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Eosinophilic Pustular Folliculitis

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Case Presentations:

Patient A

Patient: 52 year-old Caucasian male

History of Present Illness: Patient presented with a 1-month history of a pruritic red rash on his face, neck, shoulders, and chest. The patient had already completed a course of azithromycin, IM triamcinolone, and oral prednisone with only minor improvement. He experienced initial improvement in his itching with a decrease in the number of skin lesions. One month after his initial presentation, he began to experience difficulty swallowing and fatigue. He experienced swollen tonsils with neck and axillary lymphadenopathy and was diagnosed with mantle cell lymphoma.

Medical History/Surgical History: Prostate cancer

Current Medications: Indomethacin, triamcinolone cream, and hyper CVAD rituximab chemotherapy

Previous Treatments: Azithromycin, IM triamcinolone, oral prednisone, and doxycycline

Physical Examination: Multiple pink to red folliculocentric papules and pustules admixed with edematous pink plaques scattered on the face, neck, shoulders, and back. Palms, soles, and oral mucosa were clear.

Laboratory Data: Serum HIV: negative, CBC and CMP normal except as follows: eosinophils 8% (0-4%)

Studies: CT: neck, chest, and abdomen demonstrated diffuse lymphadenopathy. PET/CT: extensive metabolically active lymphoma in multiple nodal groups above and below the diaphragm with lymphomatous involvement of spleen. Axillary LN Bx: mantle cell lymphoma (CD4:CD8 1:1, CD45 (-), CD20 (+), CD5 (+))

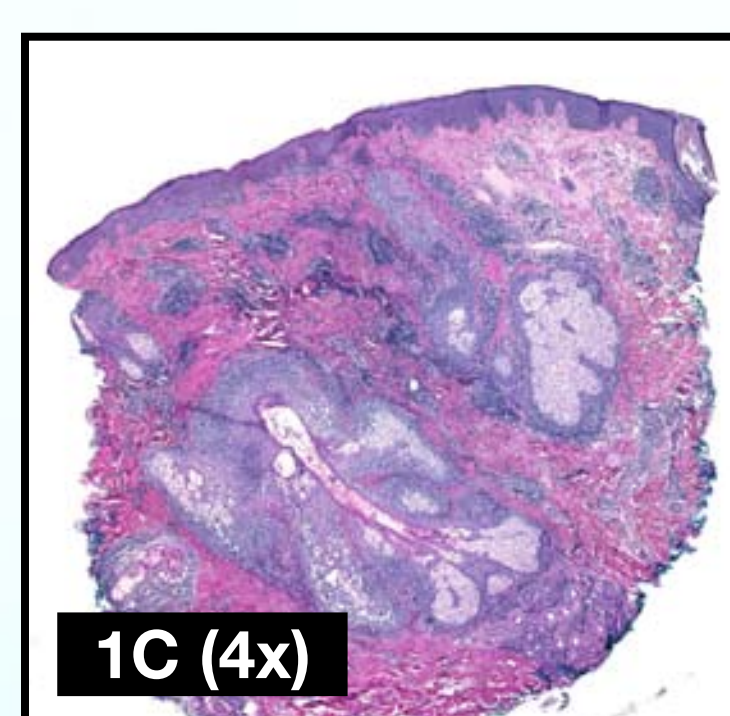
Biopsy: *Advanced Dermatology Associates, LTD* (S13-16789, 5/20/2013) Forehead: "Eosinophilic follicular spongiosis with intrafollicular Langerhans cell microgranulomas along with superficial and deep perivascular, interstitial, and perifollicular chronic inflammation."



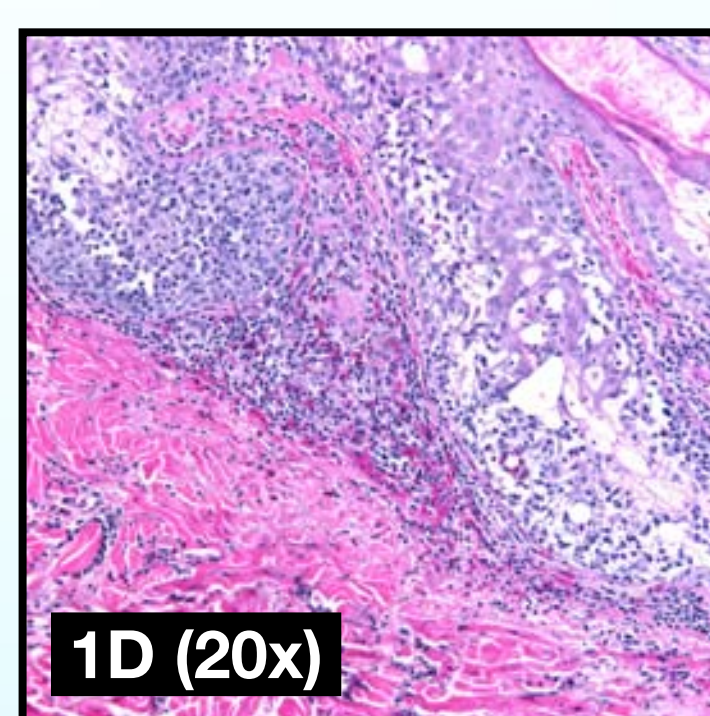
Figure 1A: Pink to red edematous papules and plaques on the face



