Lupus Overlap Syndromes

Charles A. Withers, II, M.D.
CMC NorthEast Rheumatology
January 11, 2014
Objectives

- Diagnosing autoimmune disease
- Introduce the idea of “overlap”
- Which autoimmune disease overlap?
- Review characteristics of the most common diseases that overlap with lupus
- Summarize the impact of overlap on SLE patients
What is autoimmune disease?

- Your immune system fights:
  - Viruses
  - Bacteria
  - Parasites

- Autoimmune Disease
  - Immune system targets your body
  - Antibodies vs. Autoantibodies
Causes of Autoimmune Disease

- Environmental Triggers
  - Cigarette smoke – toxins
  - Medications
  - Infections
  - Sunlight

- Genetic Factors
Making a Diagnosis

- **Is important because...**
  - Helps doctors communicate with each other
  - Helps doctors communicate with patients
  - Helps with research
  - Helps with prognosis
  - Helps with treatment choices

- **Is NOT important because...**
  - Similar medications for autoimmune disease
  - Treatment is based on symptoms more than labels
Making a Diagnosis... (cont’d)

- Requires knowledge about the cause of disease
- Pattern recognition:
  - signs and symptoms
  - Genetic markers: antibodies
- Diagnostic Criteria:
  - Good for large populations & research studies
  - Less helpful for individual patients
Some patients fit into “diagnostic boxes” – they read the textbook!

Some patients don’t meet diagnostic criteria
- Undifferentiated Connective Tissue Disease (UCTD)
  - “Incomplete Lupus”

Some patients fit into multiple categories
- Overlap Syndromes
ANIMALS

- **Group A**: animals with 2 legs
  - Humans
  - Penguins

- **Group B**: animals that can fly
  - Bees
  - Eagles

- **Overlap**: Eagles
  - Eagles have 2 legs
  - Eagles can fly
Overlapping Autoimmune Diseases

- **ANA positive Disease**
  - Systemic Lupus Erythematosus (95-100%)
  - Sjogren’s Syndrome (40-70%)
  - Scleroderma (60-80%)
  - Rheumatoid Arthritis (50%)
  - Polymyositis/Dermatomyositis (60%)
  - Antiphospholipid Syndrome (APS)
  - Mixed Connective Tissue Disease (100%)
  - Undifferentiated Connective Tissue Disease (UCTD)

- **Other organ specific autoimmune disease**
- **Non-inflammatory Disease:** fibromyalgia

*Image adopted from Lisa Criscione-Schreiber, M.D*
Antinuclear Antibodies (ANA)

- **Autoantibodies**
  - Different targets (pattern)
- **Extracted nuclear antibodies**
  - Anti-Smith
  - Anti-SSA/SSB
  - Anti-RNP
- **ANA is not a marker of disease activity**
- **Approximately 10-20% healthy people have a positive ANA**
Sjogren’s Syndrome

- Slowly progressive, inflammatory autoimmune disease
- Primarily affects exocrine glands
  - Dry eyes
  - Dry mouth
  - Enlarged parotid glands
  - Vaginal dryness
- Non-erosive polyarthritis
- Raynaud’s phenomenon
ACR Diagnostic Criteria
1. Symptoms of dry eyes
2. Symptoms of dry mouth
3. Positive Schirmer’s or Rose Bengal Test (eye dryness)
4. Positive salivary gland biopsy
5. Abnormal salivary gland function on testing
6. Positive anti-SSA (Ro) or anti-SSB (La)

To be classified as having Sjogren’s, a patient must have:
- Any 4 out of 6, including #4 or #6, or
- Any 3 of the last 4 criteria
Scleroderma (Systemic Sclerosis)

- Inflammatory disease with fibrosis
  - Skin tightening
  - Raynaud’s phenomenon
  - Gastric Reflux
  - Interstitial lung disease
  - Pulmonary hypertension
  - Renal (kidney) crisis with severe hypertension
  - Labs: ANA (anti-centromere) or Scl-70
Scleroderma (Systemic Sclerosis)
RAYNAUD’S PHENOMENON
Scleroderma (Systemic Sclerosis)
TELANGIECTASIAS
Scleroderma (Systemic Sclerosis)

SKIN THICKENING AND TIGHTENING
# Scleroderma (Systemic Sclerosis)

**ACR CRITERIA**

<table>
<thead>
<tr>
<th>Major Criteria</th>
<th>Minor Criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>Proximal sclerodactyly (proximal to the MCP)</td>
<td>Sclerodactyly</td>
</tr>
<tr>
<td></td>
<td>Digital pitting scars of fingertips</td>
</tr>
<tr>
<td></td>
<td>Or</td>
</tr>
<tr>
<td></td>
<td>Decreased tissue in finger pad</td>
</tr>
<tr>
<td></td>
<td>Bibasilar pulmonary fibrosis</td>
</tr>
</tbody>
</table>

* Must have either the Major Criteria or 2 of 3 Minor Criteria
Scleroderma (Systemic Sclerosis)

**LIMITED**
- **C**: Calcinosis
- **R**: Raynaud’s
- **E**: Esophageal dysmotility
- **S**: Sclerodactyly
- **T**: Telangiectasias

Positive anti-centromere

**DIFFUSE**
- Tight skin over hands, arms, face, torso, legs...
- Pulmonary hypertension
- Scleroderma renal crisis

Positive Scl-70
Polymyositis and Dermatomyositis
BOHAN AND PERTER CRITERIA

Individual Criteria

1. Symmetric proximal muscle weakness
2. Muscle biopsy evidence of myositis
3. Increase in serum skeletal muscle enzyme
4. Characteristic electromyographic pattern
5. Typical rash of dermatomyositis

Diagnostic Criteria

*Polymyositis*:
- Definite: all of #1-4
- Probable: any 3 of #1-4
- Possible: any 2 of #1-4

*Dermatomyositis*:
- Definite: #5 plus and 3 of #1-4
- Probable: #5 plus any 2 of #1-4
- Possible: #5 plus any 1 of #1-4
Rashes of Dermatomyositis

GOTTRON PAPULES
Rashes of Dermatomyositis

HELIOTROPE RASH
Rashes of Dermatomyositis

V-SHAPED RASH & SHAWL SIGN
Overlap of lupus, scleroderma and polymyositis
- Labs: positive RNP
- Patient symptoms can align most with 1 disease or overlap all 3
  - Hands: puffy like early scleroderma or thickening with erythema like dermatomyositis
  - Raynaud’s phenomenon
  - Malar rash
  - Lung: pulmonary hypertension
  - Muscle weakness

Specific Disease vs. undifferentiated overlap
Undifferentiated Connective Tissue Disease

- Patients have symptoms and lab tests that suggest a connective tissue disease but don’t quite meet any specific criteria
  - UCTD is different from MCTD
  - Positive ANA and possibly other labs tests
  - Symptoms can include Raynaud’s, muscle weakness, arthritis, vasculitis, rashes, lung disease, kidney disease, and fatigue
- Treat the symptoms that characterize the individual patient’s disease
- Some will progress to meet classic criteria for SLE or another disease
Antiphospholipid Syndrome
SAPPORO CRITERIA*

**CLINICAL CRITERIA**

1. **Vascular Thrombosis**: at least 1 confirmed arterial or venous event
2. **Pregnancy Morbidity**
   - 3 or more consecutive, unexplained miscarriages before 10 weeks
   - At least 1 unexplained miscarriage after week 10
   - At least 1 premature birth before week 34 due to eclampsia, extreme pre-eclampsia, or placental insufficiency

**LABORATORY CRITERIA**

The presence of at least 1 of the following test on at least 2 occasions 12 weeks apart:

1. Lupus Anticoagulant
2. Anticardiolipin antibody
3. Anti-β2-glycoprotein 1

*One clinical and 1 laboratory criteria are needed to make diagnosis*
Rheumatoid Arthritis

- Classic Symptoms
  - Morning Stiffness ≥ 1 hr
  - Symmetric, polyarticular arthritis
  - Arthritis of wrists and hands (MCPs and PIPs)
  - Rheumatoid nodules
- X-ray changes: erosions in joints
# Rheumatoid Arthritis

## 2010 ACR/EULAR CRITERIA: score ≥ 6

### Joint Involvement

<table>
<thead>
<tr>
<th>Description</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 large joint</td>
<td>0</td>
</tr>
<tr>
<td>2-10 large joints</td>
<td>1</td>
</tr>
<tr>
<td>1-3 small joints (with or without large joints)</td>
<td>2</td>
</tr>
<tr>
<td>4-10 small joints</td>
<td>3</td>
</tr>
<tr>
<td>&gt;10 joints (at least 1 small joint)</td>
<td>5</td>
</tr>
</tbody>
</table>

### Serology

<table>
<thead>
<tr>
<th>Description</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Negative RF and anti-CCP</td>
<td>0</td>
</tr>
<tr>
<td>Low-positive RF or low-positive anti-CCP</td>
<td>2</td>
</tr>
<tr>
<td>High positive RF or high positive anti-CCP</td>
<td>3</td>
</tr>
</tbody>
</table>

### Acute Phase Reactants

<table>
<thead>
<tr>
<th>Description</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal CRP and ESR</td>
<td>0</td>
</tr>
<tr>
<td>Elevated CRP or ESR</td>
<td>1</td>
</tr>
</tbody>
</table>

### Duration of Symptoms

<table>
<thead>
<tr>
<th>Description</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;6 weeks</td>
<td>0</td>
</tr>
<tr>
<td>≥6 weeks</td>
<td>1</td>
</tr>
</tbody>
</table>
Fibromyalgia

- Widespread pain: “I hurt all over”
  - Non-inflammatory
  - “volume control” in pain processing
- Symptoms for at least 3 months
  - 11 of 18 tender points
  - Insomnia
  - fatigue
- Symptoms not better explained by another disease
  - Primary: no association with autoimmune disease
  - Secondary: associated with chronic illness
- **IMPORTANT**: distinguish between symptoms of fibromyalgia and SLE
Fibromyalgia
OVERLAPPING SYNDROMES

- Tension/migraine headache
- Affective disorders
- Temporomandibular joint syndrome
- Memory and cognitive difficulties
- ENT complaints (sicca sx, vasomotor rhinitis, accommodation problems)
- Vestibular complaints
- Multiple chemical sensitivity, “allergic” symptoms
- Esophageal dysmotility
- Neurally mediated hypotension, mitral valve prolapse
- Non-cardiac chest pain, dyspnea due to respiratory mm. dysfunction
- Interstitial cystitis, female urethral syndrome, vulvar vestibulitis, vulvodynia
- Idiopathic low back pain
- Irritable bowel syndrome
- Restless legs syndrome
Impact of Overlap on SLE

- Increased risk for certain illnesses:
  - Antiphospholipid Syndrome: miscarriage
  - Scleroderma: pulmonary hypertension
- Monitoring: checking PFTs, Echo, etc.
- Treatment: guided toward individualized symptoms
Autoimmune diseases have many different characteristics

Positive ANA alone does not diagnosis SLE or any other disease

- ANA can be seen in many autoimmune disease
- ANA can be seen in healthy individuals

Multiple connective tissue diseases can overlap with SLE

Diagnosis can help with communication, monitoring, and treatment choices
Thank you!

- Questions?
- Comments?
- Concerns?