Review article: the gastrointestinal complications of myositis
E. C. EBERT

Department of Medicine, UMDNJ-Robert Wood Johnson Medical School, New Brunswick, NJ, USA
Correspondence to:
Dr E. C. Ebert, Department of Medicine, UMDNJ-Robert Wood Johnson Medical School, New Brunswick, NJ, USA.
E-mail: ebertec@umdnj.edu

SUMMARY
Background
The inflammatory myopathies are a group of acquired diseases characterized by a proximal myopathy caused by an inflammatory infiltrate of the skeletal muscle. The three major diseases are dermatomyositis, polymyositis and inclusion body myositis.

Aims
To review the gastrointestinal manifestations of myositis.

Methods
Over 110 articles in the English literature were reviewed.

Results
Dysphagia to solids and liquids occurs in patients with myositis. The pharyngo-oesophageal muscle tone is lost and therefore patients develop nasal speech, hoarseness, nasal regurgitation and aspiration pneumonia. There is tongue weakness, flaccid vocal cords, poor palatal motion and pooling of secretions in the distended hypopharynx. Proximal oesophageal skeletal muscle dysfunction is demonstrated by manometry with low amplitude/absent pharyngeal contractions and decreased upper oesophageal sphincter pressures. Patients exhibit markedly elevated creatine kinase and lactate dehydrogenase levels consistent with muscle injury. Myositis can be associated with inflammatory bowel disease, coeliac disease and interferon treatment of hepatitis C. Corticosteroids and other immunosuppressive drugs comprise the mainstay of treatment. Inclusion body myositis responds poorly to these agents and therefore a myotomy is usually indicated.

Conclusion
Myositis mainly involves the skeletal muscles in the upper oesophagus with dysphagia, along with proximal muscle weakness.

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INTRODUCTION

The inflammatory myopathies are a group of acquired diseases characterized by a proximal myopathy caused by an inflammatory infiltrate of the skeletal muscle. The three major diseases are dermatomyositis (DM), polymyositis (PM) and inclusion body myositis (IBM). The incidence of the three diseases is approximately 1 in 100,000. DM is most common, affecting both children and adults; PM is least common and generally occurs after the second decade of life and IBM is the most frequent inflammatory myopathy over the age of 50. Diagnostic criteria are shown in Tables 1 and 2.

Polymyositis and DM are characterized by the slow onset of proximal muscle weakness, whereas IBM mainly involves distal musculature. Dysphagia to both solids and liquids and sparing of ocular muscles are seen in all three types of myositis. Facial weakness may be seen in IBM, but not in PM or DM. Pulmonary fibrosis, aspiration pneumonia and ventilatory insufficiency may be caused by weakness of the thoracic muscles. Cardiac disturbances, such as atrioventricular conduction defects, tachyarrhythmias, or a dilated cardiomyopathy may be caused either by the disease itself or by hypertension from the long-term use of corticosteroids. Clinical signs include a reduction in proximal muscular strength, contractures and eventually muscular atrophy. Sensation remains normal. Deep tendon reflexes are preserved except in severely weakened or atrophied muscles. The heliotrope rash, found in DM, is characterized by purplish erythema of the eyelids often with periorbital oedema. Gottron’s signs are violaceous erythematous lesions on the extensor surfaces of the fingers. There may be a photosensitive, erythematous rash on the face, anterior chest and extensor surfaces of the arms. The enzyme most likely to be elevated is the creatine kinase (CK). If normal, then measurement of other muscle enzymes should be performed, such as aldolase, aspartate aminotransferase (AST), alanine aminotransferase (ALT) and lactate dehydrogenase (LDH). Needle electromyography shows myopathic potentials, while muscle biopsy shows inflammation.

Dermatomyositis is a complement-mediated microangiopathy affecting skin and muscle with inflammation containing a higher than normal percentage of B cells, occurring mainly perivascularly or in the interfascicular septae and around rather than within the fascicles. PM and IBM are T cell-mediated disorders, where CD8+ cytotoxic T cells invade muscle fibres expressing MHC class I antigens, leading to fibre necrosis. About 18–32% of patients with DM have associated cancer, usually breast, ovary, lung, pancreas, stomach, colon, rectum and non-Hodgkin lymphoma. The association may be higher in those aged 40 years or older. Malignancy has not been reported in the juvenile cases. The risk of cancer is the highest in the first year after diagnosis, but continues beyond the third year. Cancer may occur before or after DM is evident. Those patients with cancer are older and have more severe and acute cutaneous and muscle symptoms than do patients with primary myositis. The risk of cancer in PM is also increased, but not to the extent seen in DM.

