“37 yo M with a chronic left thigh ulcer, plan to discharge to home from the ED but want to first rule out pyoderma gangrenosum”

HPI
- 10 months prior to presentation, developed an “abscess”
- Treatments
  - I&O
  - Multiple rounds of oral antibiotics
  - Surgical debridement → enlargement of the ulcer
- Pain is now unbearable, no longer ambulating
- Now developing a new ulcer and multiple subcutaneous “bumps”

ROS
- + fatigue, night sweats, weight loss
JM

- Labs
  - CBC: wnl
  - CMP: wnl
  - CRP & ESR: elevated
  - UA: RBCs and rare red and white cell casts

JM

- DDx:
  - Infection vs PG vs malignancy

- Plan:
  - Biopsy for pan-culture and histology
  - Consider imaging left thigh for further diagnostic workup
  - Considering depth of wound and exposed tendon, would be reasonable to consider a limb viability consult
• Additional work up
  o ANA negative
  o C-ANCA: 1:256, anti-PR3: 4.3
  o P-ANCA: negative
  o RF mildly elevated
  o C3, C4 wnl
  o SPEP wnl
  o Hepatitis panel negative
  o HIV negative
• Positive C-ANCA and casts on UA prompted a Nephrology consult

• Renal biopsy:
  o Focal crescentic and necrotizing glomerulonephritis of pauci-immune type
  o Focal tubular atrophy and interstitial fibrosis
• High titer C-ANCA, renal involvement, cutaneous involvement → granulomatosis with polyangitis (Wegener’s)
JM

- **Treatment:**
  - IV methylprednisolone for 3 days → prednisone taper
  - Rituximab 1000 mg IV x 2

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“The facts we have uncovered do not prove Dr. Friedrich Wegener guilty of war crimes. However, the evidence suggests that Dr. Wegener was, at least at some point of his career, a follower of the Nazi regime.”

GPA Basics

- A multi-system disease of unknown etiology characterized by vasculitis and necrotizing granulomatous inflammation of the small and medium vessels
- Classic generalized GPA is a triad of necrotizing granulomas of the upper and lower respiratory tract, small or medium vessel granulomatous vasculitis, and glomerulonephritis

Falk, R. Clinical manifestations and diagnosis of granulomatosis with polyangiitis. In : UpToDate. (Accessed on February 18, 2015.)

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GPA Basics

- Clinical criteria (ACR)
  - Nasal or oral inflammation (painful or painless oral ulcers or purulent or bloody nasal drainage)
  - Abnormal CXR showing nodules, fixed infiltrates, or cavities
  - Abnormal urine sediment (microscopic hematuria with or without red cell casts)
  - Granulomatous inflammation on biopsy

Falk, R. Clinical manifestations and diagnosis of granulomatosis with polyangiitis. In : UpToDate. (Accessed on February 18, 2015.)

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GPA Basics

- Workup
  - Labs
    - ANCA ±
    - CBC, CMP, ANA, C3/C4, hepatitis panel, HIV, cryos, ESR, CRP
  - UA
  - CXR
  - Skin biopsy
  - Renal and/or lung biopsy

Falk, R. Clinical manifestations and diagnosis of granulomatosis with polyangiitis. In : UpToDate. (Accessed on February 18, 2015.)
GPA for the Dermatologist

- Skin involvement in 14% of patients
- In 62% of patients with skin involvement, the skin was the presenting manifestation of GPA
- Patients with cutaneous involvement had an 80% chance of renal involvement, compared to only 33% of patients with no cutaneous involvement

