“Screening” for Autoimmune Disease

Objectives

- Concept of “screening” for autoimmune disease
- Explain ANA testing
- Review common symptoms, physical findings and laboratory abnormalities associated with autoimmune diseases
- Review Systemic Lupus Erythematosus (SLE) and Fibromyalgia Syndrome (FMS)
### Case #1

- 45 year-old male patient presents to your office with complaints of generalized fatigue, diffuse arthralgias and diffuse myalgias
- PMHx is significant for HTN, PTSD
- PSHx: vasectomy
- FHx: Mother age 65 with “some kind of arthritis” affecting her hands and knees
- SocHx: Recently divorced. No children. Construction worker – recently unemployed. Smokes 1-2 ppd for 25 years. Drinks 2 beers each night, more on weekends. No IVDA.

### Case #2

- 32 year-old female patient presents with complaints of a new rash on her face, fatigue and hand pain. She states she hasn’t been able to get her rings on and off easily. Her knuckles feel swollen & stiff.
- PSHx: C-section x2.
- FHx: Sister with RA.
- SocHx: Married. SAHM. 2 children ages 3 and 6. Smokes on the weekends socially, but not daily. ETOH on weekends: 2-4 beers. No IVDA.
Overview

- Complaints of chronically low energy, arthralgias and myalgias are common
- Fact:
  - Few of these pts will have lupus or other CTD
  - Many will be diagnosed with Fibromyalgia (FMS)
- Autoantibody testing is best reserved for pts whose pretest odds of an autoimmune disease are high
- All rheum lab tests must be interpreted in the context of the history and physical exam

Demographics

- Lupus is not a common disease
  - US prevalence:
    - white women 10-50/100,000
    - black women 4-5 x’s higher
- FMS is common
  - US prevalence: 1% in women 18-29 years old; 7% in women over age 59
  - At least 20 x’s more prevalent than lupus in white women
ANA

• Short for “anti-nuclear antibody”
• Positive ANAs are commonly found in the normal population
• False positive ANAs (ie, ANAs in the absence of autoimmune disease or known antigenic stimuli) are more commonly seen in women and in elderly patients. The majority of these are present in low titer.

How common are they?

• DeVlam et al looked at healthy blood donors
  ○ 20% of women & 7% of men studied had a positive ANA
  ○ Women > 40 years old - 31% ANA+
• Tan et al studied healthy adults ages 20-60
  ○ 32% 1:40, 13% 1:80, 3% 1:160
  ○ 39% of pts with “soft tissue rheumatism” 1:40, 23% 1:80
• Slater et al reviewed 1010 ANA results
  ○ False positive rate was 72% in pts < 65; 90% in > 65 group
  ○ Even ANAs 1:320 or greater were more likely to be falsely positive (55%) than indicative of rheumatic disease (45%)
Methods of Detection

- **FANA – standard method**
  - Sera incubated with substrate cells that have been fixed with acetone
  - Bound antibodies are detected by fluorescein-conjugated anti-human IgG
  - Viewed through fluorescence microscope, antibodies bound to nuclear antigens produce a nuclear pattern
  - Dilution at which nuclear fluorescence disappears = titer
  - Results: pattern and titer

- **Others:**
  - Immunodiffusion
  - Counterimmunoelectrophoresis (CIE)
  - Immunoprecipitation
  - Immunoblot
  - Enzyme Immunossay (ELISA)

Principle of indirect immunofluorescence (diagram)
Principles of enzyme-linked immunosorbent assay (diagram)

STEP 1: Load Antigen
STEP 2: Add Serum Antibody
STEP 3: Add Antibody Enzyme Conjugate
STEP 4: Add Enzyme Substrate

Measure Optical Density

Antinuclear antibodies (photomicrographs)
Complicating factor

- Laboratory methods differ and are constantly changing
  - Often have extensive data on tests no longer in use & limited data on those currently available
  - Traditional: ANA by direct immunofluorescence (IIF) after incubation of sera with fixed Hep-2 cells
  - Newer: ELISA
- Emlen and O’Neill compared FANA to ELISA
  - 88% of known SLE pts had positive ANA by FANA
  - ELISA ranged 62-90%

In evaluating pts for systemic autoimmune disease, advances in diagnostic testing have not supplanted a carefully performed H&P
- When a pt with chronically low energy and widespread pain presents for evaluation, the history should seek clues of autoimmune disease and also evidence of FMS
- When a lab test (eg, ANA) is not very specific, it is essential to determine the pre-test likelihood of the disease
### Symptoms of ANA positive rheumatic diseases

<table>
<thead>
<tr>
<th>Lupus</th>
<th>Sjogren’s</th>
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<tbody>
<tr>
<td>Alopecia</td>
<td>Dry eyes</td>
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<tr>
<td>Oral or nasal ulcers</td>
<td>Dry mouth</td>
</tr>
<tr>
<td>Malar rash</td>
<td>Vaginal dryness</td>
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<tr>
<td>Photosensitivity</td>
<td>Parotid swelling</td>
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<tr>
<td>Raynaud’s</td>
<td>Accelerated dental caries or gingivitis</td>
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<tr>
<td>Pleuritic chest pain</td>
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<tr>
<td>Joint pain and stiffness</td>
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<tr>
<td>Unexplained fever</td>
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<tr>
<td>Unexplained weight loss</td>
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<tr>
<td>Unexplained LAD</td>
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<table>
<thead>
<tr>
<th>Myositis</th>
<th>Scleroderma/CREST</th>
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<tbody>
<tr>
<td>Insidious proximal muscle weakness</td>
<td>Hand stiffness</td>
</tr>
<tr>
<td>Rash</td>
<td>Raynaud’s</td>
</tr>
<tr>
<td>Dyspnea</td>
<td>Digital infarcts</td>
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<tr>
<td></td>
<td>Calcinosis</td>
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<tr>
<td></td>
<td>Telangectasias</td>
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<td>Heartburn</td>
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<td></td>
<td>Dysphagia</td>
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<td>Dyspnea</td>
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SLE: Diagnostic criteria

- D: discoid rash. Erythematosus raised lesions.
- O: oral and nasal ulcers.
- P: photosensitivity
- A: arthritis. (nonerosive, ≥2 jts, symm)
- M: malar rash. Fixed erythema over malar eminences.
- I: immunologic. Anti-dsDNA, anti-Sm, or APL abs.
- N: neuropsych (sz or psychosis)
- R: renal. Proteinuria or cellular casts.
- A: +ANA
- S: serositis. Pleurisy or pericarditis
- H: hematologic. (hemolytic anemia, ↓ WBCs, ↓ plts)

(Any 4 or more of the 11 criteria present, serially or simultaneously, during any interval of observation)

SLE: rash, face and neck
SLE: butterfly rash, discoid type

Alopecia, scalp
SLE: bullous lesions, palate

Raynaud’s phenomenon, blanching of hands
Raynaud’s phenomenon: hands

Raynaud’s phenomenon: cyanosis of the hands
Fusiform swelling, hand

Jaccoud’s arthropathy (clinical and radiograph)
### Photosensitivity, face and neck

![Image of skin condition]

### Laboratory abnormalities in lupus

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<tr>
<th>CBC</th>
<th>Serum Chemistry</th>
<th>UA</th>
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<tbody>
<tr>
<td>Leukopenia: usually lymphopenia, occ neutropenia</td>
<td>Elevated Cr</td>
<td>Proteinuria</td>
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<td>Anemia: chronic disease, hemolytic</td>
<td>Low albumin</td>
<td>Microscopic hematuria</td>
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<td>Thrombocytopenia</td>
<td>Polyclonal hyperglobulinemia</td>
<td>RBC or hyaline casts</td>
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<td>Elevated CPK</td>
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**History & Physical Exam**

- Differentiating lupus from FMS by history alone can be difficult
  - Fatigue, arthralgia, morning stiffness, cold intolerance, chest wall pain and subjective deficits in memory and concentration
  - The likelihood of lupus increases if the pt gives a convincing history of lupus that would not ordinarily occur in FMS
- While excluding lupus, look for fibromyalgia

**Fibromyalgia**

- Not merely a diagnosis of exclusion
- Often occurs in a setting of stress, depression, anxiety, lack of sleep, lack of exercise, and traumatic life experiences
- Related symptoms:
  - Chronic headaches, memory loss, loss of concentration, parasthesias of the extremities, irritable bowel or bladder
- Normal lab values: CBC, CMP, UA
- When the history, PE, and routine lab testing supports a diagnosis of FMS, autoantibody testing is not necessary
Fibromyalgia Tender Points

Distress

(stress related to finances, work, marriage or recent loss such as the death of a loved one)

Conscious or subconscious tension, disordered sleep

Abnormal production of pain-related chemicals in the nervous system

Lower pain threshold, heightened perception of pain

Tenderness in certain areas, such as the upper back and forearms

Symptoms of fibromyalgia
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QUESTIONS?

Bibliography