Idiopathic inflammatory myopathy

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Abstract

The idiopathic inflammatory myopathies, especially dermatomyositis and polymyositis, are systemic autoimmune diseases with significant mortality and morbidity. Muscle weakness of the proximal muscles is the most common presenting clinical feature. Since idiopathic inflammatory myopathy is relatively uncommon, randomized control trials are scarce, and no evidence-based optimal treatment regimen has been defined. Corticosteroids are first-line treatment but many patients will require further immunosuppressive or immunomodulatory treatment. Methotrexate, azathioprine and mycophenolate mofetil are among the most commonly used second-line agents, although their benefit has not been adequately studied in randomized control trials. In dermatomyositis, one randomized controlled trial showed that intravenous immunoglobulin is effective. More recently, mycophenolate mofetil and rituximab have shown therapeutic promise, but a small clinical trial of infliximab failed to demonstrate clinical effectiveness.

Keywords Autoimmune diseases; corticosteroids; dermatomyositis; immunosuppression; myositis; polymyositis

Myositis (inflammation of skeletal muscles) has many causes (Table 1). Many viruses and drugs are capable of inducing transient disease. In contrast, bacterial infection causes pyomyositis with acute focal suppuration and abscess formation. This contribution focuses on idiopathic inflammatory myopathy characterized by chronic inflammation of striated muscle (polymyositis; PM), sometimes with involvement of the skin (dermatomyositis; DM). Focal nodular myositis, giant cell myositis and eosinophilic myositis are rare conditions that have characteristic features on muscle biopsy.

Idiopathic inflammatory myopathy is classified into:

- primary idiopathic polymyositis
- primary idiopathic dermatomyositis
- dermatomyositis/polymyositis associated with neoplasia
- childhood dermatomyositis/polymyositis
- dermatomyositis/polymyositis associated with vasculitis
- polymyositis/dermatomyositis associated with autoimmune rheumatic disease
- inclusion body myositis.

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What's new?

- A large, randomized, double-blind, placebo-phase trial in patients with refractory dermatomyositis and polymyositis found that 83% of patients met the definition of improvement after treatment with rituximab
- Accumulating data suggest that physical exercise in patients with PM and DM is safe, can improve clinical outcomes and may down-regulate inflammation
- A prospective, randomized, assessor-blind, multi-centre study of combined treatment with methotrexate and glucocorticoids versus glucocorticoids alone is under way
- Mycophenolate mofetil has been increasingly used in myositis-associated interstitial lung disease[1]

Epidemiology

PM and DM affect approximately 60–80 per million population. They are more common in Afro-Caribbeans. The female:male ratio is 2.5:1. Among forms of idiopathic inflammatory myopathy (IIM) presenting over 50 years of age, the most common is inclusion body myositis, in which females and males are equally affected.

Clinical features

Inclusion body myositis can occur in association with connective tissue diseases, particularly Sjögren's syndrome. However, inclusion body myositis lacks the extra-muscular manifestations found in DM and PM.

Myositis – typically, IIM has an insidious onset. DM occurring in children or in association with neoplasia can present more acutely. Patients with inclusion body myositis have often had symptoms for several years by the time they present.

The most common presenting complaint in patients with myositis is proximal muscle weakness, leading to difficulty in lifting objects overhead, inability to comb or wash the hair, and problems with climbing stairs and rising from a chair. Muscle pain is another common feature, being present in half of those presenting. In addition to girdle muscles, other striated muscles including the bulbar and intercostal muscles can also be weak, leading to hoarseness, dysphonia and difficulty in initiating swallowing, with regurgitation of liquids and dyspnoea.

In inclusion body myositis, distal muscle weakness and atrophy can be prominent, leading to finger flexor weakness, quadriceps femoris weakness and foot drop, and falls are a frequent presentation.

Assessment of muscle strength is an important measure of disease activity.

