0A UNIQUE CASE OF DIFFUSE LARGE B-CELL LYMPHOMA, LEG TYPE PRESENTING AS LIPODERMATOSCLEROSIS

Case No. 1 **Presenters:** Aditya Sood, MD
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History: A 76-year-old female with past medical history of diabetes mellitus presented with newly developed skin lesion located on her lower left leg.

Physical Exam: Physical exam revealed erythematous, indurated, sclerotic, bound-down plaques located on the left medial proximal pretibial region. Clinical differential diagnosis included lipodermatosclerosis (sclerosing panniculitis).

Histopathology: Microscopic examination revealed dermal edema and effacement of dermal architecture by diffuse infiltrate of atypical hyperchromatic lymphocytes with scattered mitotic figures. Accompanying focal fat degeneration was seen. Immunoperoxidase stains showed the infiltrate to be strongly positive for CD20 and Mum-1. BCL-2 highlighted many cells, while CD3 revealed few scattered non-neoplastic T-lymphocytes.

Diagnosis: Anaplastic B-cell lymphoma of the leg (? Diffuse large B-cell lymphoma of Leg)

Clinical Course: The patient has been referred to oncology for systemic evaluation and staging workup.

Points of Emphasis: We present a unique case of primary cutaneous diffuse large B-cell lymphoma of the leg (PCDLBL-LT), clinically simulating sclerosing panniculitis/lipodermatosclerosis. PCDLBL-LT is an aggressive large B-cell lymphoma typically presenting in elderly females in the seventh decade of life. Classically, this lymphoma presents as multiple erythematous violaceous nodules and tumors located on the lower extremities, though 10%-15% of cases present on upper extremities, trunk, head and heck. Less commonly, it can present as pyoderma gangrenosum-like ulcerated lesions, deeply infiltrative plaques, and subcutaneous tumors. The tumor shows an aggressive behavior with 40-50% survival rate. Presentation of this lymphoma as sclerosing panniculitis is rare.

PCDLBL-LT presents with the classic immunophenotypic expression of germinal center markers (BCL-2 and BCL-6). CD10 is typically negative. The tumor expresses IRF4/MUM1, and FOXP3, consistent with an aggressive activated B-cell phenotype.

While it is more common for cutaneous T-cell lymphomas, like subcutaneous panniculitis-like T-cell lymphoma and cutaneous gamma/delta T-cell lymphoma, to present as panniculitis, B-cell lymphomas more commonly present as tumoral nodules. It is important for clinicians and dermatopathologists to be aware of the less common presentations of cutaneous large B-cell lymphomas presenting as panniculitis.

References:

1. Paulli M, Lucioni M, Maffi A, Croci GA, Nicola M, Berti E. Primary cutaneous diffuse large B-cell lymphoma (PCDLBCL), leg-type and other: an update on morphology and treatment. G Ital Dermatol Venereol. 2012;147(6):589-602.

2. Sukswai N, Lyapichev K, Khoury JD, Medeiros LJ. Diffuse large B-cell lymphoma variants: an update. Pathology. 2020;52(1):53-67. doi:10.1016/j.pathol.2019.08.013

ATYPICAL B CELL INFILTRATE FAVORING MARGINAL ZONE LYMPHOMA

Case No. 2

Presenter: Christina Carl, DO
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Foley, AL

HPI: Patient is a 69 yo female with history of metastatic malignant melanoma in remission, breast cancer, hypertension, and non-Hodgkin lymphoma. Patient follows with medical oncologist every 3 months and has PET scans because of melanoma and lymphoma history. Patient presented for a total body skin exam and was noted to have some unusual erythematous and telangiectatic plaques on her back.

Past Medical History
Malignant melanoma (right great toe, March 2020, Breslow thickness at least 2mm, ulceration, and increased mitosis. Treated with partial amputation of toe. Metastatic to lymph nodes. Treated with immunotherapy including Keytruda).
Non-Hodgkin lymphoma, Breast cancer, Hypertension, Lichen planopilaris

Physical Examination:
Left Medial Scapular Back: Erythematous edematous plaques with telangictasia.

Laboratory Data: None

Histopathology: Left Medial Scapular Back- Lateral to T5: Atypical B-Cell infiltrate, favor marginal zone lymphoma. The B-lymphocytes stain with antibodies to BCL-2 and CD 20, and there is kappa light chain restriction.

Clinical Course: Patient was referred to her medical oncologist, who recommended localized radiation to the area on her back. She completed radiation and is currently doing well.

Diagnosis: Atypical B-cell infiltrate, favor marginal zone lymphoma made based on clinical presentation and histopathology results.

Points of Emphasis: A patient with a history of non-Hodgkin lymphoma and malignant melanoma presents unique considerations. Approximately 25% of non-Hodgkin lymphoma cases present at extra-nodal site without systemic involvement, with the skin being the second most common primary site[1]. Incidence of primary cutaneous lymphoma is estimate at 0.5 to 1 case per 100,000 in Western countries, including about 20% cutaneous B cell lymphoma[1].

Primary Cutaneous Marginal Zone Lymphoma (PCMZL) accounts for 2-7% of primary cutaneous lymphomas, and about 10% of marginal zone lymphomas are primary cutaneous forms[2]. Predominantly affecting individuals in their fifth or sixth decade, PCMZL is diagnosed more frequently in men than women[3]. Potential triggers include tattoo pigment, tick bites, and antigen injections[4]. PCMZL typically presents as red to violaceous papules, plaques, or nodules localized on the trunk or upper extremities[2].

Given the patient's history of non-Hodgkin lymphoma, PCMZL is suspected to be a recurrence. Treatment is determined by lesion number, location, and symptom presence. Initial management involves local radiation therapy or surgical excision for lesions within a radiation field[2]. In cases of multiple localized lesions, second-line options include intra-lesional treatment with triamcinolone, interferon

alpha, or rituximab[2]. Regular follow-up every 6 months with comprehensive skin and lymph node examinations is recommended[2].

The prognosis for PCMZL is generally excellent, with a 5-year disease-specific survival rate close to 100%, which suggests that the patient has a high chance of recovery and long-term survival[4]. However, it is essential for the patient to undergo regular follow-up and adhere to prescribed treatment plan to ensure best possible outcome.

References:

1. Al-Katib A, Mohamed A, Primary Cutaneous B-Cell Lymphomas. Atlas of Genetics and Cytogenetics in Oncology and Haemotology 2019; 1-8

2. Vitiello P, Sica A, Ronchi A, Caccavale S, Franco R, Argenziano G. Primary Cutaneous B-Cell Lymphomas: An Update. Frontiers in Oncology 2020; 10;651;1-7

3. Servitje O, Muniesa C, Benavente Y, et al. Primary cutaneous marginal zone B-cell lymphoma: response to treatment and disease-free survival in a series of 137 patients. J Am Acad Dermatol 2013; 69:357.

4. Willemze R, Cerroni L, Kempf W, et al. The 2018 update of the WHO-EORTC classification for primary cutaneous lymphomas. Blood 2019; 133:1703.

CUTANEOUS PLASMACYTOSIS

Case No. 3a **PRESENTER:** Andrew J. DeCrescenzo, MD
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History: A 61-year-old Chinese male with no PMH presented with a pruritic and ill-defined light-pink erythematous plaques on the trunk in a geographic distribution and was treated for allergic contact dermatitis with triamcinolone 0.1% cream. The patient was lost to follow-up. The patient presented nine months later with evolution of his eruption.

Physical Examination: Examination revealed dark-red to brown papulonodules widespread predominately on the central abdomen and chest with some additional papules on the left flank. The remainder of the cutaneous surface and mucous membranes were spared. Lymph node examination did not detect any lymphadenopathy.

Laboratory Data: None.

Histopathology: Biopsy by deep shave technique from a nodule on the abdomen showed densely packed nodular aggregates of typical and mature plasma cells around vessels in the superficial and mid dermis. Immunoperoxidase stains showed a normal kappa:lambda ratio and negativity for CD20.

Clinical Course: The patient was referred to hematology-oncology for infusion of the interleukin-6 receptor inhibitor tocilizumab (Actemra).

Diagnosis: Cutaneous plasmacytosis.

Points of Emphasis: Cutaneous plasmacytosis (CP) is a rare polyclonal disorder histologically characterized by nodular aggregates of mature plasma cells. By some, it is considered a cutaneous counterpart of Castleman's disease. Clinically, CP presents with multiple red-brown papulonodules with predilection for the trunk; however, the face and extremities can be involved. It is usually seen in the Asian population—approximately 120 cases have been reported on Asian patients while about ten have been reported in Caucasians.

In the case series of five cases of this disorder by Han et al., laboratory investigation revealed elevated serum immunoglobulins (IgG in 80%) although in four cases the profile was polyclonal and in one single case a faint monoclonal restriction band was found in IgM and Igκ. In the case with a monoclonal band, there was also a polyclonal elevation of the remainder of the immunoglobulins. We therefore emphasize that if a protein electrophoresis is performed in patients with cutaneous plasmacytosis that this context be applied to prevent over treatment.

Therapy for cutaneous plasmacytosis is difficult with case reports attempting a litany of therapies with varying successes—topical steroids and topical calcineurin inhibitors, intralesional steroids, PUVA, and rituximab are all reported with few cases showing complete remission. Drs. Almazan and Jung reported in 2016 the partial response in one patient to monthly infusion (8mg/kg) of the IL-6 inhibitor tocilizumab. The pathophysiology of IL-6 inhibition inducing the remission of benign plasmacytic neoplasms stems from IL-6 being a key cytokine in terminal B-cell differentiation. Murine models support this as IL-6 null mice are unable to develop plasmacytic neoplasia. Anecdotally, the presenter (J.A.T.) has diagnosed and treated two cases of this disorder with tocilizumab infusion with complete response in both.

References:

1. Han XD, Lee SSJ, Tan SH, et al. Cutaneous plasmacytosis: a clinicopathologic study of a series of cases and their treatment outcomes. Am J Dermatopathol. 2018;40(1):36-42.
2. Aita T, Hamaguchi S, Shimotani Y, Nakamoto Y. Idiopathic multicentric Castleman disease preceded by cutaneous plasmacytosis successfully treated by tocilizumab. BMJ Case Rep. 2020;13(11):e236283.
3. Almazan TH, Jung JY. Cutaneous plasmacytosis treated with tocilizumab: a case report and review of the literature. Madridge J Dermatol Res. 2016;1(1):1-7.
4. Hilbert DM, Kopf M, Mock BA, Köhler G, Rudikoff S. Interleukin 6 is essential for in vivo development of B lineage neoplasms. J Exp Med. 1995;182(1):243-248.

TRAUMA-INDUCED METASTATIC CUTANEOUS PLASMACYTOMA

Case No. 3b

PRESENTER: Pavela Bambekova, MD
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History: A 69-year-old male with Stage III multiple myeloma diagnosed 24 years prior and previously treated with chemotherapy and palliative radiation presented with multiple, slowly enlarging masses to the right upper arm. Three months prior, he underwent intramedullary nailing for a proximal right humeral fracture. Shortly after, skin-colored papules and nodules began developing over the surgical site as well as his chin and occipital scalp.

Physical Examination: At initial presentation, physical exam revealed violaceous, firm nodules and plaques overlaying the surgical site. Additionally, two other discrete violaceous plaques were noted to the left occipital scalp and right chin.

Laboratory Data: n/a

Histopathology: Biopsy specimen showed dermal plasma cell infiltration with vesicular chromatin and prominent nucleoli. CD138, CD56, and kappa light chain were positive, while AE1/3, CD3 and lambda light chain were negative. These findings were suggestive of cutaneous plasmacytoma.

Clinical Course: Biopsy of the three sites revealed cutaneous involvement by myeloma, suggesting cutaneous plasmacytoma. Affected areas were treated by local wound care.
Chemotherapy with daratumumab, pomalidomide, dexamethasone was initiated. The patient underwent autologous stem cell transplant three months later. Over the next few months with chemotherapy, the skin nodules clinically improved; however, the patient did succumb to the disease, only 1 year after the initial biopsy and unfortunately passed away.

Diagnosis: Cutaneous plasmacytoma

Points of Emphasis: Plasmacytoma is a proliferative mass of monoclonal plasma cells, most often arising from the bone marrow. Rarely, metastatic spread of multiple myeloma after surgery may result in cutaneous plasmacytoma. Our literature review shows only a handful of cases of secondary cutaneous plasmacytomas occurring in sites of trauma, and none of which appear as severe as our case. The mechanism is unknown, but theories include direct extension from bone during the fracture, inoculation of tumor cells during surgery, or a trauma-induced plasma cell migration. Due to the small number of cases reported, there are no discrete treatment recommendations, leading to less provider awareness of this differential.

References:

1. Yoo J, Jo M, Kim MS, Jue MS, Park HJ, Choi KH. Cutaneous Plasmacytoma: Metastasis of Multiple Myeloma at the Fracture Site. Ann Dermatol. 2017 Aug;29(4):483-486. doi: 10.5021/ad.2017.29.4.483. Epub 2017 Jun 21. PMID: 28761299; PMCID: PMC5500716.
2. Gaba RC, Kenny JP, Gundavaram P, Katz JR, Escuadro LR, Gaitonde S. Subcutaneous plasmacytoma metastasis precipitated by tunneled central venous catheter insertion. Case Rep Oncol. 2011 May;4(2):315-22. doi: 10.1159/000330044. Epub 2011 Jun 30. PMID: 21738502; PMCID: PMC3130982.

HYPOPIGMENTED MACULES IN A PATIENT WITH MULTIPLE MYELOMA

Case No. 4

Presenters: Scout Treadwell, Medical Student
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History:
A 52-year-old African American male with a history of hypertension, treated Hepatitis C, and a recent diagnosis of multiple myeloma was admitted for the initiation of chemotherapy. The patient noted the presence of light spots on his skin that have been worsening over the past two years. Initially, he observed dark spots on his lower legs, which subsequently transformed into light spots and spread to involve his hands, arms, and thighs. He associates the onset of these skin changes with receiving the COVID vaccine a few weeks prior. The patient reports generalized itching and has not used any topical medications or moisturizers.

Physical Examination:
- **Arms**: Scattered hypopigmented macules coalescing into patches across the bilateral dorsal forearms, upper arms, and shoulders.
- **Legs**: Guttate hypopigmented macules scattered across the bilateral lower legs and thighs, with a few hyperpigmented scaly papules on the right proximal anterior lower leg. Mild xerosis was observed.
- **Lymph**: No palpable lymphadenopathy

Laboratory Data:
The CBC results on initial consult showed **Hgb 7.9** and a **platelet count 129**. CMP showed a **glucose level of 211**, **BUN 68.0**, **Cr 2.04**, **calcium 10.8**, and **eGFR of 38**. SPEP showed the albumin level at 3.7, gamma globulin at 2.3, and an M spike at 2.0. The LDH was slightly elevated at 211.

Histopathology:
Skin, right upper arm, biopsy:
- Superficial perivascular dermatitis with limited epidermotropism. Early evolving mycosis fungoides is not ruled out. Cutaneous amyloidosis is suspected.

Microscopic Description:
Sections show skin with superficial perivascular lymphocytic infiltrate, accompanied by mild dermal edema. Few lymphocytes within the epidermis are seen. Limited deposit of eosinophilic amorphous material in the dermis and subcutaneous tissue, highlighted weakly on the Congo red stain.

Immunophenotyping study:
CD3+, CD4+, CD5+, CD7+/-, CD8+, CD20 highlights few B-lymphocytes, CD30-, CD43+, Ki-67 (5-10%). PAS stain is unremarkable. Controls stain appropriately.

Clinical Course:
The patient initiated chemotherapy, a combination of cyclophosphamide, bortezomib, and dexamethasone for multiple myeloma and subsequently had a follow-up appointment in the dermatology clinic. Re-biopsy was recommended, but the patient declined. The patient was unable to undergo recommended nbUVB therapy due to their incarceration status. The patient was prescribed triamcinolone 0.1% cream twice daily which led to an improvement in pruritus and a mild alleviation of hypopigmentation.

Diagnosis:
Hypopigmented mycosis fungoides vs cutaneous amyloid

Points of Emphasis:
The coexistence of multiple myeloma (MM) and mycosis fungoides (MF) has been sparsely reported in the medical literature. One documented case involved a patient diagnosed with plaque-stage MF alongside MM. Notably, the onset of MF symptoms preceded those of MM, suggesting a potential predisposition of the patient to the development of the B-cell proliferative disorder, MM. [1]

In this patient, skin tumor cells were identified as originating from CD4+ T-lymphocytes, displaying a polarized Th1-type cytokine profile characterized by the expression of mRNAs for interleukin (IL)-2, interferon (IFN)-γ, and tumor necrosis factor (TNF)-β, while lacking expression of Th2 cytokines such as IL-4, IL-5, or IL-10. Furthermore, the patient exhibited an elevated CD8+/CD57+ suppressor-cytotoxic cell subpopulation in peripheral blood, which correlated with MM progression.[1]

Additionally, the study revealed that hypermethylation silenced the p16INK4A gene, a regulator of the cell cycle, in both MF cells and bone marrow plasma cells. This finding suggests that p16INK4A may contribute to the early phases of the pathogenesis of both MF and MM. This case highlights a rare possibility of two distinct types of cancer, MF and MM, in the same patient. It suggests that there may be shared molecular alterations and immune responses that contribute to the development and progression of both diseases.[1]

The diagnosis of early Mycosis Fungoides can often be challenging. The International Society of Cutaneous Lymphoma created a scoring algorithm based on clinical, histopathological, T-cell receptor clonality, and immunopathological criteria that can help in early detection. [2] A score of 4 or greater correlates with a positive diagnosis. In this patient, clinical and histopathological criteria gained him 3 points. This cannot rule out the diagnosis, and a T-cell receptor clonality study was not performed for additional scoring information.[2]

A systematic review identified 32 cases of patients concurrently affected by multiple myeloma and cutaneous manifestations of amyloidosis.[3] The majority of patients presented with hemorrhagic bullous lesions, followed by purpura/ecchymosis in 25% of cases.[3] Interestingly, all κ light chain subtypes were associated with bullous lesions and no other types of cutaneous manifestations. Unfortunately, these cases carried a very poor prognosis, with most patients surviving only six months, significantly worse than patients with either AL amyloidosis without myeloma or myeloma without amyloidosis.[3]

It is crucial to distinguish between topical steroids and the chemotherapy regimen to identify the source of lesion improvement. The patient's chemotherapy has the potential to alleviate the lesions. The improvement observed is likely due to the combination of topical steroids and systemic steroids through his chemotherapy. Furthermore, it is advisable to reconsider performing a biopsy on these lesions, as the initial biopsy did not provide a definitive diagnosis.

References:

1. Gernone A, Frassanito MA, Pellegrino A, Vacca A, Dammacco F. Multiple myeloma and mycosis fungoides in the same patient: clinical, immunologic, and molecular studies. Ann Hematol 2002;81(6):326-31. DOI: 10.1007/s00277-002-0452-9.
2. Xu C, Wan C, Wang L, Yang HJ, Tang Y, Liu WP. Diagnostic significance of TCR gene clonal rearrangement analysis in early mycosis fungoides. Chin J Cancer 2011;30(4):264-72. DOI: 10.5732/cjc.010.10344.

3. Andrei M, Wang JC. Cutaneous light chain amyloidosis with multiple myeloma: A concise review. Hematology/Oncology and Stem Cell Therapy 2019;12(2):71-81. DOI: https://doi.org/10.1016/j.hemonc.2018.09.003.

LEUKEMIA CUTIS

Case No. 5

Presenters: Jocelyn Carnicle, MD
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History: 73yo AA male with PMH of CVA, PAD, PTSD, depression, & spinal stenosis, presented to clinic for initial evaluation of a new rash which began 2 months prior to being evaluated in dermatology. He reports it initially began as a few red raised papules to posterior neck. The patient was given Triamcinolone 0.1% cream in the ED at initial onset, and incidentally was noted to have pancytopenia at time of onset of rash.

At time of evaluation with dermatology the papular eruption had progressed to involve the entire back, face, and extremities. The rash was completely asymptomatic without any associated pruritus, pain, or burning features. On further questioning the patient did endorse a 40lb unintentional weight loss in 5 months, worsening fatigue and shortness of breath, intermittent headaches and occasional drenching night sweats. The patient denied any personal or family history of skin cancer, leukemia or lymphoma. On review of EMR, it was noted that his PCP had repeated his CBC multiple times for pancytopenia on labs. The first noted evidence of pancytopenia initially began 1.5 years prior to evaluation with dermatology but no further workup was done.

