Idiopathic Inflammatory Myopathies (Myositis)

Indications for Ordering

Differential diagnosis of inflammatory myopathies in conjunction with muscle biopsy and clinical presentation

Test Description

Polymyositis and Dermatomyositis Panel
Myositis Extended Panel
- Qualitative immunoprecipitation/semiquantitative multiplex bead assay/qualitative immunoblot

Polymyositis Panel
- Qualitative immunoprecipitation/semiquantitative multiplex bead assay

Dermatomyositis Panel
- Qualitative immunoprecipitation/qualitative immunoblot

Interstitial Lung Disease Panel
- Qualitative immunoprecipitation/semiquantitative multiplex bead assay/qualitative immunoblot/semiquantitative enzyme-linked immunosorbent assay/quantitative immunoturbidimetry

3-Hydroxy-3-Methylglutaryl Coenzyme A Reductase (HMGCR) Antibody, IgG
- Semiquantitative enzyme-linked immunosorbent assay

Tests to Consider

Typical testing strategy

Initial screening tests
- Creatine kinase
- Erythrocyte sedimentation rate/C-reactive protein
- Thyroid-stimulating hormone – rule out thyroid disease as etiology for myopathy
- Metabolic profile
- Complete blood count
- Antinuclear antibodies

Antibody testing (minimum recommended)
- Antisynthetase antibodies – anti-Jo-1, anti-PL-7, anti-PL-12, anti-EJ, anti-OJ
- Nonsynthetase antibodies – anti-Mi2, anti-p155/140, anti-SRP
- Myositis associated antibodies – anti-PM/Scl-100, anti-SSA(RO), anti-U1 RNP

Definitive diagnosis
- Muscle biopsy (which can be guided by MRI) is gold standard

Primary tests

Polymyositis and Dermatomyositis Panel 2013992
- May be useful for evaluation of patients with progressive proximal muscle weakness and/or with cutaneous manifestations suggestive of dermatomyositis and/or associated connective tissue disease
- Components
  - Jo-1 antibody, IgG
  - PL-7 (threonyl-tRNA synthetase) antibody
  - PL-12 (alanyl-tRNA synthetase) antibody
  - EJ (glycyl-tRNA synthetase) antibody
  - SRP (signal recognition particle) antibody
  - OJ (isoleucyl-tRNA synthetase) antibody
  - Mi-2 (nuclear helicase protein) antibody
  - P155/140 antibody
  - SAE1 (SUMO activating enzyme) antibody
  - MDA5 (CADM-140) antibody
  - NXP-2 (nuclear matrix protein-2) antibody
  - TIF1-gamma (TIF1-y) antibody

Myositis Extended Panel 2013961
- May be useful for differential evaluation of polymyositis, dermatomyositis, necrotizing autoimmune myopathy, or overlap syndromes associated with connective tissue disease
- Components
  - SSA 52 and 60 (Ro) (ENA) antibodies, IgG
  - RNP (U1) (ribonucleic protein) (ENA) antibody, IgG
  - Jo-1 antibody, IgG
  - Mi-2 (nuclear helicase protein) antibody
  - PL-7 (threonyl-tRNA synthetase) antibody
  - PL-12 (alanyl-tRNA synthetase) antibody
  - P155/140 (TIF1-gamma) antibody
  - EJ (glycyl-tRNA synthetase) antibody
  - Ku antibody
  - U2 sn (small nuclear) RNP antibody
  - SRP (signal recognition particle) antibody
  - OJ (isoleucyl-tRNA synthetase) antibody
  - SAE1 (SUMO activating enzyme) antibody
  - MDA5 (CADM-140) antibody
  - NXP-2 (nuclear matrix protein-2) antibody
  - TIF1-gamma (TIF1-y) antibody
  - Fibrillarin (U3 RNP) antibody, IgG
  - PM/Scl-100 antibody, IgG by Immunoblot

Polymyositis Panel 2013990
- May be useful for evaluation of patients with progressive proximal muscle weakness and antisynthetase syndrome
- Components
  - Jo-1 antibody, IgG
  - PL-7 (threonyl-tRNA synthetase) antibody
  - PL-12 (alanyl-tRNA synthetase) antibody
  - EJ (glycyl-tRNA synthetase) antibody
  - SRP (signal recognition particle) antibody
  - OJ (isoleucyl-tRNA synthetase) antibody

Dermatomyositis Panel 2013991
- May be useful for evaluation of patients with characteristic cutaneous manifestations of dermatomyositis with or without muscle weakness
- Components
  - Mi-2 (nuclear helicase protein) antibody
  - P155/140 (TIF1-gamma) antibody
  - SAE1 (SUMO activating enzyme) antibody
  - MDA5 (CADM-140) antibody
  - NXP-2 (nuclear matrix protein-2) antibody
  - TIF1-gamma antibody

