally, she stated that she had white discharge on the "skin cracks" on her vagina. She believes much of this is due to the urethral stricture she developed following surgery, causing her urine to spray on her labia and upper legs when she urinates. Following a positive fungal culture, her urologist and primary care physician had treated her for a *Candida* infection with oral fluconazole, topical terbinafine and miconazole with little to no improvement. She did not take any medications for her problem.

Past Medical History:
Type 2 diabetes mellitus, gender dysphoria, generalized anxiety disorder, right inguinal hernia repair, bilateral carpal tunnel release, neuropathic pain of the left hand.

Medications:
Insulin, metformin, progesterone, estrogen, spironolactone, paroxetine, prazosin, gabapentin

Allergies:
None

Family History:
No family history of skin conditions or autoimmune conditions. No family history of skin cancer and other cancers.

Review of Systems:
No weight loss, fever, chills, nausea, vomiting, diarrhea, myalgia, joint pain or urinary frequency. Endorses dysuria.

Physical Exam:
Bilateral vulvar labia, inguinal folds and perianal skin with pink atrophic lichenified thin plaques with no scale. Fissuring of the perianal skin.

Histopathology:
Right groin, skin: parakeratosis, attenuated granular layer and acanthosis. Neutrophils are present in the stratum corneum. There is a superficial perivascular lymphocytic infiltrate. Prominent, thin-walled dermal blood vessels approach close to the epidermis. A PAS stain was also performed with adequate controls and was negative for fungus.

Treatment and Course:
The vulva, inguinal folds and perianal skin were treated with triamcinolone 0.1% ointment twice daily for 7 days and then switched to tacrolimus 0.1% ointment twice daily until clear. She no longer has tenderness, pruritus, burning or discharge. Additionally, her perianal fissure has healed. She now uses the tacrolimus ointment a few times per week for maintenance therapy.

Discussion:

The Koebner phenomenon was first described in 1876 by a German dermatologist, Heinrich Koebner. He initially described psoriasiform lesions at sites of uninvolved skin following trauma such as tattoos, excoriations and horse bites. Since then, it has been described in other diseases in addition to psoriasis such as lichen planus and vitiligo. Additionally, the definition of this phenomenon has extended to include those who get a new dermatosis at a site of trauma without preexisting cutaneous disease. Koebner phenomenon is also termed the isomorphic response, given the fact that the new lesions are clinically and histologically identical to a patient's primary cutaneous disease.

The Koebner phenomenon can be further classified into 4 different groups:

1. True Koebnerization: Reproducible response to trauma that is not due to infectious or allergic agents such as in lichen planus, vitiligo, and psoriasis.
2. Pseudo-Koebnerization: Seeding of an infectious agent at the site of trauma as seen in molluscum or by skin breakdown as seen in the pathergy phenomenon.
3. Occasional lesions: Meets some of the qualifications for the Koebner phenomenon but not all of them, as in erythema multiforme and Darier disease.
4. Questionable trauma-induced processes: All disorders that have been described to have a correlation with trauma, such as eruptive xanthomas and pemphigus vulgaris.

The Koebner phenomenon has been most extensively described in psoriasis, where the incidence has been reported to range between 11% to 75%. It has been noted to occur via numerous traumatic injuries such as insect bites, burns, infection, and surgery. However, in cases of psoriasis it appears to be unrelated to disease activity or severity. The Koebner phenomenon occurs more frequently in the winter, with increased emotional stress and at sites of scar tissue. Furthermore, those diagnosed at an earlier age and those who have been previously treated for psoriasis had a higher incidence of the Koebner phenomenon. Since not all trauma leads to the Koebner phenomenon, it has been theorized that reactivity depends on the depth of trauma. The average time to koebnerization is 10 to 20 days but can present as quickly as three days or as long as two years. There have been no regional variations regarding the Koebner phenomenon and it can occur anywhere on the body at sites of trauma. The clinical features and histopathology of the Koebner phenomenon are identical to lesions that arise spontaneously.

While the exact pathogenesis of the Koebner phenomenon is unknown, numerous theories have been developed. The most cited theory is that it is caused by an immune mediated reaction involving at first non-disease specific cytokines and substances from the traumatic insult that then trigger disease-specific effectors such as T-cell mediated reactions, keratinocyte proliferation and angiogenesis. The role of nerve growth factor (NGF) has been recently implicated in the Koebner phenomenon, whereby upregulation of NGF was noted 24 hours after trauma, which lead to keratinocyte proliferation and T-cell migration to the epidermis. This response was not seen in healthy patients nor Koebner phenomenon negative patients following trauma. Other theories posit that the Koebner phenomenon is mediated through a vascular process since the microvasculature in psoriatic patients respond differently to trauma. Other underlying mechanisms that have been proposed included neural, genetic, allergic, hormonal, infectious and enzymatic processes that lead to koebnerization.