Physical Exam:
-Diffuse erythematous firm papules, particularly noted to back, neck, head, upper extremities; sparing most of the abdomen and lower extremities
-Cervical and axillary lymphadenopathy was present
-No oral involvement or noted gingival hyperplasia

Laboratory Data on presentation to dermatology clinic:

Test	Result / Status	Flag	Units	Ref Range
IMMATURE RETIC FRACTION	0.25	L		0.30 - 0.54
WBC	2.6	L	K/uL	4.8 - 10.8
RBC	2.92	L	M/uL	4.50 - 6.10
HGB	8.0	L	g/dL	14.0 - 18.0
HCT	23.0	L	%	42.0 - 52.0
MCV	78.9	L	fL	81.0 - 98.0
RDW-CV	14.9		%	11.8 - 14.9
MCH	27.3		pg	27.0 - 32.6
MCHC	34.7		g/dL	32.2 - 34.8
PLT COUNT	57	L	K/uL	140 - 420
MPV	9.6		fL	7.4 - 10.8
SEGS%	5	L	%	44 - 77
BANDS%	2		%	0 - 11

Test	Result / Status	Flag	Units	Ref Range
LYMPHS%	38		%	16 - 46
MONOS%	45	H	%	1 - 10
EOSINO%	2		%	0 - 6
META%	2	H	%	
MYELO%	5	H	%	
ABSOLUTE NEUTROPHIL COUNT	0.2	L	K/uL	1.7 - 7.2
LYMPHS#	1.1		K/uL	0.9 - 3.4
MONOS#	1.2	H	K/uL	0.0 - 0.9
EOSINO#	0.1		K/uL	0.0 - 0.4
ATYPICAL LYMPHOCYTES	2	H	%	
ANISOCYTOSIS	1+			
POIKILOCYTOSIS	1+			
MICROCYTOSIS	1+			
PLT. EST	DECREASED			
PLT GIANT	PRESENT			
RETICULOCYTE %	<0.45		%	0.80 - 3.10
ABSOLUTE RETIC COUNT	9.90	L	K/uL	49.00 - 166.00

Test	Result / Status	Flag	Units	Ref Range
FERRITIN	1143	H	ng/mL	24 - 336
SODIUM	136		mEq/L	136 - 144
POTASSIUM	4.1		mEq/L	3.6 - 5.1
CHLORIDE	105		mEq/L	101 - 111
CO2	24		mEq/L	22 - 32
UREA NITROGEN	15		mg/dL	7 - 20
CREATININE	1.8	H	mg/dL	0.6 - 1.3
eGFR (CKD-EPI 2021)	39			
GLUCOSE	111	H	mg/dL	70 - 110
CALCIUM	8.9		mg/dL	8.9 - 10.3
SGOT	22		IU/L	15 - 41
SGPT	16		IU/L	12 - 63
ALKALINE PHOSPHATASE	39		IU/L	38 - 126
PROTEIN,TOTAL	7.5		g/dL	6.7 - 8.5
ALBUMIN	4.0		g/dL	3.5 - 5.0
TOT. BILIRUBIN	0.5		mg/dL	0.1 - 1.3
URIC ACID	8.0	H	mg/dL	4 - 7.5
IRON	169		ug/dL	50 - 170
TRANSFERRIN	151.3	L	mg/dL	180.0 - 329.0
ESTIMATED % SATURATION	89		%	
TSH	1.88		mIU/mL	0.34 - 5.6

Test	Result / Status	Flag	Units	Ref Range
FIBRINOGEN	248		mg/dL	221 - 430
D-DIMER	3.51	H	ug/mL FEU	0.00 - 0.50
THROMBIN TIME	16.1		Sec	14.0 - 21.0

Histopathology:
1/2 punch biopsy of R upper back
2/2 punch biopsy of R medial forearm
Impression: atypical monocytoid infiltrate suspicious for leukemia cutis
Both specimens consist of nonsectioned punch biopsies with similar histological features. An atypical mononuclear cell infiltrate with dispersed chromatin pattern intercalates through dermal collagen. These cells collect around blood vessels and adnexal structures. Immunostains postive for: CD33, CD4, lysozyme, and CD68. The cells of interest have a high Ki67 index. The following stains are negative: CD34, CD117, CD56. CD2, CD3, CD7, CD8, CD10, CD30, CD20, CD79a, TIA1, CD123, TdT.

Diagnosis: Leukemia Cutis

Clinical Course:
On initial dermatologic evaluation 2 punch biopsies were performed and the patient was referred directly to heme onc for further workup given such strong concern for underlying cancer. Bone Marrow biopsy was performed 2 weeks after evaluation with dermatology, which showed 1) high grade myeloid neoplasm with monocytic differentiation, 2) megakaryocytic dysplasia, and 3) marked, stage 3, reticulin and collagen fibrosis, which can be seen with acute monocytic leukemia, late stage chronic myelomonocytic leukemia, and high grade myelodysplastic syndrome. These results were particularly concerning for impending transformation to AML. Labs were negative for Calreticulin mutation analysis (CALR), MPL analysis (myeloproliferative leukemia virus oncogene), and JAK2 mutation. He was admitted for worsening anemia on multiple occasions that month while workup was being performed, each time requiring transfusions of multiple units of blood. CT head was performed which showed 2 dural based nodules (>10mm) concerning for metastatic disease. Repeat Bone Marrow biopsy was eventually performed which ultimately diagnosed the patient with AML, but the patient quickly decompensated prior to any treatment for AML and his hospitalization transitioned to focusing on palliative care. Unfortunately, 2.5 months from initial evaluation with dermatology the patient ultimately passed away due to progressive AML with metastatic disease.

Points of emphasis:
Leukemia cutis (LC), the cutaneous involvement of leukemia, occurs when neoplastic leukocytes infiltrate the epidermis, dermis, or subcutis. Cutaneous manifestation is more commonly associated with acute myeloid leukemia (AML) and chronic lymphocytic leukemia (CLL) but may also be seen in other leukemia subtypes. LC may be seen in up to 4% of patients that have AML, more commonly seen in acute myelomonocytic and moncytic subtypes.[1] Clinically, leukemia cutis lesions are polymorphous and may present as erythematous or violaceous papules, nodules, or plaques that may be localized or diffuse.[2,3] The lesions may be also be painful or pruritic. LC may resemble a wide range of neoplastic, inflammatory, or infectious skin lesions resulting in a vast differential diagnosis that may include sarcoidosis, drug reactions, lymphoma or pseudolymphoma, or mycosis fungoides.[2] Because the cutaneous presentations of LC are diverse, skin punch biopsy for examination and immunohistochemical staining are essential for diagnosis. Pathology and immunotyping vary based on the type of underlying leukemia, and histologic patterns including perivascular, interstitial nodular, diffuse, and periadnexal are seen. Lymph node biopsy and bone marrow biopsy are performed by an oncologist to make a diagnosis of systemic leukemias. More than 20% blasts in the bone marrow is required for a diagnosis of AML.[4]

Most LC is seen in patients with a prior diagnosis of leukemia as the majority of patients presenting with LC already have systemic involvement. However, in rare cases the cutaneous involvement may be the primary manifestation of systemic leukemia.[1,2] In this patient's case, the absence of an established systemic leukemia diagnosis represented a diagnostic challenge, requiring clinical and histopathological correlation. Treatment is typically aimed at addressing the underlying leukemia with systemic chemotherapy. However, Leukemia cutis is often a sign of advanced leukemia and is associated with a poor prognosis. Specifically for AML patients with LC the two-year survival rate is only 6%.[5] This case highlights the potential clinical dilemma in diagnosing leukemia cutis given its ability to resemble a variety of benign, common skin lesions. Early recognition and biopsy are thus essential for dermatologists, given the severity of rapid decline and associated poor prognosis.

References:

1. Osmola M, Gierej B, Kłosowicz A, Waszczuk-Gajda A, Basak GW, Jędrzejczak WW, Jurczyszyn A, Ziarkiewicz-Wróblewska B. Leukaemia cutis for clinicians, a literature review. Postepy Dermatol Alergol. 2021 Jun;38(3):359-365. doi: 10.5114/ada.2021.107923. Epub 2021 Jul 26.

2. Li AW, Yin ES, Stahl M, Kim TK, Panse G, Zeidan AM, Leventhal JS. The skin as a window to the blood: Cutaneous manifestations of myeloid malignancies. Blood Rev. 2017 Nov;31(6):370-388. doi: 10.1016/j.blre.2017.07.003. Epub 2017 Jul 14.
3. Su WPD, Buechner SA, Chin-Yang L. Clinicopathologic correlations in leukemia cutis. J Am Acad Dermatol. 1984;11:121-128.
4. Damon LE, Andreadis C. Blood disorders. In: Papadakis MA, McPhee SJ, Rabow MW, eds. Current Medical Diagnosis & Treatment 2016. New York, NY: McGraw-Hill; 2016:495-541.
5. Rao AG, Danturty I. Leukemia cutis. Indian J Dermatol. 2012;57:504.

SDRIFE SYNDROME

Case No. 6

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History: A 52-year-old patient presented to the dermatology clinic with an itchy "rash" on the right anterior proximal thigh. The patient first noticed the condition two weeks prior to presentation.

Physical Exam: Physical examination of the right anterior proximal thigh revealed a well-demarcated, erythematous, non-scaly plaque, approximately 6 cm in diameter. There was slight central clearing and was localized to the intertriginous area.

Histopathology: Microscopic examination revealed a superficial perivascular infiltrate of lymphocytes with a slight amount of spongiosis and epidermal hyperplasia. No lymphocytic infiltrate was seen in the superficial and deep dermis. A Periodic Acid-Schiff (PAS) stain was negative for hyphae.

Diagnosis: Symmetrical Drug-related Intertriginous and Flexural Exanthem (SDRIFE)

Points of Emphasis: The importance of clinicopathologic correlation in the diagnosis of skin lesions is emphasized by this case. In the initial differential diagnosis, the possibilities of erythema chronicum migrans, fixed drug eruption, erythema annulare centrifugum, and tinea corporis were considered. However, the clinical presentation in conjunction with histopathological findings led to the diagnosis of SDRIFE.

SDRIFE is an uncommon diagnosis typically linked to systemic drug exposure, or to contact allergens. Commonly, lesions are distributed along the buttocks and inner thighs. SDRIFE is associated with use of beta-lactam antibiotics, but has also been associated with pristinamycin, clindamycin, erythromycin, roxithromycin, and cotrimoxazole, as well as antifungal and antiviral medications.

Histopathology is variable and may present with mononuclear infiltrate, neutrophils, and eosinophils; however, vacuolar changes, subepidermal bullae, spongiosis and epidermal hyperplasia may also be present. The subtle and varied histopathologic findings in SDRIFE underscore the need for strong history taking and clinical correlation to make an accurate diagnosis.

Clinicians and pathologists should remain aware of this condition as a possible cause of localized erythema, especially in the absence of other findings suggestive of the initial differential diagnoses.

References:

1. Muresan AM, Metze D, Böer-Auer A, Braun SA. Histopathological Spectrum and Immunophenotypic Characterization of Symmetrical Drug-Related Intertriginous and Flexural Exanthema. Am J Dermatopathol. 2021;43(2):103-111. doi:10.1097/DAD.0000000000001722
2. Schuler AM, Smith EH, Chaudet KM, et al. Symmetric drug-related intertriginous and flexural exanthema: Clinicopathologic study of 19 cases and review of literature. J Cutan Pathol. 2021;48(12):1471-1479. doi:10.1111/cup.14090

ERYTHEMA NODOSUM

Case No. 7

Presenter: Christian Scheufele, DO
Michael Carletti, DO
Stephen Weis, DO
Clay J. Cockerell, MD, MBA, JD
Fort Worth, TX
Dallas, TX

History:
52-year-old female presents with a 3-week history of tender, red lesions on her bilateral thighs that gradually spread down her legs. She remembers feeling ill with generalized body aches and gastrointestinal upset a few days prior to the onset of these lesions. She's never had these lesions before. The newest lesions are acutely tender to the touch.

She takes no prescription medications, has no chronic medical conditions, and had no other recent illnesses.

She has a history of abdominoplasty in Mexico 1-1.5 years ago. She had no complications from this procedure. No other history of cosmetic procedures.

Physical Examination:
On the bilateral lateral thighs, knees, and proximal anterior legs, there are numerous erythematous to hyperpigmented subcutaneous nodules. There are scattered hyperpigmented patches.

Laboratory Data:
CBC within normal limits
QuantiFERON gold negative on 03/13/23
2-view chest XRAY negative

Histopathology:
Punch biopsies of the right medial thigh and right lateral thigh show a periseptal neutrophilic infiltrate with edema and thickening of the septae.

Clinical Course:
Patient was started on prednisone 40 mg daily. She reported improvement in her pain the day after starting treatment. She was tapered over the course of a month with improvement of the lesions. She was lost to follow up after her treatment.

Diagnosis:
Erythema nodosum (EN)

Points of Emphasis:
1. EN is the most common form of panniculitis and is often idiopathic but can be associated as the first sign of a systemic disease (including infections, inflammatory and autoimmune diseases, malignancies, and various medications).
2. EN has been associated with specific systemic diseases including Behçet disease, sarcoidosis, inflammatory bowel disease.
3. EN typically presents on the pretibial surface of the bilateral lower extremities but can less frequently involve the knees, thighs, and upper extremities.

References: (At least two recent pertinent published references)

1. Pérez-Garza, D. M., Chavez-Alvarez, S., Ocampo-Candiani, J., & Gomez-Flores, M. (2021). Erythema nodosum: a practical approach and diagnostic algorithm. *American Journal of Clinical Dermatology*, *22*(3), 367-378.

2. Requena, L., & Sánchez Yus, E. (2007, June). Erythema nodosum. In *Seminars in cutaneous medicine and surgery* (Vol. 26, No. 2, pp. 114-125). WB Saunders.

POSSIBLE PITYRIASIS RUBRA PILARIS

Case No. 8

Presenter: Alexandria Brown, MD
New Orleans, LA

History:
A 36-year-old male with no significant past medical history presented to dermatology for evaluation of a rash on his trunk and proximal arms, . The patient reported the rash started approximately two months prior on his back and proximal arms and was asymptomatic. The rash then spread to his lower chest and upper abdomen following a cholecystectomy he underwent a few weeks after the rash's onset, specifically adjacent to the skin that was shaved prior to the procedure. He denied the use of any new soaps, detergents, lotions, medications, or prodromal systemic symptoms. The patient's family history was significant for systemic lupus erythematous in his mother, otherwise non-contributory.

Physical Examination:
Throughout the posterior neck, back, proximal arms, chest, and upper abdomen there were numerous erythematous folliculocentric discrete papules coalescing into plaques with few scattered pustules and hypopigmented, alopecic patches. Palms and soles clear.

Laboratory Data:
A KOH fungal scraping was negative. A bacterial culture of a pustule showed normal skin flora.

Histopathology:
The 1st biopsy of the right upper back revealed acute folliculitis, with inflammatory infiltrate extending to the upper reticular dermis. Bacteria and Pityrosporum spores (saprophytes) were identified in the lumen of the follicular infundibulum.

Clinical Course:
The patient was started on doxycycline 100 mg twice daily for two months and ketoconazole 2% shampoo. At follow-up, the rash failed to improve and the patient was switched to minocycline 100 mg daily. Two months later, the rash persisted, and physical examination was notable for more confluent erythematous-to-orange plaques with follicular prominence and decreased islands of sparing and hypopigmented alopecic patches on the posterior neck and back. Four months after his initial visit, repeat biopsies on the right shoulder and mid-back continued to reveal non-specific findings noting acute folliculitis and perifolliculitis. The histopathologic report noted the interfollicular epidermis to show mild irregular acanthosis and spongiosis with a mild superficial perivascular lymphocytic infiltrate with occasional plasma cells and rare eosinophils. PAS was negative and there was no evidence of epidermotropism. At the most recent follow-up visit, given the initial biopsy results containing pityrosporum spores, a trial of fluconazole 200 mg daily for two weeks was prescribed in addition to an experimental trial of triamcinolone 0.1% cream twice daily and tazarotene applied to separate affected areas.

Diagnosis:
There is a high clinical suspicion for pityriasis rubra pilaris, however expert consensus would be appreciated.

Points of Emphasis:
As a result of the patient's failure to respond to multiple treatment regimens for folliculitis, in conjunction with the rash's evolution into erythematous-to-orange plaques with follicular prominence with islands of sparing and hypopigmented alopecic patches, a high clinical suspicion for pityriasis rubra pilaris remains.

Pityriasis rubra pilaris can be a diagnostic challenge and is frequently associated with diagnostic delays due to its overlap with other inflammatory conditions.

References:

1. Ross NA, Chung HJ, Li Q, Andrews JP, Keller MS, Uitto J. Epidemiologic, Clinicopathologic, Diagnostic, and Management Challenges of Pityriasis Rubra Pilaris: A Case Series of 100 Patients. *JAMA Dermatol*. 2016;152(6):670-675. doi:10.1001/jamadermatol.2016.0091

2. Ji-Xu A, Lei DK, Maloney NJ, Worswick S. Clinical course, diagnostic patterns, and treatment outcomes in patients with pityriasis rubra pilaris. *J Am Acad Dermatol*. 2022;87(6):1450-1451. doi:10.1016/j.jaad.2022.07.039

CHEMOTHERAPY-RELATED ERUPTION AND LIPODERMATOSCLEROSIS

Case No. 9

Presenters: Jacob Robertson, MD
Cassidy Nguyen, BS
Edgar Martinez, MD
Brett Keeling, MD
Khang Nguyen, MD
Austin, Texas

Case History:
58 year old female with a history of stage IV non-small cell lung cancer on 3 months of chemotherapy Pemetrexed (Alimta) who presents with a 10-day history of bilateral lower extremity edema, swelling, pain, & warmth.

She reports this swelling and erythema occurred the day after her last chemotherapy session. She was prescribed doxycycline given no improvements in her symptoms with concerns for cellulitis. Interestingly, she had a similar presentation a month prior, one day after chemotherapy. At that time, she was prescribed a course of vancomycin and doxycycline with resolution shortly thereafter.

The patient recently had bilateral lower extremity MRIs that showed soft tissue swelling without evidence of abscess, tenosynovitis, or osteomyelitis. She has a history of deep vein thrombosis and is on Lovenox daily.

There were no concerns for trauma or injury during the present case, with the patient denying subjective fevers, red streaking, arthralgias, or body aches. The patient was initially diagnosed with cellulitis and started on a course of clindamycin while admitted. The differential includes pemetrexed-induced pseudocellulitis vs venous stasis versus lipodermatosclerosis versus Sweet's syndrome.

Physical Examination:
On physical examination, there was 2+ bilateral lower extremity edema, warmth, redness, tenderness to palpation more so on the left than right ankles. No vesicles, pustules, or skin sloughing was noted. (images included demonstrating bilateral, anterior ankles, please see final pages for clinical images)

Laboratory Data:
Labs showed pancytopenia/chronic neutropenia, anemia, thrombocytopenia similar to prior labs; Low WBC (3.6) RBC (2.07) HgB (7.1) platelet (135) with elevated MCV (104.3) Electrolytes were within normal limits with exception of mild hyponatremia.
CRP was elevated to 4.2.
Sodium level (135). Glucose (144).

Histopathology:
Histopathologic findings from a 4mm punch of the left medial lower leg includes vacuolar interface dermatitis and squamous metaplasia of eccrine coils and ducts, sparse mixed interstitial inflammatory infiltrate, and widened subcutaneous fibrous septa with cystic fat degeneration.

Clinical Course:
We recommended supportive care with cleansing the area daily with gentle soap and water, dry, and reapply vaseline to the biopsy site. Patient was given prednisone 10mg as well as topical clobetasol 0.05% cream, leading to resolution of clinical symptoms.

Diagnosis:
The predominant findings in this biopsy are those of chemotherapy-related skin eruptions and lipodermatosclerosis. The mixed interstitial infiltrate is not entirely specific but could be seen in the setting of a hypersensitivity eruption. Stains were negative for infectious organisms.

Points of Emphasis:
We highlight a case of pemetrexed-associated chemotherapy pseudocellulitis. Clinical examination of patients with this hypersensitivity condition often mimic cellulitis, emphasizing the importance of considering pseudocellulitis in the differential of patients on chemotherapy.[1] Histopathology often presents very similarly to typical cellulitis, though clinical correlation, specifically demonstrating bilateral edema like that seen in our case, is critical to allow for differentiation.[2]

References:
Wollina U, Hansel G, Zschuppe E, Tchernev G. PEMETREXED-INDUCED PSEUDOCELLULITIS - A RARE CUTANEOUS ADVERSE REACTION TO MULTI-TARGETED ANTIFOLATE THERAPY. *Georgian Med News*. 2017;(267):81-84.

Tracey EH, Modi B, Micheletti RG. Pemetrexed-Induced Pseudocellulitis Reaction With Eosinophilic Infiltrate on Skin Biopsy. *Am J Dermatopathol*. 2017;39(1):e1-e2. doi:10.1097/DAD.0000000000000645

SUSPECTED WONG-TYPE DERMATOMYOSITIS

Case No. 10

Presenter: Carly Stevens, MS4
Ruby Gibson, MD
Ghaidaa Majari, MD
Leah Jacob, MD
New Orleans, LA

History: A 23-year-old female with a history of asthma but otherwise healthy was admitted to Tulane Medical Center (TMC) for rash covering 90% of body surface area (BSA) that was present and stable for 7 years. The patient reports the rash was biopsied and told she had subacute lupus and previously on hydroxychloroquine and cellcept but self-discontinued prior to admission. The patient denied any family history of connective tissue diseases and denied any systemic symptoms. She was biopsied, prescribed a prednisone 20mg taper and topical triamcinolone 0.1% cream.

Physical Examination:
Head and neck: No involvement of the scalp. Erythematous nonscaling macules coalescing into patches on malar cheeks/ears with perioral sparing
erythematous scaly reticular poikilodermatous plaques on upper/lower extremitites and trunk with notable sparing of central lower back
Nails: onycholysis, cuticular ruffling. No dilated capillary loops

Laboratory Data: The following lab workup throughout her clinical course was unremarkable: anti-nuclear antibody (Ab), anti-EJ Ab, anti-Jo-1 Ab, Anti-Ku Ab, Anti-MDA-5Ab, Anti-Mi-2 Ab, Anti-NXP-2 Ab, Anti-OJ Ab, Anti-PL, Anti-PM/Scl-100 Ab, Anti SAE1 Ab, Anti-SRP Ab, Anti SSA, Anti-TIF, Anti RNP Ab, lupus anticoagulant, antiphospholipid antibodies panel, CKMB, double stranded DNA antibody, anti-cardiolipin, urine analysis, C-reactive protein, complete metabolic panel, erythrocyte sediment rate, creatine kinase (multiple), aldolase (multiple), antibody, lipid panel , PTT
Complete blood count: Mild microcytic anemia (Hgb 10.4) and thrombocytosis (474)

Histopathology:
Lichenoid dermatitis with prominent melanin incontinence. No features of dermatomyositis are identified. Microscopic Description - lichenoid lymphocytic infiltrate accompanied by prominent melanin incontinence, basal vacuolar change, and scattered dyskeratosis. The epidermis shows mild hyperkeratosis, and parakeratosis. An Alcian blue stain highlights minimal mucin within the dermis. Pityrosporum yeasts, cocci and Demodex are identified on H&E sections in hair follicles. No microorganisms are highlighted on PAS or T. pallidum stains with adequate control.

