Thieves’ Market
What is a Thieves’ Market?

- Present a case
  - History
  - Physical Exam
  - Lab and imaging studies
  - Reveal diagnosis

- Review teaching points about the case

- Repeat for a second case
Your Role in Thieves’ Market

- Steal the diagnosis... but how?
- Interrupt and shout out the diagnosis
Requirements to Win

- Shout out the diagnosis before it appears on the screen!
- Nonspecific diagnoses won’t count
- You must say and I must repeat what you said
- I will not confirm whether a guess is correct until the end
What happens if I win?
Let's Do This!
Case 1 History

28-year-old Hispanic woman cc: weakness and chest pain

- Recurrent epistaxis
- Anemia
- Nasal procedure
- Nose bleeds less frequent

2nd trimester miscarriage
Leakage of fluid → IUFD → misoprostol
D&C for retained placenta → EBL 1800cc
Transfused 3 units PRBCs

Fever/chills
Weakness
SOB
Chest pain

-3 months
-1 months
-1 week
Case 1 History

28-year-old Hispanic woman cc: weakness and chest pain

**Fever:** x1 week, subjective, with associated chills

**Weakness:** x1 week, diffuse, progressively worsening, unable to get out of bed on her own

**Chest Pain:** worsened with exertion and deep breaths, alleviated by laying on her side

**SOB:** x3 days, at rest and with exertion
Review of Systems

Denies

- Blurry vision
- Joint pain
- Lower back pain
- Neck pain/stiffness
- Weight loss/gain
- Cough/wheezing
- Edema

- Heat/cold intolerance
- Anxiety
- Depression
- Skin lumps
- Rashes
Review of Systems

- Abdominal pain/loose bowel movements x several days
- Headache
- Mild Nausea (no vomiting)
<table>
<thead>
<tr>
<th>Histories</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Medical</strong></td>
<td><strong>Medications</strong></td>
<td></td>
</tr>
<tr>
<td>Anemia from epistaxis</td>
<td>Ferrous Sulfate 325mg every other day</td>
<td></td>
</tr>
<tr>
<td><strong>Surgical</strong></td>
<td></td>
<td>NKDA</td>
</tr>
<tr>
<td>“nasal procedure” for epistaxis</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Histories

Family History: listed as “unknown”

Social History:

- Emigrated from El Salvador 3 years ago
- Works cleaning houses
- Denies tobacco, alcohol, or drug use
- No travel outside of Alabama in 3 years
Physical Exam:

**T:** 100.3°F  **HR:** 130  **RR:** 16  **BP** 104/74  **O2:** 97%

**GEN:** Female in NAD, appears tired

**HEENT:** PERRL, EOMI

**Neck:** No JVD

**Chest:** CTA B

**CV:** Tachycardic, regular rhythm, 2/6 holo-systolic murmur at apex

**GI:** soft, BS+, NT, ND

**Skin:** no rashes

**Neuro:** difficulty following commands (with interpreter)
  
  strength: 3/5 in BUE and BLE, 5 beats L ankle clonus, brisk 2+ reflexes throughout

**Psych:** flat affect
Labs

133 | 100 | 26 | 112
4.4 | 21 | 1.5

Ca: 8.2
Mg: 2.1
MCV: 81

7.5 | 9.0 | 308

N: 86%  L: 9%  M: 4%
**Labs**

- **Ca:** 8.2
- **Mg:** 2.1
- **MCV:** 81
- **ALT:** 6
- **AST:** 15
- **N:** 86%
- **L:** 9%
- **M:** 4%
- **INR:** 1.08
- **COVID/Flu:** neg
- **HIV:** neg
- **UCG:** neg

**Blood Work**

- **Alb:** 3.0
- **T. Bili:** 0.5
- **ALT:** 6
- **AST:** 102
Labs

**Ca:** 8.2  
**Mg:** 2.1 7.5  
**MCV:** 81

**Ca:** 9.0  
**27**  
**308**

**N:** 86%  
**L:** 9%  
**M:** 4%

**CRP:** 154  
**ESR:** 83  
**UA:** 3+ prot, 3+ blood,  
>25RBCs, >50WBCs,  
12 hyal casts

**Alb:** 3.0  
**7.1**  
**T Protein**

**T. Bili:** 0.5

**ALT:** 6  
**15**  
**AST**  
**102**

**COVID/Flu:** neg  
**HIV:** neg  
**UCG:** neg  
**INR:** 1.08
ER Pelvic US

No convincing sonographic evidence of retained products of conception.
Diagnostic Studies

