Myositis 101

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What is Myositis?

- myo = muscle; -itis = inflammation
- “Idiopathic inflammatory myopathy” is most commonly used term (IIM)
- **Heterogeneous** group of autoimmune syndromes
- Muscle weakness due to inflammation in the muscle tissue
- **Systemic** complications (i.e. not just muscle)
- Unknown cause (idiopathic)
Understanding Autoimmunity

Infection

Immune Response

Control of Inflammation/Infection
Understanding Autoimmunity

- Infection
- Inflammation
- Immune Response
- Autoimmunity
- Control of Inflammation/Infection
- Immune Response Goes Awry
- Body is the target of Immune Response

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

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

- Immune response against \textit{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
Conventional Classification of Myositis

- Adult polymyositis (PM)
- Adult dermatomyositis (DM)
- Juvenile myositis (DM >> PM)
- Malignancy-associated myositis
- Myositis in overlap with another rheumatic disease
- Inclusion body myositis (IBM)

There are many other types of myositis that are much more uncommon
Systemic Targets of Myositis

- Skin
Rashes of Dermatomyositis
Systemic Targets of Myositis

- Skin
- Joint pain (arthritis)
This patient looks like they have rheumatoid arthritis
... but they also have myositis
Systemic Targets of Myositis

- Skin
- Joint pain (arthritis)
- GI tract: difficulty swallowing
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
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

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

Cutaneous
- Rashes
- Calcification
How Does Myositis Present?

- In many different ways, developing slowly or quickly
- Weakness - difficulty walking/climbing, combing hair, lifting
- Rashes or skin sores
- Severe fatigue that limits normal activities
- Joint pain or joint swelling
- Problems with swallowing or abdominal pain
- Shortness of breath or cough
- Fevers or weight loss

So ... myositis can present in many ways affecting many parts of the body and, therefore, can mimic many other diseases and be difficult to diagnose
How Does a Doctor Diagnose Myositis?

- Careful history and physical examination including tests for muscle weakness
- Blood tests for increased muscle enzymes: CK or CPK, aldolase, LDH, ALT/SGPT, or AST/SGOT
- EMG (electromyography): needle study of muscles
- Muscle biopsy: looking for characteristic pathologic changes in the muscle fibers and blood vessels
  - “immune cells” including lymphocytes
- Skin changes of dermatomyositis
- Other diagnostic approaches: autoantibody testing in blood; MRI; more specialized testing to rule out other diseases that might mimic myositis
Who Gets Myositis (Epidemiology)?

- Rare disease with annual incidence of 5-10 cases/million; possibly increasing
- Prevalence of 50-90 cases/million
- "Bimodal" incidence peaks
  - childhood (5-15 years); adult mid-life (30-50 years)
- Females > Males (2-3:1)
- IIM subsets
  - overlap CTD: younger females
  - malignancy-associated: age>50, F=M
Inclusion Body Myositis

- Most common acquired muscle disease over the age of 50
- Affects men > women at 2-3:1
- Average time from symptom onset to diagnosis is \(\sim 6\) years
Clinical Features of IBM

- Consider IBM when confronted with a PM patient who does not respond to treatment
- **Insidious** onset of painless muscle weakness with slow progression
- Tendency to **distal** (away from the trunk muscles) and asymmetric muscle involvement (“foot drop”)
- Difficulty swallowing
- Characteristic pattern of **muscle atrophy** (forearm flexors, muscles of hands, thigh)
Inclusion Body Myositis

“scooped out” forearm

“teardrop sign”
IBM: Quadriceps Atrophy

Felice, Medicine, 2001
MRI of Muscle

Normal

Dermatomyositis (TR=500 msec)

Severe quadriceps atrophy

IBM
Inclusion Body Myositis: Muscle Pathology

- Distinctive histology:
  - inflammation
  - rimmed vacuoles/red "inclusions"
Different Classifications of Myositis

Clinical groups (Adult or Juvenile)

- Polymyositis
- Dermatomyositis
- Inclusion body
- Myositis with other rheumatic syndromes
- Cancer-associated