Clinical Course:
The patient reported that the prednisone seems to be alleviating some redness and scale and denied any joint pains, muscle pain/weakness, mouth sores, weight loss, and changes in vision. At this point in her clinical course, the differential diagnosis was undifferentiated mixed connective tissue disease vs. amyopathic dermatomyositis. With this differential, the patient was recommended for malignancy screening with gynecology (negative) and a CT Chest/Abdomen & Pelvis with contrast was ordered (bilateral axillary and subpectoral lymph nodes and a 6mm calcified lung nodule). The patient was restarted on plaquenil at 200 mg BID, cellcept 500 mg BID, and continued on prednisone 10mg daily which the patient reported to help with her erythema/scale. With the prednisone taper decrease the patient was noted to have increased facial erythema but no desquamation/dryness and so cellcept was increased to 500 mg qam + 1000 mg qpm.

Five months after the initial presentation, she was re-biopsied as had minimal improvement and came back as lichenoid dermatitis. The differential diagnosis at this time included lichenoides chronica versus Wong-type Dermatomyositis versus undifferentiated mixed connective tissue disease was determined for this patient.

The patient was then switched to halobetasol propionate & tazarotene, plaquenil, prednisone 5mg (calcium and vitamin D added) and upadacitinib 15mg daily. After three months of upadacitinib and no subjective improvement, the patient was discontinued given lack of efficacy. The insurance denied apremilast. Methotrexate was restarted at 10mg weekly and her rash was unchanged and she noted occasional burning with typical application of triamcinolone.

Diagnosis:
Suspected Wong-Type Dermatomyositis

Points of Emphasis:
We present this case for discussion of diagnosis and management.
Wong-Type dermatomyositis (DM), is characterized by keratotic follicular papules that can mimic pityriasis rubra pilaris (PRP) and is a rare variant of DM. This diagnosis is hard to make and is often confused with other disorders such as PRP and discoid lupus erythematous.[1] This can be seen in our patient, who was given an initial diagnosis of subacute lupus. Pathology in Wong's DM typically reveals follicular and non-follicular epidermal invaginations filled with keratin. Our patient lacked this histopathology finding, but her clinical course was similar to others described in the literature. Wong-Type DM, like typical DM, can have associated myositis and interstitial lung disease.[2] However, unlike typical DM, the association with malignancy is not well established. Routine cancer screening should still be included as part of management for these patients.

Treatment of Wong's DM is based off on previous case reports. It depends on the severity of the patient's cutaneous and systemic disease involvement. Systemic steroids and immunosuppressants have been used and shown to have variable responses.[2,3] Medication ineffectiveness can make management of this condition difficult, leading to prolonged disease burden. Knowledge of this rare disease in association with its clinical and histopathological presentation can improve diagnosis ability and treatment, improving patient outcomes.

References:
1. Mutasim DF, Egesi A, Spicknall KE. Wong-type dermatomyositis: a mimic of many dermatoses. *J Cutan Pathol*. 2016;43(9):781-786.
2. Ashraf R, Kumar S, Chatterjee D, Sehgal IS, Vinay K. Wong-Type Dermatomyositis: A Report of Two Cases. *Indian Dermatol Online J*. 2023;14(4):547-548. Published 2023 May 25.
3. Argobi Y, Fedeles F, Schoenfeld SR. A case of Wong-type dermatomyositis treated with rituximab and IVIG. *Australas J Dermatol*. 2021;62(1):e86-e87.

GIANT DERMATOFIBROMA

Case No. 11

PRESENTER: Ciaran Smythe, DO[1]
Chris Bandel, BS[1]
Clay Cockerell, MD[1]
Dallas, TX[1]

History and Physical Examination: A 27-year-old female with a PMH of T2DM and anemia presented to a clinic with a mass on her left thigh for "several" months. The lesion had grown rapidly and become pruritic and tender. The patient denied systemic symptoms like fever or weight loss.

Histopathology: Excisional biopsy of the lesion demonstrated a bulky tumor filling the entire dermis which is composed of fibrohistiocytic cells. These cells range from plump histiocytes with abundant foamy cytoplasm to slender bipolar fibrocytes. The stroma is collagenous and varies from dense sclerotic areas to zones with minimal stroma. Dilated blood vessels are also present throughout the specimen. The overlying epidermis shows reactive basaloid hyperplasia.

Clinical Course: The lesion was removed by wide local excision. Given the benign nature of this lesion, no long term follow up was needed after wound healing had occurred.

Diagnosis: Giant dermatofibroma, aneurysmal variant

Points of Emphasis: Dermatofibromas (DFs), also known as fibrous histiocytomas, are a common benign dermal proliferations of collagen, histiocytes, fibroblasts, and capillaries. Their cause is unknown, and they tend to present as asymptomatic 0.2-2 cm skin-colored, pink, or hyperpigmented papules or nodules that persist for life. DFs most commonly appear on the legs of young adult women [1]. On histopathology, DF is characterized by a well-circumscribed proliferation of fibrohistiocytic spindle-shaped cells interspersed among thickened dermal collagen bundles; the aneurysmal variant has increased blood vessels through the lesion [2].

The diagnosis of DF is usually clinical, and treatment is typically done for cosmetic purposes. Giant DF is characterized by a size > 5 cm, typical histologic features of DF, and a benign biologic behavior. Less than 30 cases have been reported in the literature and there is no risk of recurrence when treated with full excision of the tumor [3, 4].

Although most DFs are benign, they can rarely show atypical features on histopathology with atypical tumor cells in the background of a typical DF [5]. In patients with atypical DFs, there is a small but real chance of local and even distant metastasis [5]. Fortunately, our patient's biopsy did not demonstrate atypical features, but given its large size and reportedly rapid growth, thorough examination of the biopsy slides was warranted.

References:

1. Song P, et al. Dermatofibroma. In: Goldsmith LA, ed. VisualDx. Rochester, NY: VisualDx; 2023. URL: https://www.visualdx.com/visualdx/diagnosis/?moduleId=101&diagnosisId=51413. Accessed August 6, 2023.
2. Rapini, R. P. (2021). *Practical Dermatopathology: Practical Dermatopathology E-Book*. Elsevier Health Sciences.
3. Hueso L, Sanmartín O, Alfaro-Rubio A, et al. [Giant dermatofibroma: case report and review of the literature]. *Actas Dermosifiliogr*. 2007;98(2):121-124.
4. Requena L, Fariña MC, Fuente C, et al. Giant dermatofibroma. A little-known clinical variant of dermatofibroma. *J Am Acad Dermatol*. 1994;30(5 Pt 1):714-718.

5. Kaddu S, McMenamin ME, Fletcher CDM. Atypical fibrous histiocytoma of the skin: clinicopathologic analysis of 59 cases with evidence of infrequent metastasis. *Am J Surg Pathol*. 2002;26(1):35-46.

MERKEL CELL CARCINOMA

Case No. 12

PRESENTER: Ysabelle Martinez, OMS-III
Farhad Niroomand, MD
Clay J. Cockerell, MD, MBA, JD
Fort Worth, TX
Dallas, TX

History: 69 year-old male with past medical history of HIV, malignant melanoma, BCC, SCC, solar lentigo, presents with rapid growing bumps on right forehead, right cheek, right temple, and scalp a few months after HAART regimen change 1 month ago. Patient denies fevers, chills, fatigue, unintentional weight loss, N/V/D. There are no new eruptions at follow-up visit.
Surgical and family history are non-contributory. Medications include HAART therapy (abacavir-lamivudine 600-300mg, lopinavir-ritonavir 200-50mg, Prezcobix 800-150mg, Symtuza 800-150-200-10mg).

Physical Examination:
R Upper Scalp: Large multi-nodular erythematous plaque with focal ulceration
Left Proximal Jaw: ulcerated erythematous plaque

Laboratory Data: Immunoperoxidase stains strongly positive for INSM1 and synaoptophysin with perinuclear dot pattern with cytokeratin cocktail. Cyotkeratin-20 stained weakly. Thyroid transcription factor-1 stains were negative.

Histopathology: Right Upper Scalp: Poorly differentiated malignat basal cell characterized by sheets of atypical basophilic cells, many of which are necrotic and in mitoses.

Left Proximal Jaw: Hyperkeratosis, parakeratosis, and acanthosis with lack of nuclear maturation, hyperchromatic and pleomorphic nuclei, and occasional mitoses without dermal involvement.

Clinical Course:
Merkel Cell Carcinoma prognosis is often poor even with treatment due to its highly aggressive nature with metastasis and growth. However, it may also present as a manageable manifestation of immune reconstitution syndrome as Merkel cell polyoma virus, widespread in the general population, has been associated with Merkel cell carcinoma in addition to ultraviolet light-induced mutations[3,4].

Squamous Cell Carcinoma will be treated with 5-fluorouracil due to extent of merkel cell carcinoma for now. Excision can be considered in the future.

Diagnosis: Merkel Cell Carcinoma

Points of Emphasis:
HIV positive patients have an increased risk for Merkel cell carcinoma[1,2], thus consideration of MCC should be taken in immunocompromised patients and treatment may consist of addressing underlying disease in conjunction with IL-2 therapy or with PD-I/PD-L1 therapy [3] in advanced cases.

References:
1. Burack J, Altschuler EL. Sustained remission of metastatic Merkel cell carcinoma with treatment of HIV infection. J R Soc Med. 2003 May;96(5):238-9. doi: 10.1177/014107680309600512. PMID: 12724438; PMCID: PMC539481.

2. Goldstein RH, DeCaprio JA. Merkel Cell Carcinoma in the HIV-1/AIDS Patient. Cancer Treat Res. 2019;177:211-229. doi: 10.1007/978-3-030-03502-0_8. PMID: 30523626.
3. MacDonald M, You J. Merkel Cell Polyomavirus: A New DNA Virus Associated with Human Cancer. Adv Exp Med Biol. 2017;1018:35-56. doi: 10.1007/978-981-10-5765-6_4. PMID: 29052131.
3. Ramachandran P, Erdinc B, Gotlieb V. An Unusual Presentation of Merkel Cell Carcinoma in a HIV Patient: A Case Report and Literature Review. J Investig Med High Impact Case Rep. 2019 Jan-Dec;7:2324709619836695. doi: 10.1177/2324709619836695. PMID: 30938171; PMCID: PMC6446430.
4. Wieland U, Kreuter A. Merkel cell polyomavirus infection and Merkel cell carcinoma in HIV-positive individuals. Curr Opin Oncol. 2011 Sep;23(5):488-93. doi: 10.1097/CCO.0b013e3283495a5b. PMID: 21734578.

BASAL CELL CARCINOMA IN SITU

Case No. 13

PRESENTER: Philip R Cohen, MD
San Diego California

History: A 63-year-old Fitzpatrick skin type I Caucasian man--with prior basal cell carcinomas and squamous cell carcinomas--presented with a slowly growing red lesion on his right flank of 4 months duration.

Physical Examination: On the lateral right lower abdomen was a non-tender, non-pruritic, erythematous, 2 x 2 cm scaly plaque with peripheral nodules. A shave biopsy, that included the area within the purple oval, was performed.

Histopathology: The epidermis shows contiguous extension into the underlying papillary dermis. There are basaloid tumor cells with palisading of the cells at the periphery predominantly restricted to the lower layer of the epidermis; however, there is not any non-contiguous invasion of the tumor cells into the underlying dermis.is absent. There is retracted of the dermal stroma adjacent to the tumor from the peripheral cells of the neoplasm. In the upper dermis, there are several focal areas of dense lymphocytic inflammation.

Clinical Course: Topical 5% imiquimod cream was applied (for 5 consecutive nights each week for 6 weeks) to the residual lesion and adjacent skin; the area treated became inflamed. There was no remaining tumor after the inflammation resolved. At follow-up, 21 months later, there was no skin neoplasm recurrence.

Diagnosis: Basal Cell Carcinoma In Situ

Points of Emphasis: Cancer is characterized by invasion of malignant cells. Tumor invasion is a feature of cutaneous carcinoma; specifically, neoplastic cells, that are not contiguous with the overlying epidermis, are present in the dermis. In contrast, in situ carcinoma of the skin refers to a neoplasm in which the malignant cells are restricted to the epidermis; non-contiguous invasion of the neoplasm into the dermis is absent. Based on these definitions, the tumor previously classified as a superficial basal cell carcinoma is more appropriately designated as a cutaneous basal cell carcinoma in situ. In summary, cutaneous neoplasms may present as in situ carcinoma or invasive carcinoma; the former is characterized by the contiguous extension of tumor into the dermis whereas the latter is defined by invasion of malignant cells, that are not contiguous with the overlying epidermis, into the underlying dermis. Cutaneous basal cell carcinoma in situ has recently been recognized as a unique, non-invasive, subtype of basal cell carcinoma that has a particular morphology, histology, tumor biology, and response to treatment.

References:

1.Cohen PR. Cutaneous basal cell carcinoma in situ: a case series. Cureus. 2022;14(9):e29479. PMID: 36299923. DOI: 10.7759/cureus.29479.
2.Cohen PR. Superficial basal cell carcinoma of the skin is a cutaneous basal cell carcinoma in situ [Editorial]. SKINmed. 2023; in press.

CUTANEOUS SIGNET RING SQUAMOUS CELL CARCINOMA WITH INCIDENTAL BASAL CELL CARCINOMA

Case No. 14

Presenters: George Jeha, MD
Collins Langley, MD
New Orleans, LA

History:
An 87-year-old Caucasian male with a history of non-melanoma skin cancers presented with a one-month history of an enlarging cystic papule overlying the left zygomatic arch. Initially, this lesion was suspected to be an epidermal inclusion cyst. A shave biopsy was performed, but due to its superficial nature, no cystic or other pathological features could be determined. After six weeks, the biopsy site remained unhealed and began intermittently expressing a serosanguinous discharge. Out of concern for a potential underlying malignancy, punch biopsy was performed, which subsequently revealed an infiltrative carcinoma with focal epidermal connection. The tumor was composed of epithelioid-appearing cells with eosinophilic cytoplasm and a clearing that gave them a signet ring-like appearance. Immunohistochemical (IHC) staining was positive for AE1/AE3 and negative for Mart 1. A diagnosis of cutaneous signet ring SCC was made.

Physical Examination (at time of wide local excision):
- 1.1 x 1.3 cm cystic nodule overlying left zygomatic arch
-No palpable lymphadenopathy

Histopathology:
Microscopically, the tumor showed invasive poorly-differentiated SCC with focal signet ring-like morphology and acantholytic features, with a maximum depth of invasion of 4 mm. Alongside the previously noted signet ring-like cells, a second population of basaloid cells consistent with basal cell carcinoma (BCC) was identified. There was no evidence of lymphovascular or perineural invasion, and the margins were uninvolved. IHC analysis revealed positivity for p40 and EMA, while SOX10 and mucicarmine were negative.

Clinical Course:
The patient underwent a multidisciplinary evaluation at our institution's head & neck tumor board. At the time of this evaluation, the lesion measured 1.1 x 1.3 cm, and the patient had no palpable lymphadenopathy. A computed tomography (CT) scan of the neck revealed no abnormalities within the lymph nodes or soft tissues. The patient underwent wide local excision (WLE) of the lesion with 1-cm margins, as well as left parotid sentinel lymph node biopsy (SLNB). Following 2 years of follow-up, the patient remains without signs of tumor recurrence.

Diagnosis:
Cutaneous Signet-ring Squamous Cell Carcinoma with incidental Basal Cell Carcinoma.

Points of Emphasis:
Cutaneous Signet-ring Squamous Cell Carcinoma is a rare cutaneous malignancy. Per the author's knowledge this is the 17th case reported in literature. All previously reported cases were confined to the head and neck. One reported case on the thigh occurred in a patient with Type-II Diabetes. UV radiation from 245-290nm is absorbed by DNA. This absorption drives the formation of two primary photochemical reactions that allow for mutagenesis. These photchemical reactions are: cyclobutane dimers to neighboring thymine, cytosine or pyrimidine and the formation of pyrimidone with adjacent pyrimidine bases. Recently, more cutaneous malignancies are showing relations to Human Papilloma

Virus. However, currently, Basal Cell Carcinoma remains unassociated with Human Papilloma Virus. With an identifiable transition zone between the BCC and srSCC, the two lesions could not be classified as a collision tumor.

References:

1. Findeis, S.K., Readinger, A., Mitchell, J., Agarwal, A., 2020. Cutaneous signet-ring cell squamous cell carcinoma. Baylor University Medical Center Proceedings 33, 424–426.. https://doi.org/10.1080/08998280.2020.1747342
2. S. Tornaletti & G. P. Pfeifer: UV damage and repair mechanisms in mammalian cells. BioEssays 18, 221-28 (1996)

ATYPICAL SWEAT GLAND NEOPLASM OF UNCERTAIN MALIGNANT POTENTIAL

Case No. 15 **PRESENTERS:** Nicholas Culotta, MD
Harley Davis, MD
George William Poche, MD
Baton Rouge, LA

History:
The patient is a 56-year-old male with no significant past medical history who presented to dermatology clinic for evaluation of a firm, slowly enlarging nodule to the right cheek that has been present for several years. He reports it started as a small skin-colored lesion that has slowly grown over time. It is sometimes painful with palpation and manipulation. He has not tried anything for it and has not had this before.

Physical Examination:
Right zygomatic cheek: about 1.2 cm mildly erythematous to skin-colored, firm papulonodule that is freely mobile

Histopathology:
Right zygomatic cheek, excisional biopsy: atypical epithelial neoplasm with glandular/ductal differentiation. Sections show a delineated expansive tumor with atypical epithelial cells in a dense eosinophilic stroma. An overt, infiltrating neoplasm is not identified. The differential diagnosis includes an atypical adenoma of sweat gland origin versus a primary cutaneous low grade adenocarcinoma.

Clinical Course:
The patient was seen for follow-up for suture removal at 1 week. The results of his pathology were explained in detail with recommendation for complete excision. Lymph node exam at that time was negative. He was referred to ENT for further assistance with excision of the area.

Diagnosis: Atypical epithelial neoplasm of glandular/ductal differentiation.

Points of Emphasis:
Cutaneous neoplasms of glandular/ductal differentiation are groups of benign and malignant neoplasms that are part of the adnexal epithelial types present in normal skin. There are multiple different entities that derive from apocrine or eccrine glands, sebaceous glands, or the hair follicle. The clinical findings are nonspecific. Malignancies may arise de novo or from a preexisting benign tumor. There are some triggers that have been reported including UV exposure, radiation, immunosuppression, and trauma. A biopsy is essential for making a diagnosis. Usually, complete resection of benign lesions is the optimal therapeutic approach, but some may recur. Other treatments for benign lesions include cryotherapy, CO2 laser therapy, PDT, electrodessication, 5-fluorouracil, and imiquimod with variable success. Malignant lesions require surgical intervention including wide local excision, Mohs micrographic surgery, or amputation. In summary, these neoplasms are uncommon and pathogenesis remains mostly unclear and proper diagnosis is still challenging.

References:
Płachta I, Kleibert M, Czarnecka AM, Spałek M, Szumera-Ciećkiewicz A, Rutkowski P. Current Diagnosis and Treatment Options for Cutaneous Adnexal Neoplasms with Apocrine and Eccrine Differentiation. Int J Mol Sci. 2021 May 11;22(10):5077. doi: 10.3390/ijms22105077. PMID: 34064849; PMCID: PMC8151110.

FAVRE-RACOUCHOT-LIKE SYNDROME IN IMAGE-GUIDED SUPERFICIAL RADIATION THERAPY

Case No. 16

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History:
Case 1: A 68-year-old male presented for a lesion on his forehead. He had a history of nodular basal cell carcinoma (BCC) being treated with image-guided superficial radiation therapy (IG-SRT). The lesion was initially noted within the radiation treatment field during week 6 of treatment. This is about 75% of the way through his radiation treatments. He has a history of coronary artery disease, peripheral neuropathy, and tobacco use (<1 pack per day).

Case 2: A 59-year-old female presented for a lesion on her nose. She had a history of nodular BCC of the right nasal ala treated with IG-SRT. The lesion was present at the site of previous radiation. This was first noted during her 2-week follow-up visit after completing her IG-SRT treatments. She reported scaling, irritation, and burning at this site. She reported the area feeling "hard." She has a history of hypertension, dyslipidemia, migraines, coronary artery disease, and tobacco use (1/2 pack per day).

Physical Examination:
Case 1 & 2
There are well-demarcated, round plaques with numerous open comedones at the sites of previous superficial radiation. There was loss of adnexal structures at the the biopsy site without comedones in this region.

Histopathology:
Case 2.
There are several dilated follicular orifices filled with cornified debris forming multiple comedones. Slight inflammation is present.

Clinical Course:
Case 1: The patient was treated with adapalene 0.1% gel nightly. He had additional nodular BCC on his right arm that was treated at same time as the forehead lesion with IG-SRT. 6 months later he was treated for another nodular BCC on the right clavicle with IG-SRT. No comedones formed at the clavicular or forearm treatment sites. The lesion on the forehead remained within the treatment area. Minimal to mild improvement was noted during 7 months of observation. He was lost to follow-up following the completion of his second course of IG-SRT.

Case 2: The patient was recommended to apply adapalene 0.1% gel nightly to the affected area beginning at her 2-week follow-up after completing IG-SRT. At her 3-month and 6-month follow-up, there was increased prominence of the lesion isolated to the area of radiation. At her 6-month follow-up, curettage removal was performed.

Diagnosis: Radiation-induced Favre-Racouchot syndrome

Points of Emphasis:

Radiation-induced Favre-Racouchot syndrome occasionally arises during or after treatment. It is reported to develop as long as several years after completion of treatment.[1,2] To our knowledge, these two cases are the first reported cases of radiation-induced Favre-Racouchot syndrome due to IG-SRT treatment of non-melanoma skin cancers.

It is important to note that both lesions occurred on the face, an anatomic area with dense concentrations of sebaceous glands. Additionally, both of these patients were actively smoking tobacco products throughout their radiation therapy treatments. The patient in case 1 had additional non-melanoma skin cancers on the forearm and trunk. The forearm BCC was treated at the same time as the forehead lesion. The trunk lesion began treatment 6 months after the forehead and forearm lesion were treated. Neither of these treatment sites developed comedones.

