Inflammatory Myopathies

Differential Diagnosis

Infectious/parainfectious

Autoimmune

Infiltrative

Infectious/parainfectious

- Viral-Influenza, parainfluenza, enterovirus, coxsackie, adenovirus, Hepatitis B, HIV, HTLV1
- Bacterial–staphylococcus, clostridia, lyme, Whipples
- Parasitic–toxoplasmosis, trichinosis, cysticercosis, echinococcus, schistosomiasis, trypanosomiasis

Autoimmune

- Dermatomyositis (DM)-Adult, Juvenile
- Polymyositis (PM) (things that mimic PM: DM without rash, early sIBM, rare inherited IBM (including DMRV and IBM2) with inflammation, some cases of dystrophy (PROMM, dysferlinopathy, dystrophinopathy, FSH), CTD associated myositis with or without anti-Jo abs (also assoc with interstitial pulm fibrosis)
- Inclusion body myositis (IBM)
- Overlap
- Connective tissue disease/other autoimmune disease
    - (scleroderma-35% SLE-30%, Rheumatoid arthritis-15%, Sjogrens-10%, mixed CTD, primary billiary cirrhosis, ankylosing spondylitis, Behcet's, Sprue, Myasthenia gravis, systemic vasculitis)
- Hypereosinophilic syndromes
- Eosinophilic polymyositis, Eosinophilic-myalgic syndrome, etc.
- Graft vs. Host disease
- Paraneoplastic
    - Usually indistinguishable from DM or PM, but acute necrotizing myopathy also described
    - DM more common than PM
    - Higher association between DM and malignancy in older patients; lung, breast, ovary
- Focal myositis

- Proliferative focal myositis
- Localized myositis ossificans
- Myositis ossificans progressiva

Infiltrative

- Amyloidosis
- Sarcoidosis
- Lymphoma/carcinoma

General clinical features (not present in all forms or cases):

Weakness: proximal or generalized

Myalgia: sometimes with tenderness, sometimes at rest or after exertion

Fatigue: generalized, sometimes with other constitutional symptoms

Dysphagia: mid to low dysphagia

Dyspnea: with exertion, at rest in severe cases

Myoglobinuria: with exercise

Skin rash: Dermatomyositis (DM) or myositis associated with connective tissue diseases

Other manifestations of vasculitis

Myocarditis

Important features in differential diagnosis:

- Lack of family history or exposure to muscle toxin
- Proximal distribution of weakness
- Relative preservation of reflexes and sensation
- Absence of true muscle cramps or fasciculations
- General pathological features:
- Infiltration of skeletal muscle by inflammatory infiltrates
- Muscle necrosis
- Invasion of non-necrotic fibers with inflammatory infiltrates (PM)
- Perivascular inflammation (DM or vasculitis)
- Vasculitis (alteration of vessel wall)
- Granulomatous infiltration
- Infectious infiltration

General lab features:

Bloods:

Elevated muscle enzymes (creatine kinase, aldolase, ALT, AST, rarely myoglobin or Troponin

Inflammatory markers (ESR, CRP, ENA, ANA, ANCA, anti-Jo-1, etc)

EMG:

Utility:

- Helps exclude other disorders
- Document distribution and severity
- Measure response to therapy

Limitations:

- Findings non-specific
- Difficult to differentiate from neurogenic disorders in chronic disease
- Difficult to differentiate from disease of nerve terminals
- May miss mild spotty disease

Motor NCS:

Normal or low amplitudes with normal velocities, distal latencies and F-waves

Sensory NCS:

Normal except when associated with a neuropathy

Needle Examination:

Distribution of abnormalities:

Tends to follow clinical distribution; usually proximal (including axial) > distal.

Early in disease the most sensitive muscles are:

tibialis anterior, rectus femoris, iliopsoas, gluteus medius in lower extremities

lumbar and thoracic paraspinals

biceps, deltoid and infraspinatus in the upper extremities

Insertional activity:

- Fibrillation potentials:

  Often small and in superficial layers of muscles

  Abnormalities may be patch or multifocal in early disease

  May be absent in setting of steroids

  Fibrillations are associated with necrosis or splitting of muscle fibers

  Other abnormalities of spontaneous activity include myotonic discharges and CRDs.

