The Emperor of all Maladies
IDAC Fall Symposium 2021
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ID Division
28-year-old Male with known HIV diagnosed 6 years ago, previously on Biktarvy (BIC/FTC/TAF) and history of alcohol abuse presented with abdominal pain, fevers, dysuria for 5 days
HPI

- HIV contracted via unprotected MSM with HIV + partner
- Biktarvy initiated 3 years ago, but he stopped it one year later
- Experienced the same symptoms 3 years ago....
Records from 3 year ago

- Bone marrow biopsy 3 years ago -- slightly hypo cellular marrow with no evidence for lymphoma involvement or myelodysplastic syndrome, stable pancytopenia
- Abd/pelvic CT -- stable inguinal and hypogastric LAD
- EGD w duodenal biopsy – negative
- Left axillary LN biopsy -- benign lymphoid hyperplasia with no malignancy
- R groin excisional biopsy -- fibroadipose tissue with focal lymphoid hyperplasia, flow cytometry showing many lymphoid cells and no evidence of monoclonality in B cell population
History

- PMH: HIV
- PSH: none
- Allergies: NKDA
- Home medications: none
- FH: none
Social History

- Denied IV drug use
- + methamphetamine use in the past (inhalation)
- Heavy EtOH use for the past 10 years, 10-15 shots liquor/day
- Identifies as MSM
- Last sexually active 1 year ago with 1 partner, insertive and receptive anal intercourse, condom use “most of the time”
- 6 lifetime sexual partners
- Works in retail
- Lives in apartment in Bakersfield with parents
- Born in the US
- Recent travel to Virginia, no recent travel outside of the country
Physical examination

Vitals: BP 161/96, HR 145, RR 22, T 38.8

Abdomen: mildly distended, mildly tender in suprapubic region, estimated liver span of 12cm

Skin: 3 small clustered bruise-like lesions on the left shin

Otherwise, unremarkable
Initial Workup

SARS-CoV2 (-), ESR >100, WBC 2.2, Hgb 12, Plt: 91, CRP: 17, LDH: 192

HIV viral load 95,200, CD4 count 27
Syphilis Ab, RPR, GC/Cl rRNA, Hepatitis panel: NR
Urine toxicology negative
Cocci serology serum IgM and IgG NR, titer <1:2
Cryptococcal Ag serum: not detected
Tb Quant gold negative
CMV IgG: Positive
U/A: Nitrite neg, leukocyte esterase negative, 0-2 WBCs, no bacteria seen
Chest XR

Bilateral hilar adenopathy
Workup Continued

- Blood cultures:
  - Bacterial, Fungal and Mycobacterial: all no growth to date
- Urine cultures: No growth
- ANA: Negative
- CCP <16
- Empirical antibiotics with PIP/TAZ and Vancomycin stopped.
Lumbar puncture after episode of HA

- CSF:
  - Clear
  - WBC 8, lymphocyte % 99, normal Glu and Prot
  - Cryptococcus Ag negative
  - Cocci IgM and IgG non-reactive, titer <1:1
  - HSV1/2 DNA PCR not detected
  - Gram stain: no organisms seen
  - AFB smear: not seen
  - Fungal and AFB cultures: no growth to date
CT Chest
CT Abd/Pelvis

Bilateral groins
Bone Marrow Biopsy

- Bone: Gram stain no organisms
- Aspirate: Bacterial, Fungal and Mycobacterial culture no growth to date.

**DIAGNOSIS:**
BONE MARROW, ASPIRATION AND CORE BIOPSY:
- NORMOCYTOPLASMIC MARROW WITH MEGAKARYOCYTIC HYPERPLASIA.
- DECREASED IRON.
- NO EVIDENCE OF ACID-FAST OR FUNGAL ORGANISMS.
- PANCYTOPENIA OF BLOOD.
- NO EVIDENCE OF PARVOVIRUS OR MALIGNANCY.
<table>
<thead>
<tr>
<th>Workup</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stool Clostridioides difficile</td>
<td>GDH antigen + Toxin A&amp;B +</td>
</tr>
<tr>
<td>EBV DNA serum</td>
<td>30,360 copies/mL (normal &lt;200 copies/mL)</td>
</tr>
</tbody>
</table>

Started on 10 days of PO Vancomycin
DDX?