While the exact mechanism of radiation-induced comedones is unknown, it is likely due to a combination of UV skin damage, tobacco exposure, radiation, decreased androgen levels, and immune-senescence leading to dermal and epidermal changes.[1,3-5] In these cases there was likely a correlation with tobacco smoke causing dermal changes that may resemble solar elastosis.[3] This in combination with the radiation treatment on already sun-damaged skin may be the mechanism by which these comedones form.

We have completed treatment on over 517 non-melanoma skin cancer in 250 patients. These data suggest that the frequency of this complication is approximately 0.4%. This complication is easily identified by its pattern. We present our cases to increase awareness of this potential adverse event from IG-SRT.

References:

1. Paganelli A, Mandel VD, Kaleci S, Pellacani G, Rossi E. Favre-Racouchot disease: systematic review and possible therapeutic strategies. *J Eur Acad Dermatol Venereol*. Jan 2019;33(1):32-41. doi:10.1111/jdv.15184
2. Hubiche T, Sibaud V. Localized acne induced by radiation therapy. *Dermatology Online Journal*. 2014;20(2)doi:10.5070/d3202021545
3. Yeh C, Schwartz RA. Favre-Racouchot disease: protective effect of solar elastosis. *Arch Dermatol Res*. Apr 2022;314(3):217-222. doi:10.1007/s00403-021-02202-5
4. Sutherland AE, Green PJ. Favre-Racouchot syndrome in a 39-year old female following radiation therapy. *J Cutan Med Surg*. Jan-Feb 2014;18(1):72-4. doi:10.2310/7750.2013.13011
5. Huang CF, Wang WM. Radiotherapy-induced "solar" comedones. *CMAJ*. Dec 11 2012;184(18):2015. doi:10.1503/cmaj.112098

EXTRAMAMMARY PAGET DISEASE IN BILATERAL INGUINAL AREA MASQUERADING AS INTERTRIGINOUS DERMATITIS

Case No. 17

PRESENTERS: Carly Stevens, MS4
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History:
An 83-year-old male patient, with a medical history significant for melanoma, squamous cell carcinoma, and multiple myeloma, presented in clinic for evaluation of a longstanding rash in the left groin area. The patient reported experiencing intermittent episodes of this rash for several years and had attempted over-the-counter remedies such as Lotrimin and Zeasorb with limited success. He only showed his left side initially and deferred the rest of a physical exam. However, at his follow up visit he allowed for a full exam.

Physical Examination:
-Right groin: 8x8 cm erythematous to beefy red mammillated plaque with overlying white maceration at the right groin.
-Left groin: grouping of poorly defined erythematous patches superiorly and slightly macerated/scaly erythematous plaque inferiorly

Imaging:
US pelvis: Multiple grayscale images of the bilateral groin soft tissues demonstrating mild cutaneous thickening, right greater than left. No underlying soft tissue mass or collection is identified. Mildly prominent, morphologically normal lymph nodes are seen within the left groin.
CT Abdomen/pelvis: no evidence of metastasis

Histopathology:
Right Groin: Sections show skin with confluent proliferation of atypical cells in the epidermis with prominent pagetoid spread. The tumor cells are rather atypical and highlighted by CK7, Cam 5.2 while negative for CK5/6. CK5/6 and p63 highlighted keratinocytes and adnexal structures. Foci of microinvasion into the dermis are identified. There are few foci of dermal glandular proliferation, which are also positive for CK7, Cam5.2 while negative for p63 and CK5/6. CK20 is largely negative except rare foci for positive in the Paget cells. The staining pattern supports the diagnosis of extramammary Paget's disease.

Clinical Course:
Initially, he only showed the rash on his left side and deferred the rest of a physical exam. Given this limited exam, the rash was thought to be candida intertrigo, and the patient was prescribed fluconazole 200 mg once weekly along with topical application of ketoconazole cream 2% twice daily. However, the patient's symptoms persisted with minimal improvement and at his follow up visit, he allowed for a full exam which revealed the beefy red plaque with white maceration. Subsequently, a biopsy of the right groin fold was performed, revealing a diagnosis of extramammary Paget's disease (EMPD). In light of this diagnosis and the potential association of EMPD with internal malignancies, the patient was referred for a urology evaluation. Notably, his prostate-specific antigen (PSA) levels and recent colonoscopy in 2020 were within normal limits. Cystoscopy was normal with no evidence of malignancy in the bladder or urethra.

Considering the size and thickness of the lesions, Mohs micrographic surgery (MMS) was deemed the optimal approach for achieving adequate margin clearance. The procedure was well-tolerated, and MMS confirmed clear peripheral margins. The central portion of the wound was submitted for permanent sections to evaluate depth of invasion, given the exophytic morphology of the tumor. Only minimal, focal invasion of the dermis was noted. At a subsequent follow-up appointment, the right-sided lesion had healed, and the patient's left groin was biopsied, revealing additional foci of EMPD. Mohs surgery versus topical therapy to the left groin were discussed, and the patient opted for topical imiquimod therapy to this area. At the one and half month follow up visit, he noted no significant reaction to the left groin with topical imiquimod thrice weekly and was increased to daily dosing Monday through Friday. Discussion among Dermatologist, Mohs surgeon, and patient is still ongoing, and patient has close follow up.

Diagnosis: Extramammary Paget's disease

Points of emphasis:

Extramammary Paget's Disease (EMPD) is a rare and often perplexing skin condition that primarily affects areas of the body other than the breast, where Paget's Disease is more commonly known. This dermatological disorder is characterized by the presence of red, scaly, and itchy plaques on the skin's surface, which can be mistaken for various other skin conditions initially.[1] What distinguishes EMPD is its slow progression and its potential to develop in areas with a high concentration of sweat glands and apocrine glands, such as the genital and perianal regions. Though typically non-invasive, EMPD can sometimes be associated with an underlying malignancy, most commonly prostate, urinary tract, and breast cancers.[2] Managing EMPD often involves a multidisciplinary approach, combining dermatological expertise with input from other medical specialties, and may include treatments like topical therapies, surgical excision, or Mohs micrographic surgery (MMS) to ensure complete removal of affected tissue. In this case, a hybrid surgical technique was performed: given the size of the lesion, the Mohs surgeon submitted the central portion of the lesion for vertical sectioning, then performed MMS to clear the peripheral margin.[3] Tumor infiltrates often extend beyond clinically evident areas, resulting in increased recurrence rates.[4] MMS appears to reduce recurrence rates compared with wide local excision, as en face frozen sections allow for full assessment of the peripheral margin.[5] Dermal invasion of EMPD carries an increased risk of metastatic involvement and a worse prognosis and survival rate.

When addressing EMPD, the first step typically involves a thorough diagnostic evaluation, including skin biopsies and, in some cases, imaging studies. This evaluation helps determine the extent of the disease and whether any internal malignancies may be contributing to its manifestation. Collaborative efforts between dermatologists, oncologists, gastroenterologists, and urologists are crucial in providing comprehensive care to affected individuals.

Medical treatment options for EMPD include topical therapies, such as imiquimod and 5-fluorouracil, which can be effective in treating localized lesions. Surgical intervention is the main therapeutic intervention. Tissue sparing procedures such as MMS are preferred. However, other options include partial and wide local excision procedures. One study at Mayo Clinic compared MMS to excision for EMPD. In this study, MMS had better long-term outcomes with lower recurrence rates. MMS also provides less morbidity and provides physical and psychological benefits that wide local excision procedures, including vulvectomy and reconstruction does not.[3] Additionally, regular follow-up is essential to monitor for disease recurrence and ensure prompt intervention if necessary.

This case report highlights several crucial points. First and foremost, it underscores the significance of a comprehensive evaluation of dermatological conditions in patients with a history of malignancies, especially in elderly individuals. The patient's extensive medical history, including melanoma, squamous cell carcinoma, and multiple myeloma, emphasizes the importance of vigilant skin monitoring and prompt evaluation of persistent skin issues. This case demonstrates the importance of a0 full physical examination to evaluate the patient. This is especially challenging for clinicians in resistant patients and raises the question on how best to approach these patients. In this case, what initially

appeared as a benign dermatitis turned out to be EMPD, a relatively rare but potentially serious condition, demonstrating the need for a high index of suspicion and thorough diagnostic workup. Secondly, the multidisciplinary approach employed in this case serves as a valuable lesson in the management of complex dermatological conditions. The integration of dermatology with other specialties such as gastroenterology and urology is essential in providing comprehensive care to patients with EMPD. Additionally, the choice of MMS as the surgical technique highlights its effectiveness in achieving clear margins, especially in cases with lesions of significant size and thickness. Overall, this case report underscores the importance of a holistic and collaborative approach to managing challenging dermatological cases, ensuring both effective treatment of skin conditions and potential detection of underlying malignancies.

References:

1. Kibbi N, Owen JL, Worley B, et al. Evidence-Based Clinical Practice Guidelines for Extramammary Paget Disease. JAMA Oncology. 2022;8(4):618-628. DOI: 10.001/jamaoncol.2021.7418
2. Singh, G, and Burgin, S. Extramammary Paget Disease. *VisualDx*, 7 Dec. 2021, www.visualdx.com/visualdx/diagnosis/extramammary+paget+disease?diagnosisId=52100&moduleId=101&usePassword. Accessed 14 Sept. 2023.
3. Hendi A, Brodland DG, Zitelli JA. Extramammary Paget's disease: surgical treatment with Mohs micrographic surgery. J Am Acad Dermatol 2004;52:767–73.
4. Rastogi S, Thiede R, Sadowsky LM, et al. Sex differences in initial treatment for genital extramammary Paget disease in the United States: A systematic review. Journal of the American Academy of Dermatology. 2023;88(3):577-586. DOI: https://doi.org/10.1016/j.jaad.2019.04.046
5. Kim SJ, Thompson AK, Zubair AS, Otley CC, et al. Surgical treatment and outcomes of patients with extramammary Paget disease: a cohort study. Dermatol Surg 2017;43:708–14.

ATYPICAL GRANULAR CELL TUMOR

Case No. 18

Presenter: Christina Carl, DO
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History: The patient is a 60 yo female with history of myelodysplasia, arthritis, GERD, and hypertension who presented with a firm nodule on left low back. The lesion had been present for about a year and had gradually increased in size. This lesion was bothersome to her, and she requested to have it removed. She stated that she had a previous biopsy a year prior and reported that the lump came up at the spot of previous biopsy. (Previous biopsy results were requested, and the facility said they had no record of this.)

Physical Examination:
Freely mobile subcutaneous nodule with overlying sclerotic plaque, involving Left Medial lumbar Back-Lateral to S1 (Lesion was clinically concerning for keloid vs cyst)

Laboratory Data: None

Histopathology: The preponderance of findings are those of a large benign granular cell tumor but some areas of granular cell spindling are noted, as are scattered granular cells with vesicular nuclei and prominent nucleoli. Because of atypical features and because the neoplasm extends to the deep margin in the very center of the excision specimen, a re-excision to ensure complete removal is recommended.

Clinical Course: Patient referred to general surgery and underwent excision with clear margins.

Diagnosis: Atypical Granular Cell Tumor

Points of Emphasis: Granular cell tumors are usually circumscribed, solitary, firm nodule ranging from 5-30 mm with a brownish red or flesh tint[1]. Lesions are typically benign found on the body, but almost half of all tumors appear on head or neck[1]. Patients are typically in their 3rd to 5th decade of life[2]. Malignant granular cell tumor is uncommon. Most malignant granular cell tumors are larger than benign granular cell tumors. Average size in diameter is 9 cm. Factors that have been shown to correlate with malignant behavior are infiltrative growth pattern, history of local recurrence, older patient age, presences of necrosis, increased mitotic activity, spindling of tumor cells, and nuclear staining with proliferation marker Ki67[1]. Treatment of malignant granular cell tumor is with resection. This patient's pathology showed granular cell spindling and scattered granular cells with vesicular nuclei and prominent nucleoli. These atypical features along with the deep margins were cause for concern for possible neoplasm. Patient was referred to general surgery for further excision.

References:

1. James W, Elston D, Treat J, Rosenbach M, Neuhaus I. Andrews' Disease of the Skin Clinical Dermatology 13th Edition. Elsevier 2019 28:625

2. Rejas R, Campos MS, Cortes AR, Pinto DD, de Sousa SC. The neural histogenetic origin of the oral granular cell tumor: an immunohistochemical evidence. Med Oral Patol Oral Cir Bucal. 2011 Jan 1;16:6-10

GLOMUS TUMOR

Case No. 19 **Presenters:** Jessica Sterner, MD
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History: A 45-year-old man presented with complaints of multiple draining lesions on the right axilla. He also complains of an extremely tender lesion on the right forearm that was biopsied before with normal findings. His past medical history is notable for gastric bypass and coronary artery disease. The two complaints were seemingly unrelated. The patient was initiated with treatment for Hidradenitis Suppurativa of the right axilla with significant improvement in following visits. A punch biopsy of the subcutaneous nodule on the right forearm was performed and an initial diagnosis favoring angiolipoma was made.

Physical Exam: Clinical examination of the right axilla revealed multiple erythematous papules with several scared sinus tracts. Clinical examination of the right forearm revealed a hypopigmented macule with underlying subcutaneous nodule that was exquisitely tender to light touch.

Histopathology: Surgical excision of the mass was performed to the subcutaneous level. The resected mass measured to be 1.5 cm in size. Histopathological examination of the mass in the right forearm showed solid aggregates of glomus cells surrounding inconspicuous vessels, consistent with glomus tumor. Hematoxylin-eosin stains of the glomus cells were rounded with eosinophilic cytoplasm and darkly staining oval nuclei. Immunohistochemistry assay for α-smooth muscle actin and vimentin were positive and negative for Cytokeratin AE1/AE3 and Sox 10.

Diagnosis: Pathology confirmed the mass to be a glomus tumor of the right forearm.

Points Of Emphasis:
Glomus tumors are benign neoplasms arising from the glomus body. A glomus body consists of an anastomosis of vessels that contract to control blood pressure and temperature [1]. While glomus bodies are located throughout the body, they are highly concentrated in the digits and more so in the fingertips [1]. As a result, glomus tumors typically present in the digits with blue discoloration and notable pain in response to touch and temperature [2]. Glomus tumors in extradigital locations, although less common, can be misdiagnosed due to atypical location and presentation. Early diagnosis and surgical excision is warranted for curative treatment and quick resolution of the debilitating symptoms associated with glomus tumors.

References:
1. McDermott, E.M. and A.P. Weiss, *Glomus tumors.* J Hand Surg Am, 2006. **31**(8): p. 1397-400.
2. Van Geertruyden, J., et al., *Glomus tumours of the hand. A retrospective study of 51 cases.* J Hand Surg Br, 1996. **21**(2): p. 257-60.

RECURRENT POST-IRRADIATION ANGIOSARCOMA OF BREAST AFTER MASTECTOMY

Case No. 20 **Presenter:** Natalya Gallaga
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New Orleans, LA

History: A 75-year-old female complex PMH including breast cancer 2011 and angiosarcoma of left breast s/p mastectomy 2022 presented initially for evaluation for CTCL stage Ib. Patient was referred from an outside dermatologist. Rash started on the left upper arm in late 2000s however spread rapidly to BL UE, trunk, and face within one month prior to examination. She had started chlorthalidone three months preceding the worsening of her rash. Patient was recommended to stop chlorthalidone and to use triamcinolone 0.1% cream BID. At 2 month follow up, we recommended escalation of therapy to nbUvB TIW, continued triamcinolone cream, and started Targretin gel 1% QD. At 3 month follow up, patient with mild improvement in rash, however, noted a hemorrhagic mass at her mastectomy scar which patient states had not healed since mastectomy months prior and indicated copious amount of bleeding from lesion. She also had significant abdominal pain and constipation with fatigue, leading to an ED visit with inconclusive findings. A biopsy was subsequently performed on the chest wall lesion.

Physical Examination: Fitzpatrick type V. Hyperpigmented macules and scaly plaques to cheeks, trunk, and extremities approximately 20-30% BSA. Additionally, left breast was absent with a distinctive red-purpuric hemorrhagic tumor, resembling a smooth raspberry, measuring 6-8 cm in length at the site of a previous mastectomy. No gross LAD noted.

Laboratory Data: Laboratory studies completed as the patient's initial workup for CTCL resulted in the following: normal fT4, normal lipids, CBC/CMP within normal limits. CD4:8 ratio of 1.03.

Histopathology:
Punch biopsy showed ulcer with underlying proliferation of atypical bizarre-shaped vascular spaces forming a poorly circumscribed dermal tumor, dissecting between collagen bundles. The tumor shows significant cytologic atypia with enlarged hyperchromatic nuclei and prominent nucleoli and mitoses. Red cell extravasation is prominent. The tumor cells are highlighted by CD31 stain and they are positive for c-myc favoring a post-irradiation angiosarcoma. AE1/AE3, CK7, GATA3 and SOX10 are negative in the atypical cells with adequate control.

Clinical Course:
Histopathological analysis confirmed angiosarcoma and the patient was referred for wide local excision of the chest wall growth. Later, she was hospitalized for a GI bleed, receiving 2 L of blood and a colonoscopy revealed widespread abdominal and pelvic metastasis. A chemotherapy port was placed in the left upper chest, and she is receiving ongoing Paxitaxel therapy.

Diagnosis:
Post-irradiation angiosarcoma with systemic metastases.

Points of Emphasis:
Cutaneous angiosarcoma(AS) is seen in a variety of clinical settings, such as sun-damaged sites on elderly person, Stewart,Treves syndrome (chronic lymphedema associated), and postradiation, most commonly on breast.1 Surgical treatment is recommended given it is the only therapy that is curative, potentially. Adjuvant chemotherapy/radiation is controversial. The efficacy of chemotherapy for breast AS demonstrated that weekly paclitaxel regimen was effective for unresectable or metastatic AS in several trials.2 AS commonly develops over a larger field of chest wall than initially anticipated and the majority

of secondary breast AS treated with BCS occur within one year. 3 It is imperative to monitor for skin changes closely postoperatively for this patient population.

References: (At least two recent pertinent published references)

1.Shiraki E, Kang Y, Shibayama T, Tsuyuki S. Two cases of breast angiosarcoma after breast conserving surgery. Surg Case Rep. 2020 Apr 26;6(1):81. doi: 10.1186/s40792-020-00841-w. PMID: 32337612; PMCID: PMC7183570.

2.Yin M, Wang W, Drabick JJ, et al. Prognosis and treatment of non-metastatic primary and secondary breast angiosarcoma: a comparative study. *BMC Cancer.* 2017;17(1):295. doi: 10.1186/s12885-017-3292-7.

3.Monroe AT, Feigenberg SJ, Mendenhall NP. Angiosarcoma after breast-conserving therapy. *Cancer.* 2003;97(8):1832. doi: 10.1002/cncr.11277.

TUFTED ANGIOMA

Case No. 21 **Presenter:** Caroline Savoie, MD
India Hill, MD
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New Orleans, LA

History:
This patient presented as a 6-week-old male born via uncomplicated vaginal delivery at 38 weeks EGA for evaluation of a congenital tumor. Parents report large lesion on his abdomen at birth. Ultrasound obtained suggested congenital hemangioma or possibly lymphangioma. Thus, parents were told it was a benign birthmark. The lesion continued to grow but remained asymptomatic. Other skin findings absent.

Physical Examination:
Patient was found to have a 2cm firm, mobile subcutaneous nodule to the left abdomen above umbilicus.

Laboratory Data:
CBC, CMP, DDimer, APTT, PT/INR, and fibrinogen obtained at initial clinic visit notable only for elevated DDimer of 0.82.

Histopathology:
Section of skin with underlying dermis. Confined to the dermis are scattered lobules of small capillary proliferation forming the so-called "cannonball" pattern. The proliferation includes bland small ovoid cells without atypia or increased mitotic activity. The capillary lumens are without thrombi. Inflammatory infiltrate is not significantly increased.

Clinical Course:
Surgical interventions were discussed with parents given potential for progression. The decision was made to monitor clinically. At most recent follow-up the lesion had significantly decreased in size.

Diagnosis:
The lesion was ultimately diagnosed as a tufted angioma.

Points of Emphasis:

Tufted angioma is a rare benign vascular tumor that most commonly appears during infancy or early childhood. It can be congenital or acquired. Clinical presentation varies, but it typically presents as a dusky red to violaceous ill-defined macule, papule, or plaque on neck, trunk, or extremities.[2] These lesions are often associated with pain, hyperhidrosis, and hypertrichosis.[1] These lesions are on a spectrum with kaposiform hemangioendothelioma, and both can be complicated by Kasabach-Merritt phenomenon (KMP), a consumptive coagulopathy that occurs in setting of rapid growth of a vascular tumor.[2]

The pathogenesis of tufted angioma remains unclear, but reports postulate that increased local secretion of growth factors such as interleukin-8 that stimulate vasculogenesis and promote vascular lobule formation.[1] Histologically, tufted angiomas show small tufts of capillaries and angiomatous lobules in the dermis with dilated lymphatic channels with a characteristic “cannonball” appearance. The tufts are typically encircled by an empty crescent-shaped vessel and are surrounded by fibrous dermis.[3] The proliferating cells show no atypical mitotic figures or cellular pleomorphism. The differential diagnosis for tufted angioma includes congenital and infantile hemangioma, venous malformation, venolymphatic malformation, angiosarcoma, Kaposi sarcoma, and kaposiform hemangioendothelioma.[1,2] Because of its clinical variability, histopathologic examination is required for diagnosis of tufted angioma.[3]

Currently, there are no treatment guidelines or consensus on the management of tufted angioma. Various factors such as location, size, pain, functional compromise, secondary changes, and KMP help in individualizing the treatment.[1] Treatments with local or systemic corticosteroids, surgical resection, laser,

interferon alpha, chemotherapy, and radiotherapy have been successful in individual case reports.[2] A conservative approach could be considered for an asymptomatic, uncomplicated lesion with minimal or no risk of development of KMP.[1] Due to its high mortality rate, KMP should be treated as early as possible and requires aggressive management with treatments such as sirolimus.[2]

References:

1. Singal, Archana, et al. "Indurated dusky red swelling on the forearm of an infant: Tufted angioma." Indian Journal of Dermatology, vol. 64, no. 2, 2019, p. 146, https://doi.org/10.4103/ijd.ijd_468_17.
2. Xin Su, Yu Liu, Yanghe Liu, et al. A retrospective study: Clinicopathological and immunohistochemical analysis of 54 cases of tufted angioma. Indian Journal of Dermatology, Venereology & Leprology. 2020;86(1):24-32. doi:10.4103/ijdvl.IJDVL_777_18
3. El Fekih N, Litaim N, Jones M, Fazaa B. Congenital tufted angioma. Case report. European Journal of Pediatric Dermatology. 2012;22(4):233-236. Accessed September 15, 2023. https://research-ebsco-com.ezproxy.lsuhsc.edu/linkprocessor/plink?id=2a7c82d0-2c85-3598-bd60-7c284c1ccfa6

TRICHILEMMAL CARCINOMA IN A PATIENT WITH OCULOCUTANEOUS ALBINISM

Case No. 22

PRESENTER: Jonathan Joseph, MD
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New Orleans, LA

History:
A 47-year-old female with past medical history of Oculocutaneous Albinism and numerous nonmelanoma skin cancers (NMSCs) returned to clinic to re-establish care six months after multiple biopsies were performed resulting as a nodular basal cell carcinoma and an invasive squamous cell carcinoma. Attempts to contact her to discuss biopsy results and set up surgical removal were unsuccessful.

