Hemophagocytic Lymphohistiocytosis Secondary to *Anaplasma* Infection

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Outline

• Introduction

• Case Presentation

• Discussion

• Conclusions
• Hemophagocytic lymphohistiocytosis (HLH)
  – Uncommon, but may be life threatening
  – Diagnostic and therapeutic challenge
  – Most often encountered in infants
  – Cases have been reported in older children and adults
Introduction

HLH

Primary (genetic)

Secondary

- Infections
- Autoimmune
- Malignancies
- Immunodeficiency
## Diagnostic Criteria for HLH (5 needed for diagnosis)

- Fever
- Splenomegaly
- Cytopenia in two or more cell lines
- Hypertriglyceridemia (fasting $\geq 265$ mg/dl) and/or hypofibrinogenemia ($\leq 1.5$ g/L)
- Low/absent NK-Cell activity
- Ferritin $> 500$ ng/ml
- Soluble interleukin-2 receptor $>2400$U/ml
- Hemophagocytosis in bone marrow, spleen, or lymph nodes without evidence of malignancy

Introduction

- HLH secondary to *Anaplasma* not previously reported

- Our case
  - Fulfills diagnostic criteria for HLH
  - Caused by infection with *Anaplasma phagocytophilum*
Case Presentation

• 20 year old male, previously healthy
• Two month history of:
  – Intermittent Fever
  – Nausea and vomiting
  – Diarrhea
  – Malaise
  – Headache
  – Loss of appetite
Case Presentation

• Acutely worsening symptoms over 3 days
  – Temperature elevated to 103.4

• Presented to referring hospital
  – Leukopenia
  – Thrombocytopenia
  – Splenomegaly on CT scan

• Transferred to Wichita for further evaluation
## Case Presentation

### CBC

<table>
<thead>
<tr>
<th>Test</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>WBC</td>
<td>1.2 K/ul</td>
</tr>
<tr>
<td>Hgb</td>
<td>13.3 g/dl</td>
</tr>
<tr>
<td>Hct</td>
<td>37.7 %</td>
</tr>
<tr>
<td>MCV</td>
<td>86.5 fl</td>
</tr>
<tr>
<td>Plts</td>
<td>90 K/ul</td>
</tr>
<tr>
<td>ANC</td>
<td>0.72 K/ul</td>
</tr>
</tbody>
</table>

### Other notable lab tests

<table>
<thead>
<tr>
<th>Test</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>LDH</td>
<td>932 U/L</td>
</tr>
<tr>
<td>Ferritin</td>
<td>2839 ng/ml</td>
</tr>
<tr>
<td>ALT</td>
<td>345 U/L</td>
</tr>
<tr>
<td>AST</td>
<td>294 U/L</td>
</tr>
<tr>
<td>Triglycerides</td>
<td>286 mg/dl</td>
</tr>
</tbody>
</table>
• Bone Marrow:
  – 30% cellular marrow with trilineage hematopoiesis
  – No increase in blasts; no dyspoiesis
  – No evidence of lymphoproliferative disorder or metastatic malignancy
  – Hemophagocytic histiocytes present with hemophagocytosis
Case Presentation

• Bone Marrow:
  – *Histiocytes with ingested red cells/red cell debris*
### Diagnostic Criteria for HLH (5 needed for diagnosis)

- **Fever ✓**
- **Splenomegaly ✓**
- **Cytopenia in two or more cell lines ✓**
- **Hypertriglyceridemia (fasting ≥ 265 mg/dl) and/or ✓ hypofibrinogenemia (≤ 1.5 g/L)**
- **Low/absent NK-Cell activity**
- **Ferritin > 500 ng/ml ✓**
- **Soluble interleukin-2 receptor >2400U/ml**
- **Hemophagocytosis in bone marrow, spleen, or lymph nodes without evidence of malignancy ✓**
Case Presentation

• Hematology-Oncology consulted
  – Considered starting chemotherapy
  – Decided to wait since patient was relatively stable

• ID consulted
  – Comprehensive infectious workup including viral, fungal, and tick-borne illnesses
  – All negative except for weakly positive titer (1:64) for *Anaplasma phagocytophilum* IgG
Case Presentation

• Patient started on doxycycline
  – Significant clinical improvement within 2 days
  – Afebrile
  – WBC count up to 4.1 K/ul
  – Platelets up to 200 K/ul
  – Discharged home two days after starting doxycycline
Case Presentation

• One month follow-up visit
  – *Anaplasma* IgG titer ↑ 1:128
  – Complete resolution of symptoms
  – All lab values normalized
Outline

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Discussion

• *Anaplasma phagocytophilium*
  – Bacterium
    • Transmitted to humans by bite of infected tick

*IXODES SCAPULARIS*
Discussion

• Two previous reports of HLH secondary to *Ehrlichia* \(^1,\!^2\)

• To our best knowledge, this is the first reported case of HLH secondary to *Anaplasma*

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\(^1\) Burns *et al.* J Pediatr Hematol Oncol. 2010 May;32(4):e142-3  
\(^2\) Hanson *et al.* Pediatr Blood Cancer. 2011 Apr;56(4):661-3
Discussion

- Spectrum of severity in HLH
  - Many patients have rapidly deteriorating course
  - Others have less serious illness

- Standard treatment is chemotherapy
  - Etoposide, dexamethasone, cyclosporine A
  - Intrathecal methotrexate + hydrocortisone

- Associated with significant adverse effects
• Current patient:
  – Relatively stable clinical course
  – Chemotherapy delayed while investigating for underlying cause
  – Discovery and treatment of underlying cause \(\rightarrow\) complete resolution of illness
  – Chemotherapy ultimately not needed
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Conclusions

• In patients who meet diagnostic criteria for HLH:
  – Important to consider all possible underlying causes
    • Need to investigate for various types of infections, including tick-borne illnesses

• Patients with relatively stable clinical course:
  – Identify and treat underlying cause
    • May completely resolve disease process
    • Can spare patients adverse effects of chemotherapy
Thank you

Questions?