ODAC Aesthetic, Surgical and Clinical Dermatology
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Bad Ulcers: When It's Not Pyoderma Gangrenosum

Yemi Sokumbi, MD
Associate Professor and Consultant
Mayo Clinic
Departments of Dermatology and Pathology

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DISCLOSURE OF RELEVANT RELATIONSHIPS WITH INDUSTRY
I do not have any relevant relationships with industry.

2

Objectives

- Demonstrate a rational approach to the evaluation of ulcers in complex medical dermatology cases
- Emphasize role of biopsy in ulcer evaluation
- Integrate biopsy findings with clinical presentation to develop accurate diagnosis

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Case 1

- 57-year-old male presented with lower extremity lesions x 2 years
- Developed non-healing bilateral lower extremity ulcerations that progressed over a year
- Working diagnosis of pyoderma gangrenosum
- Unresponsive to intermittent oral steroids and antibiotics
- Labs demonstrate mild pancytopenia, elevated ESR, normal LFTs, normal renal function

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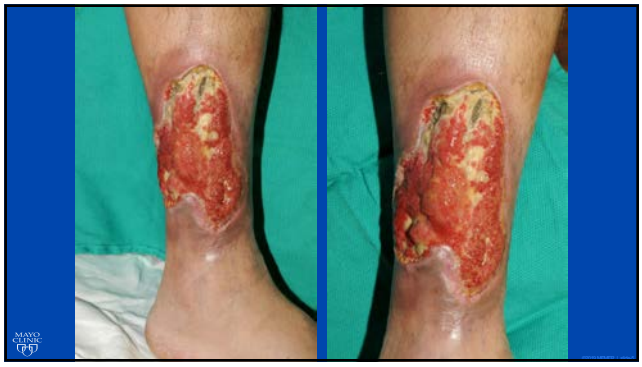

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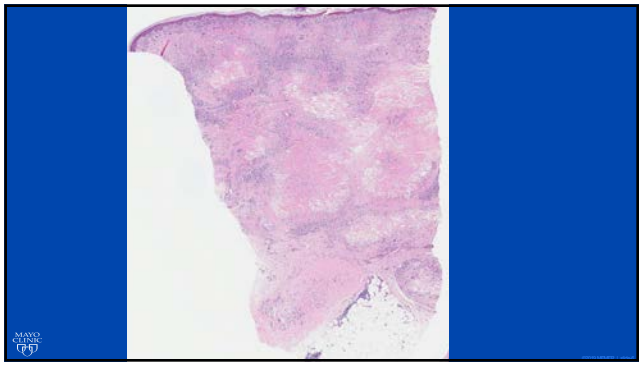

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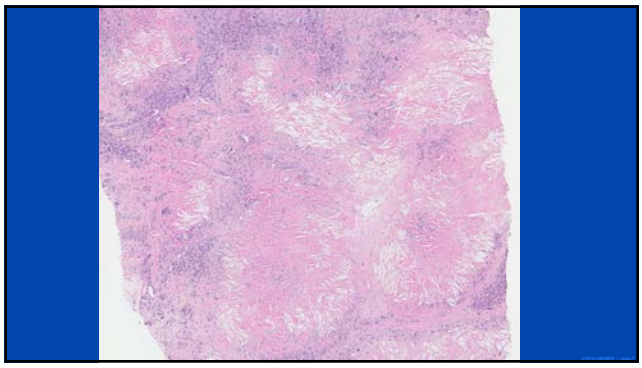

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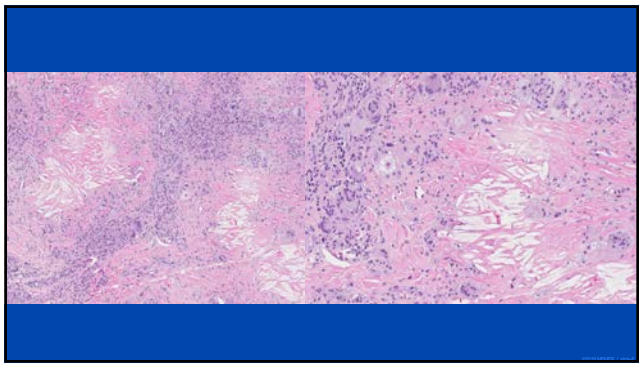

