Fever, pancytopenia, and hepatosplenomegaly in an HIV-positive patient
Disclosures

• none
Case

• 43 yo Portuguese-speaking HIV-positive female presenting with subacute fever, malaise.
Past medical history

• **HIV**: diagnosed 5 years ago, previously on ART but now off for several months
Review of systems

• **Positive:** fever, fatigue
• **Negative:** cough, SOB, dysuria, rash, joint pains, abdominal pain, headache, confusion
Physical Exam

**Vitals:** 38.6 C  BP 129/85  HR 91  Resp 26  SpO2 98% on room air

**General:** young woman resting comfortably, appears fatigued, wakes to voice

**Eyes:** no scleral icterus

**HEENT:** MMM, no oral lesions

**Neck:** No cervical LAD

**CV:** RRR, no murmurs, no JVD

**Pulm:** No accessory muscle use, clear to auscultation bilaterally

**GI:** Non-distended, soft, non-tender, palpable liver edge

**MSK:** No joint swelling or erythema

**Neuro:** CN II-XII grossly intact, no focal deficits, moving all extremities

**Skin:** No rashes, lesions, peripheral edema
### Data

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<table>
<thead>
<tr>
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<tr>
<td>128</td>
<td>94</td>
<td>9</td>
</tr>
<tr>
<td>4.1</td>
<td>23</td>
<td>0.69</td>
</tr>
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<td>96</td>
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**AG 11**

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<table>
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<tr>
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<tr>
<td>MCV 78</td>
<td>9.2</td>
<td>132</td>
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<tr>
<td>3.4</td>
<td>28.2</td>
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Lipase: 67  
INR: 1.3  
Lactate: 1.3

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<tr>
<td>8.1</td>
<td>133</td>
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<tr>
<td>7.4</td>
<td>58</td>
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<tr>
<td>2.8</td>
<td>195</td>
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</table>

0.8

Urinalysis: wnl  
Urine HCG: neg
Imaging

- **CXR**: interstitial edema, superimposed infection would be difficult to exclude
- **RUQ US**: no abnormalities
CT AP W Contrast

- RLL consolidative opacity concerning for pneumonia
- Small bilateral pleural effusion
- Hepatomegaly, splenomegaly
Additional Labs...

**HIV RNA PCR:** 71,100

**CD4 Absolute** 148, **CD4%** 21%

**HepB surface antigen** +, **HepB DNA** 53

**LP:** glucose 47, protein 29, 0 WBC
<table>
<thead>
<tr>
<th>CD4 Count</th>
<th>Opportunistic Infection</th>
<th>Prophylaxis</th>
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<tbody>
<tr>
<td>All</td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤250 cells/uL</td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤200 cells/uL</td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤150 cells/uL</td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤100 cells/uL</td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤50 cells/uL</td>
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</tbody>
</table>

Social History

- From Angola
- Moved to Brazil with husband + 7 children in 2017
- Left Brazil in 2022 and traveled through South and Central America on foot to San Antonio
- Arrived in Maine on April 1st and living in hotel with her family
Procedures

BM biopsy
- Cytology negative
- Fungal and acid-fast cultures without growth

Bronchoscopy with BAL and lung biopsy
- Cytology negative
- No pneumocystis
- Acid-fast and fungal culture without growth
  - Very rare small budding yeast forms present on GMS stain
  - >10,000 CFU/ml normal throat and mouth flora
Diagnosis

- Positive fungitell x2 384 and 178 (>60)
- Urine histoplasma antigen 1.42 (>0.2)
- Serum histoplasma antigen 5.58 (>0.2)
- Anti-histoplasma IgG EIA >80 (>10)
- Anti-histoplasma IgM EIA 68.3 (>10)
- Anti-histoplasma H FID +
- Anti-histoplasma M FID -

Significantly +++

A few weeks later... fungal culture from bronchoscopy grew mold and histoplasma species complex
Disseminated Histoplasmosis