Physical Examination:
Skin: Fitzpatrick Type I
Face: Erythematous papule with telangiectasias on right cheek, left cheek with skin graft in place
Trunk: Erythematous papule on central chest
RUE: distal medial forearm with erythematous papule with central ulceration and scattered erythematous scaly papules.
LUE: 4X2 cm Erythematous scaly plaque on volar forearm with adjacent erythematous papule with central erosion and scale.

Histopathology:
Skin with a proliferation of basaloid keratinocytes forming a nodule in the dermis with clear cytoplasm and peripheral palisading. Brisk and abnormal tripolar mitotic activity is identified. Ki-67 shows a high proliferation rate (50-60%), consistent with trichilemmal carcinoma.

Clinical Course:
The patient returned to clinic one month following the biopsy and was set up for surgical excision. The patient underwent successful excision of the Trichilemmal Carcinoma with 3.0 cm margins. Final pathology showed no residual tumor. Of note, during this process the patient was diagnosed with metastatic SCC with presumed skin as primary source. She was following with Oncology with plans to begin Pembrolizumab.

Diagnosis: Trichilemmal carcinoma

Points of Emphasis:
Trichilemmal carcinoma (TC) is a rare adnexal neoplasm derived from the outer sheath of the hair follicle. The characteristic histopathology demonstrates lobules of atypical keratinocytes with glycogen-rich clear cell change, often displaying a pattern of peripheral palisading and a high mitotic rate. Despite its aggressive histological features, the clinical behavior of trichilemmal carcinoma is typically low-grade, with local recurrences being more common than metastasis. However, it's noteworthy to mention that the potential for metastasis does exist, especially with delayed diagnosis and treatment.

Oculocutaneous albinism is a group of inherited disorders characterized by a generalized reduction in melanin pigment in the eyes, skin, and hair. Individuals with Oculocutaneous Albinism often have sun sensitivity, leading to a predisposition to sunburn and development of skin cancer. Sun protection is of paramount importance, but despite best efforts patients often develop numerous nonmelanoma skin cancers throughout their lifetime.

In the presented case, the patient's history of Oculocutaneous Albinism has invariably played a role in her vulnerability to various skin malignancies. The presence of nodular basal cell carcinoma and a later diagnosis of metastatic squamous cell carcinoma emphasizes the complexity and heightened risk faced by this demographic. The diagnosis of trichilemmal carcinoma in this setting underscores the necessity for meticulous skin surveillance in patients with oculocutaneous albinism and emphasizes importance of maintaining a broad differential diagnosis for this demographic.

References:

1. Płachta I, Kleibert M, Czarnecka AM, Spałek M, Szumera-Ciećkiewicz A, Rutkowski P. Current Diagnosis and Treatment Options for Cutaneous Adnexal Neoplasms with Follicular Differentiation. Int J Mol Sci. 2021 Apr 30;22(9):4759. doi: 10.3390/ijms22094759. PMID: 33946233; PMCID: PMC8125718.
2. Hamman MS, Brian Jiang SI. Management of trichilemmal carcinoma: an update and comprehensive review of the literature. Dermatol Surg. 2014 Jul;40(7):711-7. doi: 10.1111/dsu.0000000000000002. PMID: 25111341.

CHRONIC INTERTRIGINOUS SKIN CONDITION CONSISTENT WITH SYSTEMATIZED EPIDERMAL NEVUS

Case No. 23

Presenter: Kaycee Nguyen, BS
Landon Perry, MD
Clay J. Cockerell, MD, MBA, JD
Plano, TX
Dallas, TX

History: A 23-year-old female presented with a persistent intertriginous skin condition that had been present since infancy and progressively worsened with age. The skin lesions are present across her entire body, with the most pronounced severity observed in her intertriginous regions, especially at the base of her neck, axillary regions, and inguinal creases. The patient has no reported family history of a similar condition and denies any history of tobacco, alcohol, or drug use. Previous treatment regimens have primarily involved local wound care and antibiotics.

Physical Examination: Skin examination was notable for brown verrucous papules and plaques with pigmentary changes throughout her entire trunk. Additionally, there was skin thickening with erythema in intertriginous regions, notably in the axillary and inguinal areas.

Laboratory Data: Hemoglobin A1c was normal.

Histopathology: An excisional biopsy from the right base of the neck revealed marked epidermal hyperplasia with acanthosis and a morphology similar to that seen in a keratosis. In the context of the clinical images, these findings are suggestive of a systematized widespread variant of an epidermal nevus-like process.

Diagnosis: Consistent with systematized epidermal nevus

Points of Emphasis: Epidermal nevi are cutaneous hamartomatous growths that originate from the embryonic ectoderm and manifest along the lines of Blashko, typically present at birth. When more than one linear lesion is present, they are categorized as systematized epidermal nevi. These lesions can extend into nail folds, leading to nail splitting, discoloration, ridging, and dystrophy. Physical examination often reveals a distinctive swirled pattern of verrucous hyperpigmented papules distributed along dermatomes. Notably, certain patients may exhibit associated multisystem congenital abnormalities, particularly affecting the skeletal and central nervous systems, leading to the diagnosis of epidermal nevus syndrome.[1] Microscopic analysis often reveals epidermal hyperplasia with acanthosis and pronounced papillomatosis, with no significant inflammatory infiltrate.[2] The clinical photographs of this patient displayed a diffuse process with epidermal hyperplasia and lesions with features suggestive of keratoses, strongly suggesting an underlying genetic abnormality in this context.

Managing this condition can be challenging. Cryotherapy may be a viable option for small lesions, while laser therapy has demonstrated favorable outcomes with a reduced risk of scarring. In cases involving extensive of systematized lesions, such as those seen in this patient, full-thickness excision offers definitive treatment but may increase the risk of scarring. An alternative approach involves the use of oral acitretin, which has been effective in treating systematized epidermal nevi in some patients in the absence of epidermal nevus syndrome[3]. This treatment resulted in significant regression of lesions, often leaving behind only minor residual hyperpigmentation. For individuals diagnosed with systematized epidermal nevi, referral for genetic testing and counselling may be warranted.

References:

1. Dhanaraj M, Ramalingam M. Systematised epidermal nevus - a case report. *J Clin Diagn Res*. Feb 2015;9(2):Wd01-2. doi:10.7860/jcdr/2015/9190.5510
2. Bennett RG, Burns L, Wood MG. Systematized Epidermal Nevus: A Determinant for the Localization of Psoriasis. *Archives of Dermatology*. 1973;108(5):705-707. doi:10.1001/archderm.1973.01620260053022
3. Chhabra G, Verma P, Sharma S. A case of systematized verrucous epidermal nevus successfully treated with low dose acitretin. *Dermatol Ther*. Nov 2019;32(6):e13106. doi:10.1111/dth.13106

PALMOPLANTAR KERATODERMA

Case No. 24 **PRESENTER:** Marissa S. Ceresnie, DO
Clay J. Cockerell, MD, MBA, JD
Dallas, TX

History: A 32-year-old male with palmoplantar hyperhidrosis was referred by another dermatologist for evaluation of a rash on his palms and soles that began 14 months prior to presentation. He recalled calluses formed on his palms from weightlifting initially before turning red. He noticed his palms turned white and spongy after exposure to water. The patient did report some benefit from pumice stone exfoliation. Family history includes Wegner's granulomatosis in his mother.

Physical Examination:
Both palms had sharply demarcated erythematous and indurated plaques without central clearing with scale on the edge.

A non-indurated patch of erythema and scaling was also on both axillary vaults.

Patient sent in photos showing evolving spongy white plaques on palms and red plaques with peripheral scale on soles.

Laboratory Data:
Previous dermatologist ordered CBC, CMP, ESR, CRP, TSH, uric acid, HLA-B27, ANA, and Anti-CCP antibody, which were all within normal limits. Rheumatoid factor was very slightly elevated at 15.7 (Ref <14.0)

Histopathology:
Previous sole biopsy showed slight psoriasiform hyperplasia, but not classic for psoriasis. Changes showed mainly lichen simplex chronicus.

The patient returned to his previous dermatologist for a biopsy of his palm, which showed marked thickening of the epidermis and cornified layer. PAS and DIF were ordered and both were negative.

Clinical Course:
At his initial visit with the previous dermatologist, there was concern for psoriasis or fungal infection. However, the patient did not improve with topical clobetasol, Zoryve, Otezla, or terbinafine. The patient was directed to continue glycopyrrolate for hyperhidrosis and use topical urea lotion for exfoliation. The patient was advised to undergo genetic testing for possible hereditary keratoderma.

Diagnosis: Palmoplantar keratoderma

Points of Emphasis: Palmoplantar keratoderma is a heterogeneous group of inherited or acquired disorders that are classified based on a plethora of clinical and histopathological findings and genetic mutations. Genetic defects may involve structural proteins in the granular layer of the epidermis or cell proliferation proteins in the basal epidermis. Hereditary forms of palmoplantar keratoderma may be inherited in an autosomal dominant or recessive fashion, but may occur later in life as a "de novo"

autosomal dominant mutation. Lesion morphology may be diffuse, focal, or punctate and may be associated with additional findings such as hyperhidrosis, *transgrediens*, mutilation, pseudoainhum, or wooly hair. Many forms of palmoplantar keratoderma are syndromic, so genetic testing should be considered when a hereditary form is suspected.[1]

References: (At least two recent pertinent published references)

1. Guerra L, Castori M, Didona B et al. Hereditary palmoplantar keratodermas. Part I. Non-syndromic palmoplantar keratodermas: classification, clinical and genetic features. J Eur Acad Dermatol Venereol 2018;32:704-19.

2. Bolognia, JL., et al. "Palmoplantar Keratodermas." *Dermatology*, 4th ed., vol. 1, Mosby, London u.a., 2018, pp. 924–940.

BENIGN CEPHALIC HISTIOCYTOMA

Case No. 25

PRESENTER: Kaycee Nguyen, BS
Fred Ghali, MD
Clay J. Cockerell, MD, MBA, JD
Grapevine, TX
Dallas, TX

History and Physical Examination: An 11-month-old male with no significant past medical history presented with multiple smooth, asymptomatic, red-brown and flesh-colored papules on his face and extremities, with a few new ones still appearing. The patient is otherwise healthy.

Histopathology: A punch biopsy from the right thigh revealed a proliferation of mononuclear cells interspersed with eosinophils within the dermis and exhibited no epidermotropism. Notably, some of these cells exhibited characteristics strongly suggestive of mast cells. However, immunoperoxidase stains for tryptase and Giemsa were negative, arguing against a diagnosis of urticaria pigmentosa. Several cells were highlighted with CD68, but none were marked with CD1a or S-100 protein. Control slides were stained appropriately. Thus, these findings appear indicative of a histiocytic process, possibly analogous to a xanthogranulomatous condition. It could be somehow related to a benign cephalic histiocytosis, although the absence of staining with S-100 protein or CD1a indicates no significant Langerhans cell product.

Diagnosis: Benign cephalic histiocytoma

Points of Emphasis: Benign cephalic histiocytoma (BCH) is a rare skin disorder primarily affecting infants and young children, although it can also occur in adults.[1] This condition is characterized by the appearance of small, firm, dome-shaped, or flat-topped papules that usually appear between the ages of 2 to 34 months. These lesions are yellow-brown or skin-colored and asymptomatic. They typically occur on the face, particularly on the forehead, cheeks, and eyelids, but can also appear on other parts of the body as well. Palms, soles, mucous membranes, and visceral organs are spared. Histologically, BCH is characterized by a diffuse infiltrate of histiocytes that are positive for CD68 or CD163 and negative for Langerhans cell markers, including S-100 protein and CD1a.[2,3] Histiocytes are often interspersed with scattered lymphocytes.

Important differential diagnoses to consider include generalized eruptive histiocytoma and juvenile xanthogranuloma, both of which exhibit histological similarities to BCH. Urticaria pigmentosa also presents clinically with red-brown macules or papules akin to BCH, but it can be distinguished by the presence of erythema surrounding the lesions upon application of pressure (indicative of a positive Darier sign). Histology of urticaria pigmentosa reveals a diffuse infiltrate of mast cells in the dermis.[4]

Benign cephalic histiocytoma is typically self-limiting, and lesions usually resolve spontaneously.[3]

References:

1. Arnold ML, Anton-Lamprecht I. Multiple eruptive cephalic histiocytomas in a case of T-cell lymphoma. A xanthomatous stage of benign cephalic histiocytosis in an adult patient? *Am J Dermatopathol*. Dec 1993;15(6):581-6. doi:10.1097/00000372-199312000-00013

2. Facial Eruptions in a Child—Diagnosis. *Archives of Dermatology*. 1999;135(10):1267-1272. doi:10.1001/jamadermatol.58605

3. Koca R, Bektaş S, Altinyazar HC, Sezer T. Benign cephalic histiocytosis: a case report. *Ann Dermatol*. Nov 2011;23(4):508-11. doi:10.5021/ad.2011.23.4.508
4. Monir RL, Motaparthi K, Schoch JJ. Red-brown papules in a 13-month-old. *Pediatric Dermatology*. 2023;40(1):201-203. doi:https://doi.org/10.1111/pde.15137

MACULOPAPULAR CUTANEOUS MASTOCYTOSIS (URTICARIA PIGMENTOSA)

Case No. 26

Presenter: Christopher Wong, DO
Christian Scheufele, DO
Michael Carletti, DO
Clay J. Cockerell, MD, MBA, JD
Stephen E. Weis, DO
Fort Worth, TX
Dallas, TX

History:
A 12-year-old male presented to the dermatology clinic with a five-year history of a rash on his postauricular scalp, neck, chest, and back. The rash flares with a "tingling and burning" sensation once or twice every month, which is followed by bright red, raised lesions. Heat and exercise exacerbate this rash. The lesions eventually regress and become flat brown lesions. He has had one episode of a "scratchy feeling" in his throat but has never experienced shortness of breath, or lip or tongue swelling. He has no known allergies that cause anaphylaxis. He has no other systemic symptoms.

Physical Examination:
On the upper chest, upper back, and circumferential neck, there are numerous brown ovoid macules and thin urticarial plaques. Dermatographism was present.

Laboratory Data:
Complete blood count with differential, comprehensive metabolic panel, and tryptase levels were within normal limits.

Histopathology:
Punch biopsies of the left posterior neck and left base of neck showed similar findings. Numerous mast cells were present in the dermis with dilated blood vessels.

Clinical Course:
The patient was prescribed an epinephrine pen which he has not needed. He was prescribed loratadine 10 mg every morning and cetirizine 5 mg every evening, and topical triamcinolone 0.1% cream as needed for itching. He is scheduled for three-month follow-up.

Diagnosis: Maculopapular cutaneous mastocytosis (urticaria pigmentosa)

Points of Emphasis:
Mastocytoses result from mast cell proliferation in various tissues and are distinguished into cutaneous and systemic forms by the World Health Organization. Cutaneous forms of mastocytosis in childhood include localized mastocytoma(s), maculopapular cutaneous mastocytosis (MPCM, formerly known as urticaria pigmentosa), and diffuse cutaneous mastocytosis. Darier's sign, resulting from mast cell degranulation after physical stroking of lesions, is pathognomonic in all forms of cutaneous mastocytosis.

MPCM is the most common form of cutaneous mastocytosis in childhood and results from numerous KIT mutations. It may be further divided into monomorphic or polymorphic variants. MPCM presents as yellow, red, or brown macules or papules on the neck, trunk, extremities, groin, and buttocks; at least three mastocytomas must be present. There is rarely internal organ involvement. Histology demonstrates multifocal or diffuse mast cell accumulation. Serum tryptase is sometimes increased in monomorphic MPCM and usually not increased in polymorphic MPCM; often, no systemic mastocytosis is present in children and no further workup is warranted even if serum tryptase is elevated.

Nonsedating antihistamines are the mainstay of treatment and may be used up to four times the normal daily dose. Quality of life is rarely affected. Prognosis is excellent as childhood cases of mastocytoses often spontaneously resolve by adulthood, with a greater number of lesions increasing the likelihood of persistence.

References:

1. Nemat K, Abraham S. Cutaneous mastocytosis in childhood. *Allergol Select*. 2022;6:1-10. Published 2022 Jan 5. doi:10.5414/ALX02304E
2. Panigrahi A, Chakraborty S, Sil A. Urticaria Pigmentosa. *J Pediatr*. 2020;222:249. doi:10.1016/j.jpeds.2020.03.053
3. Heinze A, Kuemmet TJ, Chiu YE, Galbraith SS. Longitudinal Study of Pediatric Urticaria Pigmentosa. *Pediatr Dermatol*. 2017;34(2):144-149. doi:10.1111/pde.13066

PACHYDERMODACTYLY

Case No. 27

Presenters: Charles Perniciaro, M.D.
Frank Glass, M.D.
Nicole Nagrani, M.D.
Tampa, FL

History: 16-year-old male presented with asymptomatic swelling of the proximal phalangeal joints of the hands bilaterally. Began with one digit and progressed over eight months to involve several digits. There was no history of trauma, pain, redness or warmth, morning stiffness, rashes, or functional impairment. The patient was a competitive swimmer on his high school's varsity swim team and was a backstroke specialist.

Physical examination: Marked bilateral swelling with some erythema over many digits of the hands, from the MCP to the PIP joins. Some digits displayed a "webbed" appearance.

Laboratory Data: CBC, CMP, TSH, ANA, RF, EBV, Mycoplasma, CMV all normal. Negative COVID test.

Histopathology: Increased fibroblasts in the dermis with diffuse mucin deposition throughout.

Clinical course: Patient declined therapy because he felt the disorder gave him a competitive advantage in swimming competition.

Diagnosis: Pachydermodactyly

Points of emphasis: Pachydermodactyly is a form of digital fibromatosis that manifests as painless soft tissue swelling of the lateral aspects of the fingers, usually involving PIP joints of digits 2-4. More common in young adolescent boys with history of mechanical trauma. Often confused with JRA. Management includes stopping the form of hand manipulation.

References:

Bardazzi F, Neri I, Raone B, Patrizi A. Pachydermodactyly: seven new cases.
Annales de Dermatologie et de Venereologie. 1998; 125:247-250.

Verbov J. Pachydermodactyly: A Variant of the True Knuckle Pad
Arch Dermatol. 1975; 111:524.

GRANULOMA ANNULARE AND NECROBIOSIS LIPOIDICA-LIKE PALISADED GRANULOMATOUS DERMATITIS

Case No. 28a

Presenters: Zehratul Quresh, MD
Clay J. Cockerell, MD, MBA, JD
Dallas, TX

Clinical History:
50-year-old male, with a known history of sarcoidosis presented with lesions on the right medial lower leg and left ankle complaining of swelling, for a period of 1 year, suspecting granuloma annulare. No history of procedure, no significant family history, no history of diabetes mellitus.
Known history of hypertension and congestive heart failure on treatment, and herpes zoster.
Patient was first seen first at infectious diseases, suspecting for Lyme disease but later referred to dermatology for further treatment.

Histopathology:
A. Skin right medial lower leg (proximal): Punch biopsy for H&E sections showed discrete mass of palisading histiocytes surrounding collections of mucin with perivascular lymphocytes, features suggesting of classic granuloma annulare. PAS is negative for hyphae. Stains were reviewed with appropriate controls.

B. Skin left ankle medial: Punch biopsy for H&E sections showed palisading granulomatous dermatitis with central degeneration of collagen as well as some plasma cells. PAS stain was negative for hyphae. These sections are different from sections of specimen A in that they are more in favor of necrobiosis lipoidica. The histologic findings support the diagnosis of palisaded granulomatous dermatitis.

Points of emphasis:
Granuloma annulare (GA) is an idiopathic disorder affecting the dermis and subcutaneous tissue occurring as papules on the hand or feet, with its hallmark of histopathological presentation of preserved epidermis, areas of degenerated collagen in the dermis surrounded by epithelioid histiocytes and lymphocytes in a palisade along with giant cells. Reference of literature (Heite and Scharwenka) shows that in 66% of patients with granuloma annulare, 76% had features of necrobiosis with diabetes and 86% were reported as necrobiosis without diabetes with a female preponderance of 57% and 93% respectively.