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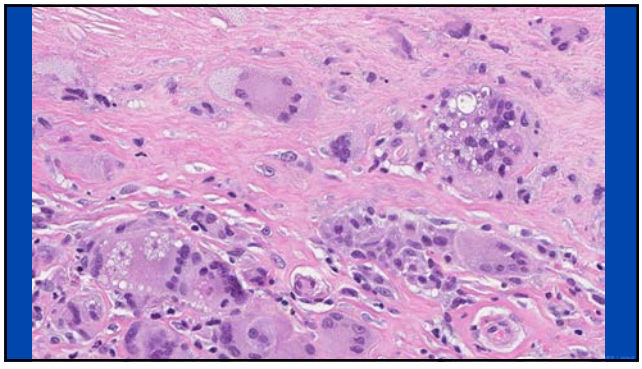

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What additional investigation should be performed in this patient?

A. T-cell gene rearrangement studies
B. B-cell gene rearrangement studies
C. Tissue cultures
D. Serum protein electrophoresis
E. Colonoscopy

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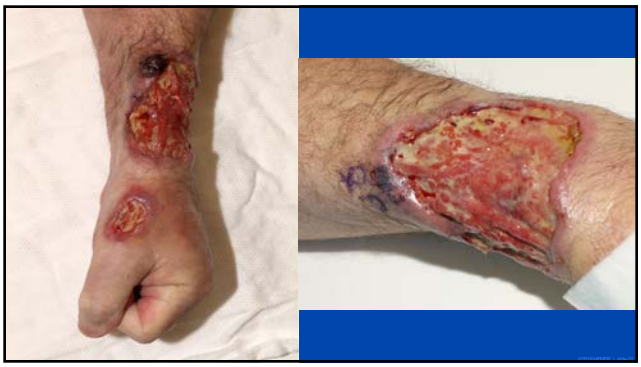

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Necrobiotic Xanthogranuloma

- Rare chronic granulomatous disorder
- Middle-aged and elderly; no gender predilection
- Initially presents with yellowish papules and nodules that coalesce into indurated plaques
- Superficial telangiectasias and ulceration in 40-50% of patients
- Most common site is the face (upper and lower lids)
  - Trunk and extremities are rare
- Underlying monoclonal gammopathy in 80% of cases
  - IgG-κ- 65%; IgG-λ (35%); less commonly IgA
  - 10-25% may develop multiple myeloma

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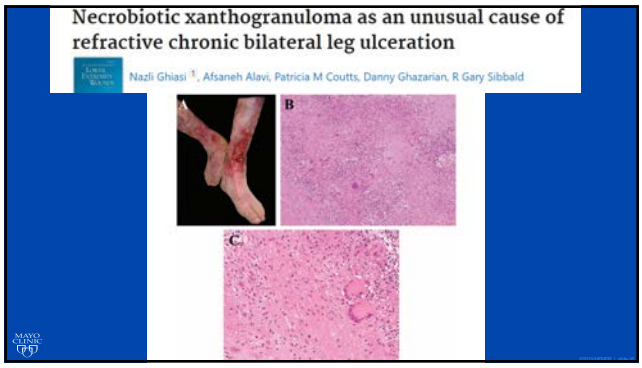

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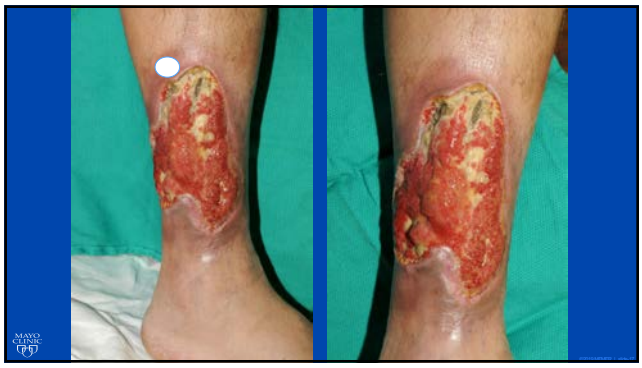

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Necrobiotic Xanthogranuloma

- Management is challenging and the disease is progressive
- Treating underlying hematopoietic d/o may not improve course
- Extracutaneous involvement may include oropharyngeal tract, bronchi, liver, lung, spleen, heart
- First line treatment
  - Corticosteroids and IVIG
- Other considerations
  - Thalidomide, lenalidomide, cyclophosphamide, chlorambucil, fludarabine, rituximab, infliximab, melphalan, cladribine, azathioprine, hydroxychloroquine, methotrexate, ECP

Steinhelfer L et al. Systemic therapy of necrobiotic xanthogranuloma: a systematic review. Orphanet J Rare Dis.