Interstitial Lung Disease Panel 2013993
- May be useful for evaluation of interstitial lung disease in the context of connective tissue disease
- Components
  - SSA 52 and 60 (Ro) (ENA) antibodies, IgG
  - Scleroderma (Scl-70) (ENA) antibody
  - Jo-1 antibody, IgG
  - PL-7 (threonyl-tRNA synthetase) antibody
  - PL-12 (alanyl-tRNA synthetase) antibody
  - EJ (glycyl-tRNA synthetase) antibody
  - Ku antibody
  - SRP (signal recognition particle) antibody
  - OJ (isoleucyl-tRNA synthetase) antibody
  - PM/Scl-100 antibody, IgG by immunoblot
  - MDA5 (CADM-140) antibody
  - NXP-2 (nuclear matrix protein-2 Ab)
  - Rheumatoid factor
  - Cyclic citrullinated peptide (CCP) antibody, IgG
  - Nuclear antibody (ANA) by IFA, IgG

3-Hydroxy-3-Methylglutaryl Coenzyme A Reductase (HMGCR) Antibody, IgG 2013101
- Differential diagnosis of myositis in patients with or without statin exposure
- In addition to clinical evaluation for muscle strength and serum creatine kinase, may be useful to monitor response to treatment

Related tests
- Creatine Kinase, Total, Serum or Plasma 0020010
- Anti-Nuclear Antibodies (ANA), IgG by ELISA with Reflex to ANA, IgG by IFA 0050080
- SSA 52 and 60 (Ro) (ENA) Antibodies, IgG 2012074
- Jo-1 Antibody, IgG 0099592
- RNP (U1) (Ribonucleic Protein) (ENA) Antibody, IgG 0050470
- Signal Recognition Particle (SRP) Antibody 2002098
- PM/Scl-100 Antibody, IgG by Immunoblot 2003040
- Fibrillarin (U3 RNP) Antibody, IgG 2012173

Disease Overview

Incidence – 4-10/million adults; rare in children

Age of onset – varies by disorder
- Dermatomyocitis (DM)
  - Bimodal – childhood and 50-70 years
- Polymyositis (PM) – rare in childhood, typically >20 years
- Inclusion body myositis (IBM) – >50 years
- Necrotizing autoimmune myositis – primarily adults, often older

Syndromes
- DM – associated with cancer
- PM
- IBM
- Necrotizing autoimmune myositis
- Overlap syndrome
- Juvenile DM and PM

Symptoms

General features
- Musculoskeletal – progressive muscle weakness (usually symmetrical and proximal)
  - Pharyngeal and neck flexion muscles frequently involved
- Arthralgias/arthritis – wrists, knees, small joints of hands
- Constitutional – fever, weight loss
- Pulmonary – fibrosing alveolitis, aspiration pneumonia
- Gastrointestinal – esophageal dysfunction, dysphagia
- Cardiovascular – myo-/pericarditis, valvular disease, rhythm disturbances
- Renal – rarely myoglobinuria, glomerulonephritis
- Dermatologic – Raynaud phenomenon, rashes, calcinosis over bony prominences

Antisynthetase syndrome
- Found almost exclusively in middle-aged women with DM or PM
- Characterized by
  - Low-grade fevers
  - Interstitial pneumonitis – major determinant of morbidity and mortality
  - Hyperkeratosis, cracking of lateral and palmar aspects of the fingers (mechanic's hands)
  - Raynaud phenomenon
  - Inflammatory polyarthritis, myalgias
- Presence of antinuclear antibodies known as antisynthetases

DM

- Characteristic photosensitive rash accompanied by symmetrical, subacute, proximal muscle weakness
  - Rash usually precedes muscle symptoms
  - Blue-purple rash – symmetrical distribution
  - Violaceous discoloration of upper eyelids with periorbital edema (heliotrope rash)
  - Erythema of metacarpophalangeal proximal and distal joints
    - Raised violaceous rash (Gottron sign) or scaly erythematous plaques over dorsal surface of bony prominences (Gottron papules) – considered pathognomonic for DM
  - Macular erythema over the lower neck and upper chest in a V-distribution (V-sign), over upper back (Shawl sign), or over upper thighs (Holster sign)
  - Telangiectasias at base of fingernails, cuticular overgrowth and periungual erythema
  - Vasculitic skin changes
    - Subcutaneous nodules, periungual infarcts, digital ulcerations
- Cancer-associated myositis
  - Most commonly associated with DM, but can be found in PM
  - May be diagnosed prior to, simultaneously with, or after myopathy
  - Increased risk of malignancy (20-25%) of any of the following types (highest risk in first 2-3 years after diagnosis)
    - Ovarian
    - Breast
    - Melanoma
    - Colorectal
    - Non-Hodgkin lymphoma
- Amyopathic DM
  - Characteristic cutaneous findings of DM >6 months without muscle involvement
  - May progress to DM
  - Some risk for lung disease, malignancy
  - Electromyography may demonstrate subtle myopathy

