Myositis and Your Lungs

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Myositis

Heterogeneous group of autoimmune syndromes characterized by chronic muscle weakness (muscle inflammation), other organ system involvement and a cause that is unknown
Autoimmunity

- Immune response against *self*
  - loss of tolerance

- Unknown cause
  - susceptibility factors (genetic)
  - environmental triggers
    - e.g. infection

- Multiple diseases and “syndromes”
  - which sometimes run in families
# Autoimmune Diseases

<table>
<thead>
<tr>
<th>Disease</th>
<th>Target</th>
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<tbody>
<tr>
<td>Rheumatoid Arthritis</td>
<td>Joints (synovium)</td>
</tr>
<tr>
<td>Systemic Lupus Erythematosus</td>
<td>Skin, joints, kidneys</td>
</tr>
<tr>
<td>Scleroderma</td>
<td>Skin</td>
</tr>
<tr>
<td>Multiple Sclerosis</td>
<td>Nervous system</td>
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<tr>
<td>Myositis</td>
<td>Muscle</td>
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</tbody>
</table>

Nearly every AI disease has *multiple* targets!
Autoimmunity (cont’d)

• Immune response against *self*
  ▪ loss of tolerance

• Unknown cause
  ▪ susceptibility factors (genetic)
  ▪ environmental triggers
    ✓ e.g. infection

• Multiple diseases and “syndromes”
  ▪ which sometimes run in families

• Formation of autoantibodies
  ▪ markers of autoimmunity

• Inflammatory in nature
Immune cells (lymphocytes) “attacking” normal muscle tissue in a patient with polymyositis.
Systemic Features of Myositis

Musculoskeletal
- Weakness
- Muscle pain/tenderness
- Muscle atrophy
- Arthralgias
- Arthritis

Cardiac
- Arrhythmias
- Congestive failure

Pulmonary
- Atelectasis from muscle weakness
- Aspiration pneumonia
- ILD

Gastrointestinal
- Dysphagia
- Reflux
- Dysmotility

Cutaneous
- Rashes
- Calcification

General
- Fever
- Fatigue
- Weight loss
- Raynaud’s

Slide, courtesy of Dr. Fred Miller
Systemic Targets of Myositis

- Skin
- Joint pain (arthritis)
- GI tract: difficulty swallowing
- **Lung**
  - Shortness of breath
  - Inflammation in lung tissue
  - Fibrosis (scar tissue)
  - Associated with markers in the blood called antibodies
Case Presentation

- 41 y.o. white male with hypertension, high cholesterol and allergies
- 3/20: swelling around eyes
- 3/27: joint pain (arthritis)
- 4/7: shortness of breath and fever
- 4/11: admitted to local hospital with abnormal chest x-ray and diagnosed with pneumonia
- 4/26: breathing worsens; poor response to antibiotics and transferred to UPMC
This patient did not have pneumonia or infection as the cause of his shortness of breath. He had interstitial lung disease (ILD) associated with his myositis.
How Common is ILD in Myositis?

- At least 30-40% of myositis patients have ILD
  - most commonly involved organ system in myositis

- There is no correlation between the extent and severity of muscle or skin disease and the development of ILD

The skin and muscle may be mild or even non-existent but the ILD may be severe
How Do We Diagnose ILD?

- Think about it!
- Chest x-rays
- High resolution CT scans
- Lung biopsy
- Pulmonary Function Tests (PFTs)
- Blood tests
  - Antibody markers
Autoimmunity

- Immune response against *self*
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- Inflammatory in nature
The patient today had a marker in his blood that is associated with ILD in myositis patients.
Case Presentation

- Lung biopsy: inflammation
- Mild myositis on further testing
- Anti-Jo-1 autoantibody
- “Anti-synthetase syndrome”
“Anti-Synthetase Syndrome”

- Acute onset of symptoms
- Lung symptoms may dominate the clinical picture in the form of ILD
  - Thus, patients may not even be seen initially by a rheumatologist or neurologist
Anti-Synthetase Syndrome

• Defines a clinically homogeneous patient population
  – Fever
  – Myositis
  – Arthritis (misdx as RA)
  – Raynaud phenomenon
  – Mechanic’s hands
  – ILD
### University of Pittsburgh Autoantibody Cohort

<table>
<thead>
<tr>
<th>Autoantibody</th>
<th>Number (% synthetases)</th>
</tr>
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<tbody>
<tr>
<td>Jo-1</td>
<td>140 (60)</td>
</tr>
<tr>
<td>PL-12</td>
<td>36 (16)</td>
</tr>
<tr>
<td>PL-7</td>
<td>27 (12)</td>
</tr>
<tr>
<td>EJ</td>
<td>11 (5)</td>
</tr>
<tr>
<td>OJ</td>
<td>6 (3)</td>
</tr>
<tr>
<td>KS</td>
<td>9 (4)</td>
</tr>
<tr>
<td><strong>Total Synthetases</strong></td>
<td><strong>229</strong></td>
</tr>
</tbody>
</table>
Autoantibody Subsets in Myositis

Anti-synthetases

Jo-1

PM

SRP

200/100

PM-Scl

U1RNP

Ku

DM

Overlap

PL-7

PL-12

EJ

OJ

KS

Mi-2

SAE

TIF-1γ

MDA-5

MJ

PL-12

PL-12

PL-12
Making the Diagnosis of Autoimmune ILD?

*Not everyone will present with the classic anti-synthetase syndrome*
Autoantibody Subsets in Myositis

- DM
- Overlap
- SRP
- U1RNP
- PM-Scl
- MDA-5
- PL-7
- PL-12
- EJ
- OJ
- KS
- PL-12
- TIF-1γ
- Mi-2
- SAE
- MJ
- PM
- 200/100
- Jo-1
- PM
- Overlap
- Ku
Anti-MDA-5

- Papules on the palms and skin ulcerations
- Rapidly progressive ILD

Fiorentino, J Am Acad Derm, 2011
Case

- 70 year old WM
- “Double pneumonia” in 6/2012
- Rash of DM in 9/2012
- Ulcerating skin changes in 1/2013
- **No muscle weakness**
- Cytoxan for ILD
Clinical Features of ILD in Myositis

- Shortness of breath with or without cough
- In about 1/3 of myositis patients, **ILD** precedes the muscle or skin manifestations
- Variable course:
  - Acute and dramatic or subacute
  - Chronic and more slowly progressive
  - Without symptoms (x-ray findings of mild fibrosis)
Monitoring Patients with ILD

- Frequent visits
- Joint monitoring by a lung specialist (pulmonologist)
- Frequent pulmonary function tests (PFTs)
- High resolution CAT (HRCT) scans
- Pulmonary rehabilitation
- Echocardiograms
  - Assessing for pulmonary hypertension
Treatment of ILD in Myositis Patients

- Steroids (prednisone) still the initial treatment
- Cyclophosphamide and azathioprine used early or in steroid-resistant cases with variable results
- CellCept is being increasingly used
- Cyclosporin A and tacrolimus (medications used to prevent rejection of transplanted organs)
- Maybe even some biologic agents like rituximab
Other Causes of Breathing Problems in Myositis

• Inflammation in the breathing muscles
• Aspiration into the lungs because of swallowing problems
  – Pneumonia/infection
• Heart involvement