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Myositis: Clinical features

Inflammatory myopathies are characterised by proximal skeletal muscle weakness and evidence of muscle inflammation. These disorders are rare (Dermatomyositis/ Polymyositis combined incidence of 2 per 100,000 annually). Myositis is generally not painful, with mild discomfort only if present but patients will have weakness on neurologic examination. Patients can also have systemic features like skin rash or interstitial lung disease.

Classification

Inflammatory myopathies form several groups according to clinical and pathologic features – all share immune-mediated muscle injury.

- Dermatomyositis
- Overlap syndromes (with another systemic rheumatic disease)
- Inclusion body myositis
- Immune mediated necrotizing myopathy – as a paraneoplastic phenomenon or in association with some medications (including statins)
- Polymyositis
- Other rarer subtypes

Key Points

Myositis related autoantibodies

- Can help define a particular clinical syndrome within the myositis spectrum including disease severity, pattern of clinical involvement and response to therapy
- May be associated with certain histopathologic features.
- Can be seen in some patients with interstitial lung disease without myositis.
- Myositis antibody testing, including HMG CoA reductase antibodies, is generally only indicated if myositis is clinically likely.

Statin associated myositis

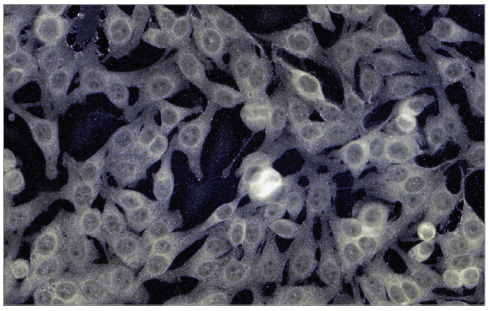
- Most adverse effects resolve with cessation of therapy. Other more severe forms (necrotizing myopathy) may require immune therapy.
- Can be associated with HMGCoA reductase antibodies in some patients.

Some patients cannot be subtyped into a specific category and are classified as having 'non-specific' myositis.

Pathology testing

General laboratory testing:

Inflammatory myopathy can increase muscle enzymes including lactate dehydrogenase (LD), creatine kinase (CK), aspartate aminotransferase (AST), and alanine aminotransferase (ALT).



Myositis positive antibody immunofluorescence.

However, these can increase with other muscle disorders, and occasionally patients with myositis have normal CK levels (uncommon and usually with localised forms of myositis).

CK levels can vary in untreated patients with myopathy, however the CK is usually at least 10x the upper limit of normal (ULN) and can reach 50-100x ULN – CK is generally a sensitive marker of muscle inflammation.

Specific laboratory testing:

Serum myositis autoantibodies can be divided into myositis-associated antibodies and myositis-specific antibodies. Myositis-specific antibodies are mainly in patients with inflammatory myositis and may inform the prognosis and potential patterns of organ involvement.

Myositis-associated antibodies occur in other autoimmune rheumatic diseases associated with myositis.

The presence of antibodies is becoming increasingly important to help classify and diagnose inflammatory myopathies.

Antibodies to 3-hydroxy-3-methylglutaryl coenzyme A reductase (HMGCR) were identified in 2010 in patients with immune mediated necrotising myopathy, 63% of these patients were on statins.

Statin associated myositis: important points

Statins lower serum cholesterol for primary and secondary prevention of cardiovascular disease and dyslipidemia. A common side effect is muscle pain and weakness, typically seen as proximal, symmetric muscle weakness or soreness with difficulty raising arms above the head, rising from sitting and climbing stairs.

Symptoms usually start within weeks to months after statin initiation but can occur at any time.

In most cases, statin related myopathy resolves after medication is stopped. However, immune-mediated necrotising myopathy can persist after cessation and may respond to immunosuppression.

Potential effects can be divided into

- Myalgia - muscle discomfort with normal CK
- Myopathy - muscle weakness with or without increased CK
- Myositis - muscle inflammation and myonecrosis with increased muscle enzymes either from base line or compared to ULN
  - Severe myonecrosis is uncommon (affects <0.5% of patients).
- Necrotizing myopathy – reported to be histologically distinct, non-inflammatory statin related myopathy with macrophagocytic engulfment of necrotic muscle fibres. Patients respond to immune therapy and this is presumed to be autoimmune in origin.
  - Antibodies to HMG CoA reductase have been seen in these patients.
  - HMG CoA reductase antibodies however, can be seen in statin-naive patients (37-62% of patients with positive antibodies and myopathy were statin-naive in some papers, another paper reported 94% of patients with antibodies had statin exposure however).
- Adverse effects are not necessarily seen as a progression from less to more severe however necrotizing myopathy and inflammatory myopathy may be a spectrum.