Recognizing the Clinical and Laboratory Presentation of Human Granulocytic Anaplasmosis

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UNIVERSITY OF WISCONSIN SCHOOL OF MEDICINE AND PUBLIC HEALTH
FRIDAY, SEPTEMBER 8, 2017
History

69-year-old male presented to a local hospital in May with fever and confusion

HPI per wife:
• Four days of acute onset fever and intermittent confusion with changes in behavior
• One episode of emesis and headache
• Bit by deer tick two weeks ago on left thigh while picking morels
• Denies diarrhea, urinary symptoms, SOB, abdominal pain, chest pain, sick contacts
• Received one dose of ceftriaxone and vancomycin at local ER before transfer to UW

PMH: HTN, Type 2 DM  
Medications: Lisinopril, Metformin

Social History: No tobacco or alcohol use
Physical exam

**Vitals:** Tmax 39.3, HR 78, RR 18, BP 197/86, SpO2 96% on RA

**General:** Disoriented to person, place, time, and situation.

**HEENT:** EOMI. No icterus.

**Neck:** Supple. No bruits.

**Heart:** RRR. No murmurs.

**Lungs:** CTAB.

**Abdomen:** Soft, non-tender, non-distended. +BS.

**Extremities:** Warm and well perfused. Minimal ankle edema.

**Neuro:** Non-focal. Normal power.

**Skin:** Indurated red papule on left thigh. No other rash.
Labs and Studies

CT Head: No acute findings. Negative for bleed or infarct. **Lumbar puncture** unable to be performed due to thrombocytopenia and patient’s refusal of blood products

Abs Lymphocytes: 330
MCV: 90
Alk Phos: 97
AST: 79
ALT: 79
LDH: 510
Haptoglobin: 24
Abs Retic: 18,000

Started on empiric doxycycline 100 mg BID
Peripheral blood smear

Morulae within neutrophils
### Hospital Course

<table>
<thead>
<tr>
<th>Hospital day 2:</th>
<th>Hospital Day 3:</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>T</strong>: 37.3</td>
<td><strong>T</strong>: 36.8</td>
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<tr>
<td><strong>WBC</strong>: 2.2</td>
<td><strong>WBC</strong>: 5.0</td>
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<tr>
<td>Abs Lymphocytes: 1230</td>
<td>Abs Lymphocytes: 3480</td>
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<tr>
<td><strong>Hgb</strong>: 10.7</td>
<td><strong>Hgb</strong>: 11.5</td>
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<tr>
<td><strong>PLT</strong>: 26</td>
<td><strong>PLT</strong>: 54</td>
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<tr>
<td><strong>Na</strong>: 135</td>
<td><strong>Na</strong>: 137</td>
</tr>
<tr>
<td><strong>K</strong>: 3.3</td>
<td><strong>K</strong>: 4.0</td>
</tr>
<tr>
<td><strong>BUN</strong>: 20</td>
<td><strong>BUN</strong>: 20</td>
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<tr>
<td><strong>Cr</strong>: 1.13</td>
<td><strong>Cr</strong>: 1.14</td>
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<tr>
<td><strong>PCR positive for Anaplasma phagocytophilum</strong></td>
<td><strong>Alert and Oriented x 4 on DC</strong></td>
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Tick-Borne Diseases of Wisconsin