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<th>Table 2. Diagnostic criteria for inclusion body myositis</th>
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<td>Pathologic criteria</td>
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<td>Electromyographic evidence of a generalized myopathy (inflammatory myopathy)</td>
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<td>Elevation of muscle enzyme levels</td>
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<td>Failure of muscle weakness to improve on a high-dose glucocorticoid regimen</td>
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<th>Table 1. Criteria to define polymyositis and dermatomyositis proposed by Bohan and Peter</th>
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<td>Symmetric weakness of limb girdle muscles and anterior neck flexors, progressing over weeks to months, with or without dysphagia or respiratory muscle involvement.</td>
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<td>Skeletal muscle histological examination showing necrosis of types I and II muscle fibres, phagocytosis, regeneration with basophilia, large sarcocellal nuclei and prominent nuclei, atrophy in a perifascicular distribution, variation in fibre size and an inflammatory exudate.</td>
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<td>Elevation of levels of serum skeletal muscle enzymes.</td>
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<td>Electromyographic triad of short, small polyphasic motor units; fibrillations, positive waves, and insertional irritability, and bizarre high-frequency discharges.</td>
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<td>Dermatologic features including a lilac (heliotrope) discoloration of the eyelids with periorbital oedema; a scaly, erythematous dermatitis over the dorsa of the hands (Gottron’s sign), and involvement of the knees, elbows, medial malleoli, face, neck, and upper torso.</td>
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ASSOCIATIONS WITH OTHER GASTROINTESTINAL DISEASES

Polymyositis and DM can be rare extraintestinal manifestations of Crohn's disease or ulcerative colitis (UC). Patients with myositis and Crohn's disease usually have colonic involvement. In general, the myositis follows the diagnosis of inflammatory bowel disease (IBD). It is usually associated with an acute exacerbation of IBD, but activity of the intestinal disease is not essential for occurrence or progression of the myositis. In most cases, treatment with mesalazine (mesalamine) and/or corticosteroids leads to improvement of the muscle disease. Myositis is also associated with coeliac disease and responds to a gluten-free diet. PM may be triggered by hepatitis B virus (HBV). An acute exacerbation of HBV induced by withdrawal of steroids for PM was controlled in one case by cyclosporin and interferon. Myositis has been found with hepatitis C virus (HCV) with immunoreactivity for HCV or HCV ribonucleic acid demonstrated in the skeletal muscle. PM and DM may be associated with primary biliary cirrhosis (PBC); in this case, treatment with immunosuppressive agents such as methotrexate, azathioprine or chlorambucil is preferred as corticosteroids worsen the osteopenia associated with PBC.

Acute PM may develop during interferon (IFN) treatment of HCV. This IFN-induced PM has a good prognosis as it usually resolves with discontinuation of the IFN and, in severe cases, with institution of corticosteroids. PM may also develop with anti-TNF therapy or with D-penicillamine for rheumatoid arthritis. Although myositis can occur in patients with rheumatoid arthritis, the temporal association of PM with anti-TNF therapy implicates the treatment as the cause. Although rare, myopathies, including PM and rhabdomyolysis, can occur during treatment with proton pump inhibitors (PPI). Improvement has been demonstrated following withdrawal of the PPI and recurrence of the myopathy with reinstatement of the drug.

PHARYNGEAL, OESOPHAGEAL AND GASTRIC DISEASES

Dysphagia caused by pharyngeal and oesophageal abnormalities was reported in 32–84% of patients with myositis. Dysphagia to both solids and liquids as well as heartburn are the most common gastrointestinal complaints. The pharynx and upper oesophageal sphincter are affected because, like peripheral muscle, they are comprised of skeletal muscle. As a result, a food bolus cannot be properly propelled into the oesophagus. The symptoms include nasal speech, hoarseness, nasal regurgitation and an inability to swallow a food bolus while recumbent. Blood has to be divided to be swallowed. Other complaints include discomfort in the sternal area, laryngitis and coughing while eating. On physical exam, one sees tongue weakness, flaccid vocal cords, and poor palatal motion. Proximal oesophageal dysfunction is demonstrated by manometry with low amplitude/absent pharyngeal contractions and decreased upper oesophageal sphincter pressure (Figure 1). Cine-esophagogram shows prolonged pharyngeal transit time with disorderly and decreased pharyngeal peristalsis, nasal reflux, tracheal aspiration and retention of barium in the distended hypopharynx, the valleculae and the atomic pyriform fossae. There may be an associated Zenker's diverticulum.

Oesophageal and gastric emptying can be delayed in PM and DM, implying malfunction of the smooth muscle of the upper GI tract. Manometry may reveal a reduced distal oesophageal sphincter resting pressure with normal relaxation and nonperistaltic low amplitude simultaneous contractions. These patients tend to have active disease, complain of reflux, and respond to anti-reflux measures and treatment of the myositis. Such findings often occur in the absence of pharyngeal involvement. Those with oesophageal dilater...
tation on barium swallow have manometric evidence of decreased motility in that region of the oesophagus. Cine-esophagram too correlates with manometric evidence of decreased peristalsis in the proximal or distal oesophagus. Endoscopy may show oesophagitis or stricture formation. There may be atrophy, fibrosis and vasculitis of the oesophagus seen on pathology. Distal oesophageal true wide-mouthed diverticuli because of atrophy and fibrosis have been described.