- Histoplasma capsulatum: dimorphic fungus
- Incidence rate ~5% for individuals with HIV
- CD4 count >300, respiratory limited disease
- CD4 count <150, increased risk of disseminated symptomatic illness

https://vividmaps.com/mississippi-river/

Clinical manifestations

- Constitutional sx: fever, fatigue, weight loss
- Pulmonary sx: cough, chest pain, dyspnea
- Disseminated = progressive extrapulmonary disease
  - Lymphadenopathy
  - Hepatosplenomegaly
  - Skin/mucosal lesions
  - Cytopenias
  - Transaminitis
  - Interstitial and reticulonodular infiltrates
  - CSF: ↑lymphocytes, ↑glucose, ↓protein
  - Enhancing brain lesions
Diagnosis

Risk factors + clinical manifestations + laboratory evidence

• Antigen detection (blood and urine)
• Peripheral smear
• Cultures/histopathology/cytology: blood, bone marrow, BAL, CSF

Serologic tests less useful
Treatment

• **Induction:** IV liposomal amphotericin B for $\geq 2$ weeks or until improvement

• **Maintenance:** oral itraconazole for $\geq 12$ months

For less severe disseminated histoplasmosis, itraconazole monotherapy
Monitoring

• Serial serum/urine antigen
• Start ART soon after initiating antifungal–IRIS rare

Stop therapy when
  o >1 year of itraconazole
  o negative fungal blood cultures
  o serum/urine antigen <4.1
  o CD4 count >150
  o ART for >6 mo
Back to our patient...

Initially treated for CAP and PJP prophylaxis, then
• Initiated on liposomal amphotericin B x9 days
• PO itraconazole x1 year
• Biktarvy (bictegravir, emtricitabine & tenofovir alafenamide) for treatment of HIV and hepatitis B
HIV for the PCP

• Screening: ages 15-65 (Grade A, USPSTF)
• Screen annually in patients at high risk

• Cancer screenings: cervical, colorectal, breast, lung
**FIGURE 2. Immunization schedule for adults infected with human immunodeficiency virus (HIV)**

<table>
<thead>
<tr>
<th>Vaccine</th>
<th>Age group (yrs)</th>
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<tbody>
<tr>
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<td>19–49</td>
</tr>
<tr>
<td></td>
<td>50–64</td>
</tr>
<tr>
<td></td>
<td>≥65</td>
</tr>
<tr>
<td>Influenza†</td>
<td>1 dose annually</td>
</tr>
<tr>
<td>Pneumococcal (polysaccharide)</td>
<td>1 dose</td>
</tr>
<tr>
<td>Hepatitis B†</td>
<td>3 doses (0, 1–2, 4–6 mos)</td>
</tr>
<tr>
<td>Tetanus, diphtheria, pertussis (Td/Tdap)†</td>
<td>Substitute 1-time dose of Tdap for Td booster; then boost with Td every 10 yrs</td>
</tr>
<tr>
<td>Human papillomavirus (HPV)†</td>
<td>Optional - see text and Table1</td>
</tr>
<tr>
<td>Measles, mumps, rubella (MMR)†</td>
<td>Do not administer to severely immunosuppressed persons</td>
</tr>
<tr>
<td>Varicella†</td>
<td>Do not administer to severely immunosuppressed persons</td>
</tr>
<tr>
<td>Hepatitis A†</td>
<td>2 doses</td>
</tr>
<tr>
<td>Meningococcal†</td>
<td>1 or more doses</td>
</tr>
</tbody>
</table>

Recommended if some other risk factor is present (e.g., on the basis of medical, occupational, lifestyle, or other indications).

For all persons in this category who meet the age requirements and who lack evidence of immunity (e.g., lack of documentation of vaccination or have no evidence of prior infection).

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*Guidelines for the Prevention and Treatment of Opportunistic Infections in Adults and Adolescents with HIV. May 2018.*
Summary

- Differential based on CD4 count
- Disseminated histoplasmosis
  - Distribution
  - Clinical manifestations
  - Diagnosis
  - Treatment
  - Monitoring
- HIV for the PCP
Questions
Sources

• Guidelines for the Prevention and Treatment of Opportunistic Infections in Adults and Adolescents with HIV. May 2018.
• Diagnosis and treatment of disseminated histoplasmosis in HIV-uninfected patients. UptoDate. Feb 28.