Figure 1B: Closer view showing pustules on the right forehead



1C (4x)



1D (20x)

Figure 1C and 1D: H&E, Follicular spongiosis with intrafollicular, interstitial, and perivascular lymphohistiocytic infiltration with numerous eosinophils

Patient B

Patient: 64-year-old African American male

History of Present Illness: Patient was admitted to the hospital for lower extremity deep vein thrombosis (DVT) in addition to a six-month history of a diffuse pruritic rash on his head, neck, trunk, and proximal extremities. Skin biopsy performed 3 months prior was consistent with a spongiotic drug reaction. However the skin rash did not improve after adjusting his medications. He describes the rash as stable and does admit to slight improvement with topical triamcinolone use at home.

Medical History/Surgical History: Chronic kidney disease s/p renal transplant with chronic allograft nephropathy and episodes of acute graft rejection, history of upper and lower extremity DVTs, hypertension, anemia of chronic disease, congestive heart failure, chronic atrial fibrillation, morbid obesity, and chronic immunosuppression

Current Medications: Prednisone, topical hydrocortisone, hydroxyzine, cinacalcet, tacrolimus, metoprolol tartate, methocarbamol, simvastatin, warfarin, furosemide and fluticasone propionate/ salmeterol inhaled

Previous Treatments: Triamcinolone ointment

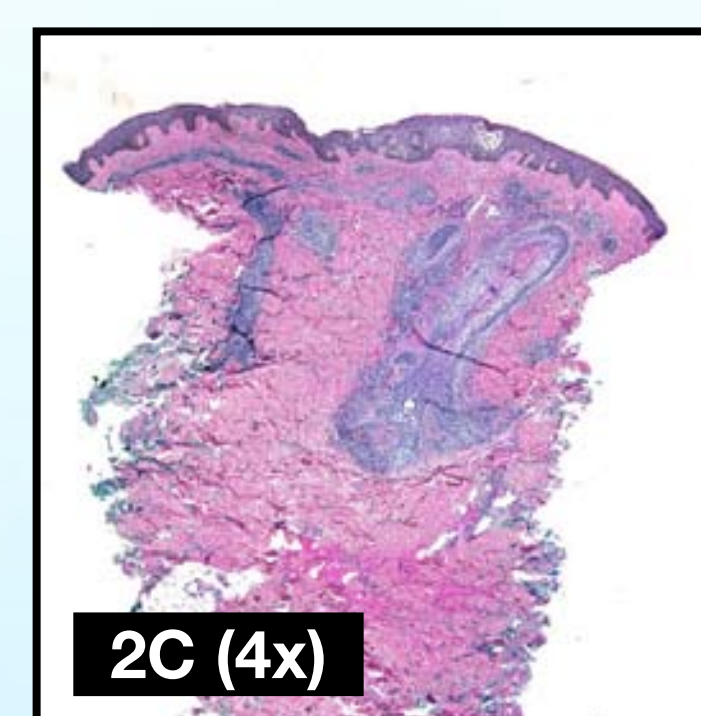
Physical Examination: Scattered hyperpigmented and firm folliculocentric papules and nodules on the head, neck, chest, abdomen, back, proximal thighs, and arms. Palms, soles, and oral mucosa are clear.

Laboratory Data: CBC: hemoglobin 11(13.5-18 g/dL) hematocrit 35 (40-54%) wbc 16 (4.5-11 thou/cmm), absolute eosinophils 9 (0-0.5 thou/cmm), eosinophils 54% (0-4%), creatinine 2.9 (0.7-1.5 mg/dL), GFR 22 (>60), UA wnl, sirolimus and tacrolimus drug levels wnl, serum HIV negative, negative for translocation (9:22) and BCR/ABL transcript product