- Anaplasmosis
- Ehrlichiosis
- Lyme Disease
- Babesiosis
- Spotted Fever Rickettsiosis: Rocky Mountain Spotted Fever and Typhus Fever
<table>
<thead>
<tr>
<th></th>
<th>Human Granulocytic Anaplasmosis (HGA)</th>
<th>Human Monocytic Ehrlichiosis (HME)</th>
<th>Lyme Disease</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Organism</strong></td>
<td>Anaplasma phagocytophilum</td>
<td>Ehrlichia chaffeensis</td>
<td>Borrelia burgdorferi</td>
</tr>
<tr>
<td><strong>Tick Vector</strong></td>
<td>-Ixodes scapularis -Ixodes pacificus</td>
<td>-Amblyomma americanum</td>
<td>-Ixodes scapularis (Eastern, North Central US) -Ixodes pacificus (Western US)</td>
</tr>
<tr>
<td><strong>Epidemiology</strong></td>
<td>-6.3 cases per million annually -RI, MN, CT, WI, NY, MD -coinfection with Lyme in 3-15% of patients in WI -spring and summer months</td>
<td>-3.2 cases per million -Southeastern, South Central, Mid-Atlantic US</td>
<td>-most common tick-borne infection in US (300,000 cases/year) -22.7 per 100,000 in WI (2015) -Northeast and North Central US -peak ages 5-10 and 35-55 -onset of disease in summer</td>
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<td></td>
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<td><strong>Laboratory Findings</strong></td>
<td>-50-90% with leukopenia, thrombocytopenia, elevated aminotransferases, LDH, alkaline phosphatase</td>
<td>-less common: anemia and elevated creatinine</td>
<td>-ESR&gt;2x ULN in 24%</td>
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<tr>
<td></td>
<td>-less common: anemia and elevated creatinine</td>
<td>-leukocytosis (5%), leukopenia (4%), anemia (3%), thrombocytopenia (1.5%)</td>
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<td><strong>Clinical Manifestations</strong></td>
<td>-rash is rare finding</td>
<td>-1/3 of patients have rash (macular, maculopapular, petechial)</td>
<td>-Early Localized (7-14 days): erythema migrans (EM) (80%), fatigue, headache, myalgia, arthralgia, fever (16%)</td>
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<td>-Early Disseminated: multiple EM lesions (days-weeks); neurologic and cardiac (weeks-months)</td>
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<td>-acute illness</td>
<td>-nausea, vomiting, arthralgias, cough in 25-50%</td>
<td>-Late (months-years): arthritis of large joints, encephalopathy, polyneuropathy</td>
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<td>-fever in all</td>
<td>-less common: mental status changes, clonus, neck stiffness</td>
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<td>-malaise, myalgia, headache, chills in 2/3</td>
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<td>-nausea, vomiting, arthralgias, cough in 25-50%</td>
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<td>-less common: mental status changes, clonus, neck stiffness</td>
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<td>Complications</td>
<td>Human Granulocytic Anaplasmosis (HGA)</td>
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<td>-opportunistic infections: herpes simplex esophagitis, invasive aspergillosis, candidiasis -7-10% mortality rate</td>
<td>-single case of rapidly progressive myocarditis -2-5% mortality rate</td>
<td>-renal failure, respiratory failure, heart failure, seizures, coma -septic or toxic shock-like illness</td>
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<td>Treatment</td>
<td>-doxycycline PO or IV 100 mg BID for 10 days or 3-5 days after resolution of fever</td>
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<td>-Early Localized: doxycycline, amoxicillin, or cefuroxime for 10-21 days -Early Disseminated: oral vs. IV therapy -Late Disseminated: ceftriaxone, cefotaxime, penicillin G for 28 days</td>
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</table>
Summary

• Anaplasmosis must be suspected in a patient who lives in an endemic area and presents with acute-onset fever and confusion without other evidence of an infectious source.

• *Anaplasma phagocytophilum* is transmitted by the same tick that transmits *Borrelia burgdorferi* but presents more commonly with fever, cytopenias, and increased ALT/AST.

• Empiric treatment with doxycycline must be initiated to treat Anaplasmosis and prevent complications such as organ failure and coma.
References


• Clinical Manifestations of Lyme Disease. [https://www-upToDate-com.ezproxy.library.wisc.edu/contents/clinical-manifestations-of-lyme-disease-in-adults?source=search_result&search=lyme%20disease&selectedTitle=1~150](https://www-upToDate-com.ezproxy.library.wisc.edu/contents/clinical-manifestations-of-lyme-disease-in-adults?source=search_result&search=lyme%20disease&selectedTitle=1~150)


• Diagnosis of Lyme Disease. [https://www-upToDate-com.ezproxy.library.wisc.edu/contents/diagnosis-of-lyme-disease?source=search_result&search=lyme%20disease&selectedTitle=3~150](https://www-upToDate-com.ezproxy.library.wisc.edu/contents/diagnosis-of-lyme-disease?source=search_result&search=lyme%20disease&selectedTitle=3~150)


References


• Lyme Disease Data Tables. https://www.cdc.gov/lyme/stats/tables.html


Acknowledgements

• University of Wisconsin School of Medicine and Public Health and University of Wisconsin Hospitals and Clinics
• Sarah Ahrens, MD
• Sean O’Neill, MD
• Bennett Vogelman, MD
Questions?

Wisconsin Ehrlichia/Anaplasma Annual Incidence
2016 (n=694)

Statewide Incidence = 12.03/100,000

Incidence per 100,000 (confirmed and probable cases)
- <1
- 1-15
- 16-30
- 31-60
- 61-90
- 91-120
- >120

This map is based on the county of residence. Some infections may have been acquired during travel to other areas.

Data Source: Wisconsin Division of Public Health

Revised 4/27/2017