Panniculitis, pancytopenia, and pathology reports: a puzzling case

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I have no conflicts of interest to disclose.
Our case

33 year old F presents with:

- Bilateral leg swelling
- Worsening of chronic skin lesions on her legs
- Nausea, vomiting, diarrhea x 2-3 days

Recent history:

- Followed by Derm x 8 mos for painful panniculitis of unclear etiology
- Recently treated for perirectal panniculitis with clindamycin
Past Medical History

PMH: panniculitis, obesity, depression
PSH: C-section, cholecystectomy, tubal ligation
Meds: escitalopram, pantoprazole, ondansetron
Allergies: NKDA
FH: father with CAD
SH: lives in rural NH. 1 PPD. No EtOH/drugs
## Physical exam

<table>
<thead>
<tr>
<th>VS: T 103.1 F</th>
<th>HR 131</th>
<th>BP 112/69</th>
<th>RR 26</th>
<th>96% on RA</th>
<th>BMI 44</th>
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<tbody>
<tr>
<td>Gen: awake, oriented to person and place, intermittently confused and agitated</td>
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<td>HEENT: no scleral icterus. No conjunctival injection</td>
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<td>CV: tachycardic, no murmurs, extremities warm</td>
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<td>Pulm: CTAB, no accessory muscle use</td>
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<td>Abd: obese, soft, nontender, nondistended</td>
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<td>Ext: significant pitting edema in BLE from the feet to the mid-back</td>
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<td>Neuro: CN intact. No focal deficits</td>
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<td>Skin: multiple tender, hyperpigmented, nodular, areas of skin breakdown over the torso and extremities</td>
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Skin exam: Panniculitis
What is panniculitis?
Panniculitis = Inflammation of subcutaneous fat

Brief differential diagnosis

• Immune-mediated
  • Erythema nodosum
  • Lupus
  • Sarcoidosis
  • Vasculitis
• Infectious panniculitis
• Trauma-induced
• Malignancy e.g. lymphoma
What are your initial thoughts?

What do you think is most likely?

What would you not want to miss?
Initial workup

ANC 1420
MCV 78.9

AST 179
ALT 46
ALP 193
Lactate 2.4

CT C/A/P: Multiple nodules in geographic fat stranding throughout the subcutaneous fat of the C/A/P
Hospital course

- Ceftriaxone + vancomycin for sepsis
- Negative infectious workup
- Developed DIC treated with cryoprecipitate
- Pancytopenia workup: ferritin **63,000**

*Differential diagnosis broadened...*
**Hemophagocytic lymphohistiocytosis:**
**HLH-2004 diagnostic criteria**

<table>
<thead>
<tr>
<th>Criterion</th>
<th>Value</th>
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<tbody>
<tr>
<td>Fever</td>
<td>&gt; 38.5 C</td>
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<tr>
<td>Splenomegaly</td>
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<tr>
<td>Cytopenias - at least 2 of 3:</td>
<td>Hgb &lt; 9, plt &lt; 100k, ANC &lt; 1000</td>
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<tr>
<td>Hypertriglyceridemia (&gt;265 fasting) and/or hypofibrinogenemia (&lt;150)</td>
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<td>Hemophagocytosis in bone marrow, spleen, lymph node, or liver</td>
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<tr>
<td>Low or absent NK cell activity</td>
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<tr>
<td>Ferritin &gt; 500</td>
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<tr>
<td>Elevated soluble IL-2 receptor alpha</td>
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<td>Elevated CXCL9</td>
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*Must meet 5 of these 9 criteria*
### Etiologies of HLH

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<th>Details</th>
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<td><strong>Key point</strong></td>
<td>- HLH in adults is usually secondary to a systemic process&lt;br&gt;- In children it is often primary</td>
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<td><strong>Infectious (~20-40%)</strong></td>
<td>- Usually viral e.g. EBV, CMV</td>
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<td><strong>Malignancy (~50%)</strong></td>
<td>- Hematologic malignancy</td>
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<td><strong>Rheumatologic/Macrophage activation syndrome (~20%)</strong></td>
<td>- Lupus, Still’s disease, sarcoidosis</td>
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**Additional workup**

### Infectious — all negative
- HIV
- Hepatitis panel
- EBV (c/w prior infection)
- CMV
- Blood cultures
- Tick panel
- Histoplasmosis
- Quant Gold TB

### Rheumatologic — all negative
- ANA
- dsDNA
- RF
- CCP
- ANCA
- ACE
- Complements
- SS-A, SS-B
- SM Ab
- Scl-70 Ab
- Jo-1 Ab

### Other
- Triglycerides 486
- Soluble IL-2 receptor positive
- Fibrinogen 160
Hemophagocytic lymphohistiocytosis: HLH-2004 diagnostic criteria

- Fever > 38.5 C
- Splenomegaly
- Cytopenias - at least 2 of 3: Hgb < 9, plt < 100k, ANC < 1000
- Hypertriglyceridemia (> 265 fasting) and/or hypofibrinogenemia (< 150)
- Hemophagocytosis in bone marrow, spleen, lymph node, or liver
- Low or absent NK cell activity
- Ferritin > 500
- Elevated soluble IL-2 receptor alpha
- Elevated CXCL9

*Must meet 5 of these 9 criteria*
Bone marrow biopsy results

No clear evidence of neoplastic lymphoproliferation

Positive clonal T-cell receptor gene rearrangement

→ raised suspicion for T-cell lymphoma

- Subcutaneous panniculitis-like T-cell lymphoma
- Gamma/delta T-cell lymphoma
Excisional skin biopsy

- Hemophagocytosis
- “Cytophagic histiocytic panniculitis”
- Ki-67+ T-cells
- TCR-gamma-positive
- CD4-/CD8-

Confirmed diagnosis of gamma/delta T-cell lymphoma
Cutaneous T-cell lymphomas: most common

- Mycosis fungoides
  - Heterogeneous skin findings
  - Preceding prodromal illness
  - Pruritus
  - Progression to extracutaneous sites

- Sezary syndrome
  - More aggressive than mycosis fungoides
  - Diffuse erythroderma
  - Malignant T cells in peripheral blood
Gamma/delta T-cell lymphoma

- Cutaneous lymphoma composed of a clonal proliferation of mature gamma/delta T-cells
- 1% of all CTCL
- Disseminated, progressive plaques/necrotic nodules
- B symptoms are common
- No RCTs, so treated similar to other peripheral T cell lymphomas (typically CHOP/CHOEP for induction)
- Median survival – 15 months
Clinical course

Treated with high-dose dexamethasone based on HLH 94 protocol. Discharged to rehab.

Treated with etoposide + MTX. Multiple readmissions to OSH with encephalopathy and septic shock.

Unfortunately she died two months after MMC admission, from complications of HLH.
Take Home Points

01
Keep HLH on your DDx in patients with fever, splenomegaly, and pancytopenia.

02
Consider a broad DDx for the inciting cause of HLH – including infectious, malignant, and rheumatologic etiologies.

03
Keep cutaneous T-cell lymphoma on your DDx in patients with evolving chronic rash with systemic symptoms.
References


Thank you! Questions?