The non-diabetic necrobiosis lipoidica (NL) also known as the Miescher's granuloma occurs primarily in adults and predominates on the legs below the knee. Primary histopathologic features in favor of GA are the presence of mucin in the center of the granulomas, while palisading necrobiotic granulomas extending into the dermis parallel to the epidermis with areas of degenerated hyalinized collagen alternating with sclerotic dermal collagen surrounded by histiocytes, lymphocytes and epithelioid cells suggests an overlapping feature of NL. (1)

Recently a case of maturity onset diabetes mellitus with a mutation of HNF1A-MODY with a clinical diagnosis of GA with overlapping features of NL was reported (2). Published literature has reported eleven cases of GA occurring with NL, two of them were in male patients. (3)

Reference:
1. josé antonio plaza, victor g. prieto, in Modern Surgical Pathology (Second Edition), 2009

2. Brandes GIG, Peixoto-Barbosa R, Meski APG, Giuffrida FMA, Reis AF. Granuloma annulare and necrobiosis lipoidica in a patient with HNF1A-MODY. Arch Endocrinol Metab. 2022 May 12;66(3):420–4. doi: 10.20945/2359-3997000000477. Epub ahead of print. PMID: 35551682; PMCID: PMC9832856.
3. Rupley KA, Riahi RR, Hooper DO. Granuloma annulare and necrobiosis lipoidica with sequential occurrence in a patient: report and review of literature. Dermatol Pract Concept. 2015;5(1):29-34. Published 2015 Jan 30. doi:10.5826/dpc.0501a03

INTERSTITIAL GRANULOMA ANNULARE

Case No. 28b

Presenters: Adeel Alam, MBBS
Clay J. Cockerell, MD, MBA, JD
Lahore, Pakistan
Dallas, TX

History: A 56 year old female presented with a non-pruritic, purplish rash on the right medial knee. The rash appeared coin-shaped and had persisted for months. There were no associated excoriations or blisters, and the area was nontender. Notably, she had no recent fever, sore throat, chills, diarrhea, or joint aches. She reported no household contacts with similar rash, no new medications, no new personal care products, and no recent infections. She had no known drug allergies.

Laboratory Data: None

Histopathology: A 4mm Punch biopsy obtained from the lesion showed an interstitial infiltrate of histiocytes with scattered lymphocytes. Some Mucin was also seen.

Diagnosis: Interstitial Granuloma Annulare

Points of Emphasis: Interstitial granuloma annulare (IGA) is a rare variant of granuloma annulare (GA), a benign inflammatory skin condition of unknown etiology. IGA is characterized by an interstitial pattern of histiocytic infiltrate in the dermis, without the typical palisading granulomas and necrobiosis seen in GA. IGA may present as macular, papular, or plaque-like lesions, often with a violaceous hue. The lesions may be localized or generalized and may affect any site of the body. The most common sites are the trunk and extremities [1].

IGA is often asymptomatic, but, in rare instances, may cause pruritus or tenderness. The course of IGA is variable, ranging from spontaneous resolution to chronic persistence or recurrence. The treatment of IGA is challenging, as there is no proven effective therapy. Topical or intralesional corticosteroids, cryotherapy, light therapy, and oral medications (antimalarials, antibiotics, Biologics) have been tried with variable results [1].

The pathogenesis of IGA is unclear, but it may be related to a delayed-type hypersensitivity reaction to various triggers, such as infections, insect bites, vaccinations, drugs, or trauma. The histiocytic infiltrate may represent a dermal response to altered collagen or mucin [2].

The differential diagnosis of IGA includes several dermatoses that may grossly appear similar , but histologically may or may not involve the dermis. These include:
- Nummular eczema: A chronic eczematous dermatitis that presents as coin-shaped plaques with scaling and crusting. It may be associated with dry skin, atopy, or contact allergy. The histopathology shows spongiosis, acanthosis, parakeratosis, and superficial perivascular lymphocytic infiltrate . [3]
- Fixed drug eruption: A drug-induced hypersensitivity reaction that presents as well-demarcated erythematous or violaceous patches or plaques that recur at the same site after re-exposure to the offending drug. The histopathology shows epidermal necrosis, basal vacuolization, pigment incontinence, and dense perivascular lymphocytic infiltrate with eosinophils [4].
- Morphea: A localized form of scleroderma that presents as indurated plaques with a lilac border and a

whitish center. It may cause atrophy and contractures of the skin and underlying structures over time. The histopathology shows thickening and homogenization of collagen bundles in the dermis and subcutis, with loss of adnexal structures and sparse lymphocytic infiltrate. Plaque Morphea initially presents as a round to oval erythematous and/or edematous plaque and is more likely to mimic IGA on gross appearance.[5]
- Mycosis fungoides: A cutaneous T-cell lymphoma that presents as patches, plaques, or tumors with variable scaling and pruritus. It may progress to systemic involvement and transformation to large cell lymphoma. The histopathology shows atypical lymphocytes with cerebriform nuclei infiltrating the epidermis (Pautrier micro abscesses) and the dermis in a band-like pattern. Immunohistochemistry can show variable results and in general is more helpful to exclude other lymphomas. CD2- and CD5- usually favours mycosis fungoides over other inflammatory diseases.[6]
- Sarcoidosis: A systemic granulomatous disease that affects multiple organs, especially the lungs and lymph nodes. It may present as various cutaneous manifestations, such as violaceous macules and papules, plaques, subcutaneous nodules, or lupus pernio. The histopathology shows noncaseating epithelioid granulomas in the dermis with or without involvement of the subcutis, with a sparse rim of lymphocytes.[7]

The diagnosis of IGA requires a careful correlation between clinical and histopathological features.
It is a rare and challenging condition that may mimic other dermatoses. The diagnosis of IGA requires a careful correlation between clinical and histopathological features. A high index of suspicion and a multidisciplinary approach are essential for the accurate diagnosis and management of this condition.

References:

1. Joshi, T.P., Duvic, M. Granuloma Annulare: An Updated Review of Epidemiology, Pathogenesis, and Treatment Options. *Am J Clin Dermatol* **23**, 37–50 (2022). https://doi.org/10.1007/s40257-021-00636-1
2. Buechner SA, Winkelmann RK, Banks PM. Identification of T-cell subpopulations in granuloma annulare. Arch Dermatol. 1983 Feb;119(2):125-8. PMID: 6218788.
3. Bruckbauer, H.R., Karl, S., Ring, J. (2000). Nummular Eczema. In: Katsambas, A.D., Lotti, T.M. (eds) European Handbook of Dermatological Treatments. Springer, Berlin, Heidelberg. https://doi.org/10.1007/978-3-662-03835-2_68
4. Cheng-Han Lee, Yi-Chun Chen, Yung-Tsu Cho, Chia-Ying Chang, Chia-Yu Chu, Fixed-drug eruption: A retrospective study in a single referral center in northern Taiwan. Dermatologica Sinica, Volume 30, Issue 1, 2012, Pages 11-15, ISSN 1027-8117, https://doi.org/10.1016/j.dsi.2012.02.002, (https://www.sciencedirect.com/science/article/pii/S1027811712000109)
5. Papara C, De Luca DA, Bieber K, Vorobyev A, Ludwig RJ. Morphea: The 2023 update. Front Med (Lausanne). 2023 Feb 13;10:1108623. doi: 10.3389/fmed.2023.1108623. PMID: 36860340; PMCID: PMC9969991.
6. LeBlanc RE. Mycosis fungoides. PathologyOutlines.com website. https://www.pathologyoutlines.com/topic/skintumornonmelanocyticmycosisfungoides.html. Accessed September 12th, 2023.
7. Sarcoidosis (cutaneous sarcoidosis) - Dermatology Advisor

PALISADED NEUTROPHILIC GRANULOMATOUS DERMATITIS (PNGD)

Case No. 29

Presenter: Lauren Chen, MD
Laura Williams, MD
Bing Han, MBBS
Yousef Al Rubaye, MD
Alun Wang, MD, PhD
Carole Bitar, MD
New Orleans, LA

History:
38-year-old male with a history of bicuspid aortic valve complicated by aerococcus viridans bacteremia and aortic valve endocarditis s/p aortic valve repair (2016) presented with fever, and chronic, asymptomatic, migratory rash on the posterior neck and extremities. Patient denies photosensitivity, arthralgias, new medications, recent travel, outdoor activity, animal exposure.

Physical Examination:
Photodistributed erythematous, indurated polycyclic plaques with central clearing

Laboratory Data:
Laboratory work-up revealed new onset pancytopenia. Autoimmune workup was negative.

Histopathology:
Neutrophilic inflammation with peri-vascular distribution in the upper dermis, poorly-formed granuloma is present. PAS is negative for fungal elements. Alcian blue highlights rare mucin with perifollicular pattern. The pathologic findings could be associated with autoimmune disorders, with entities such as neutrophilic lupus erythematosus and rheumatoid neutrophilic dermatitis.

Clinical Course:
Patient's hospitalization was further complicated by acute renal failure. Renal biopsy revealed necrotizing and crescentic glomerulonephritis with C3-dominant deposits concerning for infectious etiology. Upon further extensive workup, patient was positive on Karius cfDNA and serology for *Bartonella henselae*. Patient endorsed a distant history of one cat scratch and was diagnosed with subacute endocarditis under the Duke criteria. He was started on rifampin and doxycycline, however he suffered from a neurologic mycotic aneurysm rupture and succumbed to the disease.

Diagnosis:
Palisaded neutrophilic granulomatous dermatitis (PNGD)

Points of Emphasis:
PNGD is an inflammatory cutaneous reactive pattern with unknown pathogenesis. Most commonly associated with connective tissue disorders and arthritis, but can be seen in lymphoproliferative disorders and infections. There are other infrequent causes, such as this case of subacute bacterial endocarditis. The histologic findings of PNGD are consistent with the evolution of immune complex-mediated leukocytoclastic vasculitis that progresses to granulomatous features. A skin biopsy is required for diagnosis. Patients with cutaneous and histologic features of PNGD, who lack a diagnosis of associated systemic diseases, should be further evaluated with an extensive workup. To the authors' knowledge, this is the first case in the literature describing PNGD in *Bartonella henselae* subacute endocarditis.

References:

1. Yang C, Tang S, Li S, Ying S, Zhu D, Liu T, Chu Y, Fang H, Qiao J. Underlying Systemic Diseases in Interstitial Granulomatous Dermatitis and Palisaded Neutrophilic Granulomatous Dermatitis: A Systematic Review. Dermatology. 2023;239(2):287-298. doi: 10.1159/000527461. Epub 2022 Dec 7. PMID: 36476409.

2. Rosenbach M, English JC 3rd. Reactive Granulomatous Dermatitis: A Review of Palisaded Neutrophilic and Granulomatous Dermatitis, Interstitial Granulomatous Dermatitis, Interstitial Granulomatous Drug Reaction, and a Proposed Reclassification. Dermatol Clin. 2015 Jul;33(3):373-87. doi: 10.1016/j.det.2015.03.005. Epub 2015 Jun 5. PMID: 26143420.

CUTANEOUS METASTATIC CROHN'S DISEASE

Case No. 30 **Presenters:** Monica Bravo, MD
Leigh Hickham, MS4
India Hill, MD
New Orleans, LA

History:
The patient is a 10-year-old male with a history of poorly controlled Crohn's disease with perianal involvement (s/p fistulotomy in 2020) and duodenal stricture, treated with infliximab and methotrexate, who presented in March 2023 with new onset scrotal swelling, pain and erythema and inguinal lymphadenopathy. There was concern for testicular torsion, which was ruled out with a scrotal ultrasound. Dermatology was consulted and we had a high suspicion for a cutaneous manifestation of Crohn's disease and recommended Desonide for 2 weeks at a time. After this hospitalization, patient was seen by Urology to rule out torsion, which was not identified. There was still persistent and recurrent edema to the scrotum, and the patient was readmitted in May for scrotal and penile swelling. Urology and ID and Dermatology were consulted and there was again concern for infection. An ultrasound showed prominent tissue swelling, edema and hyperemia. We had a high suspicion for metastatic Crohn's because of the recurrent nature and his history uncontrolled Crohn's disease. A diagnostic punch biopsy and culture of the scrotum was performed under general anesthesia. Tissue cultures were negative, including fungal and acid-fast bacteria. Pathology was consistent with Metastatic Crohn's Disease. He was treated with Desonide topically for two week courses. There is discussion from Gastroenterology team about adding Stelara or Remicade to better control his Crohn's and Metastatic Crohn's.

Physical Examination:
- Erythematous papules with some excoriation in various stages of healing on the lower abdomen and proximal thighs.
- Edematous, pink phallus and scrotum.
- Right inferior buttocks with erythematous well defined edematous plaque with subtle peau d'orange change.
- No inguinal lymphadenopathy
-

Laboratory Data:
CBC with Differential: unremarkable
CMP: unremarkable
ESR: wnl
CRP: 2.3 (H)
Fecal calprotectin: 175 (H)
HLA-B51: negative
Scrotal skin biopsy and cultures: Negative AFB with smear, fungal and yeast, anaerobe
Scrotal US with soft tissue swelling and hyperemia, and bilateral testicular microlithiasis.

Histopathology:
Scrotum, Punch Biopsy: Dermal granulomatous infiltrate with perilymphatic and perivascular non-caseating granulomas. Sections show acanthotic skin with underlying thickened dermis expanded by inflammatory infiltrate primarily histiocytic (CD68 IHC) with fewer admixed lymphocytes and few scattered eosinophils. Occasional non-caseating granulomas are formed around lymphatic vessels (D240 IHC) and blood vessels. AFB stain is negative. Epidermal ulceration is not present. Acute neutrophilic infiltrate is not present in this lesion. Subcutis is not represented in this biopsy material. Controls are appropriate.

Clinical Course:

The patient clinically improved prior to discharge. While inpatient, he continued infliximab infusions and methotrexate and was followed outpatient by pediatric Gastroenterology for further management of his disease. The infliximab dose was increased after discharge with a plan to add or switch to Ustekinumab if his intestinal and scrotal disease did not respond appropriately. From a dermatologic standpoint, the patient was discharged with topical steroids to manage cutaneous lesions.

Diagnosis: Cutaneous Metastatic Crohn's Disease

Points of Emphasis:
Metastatic Crohn's disease (MCD) is an uncommon noncaseating granulomatous inflammation in skin that is noncontiguous with the gastrointestinal tract.[1] While extra-intestinal manifestations of Crohn's disease are well-documented in adults, cutaneous urogenital involvement in pediatric patients is exceptionally rare. Of the few documented cases, pediatric MCD commonly presents in the perioral, genital, and perianal areas and often precedes gastrointestinal symptoms, making proper diagnosis challenging.[1,2,3,4] In a literature review by Rani et al, pediatric MCD primarily presented as chronic or recurrent scrotal swelling (84%), plaques (15%), or ulcers in males and vulvar swelling (81%) and fissures in females.[4,5] Nearly 60% of these patients were subsequently founds to have intestinal symptoms.[5] Other studies describe metastatic skin lesions as plaques or nodules with a red to violaceous hue with possible ulceration[3] and must be distinguished from direct cutaneous extension, especially in the genital and perianal areas. Clinical and histopathological differential diagnoses for urogenital swelling in pediatric patients is vast, ranging from trauma to infectious, autoimmune or neoplastic [4]. It is reported that pediatric MCD is often misdiagnosed and treated as recurrent scrotal cellulitis prior to biopsy.[6] Unfortunately, there is no standardized protocol or evidence-based treatment regimen for MCD. This case emphasizes the importance of considering extraintestinal manifestations in pediatric patients with Crohn's disease as well as the need for further research to improve early identification and timely intervention in these patients.

References:

1. Corbett, S. L., Walsh, C. M., Spitzer, R. F., Ngan, B. Y., Kives, S., & Zachos, M. (2010). Vulvar inflammation as the only clinical manifestation of Crohn disease in an 8-year-old girl. *Pediatrics*, 125(6), e1518–e1522.
2. Ploysangam T, Heubi JE, Eisen D, Balistreri WF, Lucky AW. Cutaneous Crohn's disease in children. J Am Acad Dermatol. 1997 May;36(5 Pt 1):697-704. doi: 10.1016/s0190-9622(97)80320-9. PMID: 9146530.
3. Bernett , C., & Krishnamurthy , K. (2023, January 9). *Cutaneous Crohn Disease*. National Center for Biotechnology Information. https://pubmed.ncbi.nlm.nih.gov/29262135/
4. Kim SSY, Flannigan RK, Samarasekera D, Terry J, Macneily AE. Case: Metastatic Crohn's disease of the genitalia in a prepubescent male: An illustrative case of an uncommon diagnosis. Can Urol Assoc J. 2017 Sep;11(9):E379-E381. doi: 10.5489/cuaj.4326. PMID: 29382461; PMCID: PMC5798443.
5. Rani U, Russell A, Tanaka S, et al. Urogenital manifestations of metastatic Crohn's disease in children: Case series and review of literature. *J Urol.* 2016;92:117–21.
6. Shum DT, Guenther L. Metastatic Crohn's Disease: Case Report and Review of the Literature. *Arch Dermatol.* 1990;126(5):645–648. doi:10.1001/archderm.1990.01670290089015

PEMPHIGOID GESTATIONIS

Case No. 31 **Presenters:** Aditya Sood, MD
Jennifer Snipes, MD
Clay J. Cockerell, MD, MBA, JD

History: A 35-year-old female presented with an unidentified rash on her left posterior upper arm and upper back. The differential diagnosis based on the clinical appearance was erythema multiforme versus pemphigoid gestationis.

Physical Exam: On examination, the patient's left upper arm and back exhibited erythematous and edematous plaques, ranging from 1 cm to 3 cm in diameter. Some areas were vesiculated.

Histopathology: A 4 mm x 4 mm x 5 mm punch biopsy was taken from the left upper arm. Microscopic examination revealed a superficial perivascular infiltrate consisting mostly of lymphocytes and eosinophils, along with spongiosis in the epidermis and subepidermal vesiculation. Direct immunofluorescence studies demonstrated a smooth band positive for C3 at the dermoepidermal junction, confirming the diagnosis.

Clinical Course: The patient was started on systemic corticosteroids, as well as topical steroids to manage pruritus. Regular monitoring of both the mother and fetus is ongoing.

Diagnosis: Pemphigoid Gestationis

Points of Emphasis: Pemphigoid gestationis (PG), previously known as herpes gestationis, is a distinct dermatosis of pregnancy. It is a rare, autoimmune bullous dermatosis, with clinical and pathogenic similarities to bullous pemphigoid. Typically, it manifests during the third trimester, but may also occur less frequently during the second trimester or post-delivery, showcasing its potential to appear during any stage of pregnancy. Patients with PG present with inflammatory skin lesions accompanied by severe pruritus.

Histopathological examination often reveals a superficial perivascular band-like infiltrate of lymphocytes and eosinophils, as well as spongiosis and subepidermal vesiculation. Another diagnostic hallmark is the presence of a smooth band of C3 deposition only along the dermoepidermal junction, as seen in direct immunofluorescence findings. This distinguishes PG from erythema multiforme, which does not display this feature.

Of note, PG tends to recur in subsequent pregnancies often manifesting earlier and with increased severity. Furthermore, while it commonly resolves within two months post-delivery, there can be instances where PG may persist or worsen due to a sudden surge in antibody levels postpartum. The condition is clinically associated with hydatidiform mole and choriocarcinoma, underscoring the importance of multidisciplinary care and surveillance.

Management of PG is crucial given the significant potential for maternal and fetal morbidity. Localized disease with minimal blistering is often managed with topical corticosteroids and oral antihistamines. In more severe or unresponsive cases, intravenous immunoglobulin (IVIG) has been employed successfully. It is paramount to counsel patients about the transient nature of the disease and the possibility of flares in future pregnancies. Overall, prompt diagnosis and treatment of PG play a crucial role in optimizing maternal-fetal outcomes.

References:

1. Cobo, M. F., Santi, C. G., Maruta, C. W., & Aoki, V. (2009). Pemphigoid gestationis: clinical and laboratory evaluation. Clinics (Sao Paulo, Brazil), 64(11), 1043–1047. https://doi.org/10.1590/S1807-59322009001100002

2. Hallaji, Z., Mortazavi, H., Ashtari, S., Nikoo, A., Abdollahi, M., & Nasimi, M. (2016). Pemphigoid gestationis: Clinical and histologic features of twenty-three patients. International journal of women's dermatology, 3(2), 86–90. https://doi.org/10.1016/j.ijwd.2016.11.004

LINEAR IGA BULLOUS DERMATOSIS

Case No. 32

Presenter: Genevieve Serrano, MD
Annaleigh Harper,
Clay J. Cockerell, MD, MBA, JD
Quezon City, Philippines
Dallas, TX

History: This is an 81 year old female with bumpy, pruritic and erythematous rash on the arms, legs, and trunk present for years. She reported no other symptoms, with no new medications, no new personal care products, or recent infection. She has no recent history of antibiotic use.

Physical examination: Diffuse erythematous papules and pseudovesicles with excoriation distributed on the right anterior proximal upper arm and right anterior distal upper arm. With 40% of the body surface covered in rash.

Laboratory Data: None

Histopathology: There is subepidermal blistering disease in which there are numerous neutrophils and some eosinophils. In some areas, there are small collections of neutrophil in dermal papillae. A special stain, PAS, is negative for hyphae. Immunofluorescence studies demonstrate a smooth band positive for IgA at the interface.

Clinical course: Skin punch biopsy collected from the right upper arm was consistent with linear IgA bullous dermatosis. Patient was started on Clobetasol 0.05% topical cream twice daily in the affected area.

Diagnosis: Linear IgA bullous dermatosis

Points of Emphasis:
Linear IgA bullous dermatosis (LABD) is a rare autoimmune subepithelial vesiculobullous disease that occurs in approximately 0.2-2.3 per million population. It has a bimodal age distribution. In children, it is also known as “chronic bullous disease of childhood” with characteristic tense arciform blisters on an erythematous base in a “string of pearls” configuration.[1,2] Despite the distinct clinical appearance, its pathogenesis is similar to that of adults. This disease is caused by IgA autoantibodies against the 120kDa/97kDa portion of bullous pemphigoid BP180 in the basement membrane zone.[2,3] Causes of this IgA antibody production have been associated with autoimmune diseases, malignancy, and gastrointestinal diseases including Crohn’s.[1,3] Several human leukocyte antigens (HLA) have been implicated including HLA-B8, HLA-Cw7, HLA-DR3, and HLA-DQ2.[2]

In adults, most cases are drug-induced with vancomycin as the most common cause accounting for more than 50% of drug-induced LABD. This manifests within the first month of drug administration. Other drugs that induce LABD include antibiotics (penicillin, cephalosporin, sulfonamides), ACE inhibitors, NSAIDs, and phenytoin.[2,3] LABD lesions often have a widespread distribution in the face, limbs, or trunk. Its presentation varies from tense bullae to herpetiform-like lesions on non-inflamed or sometimes

erythematous skin. It can occasionally present similar to toxic epidermal necrolysis (TEN) with widespread blistering and loss of skin. Pruritus is often reported and mucosal involvement to the oral cavity and conjunctiva may occur.[1,2,3] In this patient they presented with widespread rash on the limbs and trunk and, while she takes medications, none of which are known offending drugs for drug-induced LABD and she instead likely have idiopathic LABD.

