Myositis for Beginners
TMA 2009
Charlotte, North Carolina

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What is Myositis?

- myo = muscle; -itis = inflammation
- “Idiopathic inflammatory myopathy” is most commonly used term
- **Heterogeneous** group of autoimmune syndromes
- Muscle weakness with inflammation in the muscle tissue
- **Systemic** complications
- Unknown cause (idiopathic)
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)

However, there are many other types of myositis that are much more uncommon
Idiopathic Inflammatory Myopathies (IIM)

Heterogeneous group of **autoimmune** syndromes characterized by chronic muscle weakness and muscle inflammation, systemic complications and a cause that is unknown.
Autoimmunity

- Immunity vs. autoimmunity
- Individual’s immune system attacks its own tissues
- The “target” of the attack can vary
- The clinical features can vary
- Disease names vary: myositis, scleroderma, lupus, rheumatoid arthritis; Sjogren’s syndrome
- Autoimmune diseases can “overlap”
Idiopathic Inflammatory Myopathies (IIM)

Heterogeneous group of autoimmune syndromes characterized by chronic muscle weakness and muscle inflammation, systemic complications and a cause that is unknown.
Lymphocytes “attacking” normal muscle tissue

Result: muscle weakness
Dermatomyositis

Perifascicular Atrophy

Perivasculare Inflammation
Idiopathic Inflammatory Myopathies (IIM)

Heterogeneous group of autoimmune syndromes characterized by chronic muscle weakness and muscle inflammation, *systemic* complications and a cause that is unknown
There are many systemic targets in patients with myositis.
Rashes of Dermatomyositis

Gottron’s Papules
Rashes of Dermatomyositis

Gottron’s sign
Other Rashes of Dermatomyositis

- cuticular overgrowth
- malar rash
- scalp rash
- V neck rash
Other Rashes of DM

calcinosis in JDM
linear extensor erythema
severe vasculitis
Mechanic’s Hands
Mechanics Hands

13 days later
Systemic Targets of Myositis

- Skin
- Joint pain (arthritis)
This patient looks like they have rheumatoid arthritis...
... but they also have myositis
This is a chest x-ray of a patient with myositis who suddenly developed shortness of breath.
Systemic Targets of Myositis

- Skin
- Joint pain (arthritis)
- **Lung**
  - Shortness of breath
  - Fibrosis (scar tissue)
  - Associated with markers in the blood called antibodies
Different Classifications of Myositis

Clinical groups (Adult or Juvenile)
- Polymyositis
- Dermatomyositis
- Inclusion body
- Myositis with other rheumatic syndromes
- Cancer-associated
- Other
  - eosinophilic
  - granulomatous
  - focal/nodular

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)
Systemic Targets of Myositis

- Skin
- Joint pain (arthritis)
- Lung
  - shortness of breath
  - fibrosis (scar tissue)
  - associated with markers in the blood called antibodies
- Gastrointestinal tract
  - difficulty swallowing (dysphagia)
  - ulcerations
How Does Myositis Present Itself?

- 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 swelling
- Problems with swallowing, reflux, diarrhea or bleeding
- Shortness of breath or cough
- Fevers, sweats 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 Do You 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 (discussed earlier)
- Newer diagnostic approaches: autoantibody testing; 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)
  - African-American women most commonly affected

• IIM subsets
  - overlap CTD: younger females
  - malignancy-associated: age>50, F=M
  - IBM: middle-aged to elderly, F:M~1:3
Questions to Consider in IBM

- What is inclusion body myositis?
- What are the clinical features?
- What is the pathogenesis (i.e. cause) of IBM?
- Is IBM an autoimmune disease?
- How do we treat this disorder?
- Why is it necessary to distinguish IBM from PM?
Inclusion Body Myositis

General Features

• Most common acquired muscle disease over the age of 50
• Prevalence of 5-10/million
• Affects men > women at 2-3:1
• Average time from symptom onset to diagnosis is ~ 6 years
Clinical Features of IBM

- Consider IBM when confronted with refractory polymyositis patient
- **Insidious** onset of painless muscle weakness with slow progression
- Tendency to **distal** (away from the trunk muscles) and asymmetric muscle involvement
- Difficulty swallowing
- Characteristic pattern of **muscle atrophy** (forearm flexors, quadriceps)
Inclusion Body Myositis

“scooped out” forearm

“teardrop sign”
IBM: Quadriceps Atrophy

Felice, Medicine, 2001
MRI of Muscle

Normal

Dermatomyositis (TR=500 msec)

IBM
Inclusion Body Myositis: Muscle Pathology

- Distinctive histology:
  - inflammation
  - rimmed vacuoles
  - may be absent in ~20% of patients with IBM
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“Pathogenesis” of IBM

• Cause is unknown

• Evidence for autoimmune/immunologic cause:
  ➢ association with other autoimmune disorders
  ➢ blood tests findings: “autoantibodies”
  ➢ muscle biopsy “resembles” polymyositis
Summary of IBM Cause

Proteins misfold and clump together in muscle tissue

Formation of “inclusion bodies”

These are “toxic” to the muscle cell

Secondary inflammation
Questions to Consider

• What is inclusion body myositis?
• What are the clinical/laboratory features?
• What is the pathogenesis of IBM?
• Is IBM an autoimmune disease?
• How do we treat this disorder?
• Why is it necessary to distinguish IBM from PM?
Difficulties in Assessing Treatment

- Rare diseases
- Published reports of treatment may “mix” different type of myositis
  - IBM and PM
- Incorrect diagnosis
  - genetic myopathies
  - toxic myopathies
Treatment Options in Myositis

- Corticosteroids (prednisone)
- Immunosuppressive agents
  - methotrexate
  - cyclosporine
  - azathioprine
  - cyclophosphamide
  - tacrolimus
  - mycophenolate mofetil
- IVIg
- Anti-TNF agents (etanercept, infliximab)
- Rituximab (depletes B cells)
- Oxandrolone (IBM)
- Other (stem cell transplant)
- Combination regimens
Approach to IBM Therapy

High dose prednisone for 6-8 weeks (after baseline measurements)

improvement

- continue prednisone but taper dose

no improvement

- add imuran, MTX or other agent to prednisone for 3 months

  no improvement

  - taper prednisone and stop the other drug
Unanswered Questions in Myositis

• How to predict those patients who need more aggressive therapy?

• How can we develop newer therapies that are adequately studied?

• What are the factors that cause and sustain myositis?
  - Genetic factors
  - Environmental risks

• How do we make the public aware that this disease deserves the same investigative efforts that other autoimmune diseases receive