GASTROINTESTINAL COMPLICATIONS OF DM AND PM

Juvenile DM may be associated with a vasculitis involving the GI tract. This may be a non-inflammatory acute endarteropathy with arterial and venous intimal hyperplasia and occlusion of vessels by fibrin thrombi in the mucosa, submucosa and serosal layers of the bowel. This narrowing and occlusion of small and medium-sized arteries lead to ischaemia. Patients present with abdominal pain, vomiting, constipation, and haematemesis with ischaemic ulceration and perforation. Radiological features include widespread thickening of mucosal folds and spiculation of small intestine, giving rise to a 'stacked coin' appearance. The role of corticosteroids and cyclosporin in these syndromes remains unclear.

Pneumatosis cystoides intestinalis has been described in DM and PM. It may occur because of retroperitoneal dissection from alveolar rupture in a diseased lung or from loss of mucosal integrity due to vasculitis. In one case, the patient developed profound GI manifestations with atomic bowel, bacterial overgrowth and malnutrition. PM has also been associated with small intestinal pseudoobstruction and pseudomonal necrotizing enterocolitis.

DIAGNOSIS AND DIFFERENTIAL DIAGNOSIS

Patients exhibit markedly elevated CK and LDH levels consistent with muscle injury. In acute cases, AST and ALT are both raised with an AST/ALT ratio of greater than 3. However, CK, LDH and AST levels decline much more rapidly than ALT levels so that the AST/ALT ratio approaches 1. These abnormalities may be misinterpreted as showing liver injury. In muscle damage without liver disease, there is a strong correlation between CK and ALT. For example, CK levels of about 1000 U/L will be accompanied by an ALT of 100 U/L. During active disease, the ESR and C-reactive protein may be increased; anti-nuclear antibodies and myositis autoantibodies may be found.

The criteria of Pearson and Bohan have been used to diagnose PM and DM in many studies (Table 1). More recently, Dalakas and Hohlfeld proposed that muscle biopsy findings should be included. A different set of criteria are used to diagnose IBM (Table 2). Old studies occurred before the concept of mixed connective tissue disease (MCTD) was known and its serological profile appreciated and therefore some of the patients labelled as PM or DM may in fact have had MCTD.

The most common diseases in the differential diagnosis of oropharyngeal dysphagia are neuromuscular disorders, including cerebral vascular accidents, motor neuron disease, myasthenia gravis and polymyelitis. Also in the differential diagnosis is steroid myopathy, which is characterized by a normal CK and histology showing atrophic rather than inflammatory changes. Muscular dystrophies generally have a family history, a relatively early insidious onset, and slow progression. Polymyalgia rheumatica has a normal CK and an absence of inflammatory histology. Other considerations are myopathies from drugs or toxins (such as alcohol and penicillamine), endocrine diseases (such as hyper- or hypothyroidism), metabolic abnormalities and infections (such as human immunodeficiency virus and tuberculosis).

Dysphagia from myositis can be distinguished from that caused by cricopharyngeal muscle dysfunction. In myositis, there is an inability to propel food in the pharyngeal phase because of weak musculature; in cricopharyngeal muscle dysfunction, there is a blockage because of the tightly constricted cricopharyngeus muscle.

TREATMENT

Corticosteroids are the mainstay of treatment although their efficacy has not been fully established in randomized, placebo-controlled trials. Other immunosuppressive drugs that can be used include methotrexate, azathioprine, cyclophosphamide, and cyclosporin A. Anti-TNF therapy can be considered in refractory PM/DM, although its efficacy has been disputed. Intravenous immunoglobulin may be effective in the muscle strength and skin rash in DM according to a double-blind placebo-controlled study and provided dramatic improvement in patients with life-threatening steroid-resistant oesophageal involvement. It may
also help in the dysphagia of IBM. IBM generally responds poorly to corticosteroids and other immunosuppressive agents; therefore, a long myotomy extending well into the constrictor muscle above and the oesophageal musculature below may be useful. Cricopharyngeal muscle obstruction is treated with a myotomy rather than with steroids. Myositis associated with cancer, which may be difficult to control with corticosteroids, may improve with successful treatment of the cancer.

PROGNOSIS

The age-adjusted risk of mortality is greater for DM than for PM because of an increased chance of dying from cancer in the former. Unfavourable prognostic signs are leucocytosis, fever (usually from pneumonia), old age, short disease history, dysphagia and failure to induce remission of the myositis. The most common causes of death are from malignancy, ischaemic heart disease and pulmonary complications. Pneumonias are caused by aspiration from dysphagia with decreased cough reflex and moderate ventilatory insufficiency with interstitial lung disease. Opportunistic infections are common, especially in the lungs and digestive tract, increasing the mortality rate.

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REFERENCES