• What to do:
  • Liver biopsy?
  • Lymph node biopsy?
  • EGD/Colonoscopy?
  • TEE?
  • PET scan?
  • Gallium scan?
  • It is all AIDS like 3 years ago? → start ART and see him in clinic
DDX

• Lymphoproliferative disorders (Hepatosplenomegaly)
• Lymphoma (for 3 years): Not a chance
• Chronic Active EBV infection
• Vasculitis: Adult-onset Still’s disease
• Castleman’s disease
• Hemophagocytic lymphohistiocytosis
• Visceral Kaposi’s sarcoma
• It is all AIDS
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<tbody>
<tr>
<td>Histoplasmosis Ag (Serum and Urine)</td>
<td>Negative</td>
</tr>
<tr>
<td>Giardia Antigen EIA (Stool)</td>
<td>Negative</td>
</tr>
<tr>
<td>Shigella, Salmonella, Campylobacter (Stool)</td>
<td>Negative</td>
</tr>
<tr>
<td>Parvo-B19 IgG (Serum)</td>
<td>Positive</td>
</tr>
<tr>
<td>Toxoplasmosis IgM, IgG (serum)</td>
<td>Negative</td>
</tr>
<tr>
<td><em>Coxiella burnetii</em>, <em>Bartonella</em> Q and H (Serum)</td>
<td>Negative</td>
</tr>
<tr>
<td>Interleukin-2 Soluble Receptor α (Serum)</td>
<td>11842</td>
</tr>
<tr>
<td>Brucella serology (Serum)</td>
<td>Negative</td>
</tr>
<tr>
<td>Parvo-B19 DNA PCR (serum and Bone Marrow)</td>
<td>&lt;100</td>
</tr>
<tr>
<td>CMV DNA PCR (Serum)</td>
<td>&lt;200</td>
</tr>
<tr>
<td>EBV DNA PCR (Serum)</td>
<td>30360</td>
</tr>
<tr>
<td>AFB and GMS Stain of Bone Marrow and AFB cx</td>
<td>Negative</td>
</tr>
<tr>
<td>Cryptosporidium (Stool)</td>
<td>Negative</td>
</tr>
</tbody>
</table>


Next step

- EGD: Negative for Metaplasia, Dysplasia or Malignancy. Negative for HELICOBACTER PYLORI
- IR Inguinal lymph node core biopsy:
  - SCANT FRAGMENTS OF LYMPHOID AND FIBROUS TISSUE
  - No Evidence of Malignancy
- Plan for inguinal excisional biopsy
Right Inguinal LN Excisional Biopsy

Serum HHV-8: 2,288,277 copies/ml
(Normal Range: <1,000)
HHV-8 associated multicentric Castleman Disease (MCD)

- 50% of MCD are HHV-8 associated in patients with HIV
- MCD: Multiple regions, hepatosplenomegaly, cytopenia and organ dysfunction

Symptoms of HHV-8 associated MCD:
- Fever – 100 percent → due to elevated IL6 (human and viral source)
- Lymphadenopathy – 96 percent
- Splenomegaly – 86 percent
- Hepatomegaly – 63 percent

Lymph node biopsy: Interfollicular plasma cells and/or germinal centers with vascularizations and “onion-skin” (hyaline vascular appearance.
Treatment for HHV-8-associated MCD

• Start and continue ART in HIV
• Based on presence of concurrent Kaposi sarcoma, organ failure and functional capacity
• Options include:
  • Rituximab
  • Pegylated liposomal doxorubicin
  • IL-6 inhibitors (Tocilizumab, Siltuximab)
  • limited data for Anti-viral therapy (Zidovudine, cidofovir, foscarnet, ganciclovir)
Prognosis

- More often a relapsing and remitting disease.
- Prior to ART, HIV patients with CD had a 15-fold increased risk of developing lymphoma

- Median survival without ART: 14-months
- This has increased to 2-year survival of more than 90% with ART
Follow up

• ART + Rituximab x 6 for several months, did well
• But he stopped ART and started ETOH
• Readmitted with fever and jaundice
• Restarted on ART and Rituximab x 3
• Due to persistent liver injury; plan is to start Doxil
“Castle on the Park”
First US hospital devoted to treat cancer
New York, Central Park, built 1887