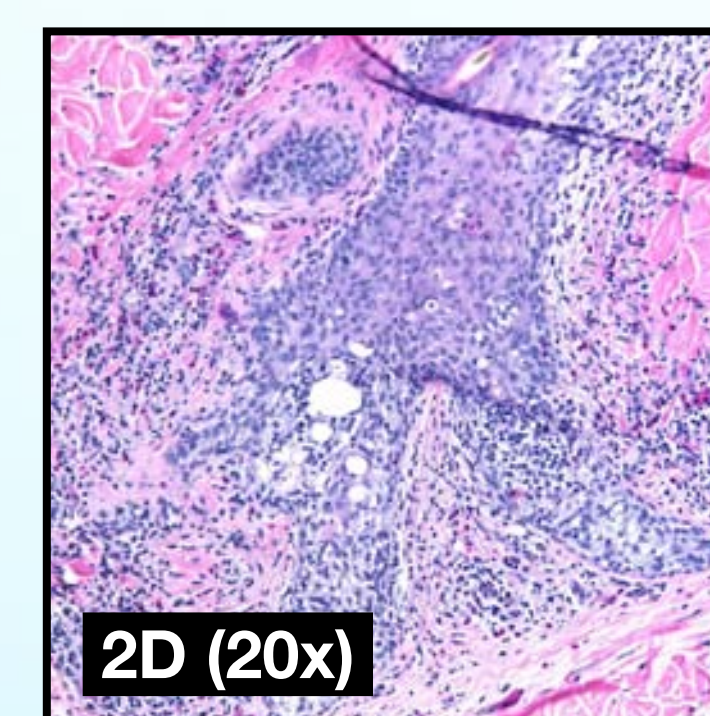
Biopsy: *Health Network Laboratories* (S13-29505, 9/4/2013): Right shoulder: "Follicular spongiosis associated with exocytosis of lymphocytes and eosinophils. There is superficial to mid dermal lymphohistiocytic infiltrate with numerous eosinophils. Focal spongiosis of overlying epidermis with a Langerhans cell microgranuloma."



Figure 2A and Figure 2B: Hyperpigmented lichenified papules and nodules on the face, chest, and abdomen



2C (4x)



2D (20x)

Figure 2C and 2D: H&E, Follicular spongiosis with overlying focal epidermal spongiosis, superficial and mid dermal lymphohistiocytic inflammation, and abundant eosinophils

Discussion:

Eosinophilic pustular folliculitis (EPF) was originally described by Ofuji in 1965 with the first case presenting as folliculocentric pustules distributed on the face, torso, and arms of a Japanese female. Since the initial description, three distinct subtypes of EPF now exist. These types include the originally described classic variant seen in the Japanese population, an immunosuppressed (EPF-IS) variant, and a rare infantile form.

All three subtypes of EPF are more commonly seen in men compared to women. The classic form has a peak incidence between the third and fourth decades. It presents as recurrent follicular papules and pustules located on the face, trunk, or extremities and more rarely the palmoplantar surfaces. Post inflammatory hyperpigmentation is common and leukocytosis with eosinophilia is seen in up to 35% of patients.

The IS subtype demonstrates intensely pruritic discrete erythematous follicular papules with palmoplantar sparing, and infrequent annular or circinate plaque forms. Frequently with the IS-HIV form, CD4 cell counts are below 300 cells/ μ l (500-1200 cells/ μ l) and 25%-50% of patients have lymphopenia with eosinophilia. The IS-Heme form has been predominantly associated with hematologic malignancies including non-Hodgkin lymphoma, leukemia (ALL and AML), and myelodysplastic syndrome. For all of these cases except two, EPF followed bone marrow transplant, peripheral blood stem cell transplant, or chemotherapy initiation. To date, no reported cases of EPF presenting prior to the diagnosis of mantle cell lymphoma have been described.

Our patient cases represent variants of immunosuppression related eosinophilic pustular folliculitis. Patient A presented initially with EPF a month before being diagnosed with mantle cell lymphoma. Patient B had a more diffuse clinical presentation secondary to his underlying chronic immunosuppression.

Histopathologically, all three identified forms of EPF show acute and chronic lymphoeosinophilic infiltrate concentrated at the follicular isthmus. In addition, scattered mononuclear cells, eosinophils, and neutrophils are typically found within the pilar outer root sheath, sebaceous glands, and ducts. Follicular mucinosis is seen in up to 40% of cases as well as follicular destruction.

The pathophysiology is believed to represent a Th2 predominant pathway (IL-3, IL-5, and IL-13) with eotaxin-3 expression, which promote eosinophil recruitment, inflammation, and tissue damage seen in EPF.

Multiple therapeutic modalities have been reported for the treatment of EPF. For all three types, moderate to high potency topical corticosteroids are considered first line of therapy while UVB phototherapy 2-3 times weekly remains the gold standard treatment. Indomethacin (50- 75mg/ day) is first line treatment for classic EPF due to its ability to limit the chemoattraction of eosinophils. Other potential treatments include prednisone, psoralen plus UVA, cetirizine, metronidazole, minocycline, itraconazole, dapson, systemic retinoids, topical tacrolimus, and topical permethrin.

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