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Back to our Patient…

- SPEP- IgG-λ
  - Didn't meet criteria for multiple myeloma
- IVIG q4weeks 0.5g/kg/day x 4days
- Prednisone 40 mg daily, Gabapentin 600 mg TID
- Ophthalmology baseline exam

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Clinical Pearls

- Ulcers deserve a biopsy!
- Most common NXG association is hematologic disorders
  - MGUS, multiple myeloma, CLL, Hodgkin lymphoma
- Corticosteroids and IVG are first line for NXG
- Beware of sequelae and ensure multidisciplinary care

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Case 2

- 65-year-old male with 4-year history of persistent ulcer
- Started on prednisone and oral antibiotics x 4-months
  - Presumed pyoderma gangrenosum with secondary infection
- Wound care support
- Denies fevers, chills, weight loss
- No other active issues

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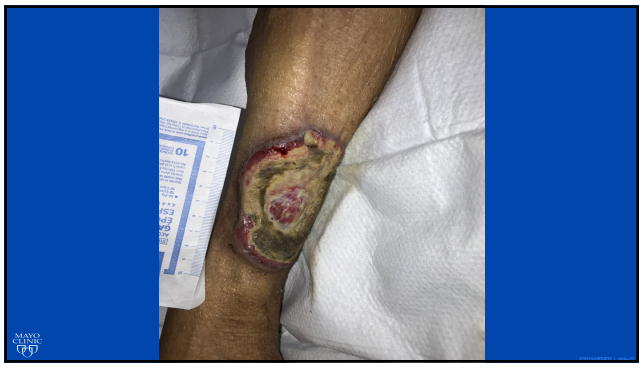

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What is your next step?

A. Biopsy for H&E
B. Biopsy for H&E and tissue cultures
C. Reinitiate oral prednisone and antibiotics
D. Evaluate for pyoderma gangrenosum associations

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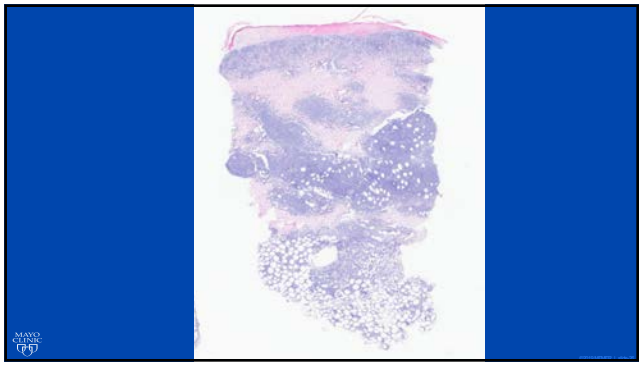

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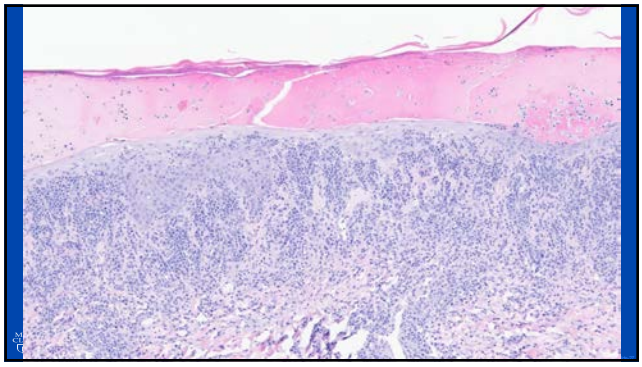