Sinus Tachycardia, RAD, LA enlargement
Diagnostic Studies

- Moderate cardiomegaly
- Left lower lobe airspace opacity may represent atelectasis. However, superimposed infection is not excluded
- There is perihilar vascular prominence without frank edema.
Labs, continued

BNP: 3,027 (0-100)
HS-Troponin: 663 (3-15)

Given chest pain with elevated troponin admitted to CCU. Admission diagnosis = Sepsis
Diagnostic Studies

Right Heart Catheterization:
1. Normal right sided filling pressures
2. Mildly elevated PCWP & left sided filling pressures
3. Normal SVR
4. Preserved CI by Fick

Left Heart Catheterization:
1. No significant obstructive CAD
Diagnostic Studies

TTE:
- LV Ejection Fraction = 40-45%.
- RV systolic function is normal.
- Normal IVC with >50% collapse with sniff. Estimated RAP is 3 mmHg.
- Mitral valve leaflets: moderately thickened, severe mitral stenosis, mild to moderate mitral regurgitation.
- The left atrium is severely dilated.

TEE: The mitral valve leaflets are severely thickened with what could possibly be thrombus. There is severe mitral stenosis.
Cardiac MRI

- Severe mitral stenosis.
- Nonenhancing areas along the mitral valve leaflets on postcontrast imaging raise suspicion of thrombi.

Lupus Anticoagulant (PTT-LA and dRVVT): neg
IgG Cardiolipin: 9
IgM Cardiolipin: 18 (<12)
Beta 2 glycoprotein: IgM <2
Beta 2 glycoprotein: 6
Diagnostic Studies

**MRI Brain:**
- Numerous foci of restricted diffusion within both the supratentorial & infratentorial brain parenchyma.
- Findings are highly concerning for *embolic infarctions*. There is *diffuse leptomeningeal enhancement* and *papilledema* which is concerning for *meningitis* likely infective etiology.

**MRI C-spine:**
- No evidence of cord compression or cord signal abnormality.
- MRA Head and neck: unremarkable
Labs

Negative

- Viral respiratory panel
- Blood cultures x 4
- Urine culture
- Throat culture
- Fungal culture
- Histo ag
- Crypto ag
- 1-3 beta-D-glucan
- Tspot TB

- Brucella IgM +, IgG –
- Q Fever IgM, IgG
- Bartonella IgM, IgG
- Trep ab
- ASO
Labs

CSF
- WBC: 3   RBC 29
- Protein: 45  Glu: 46
- Crypto ag: neg
- Culture: negative
- Fungal cx: negative
- Toxoplasma IgG: neg
- West Nile: IgG+, IgM neg

CSF
- VZV, HSV, CMV neg
- Autoimmune & Paraneoplastic ab panel negative
Consults

- Cardiology review of TTE/TEE/MRI
  - Chronic thickening, not vegetation, not thrombi
  - Further history revealed, severe sore throat and fever at age 14
  - MV = chronic mitral stenosis from Rheumatic heart disease
Problem List: 28-year-old woman w/ weakness and chest pain

- Left atrial enlargement
- Reduced LVEF
- SOB/DOE

Explained by RHD
- Mitral Stenosis
- Cerebral emboli
- Chest Pain/NSTEMI

Unexplained
- Fever
- Weakness/Confusion/Headache
- Renal Insufficiency
- Anemia
- Elevated inflammatory markers
Problem List: 28-year-old woman w/ weakness and chest pain

<table>
<thead>
<tr>
<th>Explained by RHD</th>
<th>Unexplained</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mitral Stenosis</td>
<td>Fever</td>
</tr>
<tr>
<td>Left atrial enlargement</td>
<td>Weakness/Confusion/Headache</td>
</tr>
<tr>
<td>Reduced LVEF</td>
<td>Cerebral emboli</td>
</tr>
<tr>
<td>SOB/DOE</td>
<td>Chest Pain/NSTEMI</td>
</tr>
<tr>
<td></td>
<td>Recurrent epistaxis</td>
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<tr>
<td></td>
<td>Renal Insufficiency</td>
</tr>
<tr>
<td></td>
<td>Anemia</td>
</tr>
<tr>
<td></td>
<td>Elevated inflammatory markers</td>
</tr>
</tbody>
</table>
Consults

- Neurology review of MRI
  - Embolic infarcts are numerous and tiny, more consistent with inflammation/vasculitis
<table>
<thead>
<tr>
<th>Test</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cryoglobulin</td>
<td>negative</td>
</tr>
<tr>
<td>C3</td>
<td>39L</td>
</tr>
<tr>
<td>C4</td>
<td>7L</td>
</tr>
<tr>
<td>CH50</td>
<td>22L</td>
</tr>
<tr>
<td>ANA</td>
<td>+1:640, homogenous</td>
</tr>
<tr>
<td>Ds-DNA</td>
<td>&gt;1:640</td>
</tr>
<tr>
<td>SSA</td>
<td>63H</td>
</tr>
<tr>
<td>SSB</td>
<td>23H</td>
</tr>
<tr>
<td>RNP</td>
<td>17</td>
</tr>
<tr>
<td>Anti-Smith</td>
<td>&lt;12</td>
</tr>
<tr>
<td>C3</td>
<td>39L</td>
</tr>
<tr>
<td>C4</td>
<td>7L</td>
</tr>
<tr>
<td>CH50</td>
<td>22L</td>
</tr>
</tbody>
</table>
Renal Biopsy

Focal lupus nephritis (Class IV-S) with focal glomerular necrosis (6/35) and a single crescent (1/35)

Necrotizing arteritis and arteriolar thrombosis, focal.
FINAL DIAGNOSIS

• Systemic Lupus Erythematosus with
  SLE Cerebritis
  SLE Nephritis
  SLE Myopericarditis

• She received 1 gram of methylprednisolone, Cytoxan, and hydroxychloroquine

• Improved strength and resolution of fever/systemic inflammation, kidney insufficiency and confusion ... valve replacement soon
Systemic lupus erythematosus (SLE)

- Auto-immune disease of unknown cause
- Average age onset: 16-55yo
- 10:1 Women: men ratio
- In US women prevalence:
  Asian, African American, African Caribbean, and Hispanic American >> White individuals
Systemic lupus erythematosus (SLE)

1997 ACR Criteria

- 4 of 11
- Specificity: 93%
- Sensitivity: 82%
Systemic lupus erythematosus (SLE)

2019 EULAR/ACR Criteria

- +ANA & ≥ 10 points

- Specificity: 93%
- Sensitivity: 96%

The entry criterion is necessary to classify SLE.

Entry criteria:
- ANA at a titer of ≥1:80 on HEP-2 cells or an equivalent positive test (ever). *

At least 1 clinical criterion required to classify SLE. Additional additive (clinical or immunology) criteria are counted toward the total score.

Additive criteria:
- Do not count a criterion if there is a more likely explanation than SLE.
- Occurrence of a criterion on one occasion is sufficient.
- Criteria need not occur simultaneously.
- Within each domain (e.g., musculoskeletal, complement proteins), only the highest-weighted criterion is counted toward the total score if more than 1 is present.

### Clinical domains and criteria

<table>
<thead>
<tr>
<th>Constitutional</th>
<th>Weight</th>
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</thead>
<tbody>
<tr>
<td>Fever</td>
<td>2</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Hematologic</th>
<th>Weight</th>
</tr>
</thead>
<tbody>
<tr>
<td>Leukopenia</td>
<td>3</td>
</tr>
<tr>
<td>Thrombocytopenia</td>
<td>4</td>
</tr>
<tr>
<td>Autoimmune hemolysis</td>
<td>4</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Neuropsychiatric</th>
<th>Weight</th>
</tr>
</thead>
<tbody>
<tr>
<td>Delirium</td>
<td>2</td>
</tr>
<tr>
<td>Psychosis</td>
<td>3</td>
</tr>
<tr>
<td>Seizure</td>
<td>5</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Musculoskeletal</th>
<th>Weight</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nerve palsy</td>
<td>2</td>
</tr>
<tr>
<td>Oral ulcers</td>
<td>2</td>
</tr>
<tr>
<td>Subacute tubulointerstitial lupus</td>
<td>4</td>
</tr>
<tr>
<td>Acute tubulointerstitial lupus</td>
<td>6</td>
</tr>
<tr>
<td>Serosal</td>
<td></td>
</tr>
<tr>
<td>Pleural or pericardial effusion</td>
<td>5</td>
</tr>
<tr>
<td>Acute pancreatitis</td>
<td>6</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Immunology domains and criteria</th>
<th>Weight</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antiphospholipid antibodies</td>
<td></td>
</tr>
<tr>
<td>Anti-cardiolipin antibodies</td>
<td>2</td>
</tr>
<tr>
<td>Anti-beta-2GPI antibodies</td>
<td></td>
</tr>
<tr>
<td>Anti-antiphospholipid antibodies</td>
<td></td>
</tr>
<tr>
<td>Complement proteins</td>
<td></td>
</tr>
<tr>
<td>Low C3 or low C4</td>
<td>3</td>
</tr>
<tr>
<td>Low C3 and low C4</td>
<td>4</td>
</tr>
<tr>
<td>SLE-specific antibodies</td>
<td></td>
</tr>
<tr>
<td>Anti-dsDNA antibody</td>
<td></td>
</tr>
<tr>
<td>Anti-smith antibody</td>
<td>6</td>
</tr>
</tbody>
</table>

A total score of ≥10 and ≥1 clinical criterion are required to classify SLE.

Total score
### Diseases associated with a positive ANA

<table>
<thead>
<tr>
<th>Disease</th>
<th>% with positive ANA</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Systemic autoimmune diseases</strong></td>
<td></td>
</tr>
<tr>
<td>Mixed connective tissue disease</td>
<td>100%</td>
</tr>
<tr>
<td>SLE:</td>
<td></td>
</tr>
<tr>
<td>- Active</td>
<td>98 to 100%</td>
</tr>
<tr>
<td>- Remission</td>
<td>90%</td>
</tr>
<tr>
<td>Scleroderma</td>
<td>95%</td>
</tr>
<tr>
<td>Drug-Induced LE</td>
<td>80 to 95%</td>
</tr>
<tr>
<td>Sjögren's disease</td>
<td>60%</td>
</tr>
<tr>
<td>Rheumatoid arthritis</td>
<td>45%</td>
</tr>
<tr>
<td>Raynaud phenomenon</td>
<td>40%</td>
</tr>
<tr>
<td>Polymyositis/dermatomyositis</td>
<td>35%</td>
</tr>
<tr>
<td>Juvenile idiopathic arthritis</td>
<td>15 to 40%</td>
</tr>
<tr>
<td><strong>Organ-specific autoimmune diseases</strong></td>
<td></td>
</tr>
<tr>
<td>Autoimmune hepatitis</td>
<td>70%</td>
</tr>
<tr>
<td>Primary biliary cholangitis</td>
<td>50 to 70%</td>
</tr>
<tr>
<td>Hashimoto's thyroiditis</td>
<td>50%</td>
</tr>
<tr>
<td>Graves' disease</td>
<td>50%</td>
</tr>
<tr>
<td><strong>Viral infections</strong></td>
<td></td>
</tr>
<tr>
<td>EBV</td>
<td></td>
</tr>
<tr>
<td>HIV</td>
<td></td>
</tr>
<tr>
<td>HCV</td>
<td></td>
</tr>
<tr>
<td>Parvovirus 19</td>
<td></td>
</tr>
<tr>
<td><strong>Malignancies</strong></td>
<td></td>
</tr>
<tr>
<td>Lymphoproliferative diseases</td>
<td></td>
</tr>
<tr>
<td>Paraneoplastic syndromes</td>
<td></td>
</tr>
<tr>
<td><strong>Miscellaneous diseases</strong></td>
<td></td>
</tr>
<tr>
<td>Inflammatory bowel disease</td>
<td></td>
</tr>
<tr>
<td>Interstitial pulmonary fibrosis</td>
<td></td>
</tr>
</tbody>
</table>

### ANA in Health Individuals

- 1:40: 32%
- 1:80: 13%
- 1:160: 5%
- 1:320: 3%

ANA disease prevalence: 1%

Rheumatic Fever

- Group A strep pharyngitis complications
  - Suppurative: peritonsillar abscess, sinusitis, Otitis Media
  - Nonsuppurative: rheumatic fever, scarlet fever, Acute GN

- Acute Rheumatic Fever
  - 500,000 new cases/yr worldwide (low/mid resource countries)
  - Fever, arthritis, carditis & valvulitis, Sydenham chorea

- Rheumatic Heart Disease
  - 50% of ARF develop chronic immune mediated valve damage
  - MITRAL VALVE is most frequently affected

Case 2
Case 2 History

33-year-old man cc: fevers

- Fever x 5-7 days
- Malaise, cough, myalgia
- Decreased appetite
- Daughter sick, HBV vaccine
- No sick contacts
- Upstate New York
- Cabin in the woods
- Hiking, no known ticks

-6 months
-3 months
-1 month
-2 weeks

Has felt normal between febrile periods
Case 2 History, Presentation

33-year-old man cc: fevers

**Fever:** 100.8 – 103, controlled with acetaminophen

**LAD:** nodule noted behind ear

**Eyes yellow:** noticed by family, x 1 day

**Headache:** (usually has with febrile periods)
### Review of Systems

<table>
<thead>
<tr>
<th>Denies</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Blurry vision</td>
<td>Diarrhea/constipation</td>
</tr>
<tr>
<td>Weakness</td>
<td>Easy bruising or bleeding</td>
</tr>
<tr>
<td>SOB, wheezing</td>
<td>Joint pain</td>
</tr>
<tr>
<td>Hemoptysis</td>
<td>Rashes</td>
</tr>
<tr>
<td>Chest pain</td>
<td>Numbness</td>
</tr>
<tr>
<td>Palpitations</td>
<td>Depression/anxiety</td>
</tr>
<tr>
<td>Abd pain, Naus/vom</td>
<td></td>
</tr>
</tbody>
</table>
## Histories

<table>
<thead>
<tr>
<th>Medical</th>
<th>Medications</th>
</tr>
</thead>
<tbody>
<tr>
<td>None</td>
<td>none</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Surgical</th>
<th>NKDA</th>
</tr>
</thead>
<tbody>
<tr>
<td>none</td>
<td></td>
</tr>
</tbody>
</table>
Histories

Family History: Father: DM, Mother: HTN. No family history of malignancy or auto-immune diseases

Social History:

• Born & raised India, PhD in Germany, US 7 years ago
• Infectious Diseases scientist
• Denies tobacco, alcohol, or drug use
• No travel outside of US in 3 years
• Married, 19 month old daughter, daycare
Physical Exam:

T: 101.5°F  HR: 112  RR: 18  BP 119/83  O2: 98%

GEN: NAD

HEENT: PERRL, EOMI, mild scleral icterus

Neck: small, right occipital lymph node

Chest: CTA B

CV: Tachycardic, regular rhythm, no M/R/Gs

GI: soft, BS+, NT, ND, dullness to percussion LUQ 8cm below costal margin consistent with splenomegaly

Skin: no rashes

Neuro: alert and oriented, no focal deficits

Psych: appropriate mood and affect
Labs

134 | 96 | 9 | 90
3.5 | 27 | 0.7

Ca: 8.6  Mg: 2.0  MCV: 80

3.29 | 11.4 | 39
27 | 27 | 39

N: 44%  L: 46%  M: 6%
Labs

<table>
<thead>
<tr>
<th>Test</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alb</td>
<td>3.7</td>
</tr>
<tr>
<td>T. Bili</td>
<td>4.3</td>
</tr>
<tr>
<td>ALT</td>
<td>83</td>
</tr>
<tr>
<td>Ca</td>
<td>8.6</td>
</tr>
<tr>
<td>Mg</td>
<td>2.0</td>
</tr>
<tr>
<td>Mcv</td>
<td>80</td>
</tr>
<tr>
<td>N</td>
<td>44%</td>
</tr>
<tr>
<td>L</td>
<td>46%</td>
</tr>
<tr>
<td>M</td>
<td>6%</td>
</tr>
<tr>
<td>Mg</td>
<td>2.0</td>
</tr>
<tr>
<td>T. Bili</td>
<td>4.3</td>
</tr>
<tr>
<td>ALT</td>
<td>83</td>
</tr>
<tr>
<td>Direct</td>
<td>2.6</td>
</tr>
<tr>
<td>Flu</td>
<td>neg</td>
</tr>
<tr>
<td>HIV</td>
<td>neg</td>
</tr>
<tr>
<td>INR</td>
<td>1.16</td>
</tr>
<tr>
<td>Acet</td>
<td>&lt;10</td>
</tr>
<tr>
<td>Mg</td>
<td>2.0</td>
</tr>
</tbody>
</table>
Labs

**Ca:** 8.6
**Mg:** 2.0
**MCV:** 80
**INR:** 1.16

**T. Bili:** 4.3
**Direct:** 2.6

**ALT:** 83
**AST:** 77

**Alb:** 3.7

**T. Protein:** 6.4

**Flu:** neg
**HIV:** neg
**INR:** 1.16

**CRP:** 105

**ESR:** 9
**UA:** negative

**Acet:** <10

**M:** 6%
**N:** 44%
**L:** 46%
Labs, continued

Fe: 37
TIBC: 339
Ferritin: 2,277
B12: 391
Folate: >22
Haptoglobin: 88
LDH: 623
Retic: 0.9%
Labs, continued

Fe: 37
TIBC: 339
Ferritin: 2,277
B12: 391
Folate: >22
Haptoglobin: 88
LDH: 623
Retic: 0.9%

D-dimer: 8,011
Fibrinogen: 244
Positive: ANA
Negative: RF
ANCA
CT Chest/Abdomen/Pelvis

- The lungs and pleura are unremarkable
- Bilateral axillary, mediastinal, hilar and subcarinal lymphadenopathy. 2-3cm lymph nodes
- Lymph nodes throughout abd/pelvis enlarged (up to 5 cm)
- Mild Hepatomegaly
- Splenomegaly (17cm)

- Gallbladder, adrenals, kidneys, bladder, prostate, GI tract, appendix all unremarkable. No bone lesions
Flow Cytometry

Peripheral Blood:

- No evidence of a monoclonal lymphoid or aberrant myeloid population.
Infectious Disease Labs

**Negative**

<table>
<thead>
<tr>
<th>Test</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>Crypto serum</td>
<td>1-3 Beta D Glucan</td>
</tr>
<tr>
<td>Histo Ag</td>
<td>Blood cultures</td>
</tr>
<tr>
<td>TSPOT</td>
<td>Toxo IgM, IgG</td>
</tr>
<tr>
<td>Lyme IgM, IgG</td>
<td>HSV PCR</td>
</tr>
<tr>
<td>Brucella IgM, IgG</td>
<td>CMV Ag</td>
</tr>
<tr>
<td>B Henselae IgG</td>
<td>CMV IgM</td>
</tr>
<tr>
<td>RMSF IgM, IgG</td>
<td>EBV IgG+, IgM –</td>
</tr>
<tr>
<td>Ehrlichia IgM, IgG</td>
<td>Hep A,B,C</td>
</tr>
</tbody>
</table>
Bone Marrow Biopsy

- Normocellular marrow (70%) with trilineage hematopoiesis
- No granulomas (Fite, AFB stains, GMS neg)
- No morphologic evidence of dysplasia
- Decreased storage iron
- No evidence of overt hemophagocytosis
- Flow cytometry negative
Excisional Lymph Node biopsy

- Lymph node with T-zone expansion and CD8 dominant T-cell population, favor reactive process, EBV positive.

- No evidence of a monoclonal lymphoid population.
Labs continued

EBV peripheral blood: 105,282 Int units/ml

IL-2 Soluble receptor: 1905 pg/ml (<1033)
FINAL Diagnosis

Hemophagocytic Lymphohistiocytosis (HLH) and Chronic Active Epstein-Barr Virus (CAEBV)
Hemophagocytic Lymphohistiocytosis (HLH)

- A syndrome of *excessive inflammation* and tissue destruction due to *abnormal immune activation*.

  - Triggers: infections, malignancies, rheumatologic disorders
  - Involves the absence of normal downregulation by activated macrophages and lymphocytes
HLH Diagnostic Criteria (5 of 9)

1. Fever ≥38.5°C
2. Splenomegaly
3. Bi-cytopenia or pancytopenia
4. Hypertriglyceridemia
5. Hemophagocytosis in bone marrow, spleen, lymph node, or liver
6. Low or absent NK cell activity
7. Ferritin >500 ng/mL (usually >2,000)
8. Elevated soluble CD25 (soluble IL-2 receptor)
9. Elevated CXCL9
Case 2 continued

Whole Genome Sequencing: homozygous c.1349C>T (p. T450M) missense variant in *PRF1* (*perforin*) gene

**Perforin**: pore forming protein produced by T cells and NK cells to cause apoptosis in target cells and regulate immune response
Case 2 continued

Whole Genome Sequencing: homozygous c.1349C>T (p. T450M) missense variant in **PRF1 (perforin) gene**

**Perforin**: pore forming protein produced by T cells and NK cells to cause apoptosis in target cells and regulate immune response

PRF1 mutation = cannot clear EBV, overactive immune response
Case 2 continued

- Treated with Rituximab
- HSCT recommended
- Fulminant HLH → critical illness
- Transfer to NIH → HSCT, patient died of complications

THE END
THE END

Thanks to all for playing along!