Clinical findings with cutaneous GPA

<table>
<thead>
<tr>
<th>Features</th>
<th>No. (%) of pts</th>
</tr>
</thead>
<tbody>
<tr>
<td>Palpable purpura</td>
<td>14 (47)</td>
</tr>
<tr>
<td>Pyoderma-like ulcer</td>
<td>8 (27)</td>
</tr>
<tr>
<td>Papule</td>
<td>6 (20)</td>
</tr>
<tr>
<td>Nodules</td>
<td>4 (13)</td>
</tr>
<tr>
<td>Superficial ulcerations</td>
<td>4 (13)</td>
</tr>
<tr>
<td>Petechiae</td>
<td>3 (10)</td>
</tr>
<tr>
<td>Bullae</td>
<td>3 (10)</td>
</tr>
<tr>
<td>Macules and erythema</td>
<td>2 (7)</td>
</tr>
</tbody>
</table>

Patients with cutaneous involvement had an 80% chance of renal involvement, compared to only 33% of patients with no cutaneous involvement.


GPA for the Dermatologist

- 10% of patients had cutaneous involvement
  - Most common clinical finding: palpable purpura
  - Most common histology: LCV
  - Other presentations: EN, PG, bullous

GPA for the Dermatologist

- 47% of patients had at least one mucosal or cutaneous manifestation
- Dermatologic manifestations were associated with a higher frequency of articular and renal involvement (69% vs 25% and 80% vs 47%)
- 5 year survival rates were lower in patients with dermatologic manifestations (66% vs 87%)

 Pearls from JM

- ANCA vasculitis can present as pyoderma gangrenosum like ulcers
- GPA can occur with no airway involvement
- Don’t ignore the UA
- An ulcer should prompt the same workup as palpable purpura
- Cutaneous involvement in GPA is associated with higher risk of renal and joint involvement and a poorer prognosis

UWMC General Surgery

“45 yo M with chronic buttock ulcer recently worsened after debridement, rule out pyoderma gangrenosum”

PM

- HPI:
  - Left buttock AVM treated with embolization 20+ years ago → skin breakdown and chronic ulceration
  - Treatments
    - Multiple failed flaps and grafts
    - Long-term antibiotics
    - Wound debridement
  - Wound remained relatively stable until 7 months prior when it began to rapidly enlarge and cause increasing pain
- ROS: endorses fatigue, pain, night sweats, and constipation
• DDx: chronic ulcer of known cause +/- infection, PG very unlikely
• Plan:
  o Biopsy for pan-culture and histology
CT chest/abdomen/pelvis
- Large left gluteal AVM with areas of ulceration
- Numerous spiculated cavitating lesions seen in the lungs
Lung nodule core biopsy
- Microscopic foci of poorly differentiated infiltrating malignant neoplasm
- Palliative care

Marjolin
Jean-Nicolas Marjolin (6 December 1780 – 4 March 1850) was a French surgeon and pathologist.
- In 1800 he moved to Paris where he became a favoured disciple of Guillaume Dupuytren (1777–1835)
Marjolin’s Ulcer

- Malignant degeneration that ensues over a period of time in post-burn scars, other scars, or other chronic wounds
- Presentations
  - Ulceration that fails to heal
  - Nodules developing within a wound or scar
  - Rolled or everted borders
  - Excessive granulation tissue
  - Rapid increase in size
  - Bleeding to the touch


Marjolin’s Ulcer

- 0.7-2% of post-burn wounds and scars undergo malignant degeneration
- Average latency period of 35 years
- Histology: 71% SCC, 12% BCC, 5% melanoma, 5% sarcoma, other
- At presentation LN involvement in 20-35% of patients, distant metastases in 14%
- Mortality of all MU ~21%
- Prevention and monitoring


Pearls from PM

- In the setting of a chronic wound, have an even lower threshold to biopsy
- Rapid change and increased bleeding suggest malignant degeneration
- Tissue from debridement should always be sent for histology and culture
- Role for dermatology in monitoring chronic wounds/scar?
“31 yo M with worsening abdominal wound concerning for pyoderma gangrenosum”

NH

- HPI
  - Developed a “bump” in the periumbilical region thought to be a hernia
  - Skin broke down
  - Treatments
    - Long term oral and IV antibiotics (linezolid, zosyn)
    - Wound debridement
  - Abdominal CT showing periumbilical skin thickening and edema with no evidence of abscess or hernia
- PMH: DMII, obesity
- ROS: + for decreased appetite, 30+ lb weight loss, pain
• DDx: malignancy vs less likely PG vs less likely primary infection
• Plan:
  o Tissue for pan-culture and histology
NH

