A case of systemic illness in a young HIV+ woman

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Internal Medicine - PGY3
I have no disclosures.
32-year-old woman presents to the ambulatory clinic with a chief complaint of “feeling terrible for two weeks”

- Sore throat, decreased appetite
- Lumps in neck, underarms, groin
- Pain in legs, hands, neck
- Headache with photophobia
- “Exactly like when diagnosed with HIV”
PMHx / Meds
- HIV (Biktarvy)
  - RNA QN < 20, CD4 530
- Endometriosis
- Chlamydia and syphilis s/p treatment
- Recent outbreak of vaginal sores s/p valacyclovir

Social / Family Hx
- Angola > Portugal > Texas > Maine
- 5-6 beers nightly, marijuana
- No social support system, prefers English
- Unknown family hx
T 37.4, BP 118/83, HR 97, RR 16, O₂ 98%

Physical Exam:
Gen: **Unwell appearing**, no distress
HEENT: **Eyes partially closed b/c sensitivity.** No lesions, tonsillar exudate or pharyngeal erythema.
Neck: **Posterior/right neck tenderness, chin to chest w/out pain.** Tender palpable **left posterior cervical LAD, b/l supraclavicular LAD.**
Lungs: CTAB
Cardio: RRR, no murmurs
Abd: Soft, NT
Ext: No axillary or inguinal LAD, **1+ nonpitting edema**
Neuro: CN intact, no focal deficits on limited exam

**Sent to the ED**
DAY0: ED

- MCV 74.5
diff - Abs ANC 1.35
- 11.8
- 2.7
- 371
- 137
- 102
- 9
- 4.3
- 25
- 0.81
- 108
- Ca 9.8
- Protein 8.7
- Albumin 4.5
- AST 31
- ALT 31
- AlkPhos 52
- Bili < 0.02
- bHCG: (-)
- UA: Bland
- Monospot: (-)
- CT Head: No acute process

Discharged home.

DAY7: Ambulatory Clinic
Abdominal and joint pains
10 lb weight loss
- CBC, CMP unchanged
- CD4 Count 355 (from 530)
  - tick panel (-)
  - 1 week follow up

DAY8: HIV Clinic

DAY14: Ambulatory Clinic
Labs / STAT TVUS
- 3 day follow up

DAY16: Obgyn Clinic

Sed Rate: 103
CRP: 12.1

DAY7: Ambulatory Clinic
Abdominal and joint pains
- CBC, CMP unchanged
- CD4 Count 355 (from 530)
  - tick panel (-)
  - 1 week follow up
ESR / CRP discordance
Erythrocyte Sedimentation Rate

60 min

mm/hr
## Erythrocyte Sedimentation Rate

<table>
<thead>
<tr>
<th>↑↑</th>
<th>↓↓</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infection</td>
<td>Sickle cell*</td>
</tr>
<tr>
<td>Malignancy</td>
<td>Hypogammaglobulin</td>
</tr>
<tr>
<td>Pregnancy</td>
<td>Polycythemia</td>
</tr>
<tr>
<td>MM/Waldenstrom’s Anemia</td>
<td></td>
</tr>
</tbody>
</table>

*Note: *Sickle cell* refers to sickle cell anemia.*
C – Reactive Protein
acute phase reactant

IL-1
TNFa

↓

IL-6

*IFNa

C3 fibrinogen hepcidin

Age
Women
Obesity

Lupus*

Up

Down
<table>
<thead>
<tr>
<th>DAY17 AM: Ambulatory Clinic</th>
<th>DAY17 PM: ED</th>
<th>Objective:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Unwell appearing Febrile to 104.2</td>
<td>T 37, BP 115/71, <strong>HR 115</strong>, RR 16, O2 98%</td>
<td><strong>Physical Exam:</strong></td>
</tr>
<tr>
<td>&gt; Sent to the ED</td>
<td></td>
<td>Neck: NEW submandibular LAD, unchanged cervical and supraclavicular LAD</td>
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<td></td>
<td></td>
<td>MSK: Unable to grip hands, no synovitis</td>
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<td></td>
<td></td>
<td><strong>Labs:</strong> Unchanged</td>
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<td></td>
<td></td>
<td><strong>Imaging:</strong></td>
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<td></td>
<td></td>
<td><strong>CT neck:</strong> Numerous enlarged LN through neck and upper chest</td>
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<td></td>
<td></td>
<td><strong>MR brain:</strong> No acute findings</td>
</tr>
<tr>
<td></td>
<td></td>
<td><strong>Empiric antibiotics started</strong></td>
</tr>
</tbody>
</table>
ID Workup:
- BCx x3 sets incl mycobacterial
- CMV
- EBV
- Parvovirus
- Bartonella
- Q Fever
- Treponema Pallidum
- Cryptococcus
- Toxoplasma
- Brucella
- Histoplasma
- Blastomyces
- Hepatitis
- Lyme, Anaplasma, Babesia
- Borrelia miyamotii
- Chlamydia, gonorrhea
- Biopsy Tissue: MTB
- Intraoperative cultures