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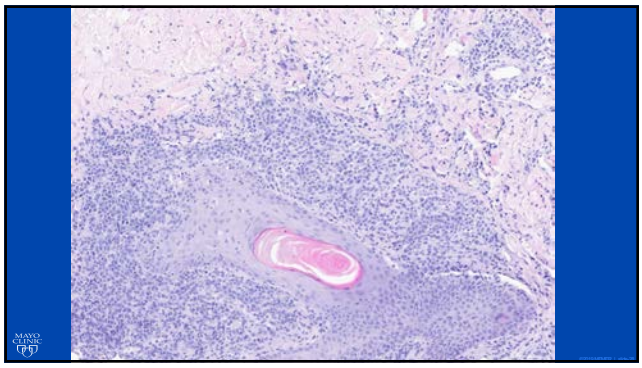

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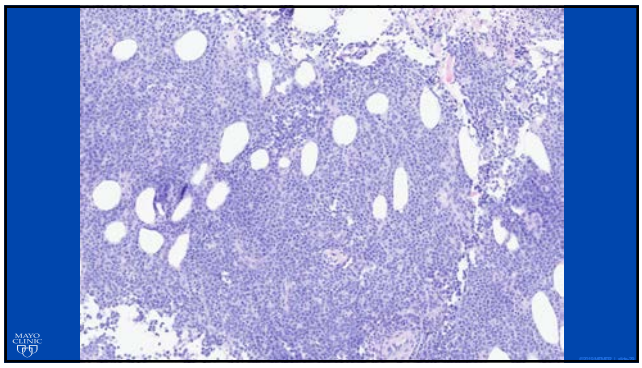

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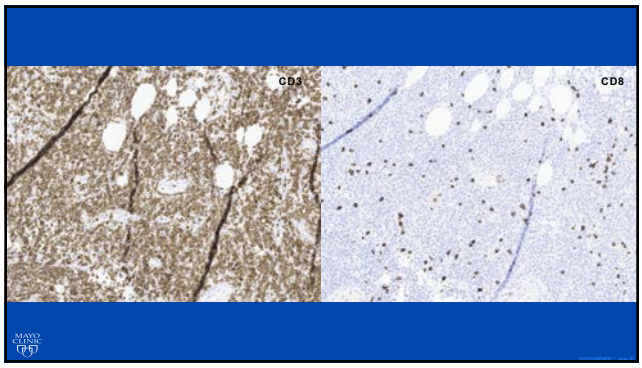

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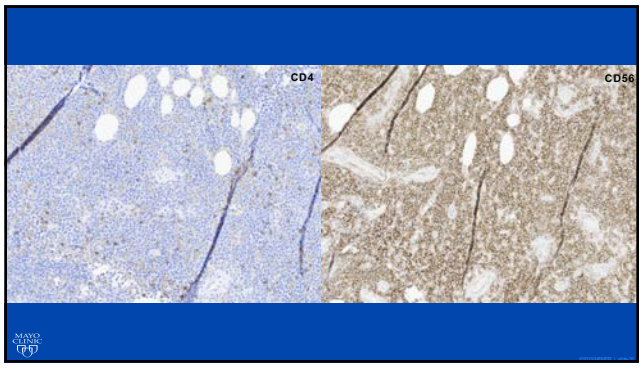

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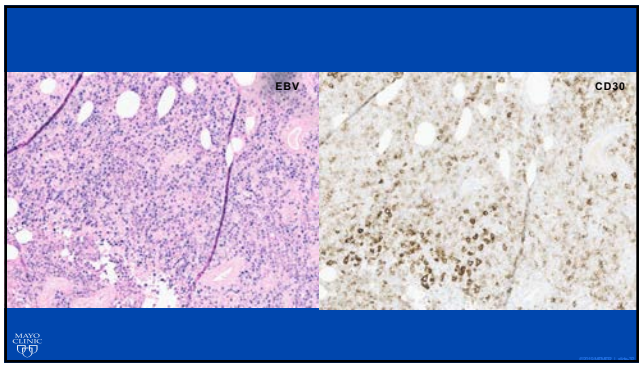