Serologic groups (Autoantibodies)

- Myositis-specific
  - Anti-Jo-1 & others (lung)
  - Anti-Mi-2
  - Anti-SRP

- Myositis-associated
  - Anti-PM/ScI (scleroderma)
  - Anti-Ku
  - Anti-U1RNP (mixed CTD)
  - Anti-MJ (JDM)
Autoantibody Subsets in Myositis
Pharmacologic Therapy of IIM

- Corticosteroids
- Immunosuppressive Agents
- Combination regimens
- IVIg
- Biologic agents
<table>
<thead>
<tr>
<th>Drug</th>
<th>Dose</th>
<th>Common side effects</th>
<th>Level of evidence for use in myositis</th>
<th>Special comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Corticosteroids</td>
<td>Starting at 1 mg/kg or 60–80 mg/d in 2 or 3 divided doses</td>
<td>Osteoporosis, steroid myopathy, glaucoma, cataract, risk of infection</td>
<td>Case series</td>
<td>Usual initial therapy with or without additional immunosuppression</td>
</tr>
<tr>
<td>Methotrexate</td>
<td>Starting at 10–15 mg/wk (orally or subcutaneously) with an increase to 25 mg/wk</td>
<td>Hepatic toxicity, bone marrow suppression, risk of infection</td>
<td>Uncontrolled cohort studies</td>
<td>First-line immunosuppression unless contraindicated</td>
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<tr>
<td>Azathioprine</td>
<td>Starting at 50 mg/d and increased by 50 mg every 2 wk up to 2–3 mg/kg/d</td>
<td>Gastrointestinal symptoms, bone marrow suppression, hepatic toxicity, pancreatitis, risk of infection</td>
<td>Uncontrolled cohort studies</td>
<td>First-line immunosuppression unless contraindicated</td>
</tr>
<tr>
<td>Cyclosporine</td>
<td>Starting at 50 mg twice daily and increasing to final dose of 100–150 mg twice daily</td>
<td>Nephrotoxicity, neurotoxicity, abnormal glucose metabolism, hyperkalemia, headache, tremor, hypertension, risk of infection</td>
<td>Case series</td>
<td>Second-line immunosuppression; some evidence of efficacy in myositis-associated lung disease</td>
</tr>
<tr>
<td>Tacrolimus</td>
<td>Starting at 1 mg twice daily and slowly increasing for trough level of 8–12</td>
<td>Similar to cyclosporine</td>
<td>Case series</td>
<td>Second-line immunosuppression; some evidence of efficacy in myositis-associated lung disease</td>
</tr>
<tr>
<td>Immunoglobulins</td>
<td>Starting at 2 g/kg/mo given over 2–5 d</td>
<td>Hypertension, volume overload, renal toxicity, headaches</td>
<td>One double-blind, placebo-controlled trial</td>
<td>Second-line immunosuppression for refractory myositis patients; some evidence of efficacy in dysphagia and refractory skin disease; can be used in patients with infection</td>
</tr>
<tr>
<td>Mycophenolate</td>
<td>Starting at 500 mg twice daily, slowly increasing to 2–3 g/d</td>
<td>Bone marrow suppression, gastrointestinal intolerance, risk of infection</td>
<td>Case series</td>
<td>For refractory cases; some efficacy in refractory skin disease and possibly in interstitial lung disease</td>
</tr>
<tr>
<td>Cyclophosphamide</td>
<td>Oral: 2-mg/kg/d dose</td>
<td>Malignancy, bone marrow suppression, hepatotoxicity</td>
<td>Case reports</td>
<td>Limited to very refractory cases with interstitial lung disease</td>
</tr>
<tr>
<td>Rituximab</td>
<td>2 doses of 1,000-mg intravenous infusion 2 wk apart</td>
<td>Risk of infection</td>
<td>Case series</td>
<td>For refractory cases; possible use in interstitial lung disease</td>
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Aggarwal/Oddis, Curr Rheum Rep, 2011