Treatment of Koebner phenomenon lesions is identical to the treatments for the underlying disease. However, in studies of the Koebner phenomenon in vitiligo it has been suggested that there was an overall lower response to treatment in patients who exhibited koebnerization, suggesting that it can be used as a predictor of treatment response.

Our patient had no history of psoriasis and the koebnerization of her gender-affirming surgery was the presenting sign for diagnosis. Fortunately, she was well-controlled with topical steroids and topical calcineurin inhibitors. We present this unique case as the first report to our knowledge of a patient who underwent gender affirmation surgery and exhibited koebnerization as a result. Moreover, we seek to highlight the need to educate our non-dermatologic colleagues of this relatively common phenomenon to prevent future delays in diagnosis. Finally, we would like to bring attention to the possibility of the Koebner phenomenon in those who undergo gender affirmation surgery, especially with the recent increase in number of cases performed per year.

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Case Presented by Samantha Hunt, MD
Marylee Braniecki, MD, Michelle Bain, MD and Sheryl Hoyer, MD

Patient 1:

History of Present Illness:

A 36-year-old male was seen in the dermatology clinic for evaluation of lower lip swelling that was present for four months. The swelling was greatest on the left portion of the lower lip and each episode lasted for a few days. He was unable to identify any inciting events or triggers. The patient had previously tried antihistamine medications without improvement. He denied any surface changes, pain, or dryness of the lips. He also denied dyspnea, difficulty swallowing, and facial or tongue swelling. He did endorse drooling more often from the left side of his mouth. A review of systems was otherwise negative. He denied any recent medication changes or nonsteroidal anti-inflammatory drug use.

Past Medical History:

Allergic rhinitis, generalized anxiety disorder

Medications:

Cetirizine and sertraline

Allergies:

None

Family History:

Systemic lupus erythematosus in maternal grandmother and maternal aunt

Physical Examination:

There was a non-tender edema of the lower left lip without any overlying surface changes. The oral cavity was otherwise unremarkable.

Histopathology:

Left lower vermillion lip, skin: noncaseating microgranuloma in the submucosa with modest submucosal vascular ectasia and perivascular lymphoplasmacytic infiltrates.

Labs and Imaging:

CBC, angiotensin-converting enzyme (ACE) level, erythrocyte sedimentation rate, C-reactive protein, antinuclear antibodies, and complement levels all were normal.
Serum environmental allergen test was reactive to ragweed.
Fecal calprotectin was normal.
Chest radiograph was unremarkable.

Diagnosis:

Cheilitis granulomatosa (Cheilitis granulomatosa of Miescher)

Treatment and Course:

ACE level and chest radiograph performed to evaluate for sarcoidosis were normal. The patient was referred to gastroenterology to screen for inflammatory bowel disease. Fecal calprotectin ordered by gastroenterology was negative. The patient was treated with intralesional steroid injections of the lower lip. He underwent an initial intralesional injection of 5mg/mL triamcinolone

acetonide with five additional maintenance injections of 2.5 mg/mL to 5 mg/mL of triamcinolone acetonide every two to four months. The patient experienced complete resolution of his symptoms.

Patient 2:

History of Present Illness:

A healthy 17-year-old male presented with intermittent lower lip swelling for four years. Each episode lasted two weeks. He also reported recurrent, painful ulcers on the inner mucosal surface of the lower lip. He denied swelling in other areas of the face or the tongue. He had previously tried antihistamine medication without improvement. A review of systems revealed intermittent episodes of diarrhea but was otherwise negative.

Past Medical History:

None

Medications:

None

Allergies:

None

Family History:

Non-contributory

Physical Examination:

Lower lip with diffuse, firm, nodular enlargement with accentuation of folds at midline and bilateral ends. No active ulcerations were noted.

Labs and Imaging:

CMP and CBC were normal.

Quantitative immunoglobulin levels, erythrocyte sedimentation rate, C-reactive protein level, antinuclear antibodies, quantiferon gold, complement levels, and serum angiotensin-converting enzyme level were all normal.
Fecal calprotectin level was positive.

Histopathology:

Oral mucosa, skin: subacute spongiotic mucositis with mild squamous hyperplasia and was negative for granulomas.

Colonoscopy and endoscopy: two noncaseating microgranulomas in the lamina propria. Transverse colon mucosa, aphthous erosion: multiple noncaseating microgranulomas.