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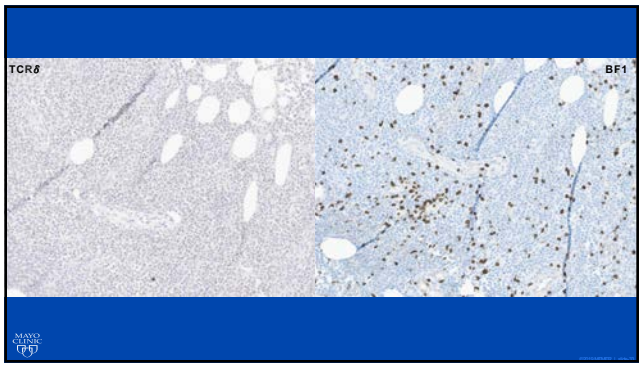

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Extranodal NK/T cell lymphoma

- Aggressive malignancy of NK cell origin
- Defining feature of EBV infection of the lymphoma cells
- Occurs mostly in the nose or upper aerodigestive tract tract (80%)
  - Nasal obstruction, epistaxis, destructive mass of nose, sinuses, or palate
- Less commonly in non-nasal areas (skin, GI, testis)- 20%
- Predilection for Asian, Central and South American origin
- Chemotherapy and radiotherapy

Tse, E. et al. The diagnosis and management of NK/T-cell lymphomas. *J Hematol Oncol* 10, 85 (2017).

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Extranodal NK/T cell lymphoma

- When compared with nasal NK/T cell lymphoma, extranasal NK/T cell lymphoma more likely to
  - Present with stage II or greater disease (56 versus 20%)
  - B symptoms (54 versus 37%)
  - Outcomes were similar for both when matched for stage
- Approximately 3% of ENKL are associated with the hemophagocytic syndrome
  - Often fatal complication- high fevers, failure to thrive, CNS symptoms, hepatosplenomegaly, lymphadenopathy, cytopenias, coagulopathy, abnormal liver function tests, or extremely high serum ferritin levels

Tse, E. et al. The diagnosis and management of NK/T-cell lymphomas. *J Hematol Oncol* 10, 85 (2017).

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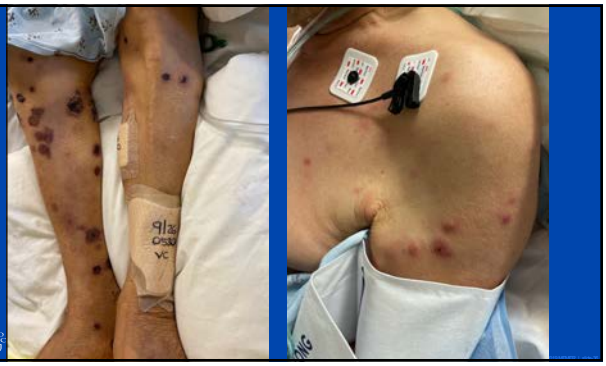

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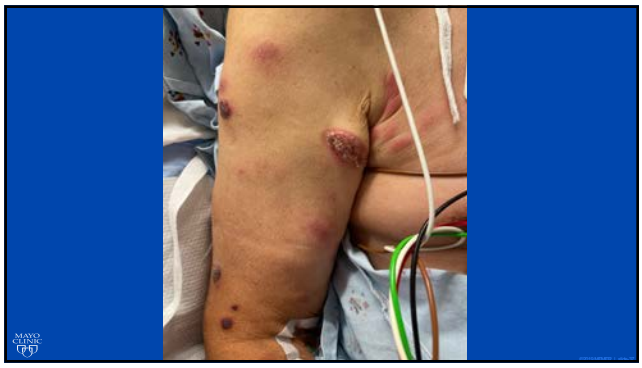

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Back to our patient

- 40-50% cells positive for CD30
  - CD30 targeted therapy with brentuximab 1.3 mg/kg q2 weeks
  - Chemotherapy regimen with ICE (Ifosfamide, Carboplatin and Etoposide)
- MRI with concern for cardiac involvement
- Right ventricular endomyocardial biopsy
  - Myocardium involvement of NK/T cell lymphoma
- Cardiogenic shock
- Rapidly declined and expired