- Additional workup
  - Flow cytometry on tissue
    - Abnormal T cell population (9.7%)
  - Cytogenetics
    - Translocation 4;7 of unclear significance
- Diagnosis: primary cutaneous peripheral T-cell lymphoma unspecified

NH

- PET scan
  - Ventral abdominal wall surgical defect
  - Intra-abdominal lymphadenopathy
  - An indeterminate soft tissue lesion extending from the lingula to the left chest wall
  - Splenomegaly
- Underwent CT-guided biopsy of the lingula lesion which demonstrated adenocarcinoma in situ c/w mucinous bronchoalveolar type

NH

- Therapy
  - Multi-agent chemotherapy (dose-adjusted EPOCH) with attainment of complete remission of his lymphoma
  - Resection of lung carcinoma
  - Diagnosed with retroperitoneal fibrosis, treated with steroids and rituxumab
Primary Cutaneous Peripheral T-cell Lymphoma Unspecified

- **Clinical features:**
  - Adults who present with solitary, localized, or generalized nodules or tumors
- **Histopathology:**
  - Nodular or diffuse infiltrates with variable numbers of medium-to-large-sized pleomorphic T cells, large neoplastic cells represent at least 30% of the total tumor cell population
- **Immunophenotype:**
  - Most cases show an aberrant CD4 T-cell phenotype with variable loss of T-cell antigens, CD30 staining is negative or restricted to a few scattered tumor cells
- **Prognosis:**
  - Generally poor, 5-year survival rates of less than 20%
- **Treatment:**
  - Multi-agent chemotherapy

**Pearls from NH**

- Cutaneous T-cell lymphoma is even more confusing than I thought
- Always send debrided tissue for histology and pan-culture
- Don’t ignore the ROS
Skin Ulcers Misdiagnosed as PG

- 10% of patients referred to a tertiary care center for PG did not have PG

Most common PG mimics

- Vascular occlusive or venous disease
  - APAS, livedoid vasculopathy, venous stasis
- Vasculitis
  - GPA, PAN, cryoglobulinemia
- Malignancy
  - T cell lymphoma
- Infection
  - Sporotrichosis, aspergillus, cryptococcus, chronic HSV, TB
- Drug-induced, exogenous
  - Factitial, hydroxyurea
- Other inflammatory disorders
  - Crohn’s, NLD


Skin Ulcers Misdiagnosed as PG Pearls

- More than half the patients from this study who had biopsies had histopathological evidence of an alternative diagnosis
  - Although the rate of pathergy in patients with PG is unknown, we propose that the need to rule out an alternative disease should override the fear of exacerbating the condition by performing a biopsy
- A substantial number of the patients we analyzed who were treated for PG had ulcers that were refractory to treatment
  - These cases emphasize the need to reconsider the diagnosis of PG when the condition fails to respond to standard treatment

Suggested Ulcer Workup

- History:
  - Pathergy, symptoms of associated disease, medication history
- Physical exam:
  - Rolled edges, undermined borders, necrosis
- Skin biopsy to rule out diagnoses that mimic PG:
  - Send for histology and culture
- Labs to rule out diagnoses that mimic PG:
  - CBC, CMP, protein electrophoresis, coagulation panel, ANCAs, cryes
- Arterial and venous studies
- If no response to therapy, reconsider diagnosis and repeat biopsy

Ulcer Pearls

- Always, always, always biopsy an ulcer
- Pyoderma gangrenosum is a diagnosis of exclusion
- Diagnostic momentum and anchoring bias can be dangerous
- Ulcers represent a unique opportunity to interface with other specialties (rheumatology, nephrology, general surgery, oncology, infectious disease) and our role as dermatologists is critical