Diagnosis:

Crohn's Disease

Treatment:

The patient was referred to gastroenterology at an outside facility for the management of Crohn’s disease. The patient was lost to follow up with dermatology.

Discussion:

Cheilitis granulomatosa is an uncommon, granulomatous disorder characterized by recurrent swelling of the lips. It may be seen in a triad with orofacial edema, fissured tongue, and recurrent peripheral facial nerve palsy, which is otherwise known as Melkersson-Rosenthal Syndrome (MRS). When it occurs in isolation, it is known as cheilitis granulomatosa of Miescher (CGM). This monosymptomatic form of MRS is the most common form, as the complete triad of symptoms is only present in 8 to 18% of patients. There is no clear etiology for CGM, however, genetic, immunologic, allergic, and infectious mechanisms have been postulated. The incidence of CGM peaks at 20 to 40 years of age and is estimated to be equal among the sexes.

CGM presents clinically as painless orofacial edema, generally limited to the lips. Periods of edema are recurrent, lasting anywhere from minutes to a few weeks and, gradually, permanent edema may be observed. The differential diagnosis of persistent lip swelling includes, but is not limited to, acquired or hereditary angioedema, foreign body reactions, and oral manifestations of granulomatous diseases such as Crohn's, sarcoidosis, granulomatosis with polyangiitis, and tuberculosis. The diagnoses of both MRS and CGM are mainly clinical, however, histopathology revealing a noncaseating granulomatous infiltrate may help confirm the diagnosis. A tissue biopsy may also be negative early in the disease course.

In patients with persistent lip swelling, systemic granulomatous diseases should be considered based on the clinical scenario. CGM has been reported in the literature to possibly represent an extra-intestinal manifestation of Crohn's disease. Some case studies claim that CGM may even precede a diagnosis of intestinal Crohn's disease, while others refute any association. A diagnosis of Crohn's disease may be supported by other oral findings such as aphthous-like ulcers, fissuring, or cobblestoning of the buccal mucosa. A detailed gastroenterologic history should also be taken. Performing a routine colonoscopy in patients without gastroenterological symptoms or other features suggestive of Crohn's disease is debated. The diagnosis of sarcoidosis should also be considered in these patients. Work-up may include chest imaging, serum calcium, or serum angiotensin-converting enzyme levels. Oral sarcoidosis is usually seen in those with systemic disease, thus, concurrent pulmonary, joint, or eye symptoms may support this diagnosis.

Treatment of idiopathic CGM is aimed to reduce the intensity and recurrence of swelling to prevent permanent swelling and subsequent cosmetic and functional concerns. The use of corticosteroids either topically, intralesionally, or even systemically is the current mainstay of therapy. Current literature supports the efficacy of intralesional injections in particular. Various other systemic therapies including clofazimine, metronidazole, tetracycline and macrolide antibiotics, and immunomodulators such as tumor necrosis factor inhibitors and methotrexate have been studied with variable outcomes. For more severe cases and those causing disfigurement, surgical management with cheiloplasty may be considered, however, it may not necessarily provide definitive. We present this case series to highlight important differential diagnoses to consider in patients who present with persistent lip swelling.

Essential Lessons:

- Cheilitis granulomatosa of Meischer is an uncommon, poorly understood disorder that may lead to permanent cosmetic and functional concerns in patients. Prompt diagnosis and treatment may result in improved outcomes.
- Idiopathic CGM is a diagnosis of exclusion and workup for other systemic granulomatous conditions should be carefully considered based on the clinical scenario

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Case Presented by Neha Chandan, MD, MPH
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History of Present Illness:
A seventy-year-old male with a history of monoclonal gammopathy of unspecified significance (MGUS) presented for evaluation of a new, enlarging lesion on his back. The patient stated it started out as a "pimple" and persistently increased in size with some areas of healing and then reopened again. He noted pain, odor, and purulence from the lesion but no fevers or chills. Two months into treatment of the prior lesion, a new lesion developed on the patient's left shoulder. The patient stated this lesion began as a small, red bump that progressively grew in size and sometimes bled with minor trauma.

Past Medical History:
MGUS, diagnosed in 2011. Patient was not following with oncology.
Pyoderma gangrenosum (PG), biopsy confirmed which was diagnosed in 2011 on the right buttock, left neck, bilateral posterior thighs, left ankle.

Medications:
Patient had self-discontinued all medications.
Previous Medications: doxycycline, minocycline, pentoxifylline, prednisone, triamcinolone 0.1% ointment, dapsone (discontinued due to thrombocytopenia), IVIG 2g/kg for 4 days in 11/2018

Allergies:
None

Family History:
Unremarkable

Review of Systems:
The patient endorsed pain and active, purulent drainage from back. He denied fevers, chills, adenopathy, bone pains, issues with bleeding or bruising, headaches, dizziness, or lightheadedness.