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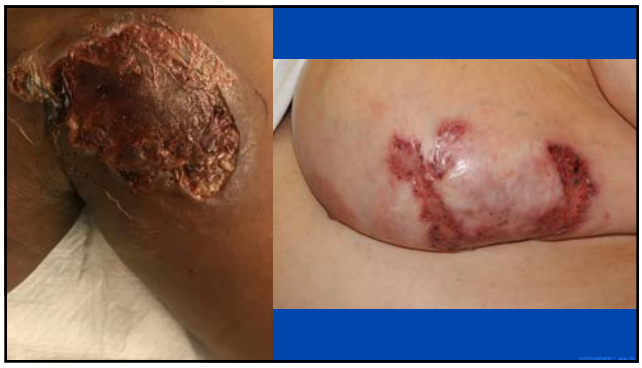

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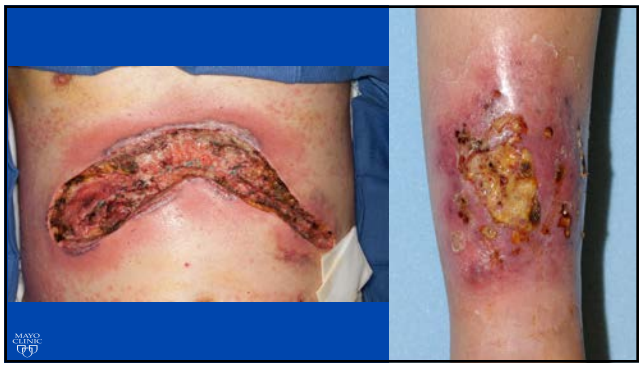

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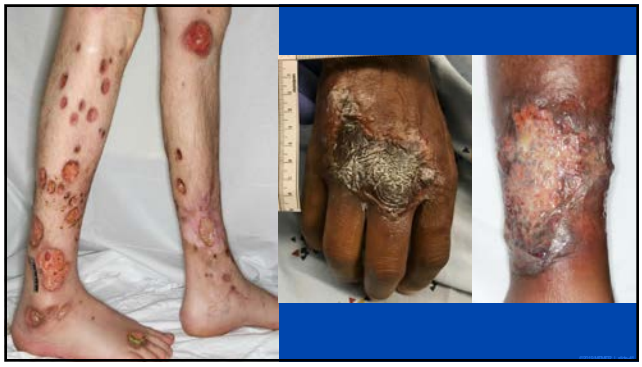

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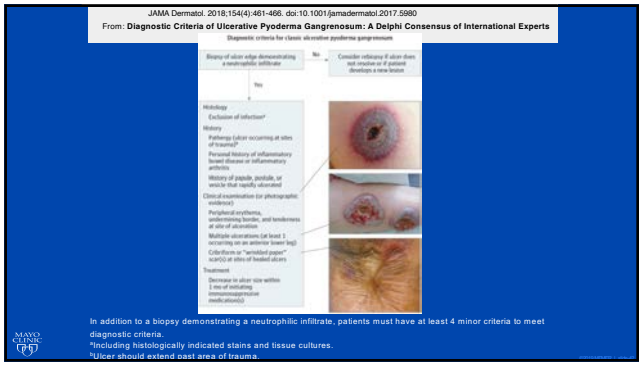
JAMA Dermatol. 2018;154(4):461-466. doi:10.1001/jamadermatol.2017.5980
From: Diagnostic Criteria of Ulcerative Pyoderma Gangrenosum: A Delphi Consensus of International Experts
In addition to a biopsy demonstrating a neutrophilic infiltrate, patients must have at least 4 minor criteria to meet diagnostic criteria.
[a]Including histologically indicated stains and tissue cultures.
[b]Ulcer should extend past area of trauma.

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Final Pearls

- Thorough evaluation is recommended for all ulcerations
- Although PG is a clinical diagnosis, skin biopsy is important to exclude other causes of ulceration
  - Biopsy active border of ulcer and penetrate deep to fat
  - H&E and tissue cultures (bacterial, mycobacterial and fungal cultures)
- Keep an open mind! A lot things can present as an ulceration
  - Arterial and venous disease, sickle cell disease, cryoglobulinemia, anti-phospholipid syndrome, vascular occlusion, vasculitis, infections, calciphylaxis, drug-induced ulceration, inflammatory conditions, primary or metastatic tumors

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Thank you!

sokumbi.olayemi@mayo.edu

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