PM

- Dominated by muscular presentation
  - No rash
- Usually subacute presentation
- May be associated with other autoimmune diseases
- Diagnosis of exclusion – must rule out the following
  - Neuromuscular disease
  - Endocrinopathy
  - Muscular dystrophy
  - Known biochemical muscle disorder or familial biochemical disorder
  - Drug-induced myopathy

IBM

- Two types – sporadic, hereditary
- Muscle involvement
  - Muscle atrophy early in disease
  - Distal weakness is most common – deep finger flexors and foot extensors common
  - Asymmetric distribution is common
  - Proximal muscles less frequently involved
  - Specific muscles
    - Small muscles in hand frequently involved
    - Quadriceps involvement common – associated with frequent falls
    - Facial muscles frequently involved
- Extramuscular disease rare – dysphagia is the exception (>50% of patients)
- May be misdiagnosed as PM, adult-onset muscular dystrophy, or motor neuron disease
- Associated with other autoimmune diseases

Necrotizing autoimmune myositis

- Acute or subacute presentation
- Severe proximal muscle weakness – clinically indistinguishable from PM
- May occur in association with cancer, other CT diseases, or drug use (eg, statins)
- Diagnosis of exclusion

Overlap syndrome

- Most common in DM but can occur with other inflammatory myopathies
- Myositis in conjunction with connective tissue disease
  - Most common – systemic sclerosis, mixed connective tissue disease, systemic lupus erythematosus
- Rash – faint or transient
- Frequent association with antisynthetase antibodies
- Myopathy varies from mild to dominant presentation

Juvenile disease

Juvenile dermatomyositis (JDM)

- ~85% of juvenile idiopathic inflammatory myopathy (JIIM)
- Symmetrical and proximal muscle weakness
- Gottron papules
- Heliotrope rash
- Periungual telangiectasia
- Vasculitis – more common than in adults
- Other organs
  - Cardiac
  - Joints
  - Gastrointestinal
  - Pulmonary
- May have family history of other autoimmune diseases
- Amyopathic (hypomyopathic form)
  - Inflammatory rashes without muscle weakness
  - ~25% develop full-blown dermatomyositis

Juvenile polymyositis

- 4-8%
- Proximal and distal muscle weakness
- Frequent falling episodes
- Cardiac damage

Juvenile connective tissue disease myositis

- 6-11% of JIIM
- Occurs in conjunction with another connective tissue disease
- Raynaud phenomenon
- Arthritis
- Malar rash
- Interstitial lung disease

Diagnostic issues

May be difficult to distinguish between myopathies

- Antibody testing in conjunction with clinical presentation and muscle biopsy help to confirm the diagnosis
- Distinction may be important for therapy and prognosis

Antibody testing

- Myositis-specific antibodies
  - Antisynthetase antibodies
    - Anti-Jo-1 (histidyl-tRNA synthetase) – more common in polymyositis
    - Anti-PL7 (threonyl-tRNA synthetase)
    - Anti-PL-12 antibodies (anti-alanyl-tRNA synthetase)
    - Anti-EJ (glycyl-ts RNA synthetase)
    - Anti-OJ (anti-isoleucyl-tRNA synthetase)
    - Anti-KS (asparaginyl tRNA synthetase)
    - Anti-Ha (tyrosyl tRNA synthetase)
    - Anti-Zo (phenylalanyl tRNA synthetase)
  - Nonsynthetase antibodies
    - Anti-signal recognition particle (anti-SRP)
      - Necrotizing myopathy
      - Severe cardiac involvement
    - Anti-p155/140
      - JDM , DM, and ulceration
      - Adults – DM, increased malignancy risk
    - Anti-Mi-2
      - DM
      - Not associated with increased malignancy risk
      - Steroid responsiveness
    - Anti-CADM-140
      - CADM
      - Rapidly progressive ILD
    - Anti-p140
      - JDM, DM, and calcinosis
      - Adults – DM, increased malignancy risk, ILD
    - Anti-SAE
      - DM
    - Anti-HMGCR
      - Necrotizing myopathy
- Response to short-term statin withdrawal
- Myositis-associated antibodies – usually associated with connective tissue disease/overlap syndrome
  - Anti-PM-Scl – polymyositis-scleroderma
  - Anti-U1 RNP
  - Anti-Ku
  - Anti-Ro (SSA)

Test Interpretation

Results

- Positive – as a single test, not diagnostic for inflammatory myopathy
- Negative – does not rule out inflammatory myopathy

Limitations

- Results by themselves are not diagnostic; strong clinical correlation is recommended
- Negative results do not rule out a diagnosis of inflammatory myopathy or overlap syndrome