Histologically, subepidermal blisters containing inflammatory cells of neutrophil and sometimes eosinophils are appreciated. The upper dermis may show perivascular and diffuse interstitial infiltrate of neutrophils and lymphocytes.[2,3] Some also have focal necrotic keratinocytes[3]. Since its histologic and clinical features mimic those of other blistering conditions, LABD is best diagnosed through direct immunofluorescence of the skin adjacent to the blister. On direct immunofluorescence it appears as a linear IgA band at the dermo-epidermal junction.[1,2] This is in contrast to the granular IgA deposit in dermatitis herpetiformis. Idiopathic LABD may occasionally be accompanied by IgG deposits while drug-induced LABD sometimes present with linear deposition of C3 at the basement membrane zone. There is however no specific pattern that differentiates idiopathic from drug-induced LABD.[2,3]

References:

1) Genovese, G., Venegoni, L., Fanoni, D., Muratori, S., Berti, E., and Marzano, A. (2019). Linear IgA bullous dermatosis in adults and children: a clinical and immunopathological study of 38 patients. *Orphanet Journal of Rare Disease* 14(115): https://doi.org/10.1186/s13023-019-1089-2
2) Juratli HA, Sárdy M. (2019). LInear IgA bullous dermatosis. *Hautarzt* 70(4): 254-259. doi: 10.1007/s00105-019-4377-9.
3) Lammer J, Hein R, Roenneberg S, Biedermann T, Volz T. (2019). Drug-induced Linear IgA Bullous Dermatosis: A Case Report and Review of the Literature. *Acta Dermato-Venereologica* 99(6): 508-515. doi: 10.2340/00015555-3154. PMID: 30809685.

BULLOUS DISEASE WITH SWEAT GLAND NECROSIS

Case No. 33

PRESENTER: Vivien Chen, MD
Callie Cross, MS4
Carole Bitar, MD
Richard Marshall, MD
Pamela Martin, MD
New Orleans, LA

History:
A 61 year old female with a history of anxiety, depression, breast cancer, arthritis s/p right shoulder arthroplasty with revision and recent extended course of doxycycline who presented with a rash and blistering on her foot for the past few days. Patient awoke with pink asymptomatic patches scattered on the body followed by swelling and progressive blistering of the left foot. She denied new mediations but later revealed taking an extra dose of trazodone resulting in a fifteen-hour sleep prior to onset of lesions.

Physical Examination:
Skin exam notable for erythematous patch with surrounding hypopigmentation and well-healing biopsy site on right posterior thigh, erythematous patch on right posterior heel and left dorsal foot, deroofed blister on right lateral hallux, tense bullae on right medial hallux.

Laboratory Data:
At time of diagnosis, patient had an ESR of 95 mm/h. CBC, CMP, C3 and C4 complement levels were within normal limits. UA significant for abnormal protein (20mg/dL) and urobilinogen (3mg/dL). Bacterial culture of interdigital skin of left foot grew mixed skin flora. Bullae fluid culture was negative.

Histopathology: Punch biopsy of lesion on right buttock revealed leukocytoclastic vasculitis with sweat gland necrosis within the deep dermis.

Clinical Course:
While pending biopsy results, patient started a 7-day course of amoxicillin and held doxycycline and new multivitamin. At follow up, she noted interval improvement to rash and decrease of left foot bullae. She was given triamcinolone ointment for use on pruritic lesions on flank and instructed to hold trazodone.

Diagnosis: Bullous disease with sweat gland necrosis, suspected secondary to prolonged immobilization from trazadone use.

Points of Emphasis:
Coma bullae are blistering lesions most commonly in comatose patients taking barbiturates or other psychoactive drugs. Patients initially develop erythematous patches or plaques followed by tense fluid filled bullae on pressure dependent areas 48-72 hours after onset of unconsciousness. Lesions are self-limited and resolve within 1-2 weeks.1 While etiology is uncertain, it is postulated that eccrine gland necrosis and bullae formation result from cytotoxic drug excretion by eccrine sweat glands and/or prolonged pressure that can be exacerbated by low blood flow states.2 Historically, barbiturates have been associated but more recently other medications including opiates, tricyclic antidepressants,

benzodiazepines, hypnotics, antipsychotics, and alcohol have been implicated.3 This case highlights a unique presentation of bullae and sweat gland necrosis in context of trazodone use.

References:

1. Dinis-Oliveira, R. J. (2019). Drug overdose-induced coma blisters: Pathophysiology and clinical and forensic diagnosis. *Current Drug Research Reviews*, *11*(1), 21–25. https://doi.org/10.2174/1874473711666180730102343

2. Shakshouk, H., Johnson, E. F., Peters, M. S., Wieland, C. N., Comfere, N. I., & Lehman, J. S. (2021). Cutaneous eccrine inflammation and necrosis: Review of inflammatory disorders affecting the eccrine apparatus including New Associations. *Human Pathology*, *118*, 71–85. https://doi.org/10.1016/j.humpath.2021.08.005

3. Muirhead, T., Rudner, E., & Lim, H. W. (2011). A case of coma blisters in a non–pressure dependent distribution. *MD*, *64*(2). https://doi.org/10.1016/j.jaad.2010.09.419

ATYPICAL SPITZ TUMOR WITH LMNA-NTRK1 FUSION

Case No. 34

Presenters: Anika Koka
Kristopher McCay, MD
Dipti Anand, MD
Atlanta GA

History: A 40-year-old male with no previous medical history presented with a painless lesion on his arm since, 6 months.

Physical Exam: Physical exam revealed erythematous non-tender papule measuring approximately 5mm on the left mid-lateral posterior arm. Clinical differential diagnosis included dermatofibroma, Spitz nevus and basal cell carcinoma.

Histopathology:
Shave biopsy showed a compound, asymmetric but relatively well-circumscribed proliferation of epithelioid melanocytes arranged as large, irregular, and elongated nests surrounded by a small amount of clefting, with focal pagetoid extension. Individual cells showed variable nucleoli with moderate nuclear pleomorphism and focal hyperchromasia. Bridging of rete ridges was present, and occasional eosinophilic bodies were noted. Within the dermis, surrounded by moderately dense inflammation, were nests of similar enlarged melanocytes. Occasional superficial mitotic figures were identified. There was some decrease in cell size and nest size with depth. Ki67/Melan-A stain dual immunostain showed increased superficial dermal proliferation. Both PRAME and ALK-1 stains were negative. p16 was diffusely positive. ROS-1 and BRAF V600E immunostains were negative with adequate controls. Pan-TRK was strongly positive. FISH study was negative, and Next Generation Sequencing detected LMNA-NTRK1 fusion. Additionally, TERT gene promoter mutation analysis was negative.

Clinical Course: Due to the focal involvement of the specimen edge, conservative excision was recommended. The lesion was excised with clear margins. Patient currently reports no recurrence of the tumor.

Diagnosis: Atypical Spitz Tumor with LMNA-NTRK1 fusion
Points of Emphasis:

Spitz nevi harbor a unique set of initiating oncogenes that distinguish them from other types of nevi and these genetic alterations form the basis for defining Spitz tumors, ranging from benign (Spitz nevi) to malignant (Spitz melanoma). By integrating molecular findings Spitz tumors can now more precisely and reproducibly be distinguished from Spitz-like (spitzoid) melanocytic neoplasms. Spitz melanocytoma is a recently defined term that refers to tumors with a Spitz nevus initiating mutation and additional genetic progression that fall short of melanoma.

Translocations involving tyrosine kinases have been identified in the majority of Spitz neoplasms. They occur in in a mutually exclusive pattern, involving ROS1, ALK, NTRK1, NTRK3, BRAF, RET, MAP3K8 or MET. Each rearranged kinase may have various fusion partners. The fusion partner replaces the normal regulatory site on the tyrosine kinase, resulting in constitutive activation. Some fusions are associated with distinct morphological findings. NTRK1-rearranged Spitz tumors tend to display rosettes, filigree-like epidermal rete ridges, lobulated nests or exhibit exaggerated maturation. The more common fusion partners of NTRK1 gene include LMNA, TPM3, and TP53, with the former, as seen in our case, being the most common. In addition to Spitzoid neoplasms, NTRK1 fusions have been described in adenocarcinoma of lung, glioblastoma, papillary thyroid carcinoma, and in soft tissue neoplasms and

sarcomas. In Spitzoid neoplasms, NTRK1 fusions have been detected in ~16% of cases, being equally common in benign Spitz nevi, atypical Spitz tumors, and Spitzoid melanomas.
It is important for dermatopathologists to be aware of kinase fusions in spitzoid neoplasms, aiding in the precise classification of these tumors. Presence of NTRK1 fusion in the absence of other genetic aberrations, especially homozygous deletion of chromosomal 9p21, is associated with a benign outcome. However, conservative excision with clear margins is recommended.

References:

1. Cheng TW, Ahern MC, Giubellino A. The Spectrum of Spitz Melanocytic Lesions: From Morphologic Diagnosis to Molecular Classification. *Frontiers in Oncology*. 2022;12(889223). doi:https://doi.org/10.3389/fonc.2022.889223

2. Cappellesso R, Nozzoli F, Zito Marino F, et al. NTRK Gene Fusion Detection in Atypical Spitz Tumors. *International Journal of Molecular Sciences*. 2021;22(22):12332. doi:https://doi.org/10.3390/ijms222212332

MELANONYCHIA

Case No. 35

PRESENTER: Julia Accetta, MD
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History:
A 57 year old female with history of mitral valve replacement on warfarin presented for a dark-colored line on her right thumb that had been present for several years. The lesion has become wider and darker over time and she noted crumbling and thinning of the nail plate (Figure 1). Patient denied personal or family history of melanoma or non melanoma skin cancer.

Physical Examination:
On exam the right first thumbnail is noted to have longitudinal melanonychia, several bands, distal onychodystrophy with a central longitudinal ridge with lateral hyperkeratosis, and central periungual black-brown pigment to proximal nail fold. Other nails have artificial nails.

Laboratory Data:
INR of 1.5, no other pertinent laboratory data.

Histopathology:
Sections of the skin show basal hyperpigmentation. No atypia was identified. Melan-A, Sox-10, and PAS were unremarkable. Histologically this lesion was consistent with a lentigo. The evaluation was suboptimal due to a lack of nail base. No evidence of melanoma or infection was identified.

Clinical Course:
The patient is healing well from the biopsy and has no further dermatologic problems.

Diagnosis:
Melanonychia

Points of Emphasis:

The differential diagnosis for longitudinal melanonychia can be subdivided into melanocytic and non-melanocytic causes. Non-melanocytic causes of nail pigmentation include subungual hematoma, fungal melanonychia, and exogenous pigment due to exposure to chemical agents, application of silver nitrate, tobacco, dirt, and cosmetic products (henna, hair dyes). Melanocytic causes can be the result of melanocytic activation or hyperplasia, and can be either benign, as in a nevus, or malignant, such as nail unit melanoma. Other causes of melanocytic hyperplasia can be seen with onychomycosis, chronic paronychia, psoriasis, lichen planus and chronic radiodermatitis as well as systemic disorders such as Addison's disease, Cushing syndrome, hyperthyroidism, porphyria, genetic syndromes, et cetera. Melanocytic activation occurs more commonly in higher Fitzpatrick levels. Since the above etiologies can present similarly to subungal melanoma, nail biopsies are often merited.

There is limited research investigating the clinical differences of benign melanonychia in biopsied versus non-biopsied patients. A study by Lee et al. investigated the clinical and dermoscopic features in diverse skin types and found that darker skinned individuals more frequently had greater mean band width, lower band brightness (i.e. darker color) and overall received more nail matrix biopsies than lower Fitzpatrick types. Of the 248 patients they studied, 19% underwent nail biopsy and all received a histopathological diagnosis of melanotic macule. Those who underwent biopsy had less multidigit band involvement, higher mean band width percentage, darker bands, and more nail changes than patients who did not undergo nail biopsy.

Guidelines for nail matrix biopsies have not been established and clinicians are still instructed to use ABCDEF rule (age, brown-black band, change, digit – thumb or hallux, extension of color, family history of melanoma) to determine whether nail matrix biopsy is warranted. A smaller study by Ko et al found that using the above criteria, subungual melanoma usually presented with wider band percentage but there was no difference between the number of ABCDEF criteria met between melanoma and benign melanonychia, and also noted that dermoscopic findings were inconsistent. They recommend that any concerning band with a width percentage greater than 40% should undergo biopsy.

References:

1. Lee D, Chang M, Desai A, Lipner S. "Clinical and dermoscopic findings of benign longitudinal melanonychia due to melanocytic activation differ by skin type and predict likelihood of nail matrix biopsy." Journal of the American Academy of Dermatology. 87, 4 (2022): 792-799.
2. Lee, Debra K, and Shari R Lipner. "Optimal diagnosis and management of common nail disorders." *Annals of medicine* vol. 54,1 (2022): 694-712. doi:10.1080/07853890.2022.2044511
3. Ko D, Oromendia C, Scher R, Lipner S. "Retrospective single-center study evaluating clinical and dermoscopic features of longitudinal melanonychia, ABCDEF criteria, and risk of malignancy." J Amer Acad Derm. 80, 5 (2019):1272-1283.

CUTANEOUS NEUROCRISTIC HAMARTOMA WITHIN A GIANT CONGENITAL MELANOCYTIC NEVUS

Case No. 36

Presenters: Haley Caire, MD
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New Orleans, LA

History: A 5-year-old female with a known history of atopic dermatitis and giant congenital melanocytic nevus (CMN) was referred to pediatric dermatology for further evaluation. The lesion had been present since birth, but her parents noted gradual growth of the lesion and development of numerous satellite nevi. They also noted focal skin thickening of the lesion within the past few years associated with intermittent painful episodes. She denied any neurological deficits. The lesion was biopsied at 6 months of age at an outside facility, which her parents reported as benign, but the official pathology was unavailable.

Physical Examination: The patient is a well appearing Fitzpatrick type V female who measured 1.136 meters (3.73 feet) in height and weighed 22.1 kilograms (48.72 pounds). Skin exam was significant for a large hyperpigmented patch measuring > 40 cm on her lower back and extending to both flanks, round in shape. There was a focal area of thickening over the central back associated with a hyperpigmented, slightly lichenified patch. In addition, there are > 15 round, uniformly hyperpigmented macules scattered on the neck, trunk, arms, and legs. There were also 2 intraoral melanotic macules noted, one on the left hard palate and the other on the right floor of the mouth.

Histopathology:

1. Skin, area of thickening within congenital melanocytic nevus: Specimen consists of horizontally oriented collagen bundles and fascicles of bland spindle cells showing fibroblastic or myofibroblastic differentiation. The cells have corkscrew nuclei running parallel to the epidermis, without prominent nucleoli and cytologic atypia. The epidermis contains hyperpigmentation and hyperkeratosis. There is subepithelial collagen plaque. These features fit the diagnosis of neurocristic hamartoma with overlying junctional melanocytic nevus.

Clinical course: At the patient's initial clinic visit, an ultrasound and punch biopsy were performed. Ultrasound of the back revealed two areas of plaque-like decreased echogenicity in the dermis with extension to subcutaneous fat; one at the site of the biopsy with a similar area on the left back, 2.3 cm wide and 2.8 cm wide respectively. The biopsy result was consistent with neurocristic hamartoma with an overlying junctional melanocytic nevus with no identifiable dysplasia or malignancy. Because both CMN and neurocristic hamartomas have potential for malignant transformation, an MRI was performed and showed infiltrates in the deep lumbar subcutaneous soft tissues without extension into the paraspinal musculature or underlying lumbar spinous processes. Additionally, other ill-defined lobulated heterogeneously enhancing lesions were noted more superficially on the back. Because of the large size of the lesion, MRI abnormalities, and risk of malignant transformation, staged excision was recommended. The patient is currently being evaluated by plastic surgery.

Diagnosis: Giant congenital melanocytic nevus with biopsy proven neurocristic hamartoma

Points of Emphasis:
Congenital melanocytic nevi (CMN) are proliferations of benign melanocytes that are present at or develop shortly after birth. Its estimated incidence is less than 1 in 20,000 newborns. They usually present as brown patches with well-demarcated borders (1). The nevus grows at the same rate the body grows and is classified based on expected adult size. The patient in this case meets the criteria for a giant CMN, as

the diameter is greater than 40 centimeters in diameter. The surface features can vary thoughout the nevus and can change over time. Affected individuals often have other nevi that are smaller and referred to as satellite or disseminated nevi. The pathogenesis involves somatic mutations in genes (NRAS and BRAF) that control proliferation of neural crest cells, the precursor to melanocytes (2). Treatment is individualized based on close clinical monitoring for any changes in the lesion. Surgical excision is indicated if malignancy develops within the lesion (1).

Cutaneous neurocristic hamartomas (CNH) are very rare, pigmented lesions of the skin and soft tissue resulting from abnormal development of cells of neural crest origin including melanocytes, schwann cells, and pigmented dendritic and spindled cells. Although CNHs can share some features with other dermal melanocytic neoplasms, they have distinct histologic features (3). Histopathology usually reveals a lesion extending deep into the dermis, involving the subcutis. Higher power examination can show a mixture of nevomelanocytes, Schwann cells, and dendritic blue nevus cells. Immunohistochemistry can demonstrate Melan-A, S100, HMB-45, and vimentin positivity. CNH has a reported association with the development of malignancy, but the exact incidence of neither CNH nor malignancy arising within CNH is not well quantified in the literature. The melanomas that may develop are often subepidermal, multinodular tumors, composed of small, round to spindle cells in a trabecular or nested growth pattern (4,5).

This case presents a neurocristic hamartoma arising in the setting of a giant congenital melanocytic nevus (6). The presence of a giant congenital melanocytic nevus alone is associated with a 5 to 10 percent lifetime risk of developing melanoma. Melanoma often begins in the nevus, but it can also develop when the melanocytes invade other tissues like the brain and spinal cord. Unfortunately, when melanoma develops in patients with giant CMNs, the survival rate is low (2). On further literature review, by 2011, 7 cases of malignant transformation in neurocristic hamartomas were found in the literature. The mean time until diagnosis of malignancy was 32 years after identification of congenital CNH and 3.5 years for acquired CNH. Patients with congenital lesions reported multiple recurrences and death within an average of 9 years (4). These patients require close clinical follow up and evaluation for surgical management to monitor for the development of malignancy. We present this case not only to highlight the compounded risk of malignancy and mortality in patients with neurocristic hamartomas developing within giant congenital melanocytic nevi but also for discussion and management recommendations. Due to the size of the lesion, MRI abnormalities, and risk of malignant transformation, the patient is pending staged excision, but it is unclear how aggressive management should be in this situation.

References:

1. Viana AC, Gontijo B, Bittencourt FV. Giant congenital melanocytic nevus [published correction appears in An Bras Dermatol. 2014 Jan-Feb;89(1):190]. *An Bras Dermatol*. 2013;88(6):863-878. doi:10.1590/abd1806-4841.20132233. Giant congenital melanocytic nevus - PubMed (nih.gov)
2. MedlinePlus [Internet]. Giant Congenital Melanocytic Nevus: National Library of Medicine (US); [updated Dec 2014; cited 2023 Sep 16]. Available from: Giant congenital melanocytic nevus: MedlinePlus Genetics
3. Mezebish D, Smith K, Williams J, Menon P, Crittenden J, Skelton H. Neurocristiccutaneous hamartoma: a distinctive dermal melanocytosis with an unknown malignant potential. *Mod Pathol*. 1998;11(6):573-578.
4. Pearson JP, Weiss SW, Headington JT. Cutaneous malignant melanotic neurocristictumors arising in neurocristic hamartomas. A melanocytic tumor morphologically and biologically distinct from common melanoma. *Am J Surg Pathol*. 1996;20(6):665-677. doi:10.1097/00000478-199606000-00003
5. Patterson JW. (2016). Lentigenes, Nevi, and Melanomas In Weedon' s Skin Pathology (fourth edition, pp. 910-913). Text, Elsevier.

6. Garrido MC, Maroñas-Jiménez L, Ruano Y, Rodriguez-Peralto JL. Proliferating Neurocristic Hamartoma Arising in a Giant Congenital Nevus: Comparative Genomic Hybridization Findings. *Am J Dermatopathol*. 2019;41(6):438-442. doi:10.1097/DAD.0000000000001319

MALIGNANT MELANOMA AND GENE EXPRESSION PROFILING

Case No. 37 **PRESENTER:** Etan Marks, DO
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History:
Patient is a 60-year-old male that noticed a lesion on the left proximal calf that had been changing over several months. It had some elevation to it. The patient does not regularly see a dermatologist. The patient's significant other had photographs that demonstrated the character as well as the black and brown raised area. Patient has a family history of pancreatic cancer in mother and paternal grandfather ages 58 and 85, respectively. However, the patient had no history of melanoma or other skin cancer. He also has type 2 diabetes and hypertension.

Physical Examination:
There is a 0.7 cm x 0.5 cm area of pigmentation with a volume to it and is raised roughly 1 mm. There are no satellite or in-transit lesions. No popliteal or inguinal lymphadenopathy. Total body cutaneous examination finds no atypical lesions with moderate bronzing bathing trunk distribution.

Laboratory Data:
Vital signs: BP 118/63 seated, 70 pulse and regular, respirations 18, oxygen saturation 95%, BMI of 29. LDH normal at 120. Pre-operative chest x-ray was negative.

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Histopathology:
Punch biopsy of a compound melanocytic proliferation with unusual features. There is some pagetoid spreading melanocytes, pleomorphism among some of the melanocytes, as well as dusky cytoplasm. There is abundant melanin pigment, some in melanophages and an inflammatory response. Immunohistochemical stains for Sox10 and PRAME were performed. Sox10 highlighted the melanocytes, but PRAME was only focally and weakly positive. Therefore, in light of the worrisome clinical and histological features 23-gene expression profiling was pursued (GEP)(Castle Biosciences' MyPath) which returned a result suggestive of a malignant neoplasm.