Heme Workup:
- SPEP, UPEP, FLC
- Iron (↓)
- Ferritin (↑)
- Reticulocyte count (↓)
- DIC panel (ddimer, fibrinogen ↑)
- Haptoglobin (↑)
- Lactate dehydrogenase (↑)
- LN biopsy pending

Rheum Workup:
- ANA (-)
- DS-DNA (-)
- RF (-)
- Smith 4.2 (↑) (< 1 neg)
- RNP 1.8 (↑) (< 1 neg)
- CCP (-)
- ANCA mass gen: (-)
- Sjogren’s SSA + SSB (-)
- C3 + C4 (WNL)
- IgG 1790 (↑) (700-1600)
- IgG subclasses, total (↑)
- IgA, IgM (WNL)
FINAL DIAGNOSIS:
Lymph node, posterior cervical region, excisional biopsy:

1. Necrotizing lymphadenitis.
2. Special stains negative for acid fast bacilli and fungal organisms.
3. Negative for malignancy. See comment.
Kikuchi-Fujimoto Disease
histiocytic necrotizing lymphadenitis

**Epidemiology:** Young women

**Clinical Features:**
- **Exam:** Tender posterior cervical LAD + fever
- **Labs:** Normal (+/- anemia, leukopenia, LDH, AST/ALT)

**Etiology:** ?Viral ?Immune mediated

**Treatment:** Symptomatic

**Prognosis:** Benign, self-limited disease

**Ddx includes infection, malignancy, connective tissue disorder (SLE)**

**Histology:** Partially preserved architecture + follicular hyperplasia w/ areas of nongranulomatous necrosis.
Labs 10 days later (HD13)

POSITIVE ANA
1:80 Speckled
Lupus anticoagulant (dRVVT)
2019 European League Against Rheumatism/American College of Rheumatology classification criteria for systemic lupus erythematosus

**Entry criterion**

Antinuclear antibodies (ANA) at a titer of ≥1:80 on HEp-2 cells or an equivalent positive test (ever)