  DO NOT see cramps or fasciculations

  May see increased resistance to needle movement in infiltrative myopathies

- Voluntary activity:

  Small, polyphasic MUP with rapid recruitment

  Severity of MUP abnormalities (size) should correlate with the degree of rapid recruitment

  Mixed small and long complex MUP in chronic disease or if associated neuropathy

- Interference pattern analysis:

  Nonspecific and relatively insensitive but should show increased turns/amplitude ratio

- Single fiber EMG:

  Increased jitter and blocking due to denervation and reinnervation of muscle fibers

  Reinnervated nerve terminals have reduced safety margin of neuromuscular transmission

Polymyositis

- <u>Epidemiology</u>

- Incidence of PM and DM combined 2-7 per million, women 2x>men; prevalence 10-63 per million
- Peak incidence of PM ages 45-85 (30 % after the age of 65)
- Pathogenesis
    - Cell mediated disease with CD8 cells and macrophages invading non-necrotic muscle fibers
- Clinical Manifestations
    - Acute, subacute, chronic progressive weakness
    - Proximal > distal muscles
        - Shoulder and hip girdles, tibialis anterior, neck flexor and extensor, respiratory and facial muscles
    - Dysphagia due to weakness of skeletal muscle in upper to middle 1/3 of esophagus
    - Symmetrical distribution very common (asymmetric or monomelic distribution rare)
    - Myalgia may occur
    - Reflexes preserved unless weakness is severe
    - Atrophy is a late sign
    - Contractures of elbows, hips, knees, ankles may occur
    - Lung- interstitial fibrosis in 30% (associated with anti-Jo-1 antibodies in PM but not DM)
    - Cardiac- myocarditis or pericarditis
- Laboratory
    - *Blood:* elevated CK, aldolase, ALT, AST, in some increased ESR and autoantibodies
    - *EMG:* see general section
- *Muscle biopsy:*
    - Cell mediated attack on muscle fibers
    - Endomysial infiltration of CD8 cells and macrophages (MHC class I)
    - Invasion of non-necrotic fibers

Natural History and Treatment

Tends to progress without continuous immunosuppressive Rx, but spontaneous short and long term remissions due occur

Corticosteroids

- Oral: 40-60 mg for 4-8 weeks, then taper according to clinical response, CK, ESR, etc.
- IV: 500-1000 mg MP 3-4 days consecutively; repeat as needed

Imuran

- 2-3 mg/kg/day in divided doses
- minimum of 4-6 months before effect is observed

Cellcept

- 500-2000 mg BID
- minimum of 4-6 months before effect is observed

Methotrexate

- 5-10 mg per week
- onset of effect over 4-8 weeks

Cytoxan

- 1-2 mg/kg/day in divided doses
- adjust to keep WBC 2500-3500
- onset of effect over 4-8 weeks

IVIg

- 400 mg/kg/infusion
- 3-4 days consecutive in severe disease
- 1-2/week for 4-6 weeks, then slowly increase interval between Rx)

Plasmapheresis

- same interval as IVIg

Cyclosporine

- 5-6 mg/kg/day in divided doses
- onset of effect over 4-8 weeks
- close monitoring of blood level, renal function, lytes, BP

Total body irradiation

- only a few cases reported in refractory cases

Dermatomyositis

- Epidemiology
  - See PM
- Pathogenesis
  - Immune complex disease directed against vascular endothelium of muscle (vasculitis of muscle)
- Clinical Manifestations
  - *Muscle*
    - Acute, subacute, chronic progressive weakness

        - Proximal > distal muscles
            - Shoulder and hip girdles, tibialis anterior, neck flexor and extensor, respiratory and facial muscles
        - Dysphagia due to weakness of skeletal muscle in upper to middle 1/3 of esophagus
        - Symmetrical distribution very common (asymmetric or monomelic distribution rare)
        - Myalgia may occur
        - Reflexes preserved unless weakness is severe
        - Atrophy is a late sign
        - Contractures of elbows, hips, knees, ankles may occur
    - *Skin*
        - May come before or after myopathy;
        - Heliotropic rash- violaceous macular rash with edema; located over malar and sun exposed regions
        - Gottron's nodules- subcutaneous papules over extensor surfaces (MCP, IP, elbow, knee joints)
        - Capillary telangiectasias- nail beds or skin
        - Subcutaneous calcinosis (50% of kids)
        - Raynaud's phenomenon
    - *Lung*
        - Interstitial fibrosis in 30% (associated with anti-Jo-1 antibodies in PM but not DM)
        - *Cardiac*- myocarditis or pericarditis
        - *GI*- ulceration and bleeding particular in childhood DM
        - Laboratory
    - *Blood*
        - See PM and general section
    - *EMG*
        - See general section
    - *Muscle biopsy*
        - Humorally mediated microangiopathy
        - Perifascicular infiltration of CD4+ lymphocytes, B-cells and macrophages
        - Predominant involvement of microvessels (endothelial hyperplasia, reduced capillary density)
        - Ischemia with perifascicular necrosis and atrophy of muscle fibers
- Natural History and Treatment
    - Poorer prognosis if multiple organ involvement, calcinosis and in either very young or old