Clinical Course: Patient was referred to oncology where lesion was resected with 1.5 cm margins. Sentinel lymph nodes were taken from the left superficial groin, which were negative (0/2). Residual melanoma was seen at a depth of 0.75 mm

Diagnosis:
Malignant melanoma, left proximal calf, 0.7 mm in depth. Stage IB melanoma pT1b N0 M0.

Points of Emphasis:
Worrisome clinical lesions are often biopsied but can be histologically difficult to come to a definitive diagnosis. This is especially true when the sampling technique used prevents some histologic features from being assessed. For example, a punch biopsy of a pigmented lesion can prevent assessment of circumscription or can simply only represent a partially sampled lesion. Additionally, even if worrisome features are present, there may be ambiguous features histologically, such as inflammation and irritation without mitotic figures or ulceration. Lastly, PRAME has been shown to be very helpful in the diagnosis

of melanoma when diffusely positive.[1] However, when a worrisome lesion is negative for PRAME, this lesion could still represent a PRAME negative melanoma.

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In these difficult or ambiguous lesions, molecular testing can be very useful. Each molecular test has its benefits and its drawbacks. In our case, we used the MyPath test which has been shown to be highly sensitive and specific (90%-95% for both) thanks to its inclusion of a variety of markers for tumor microenvironment as well as cell specific markers.[2] Therefore, when any doubt about an ambiguous melanocytic lesion occurs, consideration of using GEP is appropriate as it can help lead to a definitive diagnosis and appropriate treatment as was done in this case.

References:

1. Lezcano C, et al. *Am J Surg Pathol*. 2018 Nov;42(11):1456-1465.
2. Clarke LE et al. *Cancer*. 2017;123:617–628.

DISSEMINATED BLASTOMYCOSIS WITH SECONDARY MENINGITIS AND ENCEPHALOPATHY IN AN IMMUNOCOMPETENT MALE

Case No. 38

PRESENTERS: Sammi Jo Albucker, MS4
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History:
38-year-old male with nonpainful skin lesions that first developed on the scalp and spread to the nose, lip, neck, chest, and leg. He presented to the hospital after an unresponsive episode at home. He reported month-long worsening headaches, blurry vision, weight loss (20 pounds), dizziness, nausea, vomiting, and lethargy. Prior to his hospitalization, he was otherwise healthy with no significant past medical history and no medications. He lives in southern Mississippi and denied recent travel, exposure to exotic animals or swimming in any bodies of water. He has no history of immunosuppression, HIV, or other sexually transmitted infections.

Physical Examination:
Vertex scalp- two verrucous plaques with heme crust and ulceration
Right lateral canthus, right inferior nares, and chin - three verrucous plaques with ulceration and friability
Chest - scattered follicular papules and pustules on the chest, and scattered hyperpigmented macules
Left lower extremity -few verrucous crusted papules on the left lower extremity.

Laboratory Data:
Lab results for acid fast smear, serum histoplasma antigen, serum blastomycosis antigen, cryptococcus antigen, HIV, hepatitis C, and treponemal pallidum antibody were negative. CSF cytology was negative for malignant cells and blastomycosis CSF antigen was positive. MRI brain without contrast demonstrated meningeal enhancement of the basal cisterns, compatible with meningitis. There was moderate hydrocephalus and subacute ischemic infarcts involving several regions of the brain.

Histopathology:
Two punch biopsies of the right upper lip lesion were sent for Hematoxylin and Eosin (H&E) and tissue culture. On H&E, pseudoepitheliomatous hyperplasia was seen. GMS stain confirmed the presence of broad-based budding yeasts, suggestive of blastomycosis.

Clinical Course:
Tissue pathology along with blastomycosis CSF antigen positivity confirmed the diagnosis of disseminated blastomycosis with secondary meningitis and encephalopathy. Patient was treated with IV amphotericin and voriconazole. He developed seizures with cerebral vasospasms and his condition continued to worsen. He died weeks later.

Diagnosis:
Disseminated blastomycosis with secondary meningitis and encephalopathy

Points of Emphasis:

Blastomycosis is a dimorphic, fungal infection caused by Blastomyces dermatitidis, which is endemic to the Ohio and Mississippi River Valleys, Great Lakes region, and southeastern United States.[1] As this patient was immunocompetent, the frequency of a disseminated presentation of blastomycosis in healthy populations was of interest. In a retrospective study of 106 adult patients with blastomycosis (2004-2016), immunocompromised patients had higher rates of acute pulmonary disease (p=0.03), more severe infection (p=0.007), respiratory failure (p=0.010), and increased mortality (p=0.02).[2] However, the rate of disseminated blastomycosis was similar among non-immunocompromised (48.6%) and solid organ transplant recipients (47.4%), suggesting that pathogen-related factors may have a greater impact on dissemination for blastomycosis than immunity levels.[2]

Of note in this patient, the blastomycosis serum antigen test was negative. In a retrospective study evaluating the use of *blastomycosis* urine, serum, and bronchoalveolar lavage fluid antigen assays for blastomycosis diagnosis, serum antigen testing was positive in 9/14 (64.3%) patients with isolated pulmonary disease, 1/3 (33.4%) patients with disseminated infection, and 0/1 (0%) patients with extrapulmonary infection (p=0.08).[3] Though not statistically significant and limited by a small sample size of disseminated extrapulmonary infection, the study demonstrates that when one has a high degree of suspicion for blastomycosis, antigen testing alone should not be employed to exclude the diagnosis, and culture and cytopathology remain the gold standard for diagnosing blastomycosis.[3]

In summary, this case demonstrates that disseminated blastomycosis can significantly affect the skin and central nervous system. It highlights the importance of keeping this diagnosis on the differential regardless of patients' immunocompetency or negative serology.

References:

1. Hashim S, Barrios C. Disseminated blastomycosis. *IDCases*. 2020;21:e00786. Published 2020 May 14. doi:10.1016/j.idcr.2020.e00786
2. McBride JA, Sterkel AK, Matkovic E, Broman AT, Gibbons-Burgener SN, Gauthier GM. Clinical Manifestations and Outcomes in Immunocompetent and Immunocompromised Patients With Blastomycosis. *Clin Infect Dis*. 2021;72(9):1594-1602. doi:10.1093/cid/ciaa276
3. Frost HM, Novicki TJ. Blastomyces Antigen Detection for Diagnosis and Management of Blastomycosis. *J Clin Microbiol*. 2015;53(11):3660-3662. doi:10.1128/JCM.02352-15

CUTANEOUS ATYPICAL MYCOBACTERIAL INFECTION

Case No. 39 **PRESENTERS:** William Goodman, MS2
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History:
Patient is a 45 year old female with a past medical history of latent tuberculosis (s/p treatment in 2017) and rheumatoid arthritis (on plaquenil, infliximab, methotrexate) who presented 05/2023 with tender subcutaneous nodules on left forearm. She denies preceding trauma or systemic symptoms. Of note, patient previously with LLE ulceration of unknown etiology (02/2023 from which biopsy showed nonspecific granulomatous dermatitis without evidence of vasculitis or infection) which had resolved s/p intralesional kenalog.

Physical Examination:
- General Appearance: Well-appearing.
- Psych: Pleasant.
- Skin:
- Right Arm: No lesions.
- Left Arm: Irregular, flesh colored subcutaneous nodule/cords to ventrolateral forearm.
- Right Leg: No lesions.
- Left Leg: Atrophic plaque without erosion to pre-tibia.

Laboratory Data:
Tissue Culture, AFB with smear: Stain + for acid-fast bacteria with culture growing *Mycobacterium chelonae.*
Send-out antibiotic susceptibility testing confirmed susceptibility to macrolide antibiotics
Tissue PCR send-out to University of Washington confirming presence of *M chelonae.*

Histopathology:
Skin, left lower arm, biopsy
- Caseating granulomatous dermatitis
Note: Mycobacteria-like organisms are identified on Fite and GMS stains. Further study, including PCR and culture is recommended for microorganism identification.

Clinical Course:
Tissue PCR confirmed *Mycobacterium chelonae* with susceptibility to macrolides. She was prescribed clarithromycin 500mg BID per infectious disease consultation with an anticipated 3-6 month course. July 2023 clinic visit with resolution of left arm subcutaneous nodules.

Diagnosis:
Atypical mycobacterial infection - *Mycobacterium chelonae* in the setting of immunosuppression.

Points of Emphasis:
It is important to consider atypical pathogens in cases where immunosuppression is a factor. Other risk factors include trauma, nail salons, and medical procedures (e.g., liposuction, implants). Initially, it was unclear whether the skin condition represented cutaneous TB or atypical mycobacteria. Additionally, it is still unclear if the LLE pretibial ulceration is related to LUE nodules as this resolve prior to clarithromycin treatment.

One should have high suspicion for atypical mycobacterial infection in immunosuppressed patients with lesions displaying sporotrichoid pattern, accompanied by granulomatous inflammation on histopathology.

When using staining techniques to confirm mycobacteria infection, AFB stain sensitivity can widely vary. Host immune response, mycobacterial load, and the mycobacteria species being tested can all alter the test's sensitivity, which generally ranges from 20% - 80%. Even though AFB stain was positive in this case, the wide range highlights the limitations of AFB staining as a standalone diagnostic tool.

After biopsy, the diagnostic workup included tissue culture and PCR, which are necessary for identification of the specific mycobacterial species. It is important to note that atypical mycobacteria can have varying growth rates in culture. *M. Chelonae* is considered a rapid grower as it can produce visible colonies in 3-5 days, while slow growers can take several weeks. In addition to culture, PCR may also be used as a send out diagnostic test. Generally, PCR has a higher sensitivity and lower specificity compared to culture. Even though PCR has the ability to detect mycobacterial DNA when cultures are negative, they are still essential in determining antimicrobial susceptibility.
With these factors contributing to the complexity of diagnosis, interdisciplinary management with infectious disease should be considered for antimicrobial recommendations.

References:

1. Hrvatin Stančič B, Žgavec B, Bergant Suhodolčan A. Mycobacterium chelonae infection in an immunocompromised patient presenting as multiple papulonodules on the leg. Acta Dermatovenerol Alp Pannonica Adriat. 2022 Mar;31(Suppl):S21-S24. PMID: 35339138.
2. Olesen, Jens Steen, et al. "*mycobacterium chelonae*hand infection after steroid injection in a patient with rheumatoid arthritis receiving long-term linezolid therapy." *BMJ Case Reports*, 2017, https://doi.org/10.1136/bcr-2016-217257.

CUTANEOUS TUBERCULOSIS

Case No. 40 **Presenter:** Gavin Dennis, MS2
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History:
Patient is a 40 year-old female with a complex past medical history including hidradenitis suppurativa on Humira, mast cell activation disorder, Ehlers-Danlos syndrome, IgG deficiency, and familial Mediterranean fever.

She presented to dermatology with a several month history of erythematous plaques with ulceration on her left lower extremity (LLE). The lesions reportedly started after scratching the back of her leg on a blackberry bush. Three months prior to presentation, she was hospitalized for suspected LLE cellulitis, where she received various IV antibiotics (e.g. piperacillin/tazobactam, vancomycin, and levofloxacin) and her Humira was held. Nevertheless, her LLE ulcers continued to worsen. The patient then had a biopsy which was interpreted as non-specific ulceration with calcinosis cutis and she was started on minocycline 100 BID. Bacterial and fungal cultures were done at that time, showing no growth.

Physical Examination:
Several discrete, punched out ulcers with scalloped borders and surrounding violaceous erythema affecting the distal left lower extremity and dorsal foot.

Laboratory Data:
Vitals within normal limits.
Admission labs (6/17/23): Lactate 3.3, WBC 13.0, Hgb 17.5, ESR 18, CRP 0.9
Imaging (6/17/23): X-ray LLE: dermal vs soft tissue calcification in left lower leg.

Histopathology:
Examination of punch biopsy from the left lower extremity showed a dense mixed inflammatory infiltrate in the dermis composed of epithelioid and foamy histiocytes, multinucleate giant cells, lymphocytes and rare scattered neutrophils surrounding an area of necrosis. Focal areas of fat necrosis and lymphohistiocytic infiltrate in association with dystrophic calcifications, highlighted by Von Kossa stain were also identified. Scattered medium sized blood vessels showed calcification of vessel wall media. Gram stain showed scattered Gram positive/variable bacilli within the lesion. Acid-Fast Bacteria (AFB) and Fite stains highlighted scattered bacilli within the inflammatory infiltrate. Periodic Acid-Schiff (PAS) and Grocott methenamine silver (GMS) stains were negative for fungal microorganisms.

Overall, given that AFB and Fite stains highlighted bacilli coupled with granulomatous inflammation and necrotic material, these findings were consistent with an infectious process such as a variant of cutaneous tuberculosis. Nontuberculosis mycobacterium was also considered.

Clinical Course:
Given that the ulcers continued to progress despite various treatments, the patient's biopsy was then sent to the UPMC dermatopathology in consultation and suspicion for cutaneous tuberculosis versus nontuberculous mycobacterium was raised based on aforementioned pathologic findings. At the time of writing, molecular speciation of mycobacteria by polymerase chain reaction (PCR) and repeat tissue culture for AFB were pending. Chest x-ray showed a 2cm right lung nodular density.

Diagnosis:
Cutaneous tuberculosis vs atypical mycobacterial infection

Points of Emphasis:

1. The diagnosis of cutaneous tuberculosis in this case highlights the importance of maintaining a high index of suspicion even in low-prevalence areas such as the United States. AFB cultures should be considered when submitting tissue for culture, especially in immunosuppressed individuals.

2. Our case emphasized the difficulty in identifying mycobacteria using AFB/Fite stains due to the limited number of bacteria detected in the biopsied tissue sample.

References:

1. Charifa A, Mangat R, Oakley AM. Cutaneous Tuberculosis. [Updated 2023 Aug 14]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2023 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK482220/

2. Chen Q, Chen W, Hao F. Cutaneous tuberculosis: A great imitator. Clin Dermatol. 2019 May-Jun;37(3):192-199. doi: 10.1016/j.clindermatol.2019.01.008. Epub 2019 Jan 11. PMID: 31178102.

SECONDARY SYPHILIS

Case No. 41

Presenter: Giuseppe Tripodi, MD
Anna Sompayrac, MS4
Erin Boh, MD
Ghaidaa Majari, MD
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History:
A 66-year-old male presented to clinic for evaluation of an 8-month history of painless, mildly pruritic rash beginning on the abdomen that later progressed to involve the neck, back, and extremities. Patient denied fever, chills, lymphadenopathy, weight loss, or gastrointestinal symptoms. Biopsy from outside dermatologist demonstrated findings concerning for B-cell lymphoma; subsequent PET-CT, EGD, colonoscopy, and bone marrow biopsy were unrevealing for malignancy.

Physical Examination:
Physical examination demonstrated intensely erythematous, polymorphic patches and plaques without significant scale involving the trunk and extremities with approximately 35-40% total BSA involvement. No palpable lymphadenopathy was present in cervical, supraclavicular, axillary, or inguinal areas. Repeat punch biopsies of the left shoulder and thigh were performed due to concern for cutaneous T-cell lymphoma given morphology and distribution of rash and previous biopsy data.

Laboratory Data:
CBC with differential, CMP, and LDH were unremarkable aside from mild thrombocytopenia of 142,000/uL and elevated total protein of 9.1 g/dL with gamma gap of 5.1.

Histopathology:
Surgical pathology of both sites revealed lymphoplasmacytic infiltrate with presence of spirochetes consistent with diagnosis of syphilis.

Clinical Course:
RPR titers were elevated to 1:512 and the patient was referred to infectious diseases and later allergy/immunology for penicillin desensitization. Sexual history was notable for a single sexual encounter two months prior to the development of rash. HIV screen was negative. Patient underwent treatment with single dose benzathine penicillin G 2.4 million units IM. He tolerated treatment without negative side effects and rash resolved.

Diagnosis: Secondary syphilis

Points of Emphasis:
Clinical presentation of syphilis is highly variable and can mimic conditions such as cutaneous T-cell lymphoma. Dermatopathology of lesional skin shows dermal lymphoplasmacytic infiltrate and Steiner stain can be used to confirm presence of spirochetes.

References:
1. Whiting C, Schwartzman G, Khachemoune A. Syphilis in Dermatology: Recognition and Management. *Am J Clin Dermatol*. 2023;24(2):287-297. doi:10.1007/s40257-022-00755-3
2. Harris E. STI Epidemic Worsened in 2021, Syphilis Cases Surged. *JAMA*. 2023;329(19):1633. doi:10.1001/jama.2023.6620
3. Preliminary 2021 STD Surveillance Data. Centers for Disease Control and Prevention; [Accessed September 16, 2023]. Published September 1, 2022. https://www.cdc.gov/std/statistics/2021/default.htm

INVASIVE ASPERGILLOSIS PRESENTING AS NON-HEALING ULCERS

Case No. 42

PRESENTER: Vivien Chen, MD
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History:
An 80 year old female with hypertension, type 2 diabetes mellitus, and recently diagnosed diffuse large B cell lymphoma (DLBCL) s/p first chemotherapy cycle of rituximab and EPOCH who presented with a non-healing wound on her left leg. She was evaluated in the inpatient setting, admitted for neutropenic fever and E.coli bacteremia. The wound was present for the past month, first starting as a small blister. The patient noted clear fluid drainage, and tenderness to the surrounding area. She had similar lesions on the calf and right finger, and denied any recent trauma to the sites.

Physical Examination:
Skin exam notable for an ulcer on the left anterior leg with yellow, fibrinous wound bed and violaceous rolled border, surrounding erythema and induration. Pitting edema +3 of bilateral legs.

Laboratory Data:
At the time of diagnosis, the patient had a WBC of 0.3 K/uL with ANC 0.10 K/uL, platelet count of 18 K/uL, and hemoglobin of 10.9 g/dL with MCV 80.5 fL. CMP was significant for potassium of 2.5 mmol/L and phosphorus of 0.7 mg/dL, elevated alkaline phosphatase 162 units/L. AST and ALT were within normal limits.

Histopathology:
From punch biopsy of wound edge, H&E revealed multiple septated hyphae throughout epidermis and dermis, and vessel walls. Confirmed with positive PAS stain.

Clinical Course:
Following biopsy results, tissue cultures grew *Aspergillus flavus*. CT chest showed multifocal ground glass pulmonary nodules concerning for lung involvement. The patient was discharged to a subacute rehab center to complete a 6 week course of isavuconazonium (Cresemba).

Diagnosis: Invasive aspergillosis

Points of Emphasis:
Angioinvasive fungal infections are aggressive, with complications resulting in mortality rates from 50% to up to 100%1. Timely diagnosis with histopathologic and culture confirmation is important for prompt treatment1,2. Angioinvasion occurs rapidly, causing necrosis and tissue hemorrhage. Clinically, primary cutaneous lesions present as red to violaceous macules or papules that develop into vesicles with central hemorrhage and subsequently ulcerate3. Risk factors include immunosuppression, COPD, and decompensated liver disease2.

References:
1. Berger AP, Ford BA, Brown-Joel Z, Shields BE, Rosenbach M, Wanat KA. Angioinvasive fungal infections
impacting the skin: Diagnosis, management, and complications. J Am Acad Dermatol. 2019;80(4):883-898.e2.
doi:10.1016/j.jaad.2018.04.058
2. Cadena J, Thompson GR 3rd, Patterson TF. Invasive Aspergillosis: Current Strategies for Diagnosis and

Management. Infect Dis Clin North Am. 2016;30(1):125-142. doi:10.1016/j.idc.2015.10.015
3. Shields BE, Rosenbach M, Brown-Joel Z, Berger AP, Ford BA, Wanat KA. Angioinvasive fungal infections
impacting the skin: Background, epidemiology, and clinical presentation. J Am Acad Dermatol. 2019;80(4):869-880.e5. doi:10.1016/j.jaad.2018.04.059

FACIAL HERPES VEGETANS IN AN HIV-POSITIVE PERSON WITH UNDETECTABLE VIRAL LOAD

Case No. 43

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History:
A 51-year-old woman with a past medical history of asthma and gastroesophageal reflux disease presented to the emergency department with a four-week history of a rapidly progressive, ulcerating nodule on the right nasal ala. The patient is an HIV-positive person, well-controlled on bictegravir/emtricitabine/tenofovir alafenamide. She reported adherence to antiretroviral therapy with no lapses in care.

Physical Examination:
Physical examination was significant for a round, exophytic plaque abutting the right nasal opening, extending medially to the columella and inferiorly to the upper lip. Physical examination was otherwise within normal limits.

Laboratory Data:
The patient's viral load was undetectable and her CD4+ cell count was 382 cells/μL. Viral swab of the lesion revealed positive herpes simplex virus 2 (HSV 2).

Histopathology:
A lesional punch biopsy revealed impetiginized, purulent scale crust and markedly inflamed granulation tissue with rare multinucleated cells.

Clinical Course:
The patient was first given high-dose oral valacyclovir (1000mg daily) but failed to respond, prompting the initiation of topical imiquimod 5% cream, which reduced the lesion's size by 50%. Ultimately, the patient is awaiting surgical intervention for removal of the residual plaque.

Diagnosis:
Herpes vegetans

Points of Emphasis:
1. Despite herpes vegetans classically presenting in the anogenital region of severely immunocompromised patients, clinicians must consider herpes vegetans on the differential for HIV-positive persons presenting with a verrucous plaque, irrespective of the lesion location or the patient's viral load.
2. Herpes vegetans may mimic neoplastic or atypical infections, and prompt identification of the correct diagnosis is essential for proper treatment and favorable outcomes.

References:

1. Ronkainen SD, Rothenberger M. Herpes Vegetans: an Unusual and Acyclovir-Resistant Form of HSV. *J Gen Intern Med*. 2018;33(3):393. doi:10.1007/s11606-017-4256-y

2. Yen-Fen Y, Yu-Hung W. Herpes vegetans. *Dermatologica Sinica*. 2013;31(3):163-164. Published 2012 Dec 12. Doi:10.1016/j.dsi.2012.12.001.