Cutaneous features – the rash of DM can precede myositis or can occur without apparent muscle involvement (clinically amyopathic dermatomyositis [CADM]). Erythematous or heliotropic rashes characteristically affect the eyelids (Figure 1), malar areas, 'V' areas of the anterior chest and upper back. Gottron's papules are erythematous, scaly plaques over the knuckles or fingers (Figure 2), which extend into the forearm. Machinist's hands, characterized by brawny induration of the fingers with darkened or

Causes of myositis

Infectious agents

Viral

- Influenza A and B
- Hepatitis B
- Coxsackie
- Rubella (natural infection and live-attenuated vaccine)
- Echovirus
- Human immunodeficiency virus

Bacterial

- *Staphylococcus*
- *Streptococcus*
- *Clostridium*
- Tuberculous leprosy

Parasitic

- Trichinosis
- Toxoplasmosis

Drugs and toxins

Cholesterol-lowering agents

- Statins
- Gemfibrozil
- Clofibrate
- Bezafibrate

Drugs for infections

- Rifampicin
- Sulfonamides
- Griseofulvin
- Zidovudine

Cytotoxic agents and immunomodulators

- Hydroxycarbamide
- Vincristine
- Ciclosporin
- Interleukin-2

Toxins

- L-Tryptophan
- Alcohol

Others

- Cimetidine
- Colchicine
- Penicillamine
- Phenylbutazone
- Procainamide
- Propylthiouracil
- Carbimazole
- Growth hormone
- Tretinoin

Focal nodular myositis

Eosinophilic myositis

Idiopathic inflammatory myopathies

- Dermatomyositis
- Polymyositis
- Inclusion body myositis

Table 1

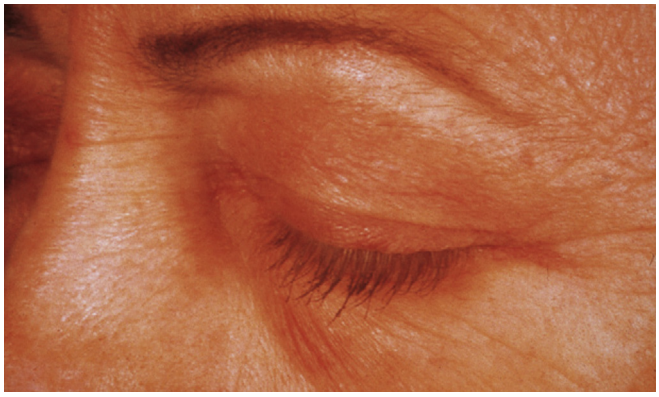

Figure 1 Heliotropic rash over the eyelid. (Copyright of King's College Hospital NHS Foundation Trust photography department).

'dirty' horizontal lines across the lateral and palmar aspects, occur specifically in patients with the antisynthetase syndrome.

Pulmonary involvement — interstitial lung disease is common in IIM and, after malignancy, is the greatest cause of mortality.[2] The most common pattern of disease is non-specific interstitial pneumonitis, although cryptogenic organizing pneumonia, diffuse alveolar damage and usual interstitial pneumonitis also occur.[3]

In a cohort of newly diagnosed patients with PM and DM, interstitial lung disease, detected by high-resolution computerized tomography (HRCT) and lung function testing, was found in 65% of cases,[4] although clinically significant disease was less frequent. Among patients with antisynthetase antibodies, in whom lung disease can predate muscle disease, the frequency of interstitial lung disease is particularly high. In Japan, recently, a group of patients with CADM and anti-CADM-140 antibodies has been described, in whom interstitial lung disease was rapidly progressive.[5]

IIM can also result in respiratory muscle weakness, causing symptoms that range from mild dyspnoea to respiratory failure. Sniff nasal inspiratory pressure (SNIP) is a reliable and reproducible method for monitoring diaphragmatic weakness, which characteristically improves in parallel with improvement of skeletal muscle strength. In patients who present in this way, respiratory muscle strength of <30% expected and a forced vital capacity <55% expected are predictive of hypercapnia.[3]

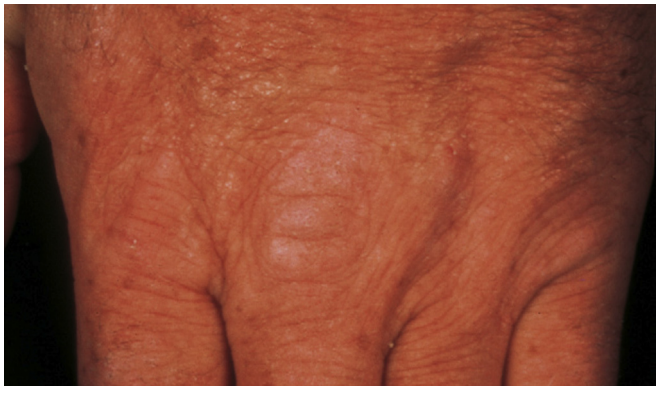

Figure 2 Gottron's papules over the knuckle. (Copyright of King's College Hospital NHS Foundation Trust photography department).