HOW ATYPICAL CAN AN ATYPICAL PATIENT BE?

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NO DISCLOSURES OF FINANCIAL RELATIONSHIPS.

No disclosures of financial relationships.
PRESENTATION

❖ Who? 17 year old obese, previously healthy, African American female

❖ What? Fevers, generalized edema, weakness, myalgias, vomiting, diarrhea

❖ When? 1 month

❖ What brought her in? Discomfort from worsening dyspnea and orthopnea

WHY?
TO THE ED

Physical Findings:

- Afebrile (37.1°C), Tachypnic (28-45 bpm), Tachycardic (110-122 bpm), Hypertensive (141/80 mmHg)
- General Appearance: uncomfortable in moderate distress sitting upright in bed; alert, but fatigued
- Pertinent Positives: diminished breath sounds at the right lower lung base, pale with cool distal extremities, 2+ pitting edema most notable in bilateral lower extremities

What to do?

INITIAL WORKUP

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<tbody>
<tr>
<td>MCV</td>
<td>73.7</td>
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<tr>
<td>Bands</td>
<td>3%</td>
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<tr>
<td>Metamyelocytes</td>
<td>8%</td>
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<tr>
<td>Eos</td>
<td>10%</td>
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<tr>
<td>ANC</td>
<td>8550</td>
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<tr>
<td>Reticulocyte count</td>
<td>7.13</td>
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<tr>
<td>Blood smear</td>
<td>+3 schistocytes</td>
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<th>136</th>
<th>102</th>
<th>59</th>
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<tbody>
<tr>
<td>Albumin</td>
<td>2.3</td>
<td></td>
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<tr>
<td>AST, ALT</td>
<td>58, 16</td>
<td></td>
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<tr>
<td>Coags: PT</td>
<td>13.2, PTT</td>
<td>29.7</td>
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<tr>
<td>D dimer</td>
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<tr>
<td>Fibrinogen</td>
<td>496</td>
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ESR/CRP: 8.6/79
CPK 87
LDH 3330
Lactic Acid 0.8
Ferritin 5269
VBG: pH 7.42, pCO2 33, bicarb 21
CXR: enlarged cardiac silhouette and bilateral pleural effusions
EKG: sinus tachycardia
- Acute kidney injury
- Thrombocytopenia
- Microangiopathic hemolytic anemia

**DIFFERENTIAL**

**THROMBOTIC MICROANGIOPATHIES**

- Infection
  - Streptococcus pneumoniae
  - Influenza A/H1N1
  - STEC

- Coexisting disease
  - Malignancy
  - Autoimmune disorders
  - Drug associated
  - HIV
  - Transplant patients
  - Malignant hypertension
  - DIC

- Complement defects
  - Cobalamin C
  - DGKE mutation
  - CFH antibodies
  - Alternative complement pathway abnormality (CFH, CFI, MCP, C6, CFB, THBD mutations)

- Pregnancy: HELLP syndrome

- Thrombotic thrombocytopenic purpura: ADAMTS13 activity <10%

- Hemolytic uremic syndrome
**FURTHER WORKUP**

**Nephrology**
- Urinalysis: Large blood, >500 protein, 4 RBC, 17 WBC
- Renal sonogram: Renal cortical echogenicity compatible with renal disease, no hydronephrosis
- Urine and stool cultures: NEGATIVE
- Urine protein, Cr, lytes

**Hematology**
- Transfusion
- Trend ferritin
- ADAMTS13 activity

**Cardiology**
- Echocardiogram: Trivial pericardial effusion without structural abnormalities, normal function

**Rheumatology**
- Anti-cardiolipin, -Ro, -La, -Sm, centromere
- IgA, IgM, IgE, IgG
- C-3, C-4

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**SO WHAT NEXT?**

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HOSPITAL COURSE

Worsening kidney function and persistent cytopenias

Lasix and transfusions with pRBCs

Plasmapheresis, hemodialysis, and blood pressure control with norvasc and isradipine PRN

CONTINUED...

Finally, on PICU day five ADAMTS13 activity resulted:

56%

Eculizumab
**ECULIZUMAB?**

- AKA “Soliris”
- Humanized monoclonal antibody and a terminal complement inhibitor

**Lectin Pathway**

**Classical Pathway** → C3 → C5b (MAC) → tissue damage, hemolysis, inflammation, thrombosis

**Alternative** → C5a → anaphylaxis, inflammation, thrombosis

**Diagnostic Considerations**

- Sufficient ADAMTS13 activity
- Negative infectious disease work up and stool studies for typical HUS
- Negative rheumatological work up for SLE/vasculitis
- Normal complement levels and no anti-CFH antibodies

**ATYPICAL HEMOLYTIC SYNDROME**

- with unusually high ferritin, eosinophilia, serositis & acute interstitial nephritis
GENETIC DEFECT

- Large CFHR1-CFHR3 homozygous deletion (Factor H autoantibody negative)
- DGKE heterozygous missense variant (more common in African Americans)
- Silent variants of unknown significant in exon 2 of CFI and exon 29 of C3


PROGNOSIS AND TREATMENT

- Eight rounds of hemodialysis
- Epoetin injections due to persistent hemolysis
- Pericardiocentesis due to large effusion on repeat imaging
- Interstitial nephritis on renal biopsy, therefore, steroid therapy initiated
- Four weekly doses of eculizimab received inpatient and continued every two weeks thereafter as an outpatient indefinitely
- Blood pressure control with enalapril & amlodipine, as well as statin therapy
- Most recent BUN/Cr 13/0.81
FINAL THOUGHTS

THANK YOU


