Myositis Overlap Syndrome

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University of Pittsburgh Myositis Center

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



Understanding Autoimmunity



Understanding Autoimmunity









Autoimmunity

- Immune response against self
 - loss of tolerance
- Unknown cause
 - susceptibility factors (genetic)
 - environmental triggers
 - e.g. infection (virus)
- Multiple diseases and "syndromes"
 - which sometimes run in families

Autoimmune Diseases

Disease	Target
Rheumatoid Arthritis	Joints (synovium)
Systemic Lupus Erythematosus	Skin, joints, kidneys
Scleroderma	Skin
Multiple Sclerosis	Nervous system
Myositis	Muscle

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Nearly every AI disease has multiple targets!

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- Formation of autoantibodies
 - markers of autoimmunity

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- 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

Subsets of Myositis

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

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This patient looks like they have rheumatoid arthritis



This patient looks like they have rheumatoid arthritis ... but they have myositis in overlap with RA and scleroderma



Autoantibody Subsets in Myositis



Univ. Pittsburgh Myositis Cohort

	PM	DM	Overlap
# Patients	373	510	267

Anti-synthetase Syndrome

- Defines a subset of myositis patients with several clinical features:
 - -Fever
 - Myositis
 - -Arthritis (misdiagnosed as RA)
 - Raynaud phenomenon
 - 'Mechanic hands'
 - -Interstitial Lung Disease



Clinical Features: Anti-synthetase Syndrome



General Concepts: Myositis Therapies

- Myositis is inflammatory and autoimmune
- Drugs will:
 - Decrease inflammation (e.g. steroids)
 - Suppress the immune system
- Borrowed from oncologists
 Methotrexate, imuran, cytoxan and rituximab
- Borrowed from transplant surgeons

 Cyclosporine, tacrolimus, MMF (CellCept)

Myositis is not a single disease!















Myositis Medications

- Glucocorticoids (steroids)
- Immunosuppressive Agents
- Combinations of drugs
- IVIg (gamma globulin)
- Biologic agents
- Others

Medications After Prednisone

- Most physicians choose glucocorticoids as their initial treatment
- Most patients needs additional drugs

 Steroids: side effects, intolerance, ineffective alone, flare ups on tapering
- Methotrexate is often given next or even concomitantly with steroids
- Azathioprine may be given using same rationale

Drug	Level of evidence for use in myositis
Glucocorticoids	Retrospective studies
Methotrexate	Retrospective uncontrolled cohort studies
Azathioprine	Retrospective uncontrolled cohort studies
Mycophenolate mofetil	Retrospective uncontrolled studies
Cyclosporine	Retrospective controlled studies
Tacrolimus	Retrospective controlled studies
Cyclophosphamide	Prospective uncontrolled studies on myositis-ILD; case reports on myositis

Myositis Medications

- Glucocorticoids (steroids)
- Immunosuppressive Agents
- Combinations of drugs
- IVIg (gamma globulin)
 Difficulty swallowing
 - Severe rash

Main Features Requiring Treatment in Myositis

- Muscle (myositis)
- Skin
- GI tract: difficulty swallowing
- Joint pain (arthritis)
 - May get treated like you have rheumatoid arthritis (RA)
 - Multiple biologic agents approved for RA

Main Features Requiring Treatment in Myositis

- Muscle (myositis)
- Skin
- GI tract: difficulty swallowing
- Joint pain (arthritis)
- Lung (ILD)
 - Shortness of breath
 - Inflammation in lung tissue
 - Fibrosis (scar tissue)

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

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)
- Emerging use of biologic agents like rituximab

Monitoring Patients with ILD

- Frequent doctor visits
- Joint monitoring with a lung specialist (pulmonologist)
- Frequent pulmonary function tests (PFTs)
- High resolution CT (HRCT) scans with flare
- Pulmonary rehabilitation
- Echocardiograms

Assessing for pulmonary hypertension

Myositis Medications

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Biologic Drugs	Level of evidence for use in inflammatory myopathy
Rituximab (RIM Trial)	Double-blind (improvement in 83% of PM, DM and JDM pts) and multiple case series