If absent, do not classify as SLE

If present, apply additive criteria

**Additive criteria**
<table>
<thead>
<tr>
<th>Clinical domains and criteria</th>
<th>Weight</th>
<th>Immunology domains and criteria</th>
<th>Weight</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Constitutional</strong></td>
<td></td>
<td><strong>Anti phospholipid antibodies</strong></td>
<td></td>
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<tr>
<td>Fever</td>
<td>2</td>
<td>Anti-cardiolipin antibodies OR</td>
<td></td>
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<tr>
<td><strong>Hematologic</strong></td>
<td></td>
<td>Anti-β2GP1 antibodies OR</td>
<td></td>
</tr>
<tr>
<td>Leukopenia</td>
<td>3</td>
<td>Lupus anticoagulant</td>
<td>2</td>
</tr>
<tr>
<td>Thrombocytopenia</td>
<td>4</td>
<td><strong>Complement proteins</strong></td>
<td></td>
</tr>
<tr>
<td>Autoimmune hemolysis</td>
<td>4</td>
<td>Low C3 OR low C4</td>
<td>3</td>
</tr>
<tr>
<td><strong>Neuropsychiatric</strong></td>
<td></td>
<td>Low C3 AND low C4</td>
<td>4</td>
</tr>
<tr>
<td>Delirium</td>
<td>2</td>
<td><strong>SLE-specific antibodies</strong></td>
<td></td>
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<tr>
<td>Psychosis</td>
<td>3</td>
<td>Anti-dsDNA antibody* OR</td>
<td></td>
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<tr>
<td>Seizure</td>
<td>5</td>
<td>Anti-Smith antibody</td>
<td>6</td>
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<tr>
<td><strong>Mucocutaneous</strong></td>
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<tr>
<td>Non-scarring alopecia</td>
<td>2</td>
<td></td>
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<tr>
<td>Oral ulcers</td>
<td>2</td>
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<tr>
<td>Subacute cutaneous OR discoid</td>
<td>4</td>
<td></td>
<td></td>
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<tr>
<td>Lupus</td>
<td>6</td>
<td>Acute cutaneous lupus</td>
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<tr>
<td><strong>Serosal</strong></td>
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<tr>
<td>Pleural or pericardial effusion</td>
<td>5</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Acute pericarditis</td>
<td>6</td>
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<tr>
<td><strong>Musculoskeletal</strong></td>
<td></td>
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<tr>
<td>Joint involvement</td>
<td>6</td>
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<tr>
<td><strong>Renal</strong></td>
<td></td>
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<tr>
<td>Proteinuria &gt;0.5g/24h</td>
<td>4</td>
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<tr>
<td>Renal biopsy Class II or V lupus nephritis</td>
<td>8</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Renal biopsy Class III or IV lupus nephritis</td>
<td>10</td>
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Classify as Systemic Lupus Erythematosus with a score of 10 or more if entry criterion fulfilled.
American College of Rheumatology

View all recommendations from this society

Released February 21, 2013

**Don't test ANA sub-serologies without a positive ANA and clinical suspicion of immune-mediated disease.**

Tests for anti-nuclear antibody (ANA) sub-serologies (including antibodies to double-stranded DNA, Smith, RNP, SSA, SSB, Scl-70, centromere) are usually negative if the ANA is negative. Exceptions include anti-Jo1, which can be positive in some forms of myositis, or occasionally, anti-SSA, in the setting of lupus or Sjögren's syndrome. Broad testing of autoantibodies should be avoided; instead the choice of autoantibodies should be guided by the specific disease under consideration.
HD1: Total D17
HD2: Infectious Disease
HD3: Rheumatology + Gynecology
HD4
HD5
HD6: Heme + SurgOnc
HD7: LN biopsy Ex-lap
HD8:
HD9
HD10
HD11: AKI, UA protein
HD12: Rheum note
HD13
HD14: Path Result
HD15: Dx
HD16
HD17: D33 D/c

Lupus
DAY0: ED

- MCV 74.5 Diff
- Abs ANC 1.35
- Ca 9.8
- Protein 8.7
- Albumin 4.5
- < 0.02 Bili
- bHCG: Neg
- UA: Unremarkable
- Monospot: Neg
- CT Head: Unremarkable
- Discharged home.

DAY7: Ambulatory Clinic

- Abdominal and joint pains
- CBC, CMP unchanged
- CD4 Count 355
- tick panel negative
- 1 week follow up

DAY8: ID Clinic

- 3 month follow up

DAY14: Ambulatory Clinic

- Labs / STAT TVUS
- C/f tuboovarian abscess
- 3 day follow up

DAY16: Obgyn Clinic

- imaging improved
- reassuring exam

Sed Rate: 103
CRP: 12.1
C – Reactive Protein
> acute phase reactant

*IFNa

IL-1
TNFa

↓

IL-6

CRP
fibrinogen
hepcidin

C3

*Rises in 4 hours, days to normalize

Obesity
Age

Lupus*

*IFNa

*Rises in 4 hours, days to normalize
ESR / CRP discordance

- high ESR, low CRP in Lupus flare
- IF high CRP - THEN think INFECTION
Take Away Points:

• ESR: ↑ positively charged proteins
• CRP: Acute phase reactant - ↓ in Lupus
• ESR / CRP discordance may provide diagnostic clues!
• Necrotizing lymphadenitis > Kikuchi-Fujimoto
  • think Lupus!
• ANA is REQUIRED for a Lupus diagnosis
Thank you,

Kenneth O’Rourke, MD
Matthew Clark, DO
Natalie Channell, MD
Elizabeth Eisenhardt, MD
My MANY colleagues who put hours of thought, effort, and care into this case

Sources: