Mechanic’s Hands in an Excavator?

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Maine ACP Annual Meeting
Clinical Vignette- September 16, 2017
48 year old male with diffuse pain and swelling.
- Fatigue, weakness, difficulty sleeping
- Diarrhea
- Joint pain, myalgias
- Weight Loss

Symptoms are limiting mobility and ability to work

Evaluated at urgent care clinic

Thought to be Lyme, started on Doxycycline
March:

- **PCP:**
  - Lab Tests Revealed:
    - RF Negative, CRP 2.3, ESR 34, ANA NL
    - ?Fibromyalgia: Started on Pregabalin
April:

- Rheumatologist:
  - Myalgias, Arthralgias and Muscle Weakness
  - Desquamation of fingers and Toes with pain
  - Mechanics Hands
    - ?myositis or anti-synthetase syndrome
  - Started on Prednisone 40 mg daily and sent off lab tests
May:
* PCP
* Returned after no improvement in symptoms.
  
  * CBC: 0.6 349
  * ANC: 0.17
  
  - Sent to ED
Presenting Complaints

- 3 months diffuse joint pain and weakness
- Rash on hands: desquamating and purple
- Pain when the rash peels
- Night sweats, chills, 20 lb weight loss
Past Medical History:
- HTN
- HLD
- Anxiety
- Steatohepatitis

Past Surgical History:
- None

Family History:
- Mother: Diabetes Mellitus, Type 2
- Father: Hypertriglyceridemia
- Daughter: Celiacs Disease
Home Medications

- Alprazolam 0.5 mg BID
- Fluticasone 2 sprays each nare daily
- Meloxicam 15 mg daily
- Pregabalin 225 mg BID
- Tramadol 50 mg BID
- Gemfibrozil 600 mg BID
- Vilazodone HCl 30 mg daily
- Prednisone 40 mg daily
Married and lives with his wife, son, and 2 dogs.
Works as an excavator
No recent travel
Former Smoker: 1.5 packs per day from Age 18-38.
Chews Nicorette Gum
Usually drinks 10 beers daily, recently cut to 2-3 beers a day.
No IVDU
Physical Exam

Vitals: 119/75  HR 73  Temp: 36.9  RR 20  Wt 78 kg  BMI 26  SpO2 98%

* General: Appears uncomfortable but in no acute distress
* HEENT: Pupils equal, round and reactive to light, Sclerae nonicteric, no adenopathy,
* CV: Normal rate, regular rhythm, no murmurs or gallops
* Pulm: Clear with no rubs, rales, rhonchi or wheezing
* Abdomen: Non-distended, normoactive bowel sounds, soft, non-tender, no HSM
* MSK: Hands are diffusely puffy with synovitis noted at the right 3rd PIP joint. Range of motion is limited. There is periarticular erythema and some nail fold capillary overgrowth. Wrists have mildly limited range of motion and are diffusely swollen. Elbows: normal ROM. Shoulders: Painful limited ROM. Knees: Near normal ROM. Ankles: Normal ROM
* Neuro: Normal distal strength, Mild weakness in shoulders.
* Skin: There is splotchy, purplish red erythema on bilateral hands. There are multiple small hyperkeratotic ulcerated lesions on the radial side of the 2nd and 3rd fingers, both thumbs as well as both great toes.
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I received verbal consent to obtain above photos of patient's hands. There are no identifying information or features in the photos.
Labs

- PMN 44%
- Lymph 18%
- ANC 0.35
- ANA: 1:1280
- AST 86
- ALT 94
- ALK Phos 111
- Alb 3.7
- CRP 22.7
- ESR 88
- 110
- 94
- 16
- 132
- 266
- 0.8
- 3.9
- 23
- 0.74
- 33.5
Previously Healthy, 48 year old male with 3 months of pain, swelling, and fatigue.

Presents with profound leukopenia and neutropenia.

Now elevated ANA
* Patient had regular spiking fevers early on during his hospital stay.
Hospital Course

* Infectious Disease was consulted:
  * He was started on Cefepime for empiric treatment of neutropenic fever.
  * Blood Cultures, UA (+ for protein), Urine culture, and CXR were obtained
Hospital Course

- Tick Panel: Negative
- HIV: Non-reactive
- Histoplasma: Negative
- Cryptococcus: Negative
- Brucella: Negative
- Beta D Glucan: Negative
- Q Fever Antibody: Negative
- **Epstein-Barr Virus:**
  - Early Ag IgG: NEGATIVE
  - **Nuclear Antigen Ab IgG**: POSITIVE
  - Capsid Ab IgM: NEGATIVE
  - **Capsid Ab IgG**: POSITIVE
- CMV Ab: IgM Positive, IgG Negative
- ECHO: Normal
CT: Chest/Abdomen/Pelvis
Hematology was consulted: Bone Marrow Biopsy performed

• Bone Marrow Results:
  • Culture: Neg
  • AFB: Neg
  • Anaerobic: Neg
  • Fungus: Neg
  • Virus: Neg
  • Cytogenetics: Normal

• Peripheral Blood:
  • Hairy Cell Leukemia Flow Cytometry : Neg
  • Lymphoma Panel : Neg
Rheumatology Work-Up
- CK: Normal
- ANCA: Neg
- Anti DsDNA: Neg
- CCP: Neg
- RF: Neg
- SSA/SSB: Neg
- Smith Ab: Neg
- RNP Ab: Neg
- SCL 70: Neg
- Jo 1 Ab: Neg
- Anti HMGCR: Neg
- MyoMarker Panel 3: Neg
- C3: 81 (Low)  C4: NL
MyoMarker Panel 3

- Anti Jo 1
- PL-7
- PL-12
- EJ
- OJ
- SRP
- MI-2
- TIF 1 Gamma
- MDA-5
- NXP-2
- Anti-PM/SCL 100 Ab
- Fibrillarin
- U2 snRNP
- Ku
- Anti-SS-A
Rest of Hospital Course

* Patient was started on:
  * Prednisone: 20 mg daily
  * Hydroxychloroquine: 200 mg BID

* Rash & Polymyalgia’s improved
White Count and ANC Trend

Leukocytes
ANC

0 1 2 3 4 5 6 7 8
Following Discharge

- Anti-Histone AB: Positive
Back to his Home Meds..

- Alprazolam 0.5 mg BID
- Fluticasone 2 sprays each nare daily
- Meloxicam 15 mg daily
- Pregabalin 225 mg BID
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- Vilazodone HCl 30 mg daily
- Prednisone 40 mg daily
Diagnosis?

- Idiopathic vs Drug Induced?
- What about the CMV IgM Antibody?
Questions/Thoughts?

International Seaplane Fly-In. Greenville, Maine
Systemic Lupus Erythematosus

- Mid 1800s: Two Viennese physicians wrote about the symptoms of lupus.
- Lupus is latin for wolf.
- Two Accounts:
  - Used to describe the facial lesions that resembled a wolf's bite
  - Facial rash similar to the distinctive marks on a wolf’s face
Systemic Lupus Erythematosus

- Chronic and Recurrent activation of the immune system -> antibodies and protein products -> inflammation and tissue damage
- Female > Male
- Highest Prevalence: African-American and Afro-Caribbean women
- Lowest Prevalence: White men
General:
- Fatigue
- Fever

Arthritis
- Arthralgias
- Myalgias

Acute Cutaneous Lupus
- Erythema

Pulmonary:
- Pleuritis, Fibrosis

Lupus Nephritis

GI:
- Nausea, Diarrhea, Increased AST/ALT

Cardiac Disease
- Pericarditis
- Myocarditis
- Fibrinous Endocarditis
- Increased risk MI

Keratoconjunctivitis Sicca

Retinal Vasculitis

Hematologic:
- Anemia of Chronic Disease
- Leukopenia
- Mild Thrombocytopenia

Splenomegaly

Lymphadenopathy

Raynaud’s

Thrombosis

Arthritis
- Arthralgias
American College of Rheumatology Criteria

Must have 4 of the 11 Criteria

- Malar Rash
- Discoid Rash
- Photosensitivity
- Nonerosive Arthritis
- Pleuritis or Pericarditis
- Oral Ulcers
- Renal Disease
- Positive ANA
- Neurologic Disease
- Hematologic Disease
- Immunologic Disease

2+ peripheral Joints: Tenderness, Swelling, or Effusion

Persistent Proteinuria >0.5 g per day or >3+ if can't quantify
OR
Cellular Casts

Seizures or Psychosis

Hemolytic Anemia, Leukopenia, Lymphopenia, Thrombocytopenia

Anti- DNA, Anti-Sm or Antiphospholipid
**Clinical Criteria**

- Acute Cutaneous Lupus
- Chronic Cutaneous Lupus
- Oral or Nasal Ulcers
- Non-scarring Alopecia
- Arthritis
- Serositis
- Renal Involvement
- Neurologic
- Hemolytic Anemia
- Leukopenia
- Thrombocytopenia

**Immunologic Criteria**

- ANA
- Anti-ds DNA
- Anti-Sm
- Antiphospholipid Ab
- Low Complement (C3, C4, CH50)
- Direct Coombs Test
- Pleurisy, Pericarditis
- UPCR: 500 mg/24 hours or RBC casts
- Seizures, Psychosis, Mononeuritis Multiplex, Peripheral or Cranial Neuropathy, Acute confusional State

≥4 Criteria (at least 1 clinical and 1 immunologic criteria) OR biopsy proven lupus
Tends to occur in patients >50.

Increased incidence among whites

Females = Males

Usually starts months after starting the drug

Less end-organ damage and renal and CNS involvement is uncommon.

Skin findings and Raynauds less common

Higher incidence of purpura and erythema nodosum
<table>
<thead>
<tr>
<th>Characteristics</th>
<th>DILE</th>
<th>SLE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age of onset</td>
<td>Older</td>
<td>Child-bearing years</td>
</tr>
<tr>
<td>Female : male</td>
<td>1:1</td>
<td>9:1</td>
</tr>
<tr>
<td>Clinical course</td>
<td>Remits with drug cessation</td>
<td>Chronic, relapsing</td>
</tr>
<tr>
<td>Symptom severity</td>
<td>Generally mild</td>
<td>Mild to severe</td>
</tr>
<tr>
<td>Major organ involvement</td>
<td>Rare</td>
<td>Common</td>
</tr>
<tr>
<td>Cutaneous involvement</td>
<td>Purpura, erythema nodosum SCLE</td>
<td>Malar, discoid rash, photosensitivity, oral ulcers</td>
</tr>
<tr>
<td>Serologic features</td>
<td>ANA (homogenous)</td>
<td>ANA (homogenous, speckled)</td>
</tr>
<tr>
<td></td>
<td>Anti-histone (up to 95%)</td>
<td>Anti-histone (up to 50%)</td>
</tr>
<tr>
<td></td>
<td>Anti-dsDNA (&lt;5%)</td>
<td>Anti-dsDNA (50–70%)</td>
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</tbody>
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Pathophysiology

* Theory:
  * Reactive metabolites of medications: Increased lupus-like antibody formation
  * Slow acetylators with genetic deficiency of N-Acetyltransferase are at high risk.
Lab Tests

* Less likely to show:
  * Anemia
  * Thrombocytopenia
  * Decreased C3 & C4
  * Abnormal Liver or Kidney Function

* ANA can be positive in both

* Anti-Histones are classically associated with drug-induced, however they can occur in up to 50% of patients with idiopathic SLE.
Which Drugs?

Most Common: Hydralazine & Procainamide

TB Meds: Isoniazid, Pyrazinamide, Rifabutin

Anticonvulsants: Phenytoin, Valproate, Carbamazepine

Antimicrobials: Minocycline, Terbinafine

TNF Alpha Inhibitors: Etanercept, Infliximab

Antiarrhythmics: Procainamide, Quinidine, Propafenone

Anti-Hypertensives: Hydroxyzine, Mionxidil, Timolol

Antihyperlipidemics: Lovastatin, Atorvastatin, Gemfibrozil
Treatment

- Discontinue the medication
- Symptoms should improve within weeks
- Severe: Steroids and NSAIDS
A few weeks later….

* Presented to the ED with chest pain…..

* Painful with deep inspiration
* EKG: Sinus Tachycardia
* CTA for PE: No PE, Small left effusion
* Diagnosis: ?
* Pleurisy

* Treatment:
  * NSAIDS
  * No response in 1-2 weeks? Steroids
Remains on Prednisone 20 mg daily and Hydroxychloroquine

At his next office visit the rheumatologist is going to discuss switching to steroid sparing agent such as Azathioprine or Mycophenolic Acid

Repeat CT abdomen: Improved inflammation around pancreas and no enlarged lymph nodes.
Rash?

Chillbains Lupus Rash?

http://www.lupusimages.com/browser/fancybox/33/Chilblains%20lupus%20erythematosus
References

Special Thanks to:

* Dr. Steve Hayes
* Dr. Stephanie Gartner-Fanburg
* Infectious Disease Team
* Hematology/Oncology Team
* Warene Eldridge
* ACP Mentors, MMC Faculty
Thank you! Questions?