Physical Examination
There is a 10 mm x 7 mm pink pearly papule with arborizing vessels on the left posterior shoulder. Localized to the patient's central, mid back was a 13 cm x 15 cm ulcer with gun-metal gray rolled borders. A hemorrhagic and necrotic exudate was present at the superior portion and a purulent exudate was present at the center of the lesion.

Laboratory Data/Diagnostic Procedures and Tests:
SPEP: Total serum protein 7.3. IgA monoclonal immunoglobulins detected
Kappa Quant Free Light Chains: 18.98 (within normal limits)
Lambda Quant Free Light Chains: 16.39 (within normal limits)
CBC and CMP were within normal limits
The patient had a biopsy in 2011 of a similar lesion on his buttock that confirmed PG.

Diagnosis:
Basal cell carcinoma (BCC), infiltrating nodular type (L posterior shoulder)
Ulcerative pyoderma gangrenosum (back)

Treatment and Course

PG

Treatment with topical clobetasol ointment 0.05% BID and cyclosporine 100 mg TID was initiated following baseline labs. The patient was followed closely every two weeks in clinic with repeat labs. He noted pain and reduction in the size of the lesion and continues to tolerate the treatment well without side effects.

BCC

Given the size of the BCC and the aggressive pathology, the lesion was appropriate for Mohs micrographic surgery (MMS). A total of two Mohs stages were taken until the surgical site was free of tumor and no microscopic tumor was found in any of the specimens comprising the final Mohs stage. A complex linear closure was performed. Following suture removal, the patient was instructed to apply clobetasol 0.05% ointment twice daily to the area to prevent occurrence of PG at the site. At three month follow up, the site was healing well and no occurrence of PG was noted.

Discussion

Pyoderma Gangrenosum (PG) is an ulcerating inflammatory neutrophilic dermatosis that is characterized by pathergy. The pathogenesis involves neutrophil dysfunction, inflammatory mediators, and genetic predisposition. Between 50% to 70% of PG cases have associated systemic diseases, with the strongest associations being inflammatory bowel disease, rheumatologic conditions, and hematologic disorders. Of the 5 clinical subtypes of PG, ulcerative PG is both the most common and the most frequently associated with monoclonal gammopathies, which can be seen in up to 15% of patients and is often composed of IgA.

Monoclonal gammopathy of unspecified significance (MGUS) is a plasma cell disorder characterized by a level of serum M protein of less than 3g/L with less than 10% plasma cell infiltration in the bone marrow and the absence of hypercalcemia, renal insufficiency, anemia, or bone lesions. One study evaluating treatment of MGUS-related PG found that all patients with Ig populations other than IgA experienced complete resolution of cutaneous PG following treatment without recurrence, while all MGUS-IgA type patients continued to have recurrence of PG following treatment despite varying treatment regimens. This data suggests no durable remission of PG can be expected in MGUS IgA type unless the MGUS is treated and this emphasizes the need for patients to have concurrent follow up with oncology.

Cutaneous cancer treatment in PG patients presents its own challenge and, per literature review, there are no established guidelines. A 2017 retrospective analysis studying the risk of post-operative PG in patients with a known history found that 5.5% of surgical procedures that pierced the skin led to development or recurrence of PG. However, when PG was chronically present at the time of the procedure, the risk was approximately 4.5 times higher (OR 4.58 [95% CI, 1.72-12.22]). Of note, immunosuppression, time from the original PG diagnosis, and location of the original PG or procedure location did not significantly affect risk. Compared with skin biopsy, MMS and skin excision, which were grouped into the same category, had an OR of 6.47 for pathergy (95% CI, 1.77-23.6). Although not explicitly stated in literature, we expect that MMS will have a lower risk of PG pathergy than excision given the tissue sparing nature of MMS.

Herein we present a challenging case of PG in a patient with a known history of MGUS to raise awareness of the complex relationship between MGUS-IgA type and PG and to highlight the need for MGUS treatment . We also present a case of BCC successfully treated by MMS in a patient with chronically active PG without development of a new PG lesion.

Essential Lesson:

- Monoclonal gammopathies can be seen in up to 15% of PG patients and is most frequently IgA type.
- Prognosis of cutaneous PG associated with MGUS IgA type may differ from other monoclonal gammopathies, and it may be necessary to achieve successful treatment of MGUS in order to achieve complete resolution of PG.
- The risk of post-operative PG increases in patients whom have chronic, active PG and may be decreased by utilizing tissue sparing procedures, such as MMS.

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