

Inflammatory Muscle Disease

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Introduction

Inflammatory muscle disease is a generic term used to include polymyositis (PM), dermatomyositis (DM) and inclusion body myositis (IBM). The latter does not respond to immunosuppression suggesting that the inflammation may be a secondary phenomenon rather than a causal factor. PM and DM on the other hand, are immune mediated.

Epidemiology

The prevalence and incidence figures vary widely from study to study. The prevalence of PM is in the order of 1-7/100,000 and DM 1-10/1,000,000. DM is the commonest childhood myositis with a prevalence of around 3/1,000,000 children.

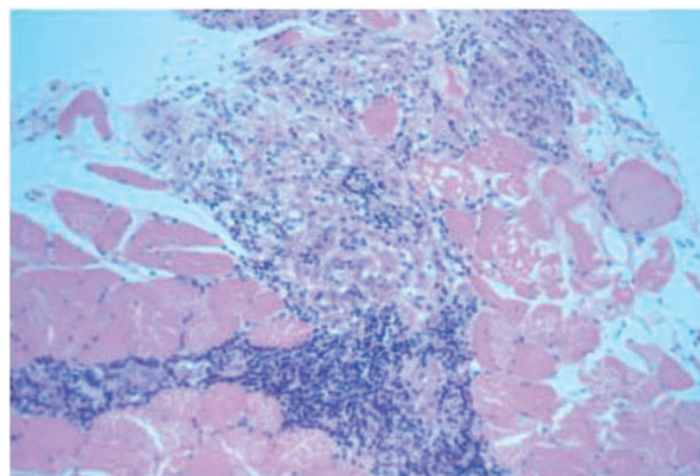
Both PM and DM affect woman approximately twice as often as men. Whereas PM is a disease of adults (with only rare exceptions), DM affects both adults and children showing 2 peaks between the ages of 14-16 and 45-65. IBM is a disease predominantly of older men. It affects men three times as often as females and is only rarely seen under the age of 50.

Association with an underlying malignancy

Again the figures vary from report to report. What can be said with more certainty is that an associated malignancy is not a feature of childhood myositis or of IBM. Some reports suggest an underlying malignancy is only found with DM whereas others with both DM and PM. More recent studies suggest a modest increase in relative risk with PM and a more significant increase with DM especially in patients over 50 (reviewed in 1). Therefore, particularly in older patients, a search for an underlying malignancy is warranted. This should include a physical examination concentrating on breast, lungs and abdomen and pelvis and appropriate blood analysis and radiological screening. Initial screening may be normal and the malignancy declare itself sometime (maybe years) after presentation with myositis. For this reason, some authors advocate repeat screening at 6 monthly intervals for several years².

Overlap Syndromes

In some cases myositis is seen as part of a wider autoimmune condition, often associated with systemic lupus erythematosus, rheumatoid arthritis, scleroderma, mixed connective tissue disease etc. In Sjögren's syndrome myositis is associated with interstitial lung disease. Antibodies to histidyl-tRNA synthetase, known as Jo-1, are found in the majority of patients with myositis and interstitial lung disease and may indicate a worse outcome secondary to respiratory distress syndrome. Interstitial lung disease is found in approximately 10% of patients with DM and PM.



Muscle from patient with polymyositis. Dense inflammatory cell infiltrate is shown.

Presentation

PM has a sub acute, insidious onset over months. Patients experience proximal weakness often without myalgia. Cardiac involvement includes both problems with conduction and cardiomyopathy. DM is an easier diagnosis due to the characteristic rash that may precede the muscle involvement. One sees a heliotropic rash around the eyelids that may spread to the cheeks and erythematous, raised scaly lesions on the knuckles (Gottron's patches) and similar lesions on the elbows. Calcinosis of the subcutaneous tissue and intermuscular fascia, which may ulcerate, is mainly seen in the childhood form of DM but is occasionally seen in adults. Other manifestations include dysphagia, cardiac and pulmonary involvement (as above), associated vasculitis and contractures (childhood DM). Systemic features including fever, malaise and weight loss may be seen in either PM or DM.

Focal myositis is an entity that does exist. It is mostly restricted to the thigh, neck or shoulder girdle and occasionally large limb muscles such as in the forearm but is also reported in small foot muscles³. Focal myositis may present as a local pseudotumour or may have systemic features.

Whereas PM and DM tend to have symmetrical presentations, IBM is usually asymmetrical. It again tends to affect proximal muscles particularly the quadriceps femoris but often affects the long finger flexors early such that patients may present with complaints such as being unable to use aerosols. There is also preferential involvement of iliopsoas, biceps and triceps. Mild facial weakness (not a feature of PM or DM) is seen in 60% of cases and dysphagia common.

Diagnosis

Serum creatine kinase (CK) is not necessarily raised. In PM and DM it is very occasionally normal though is usually raised and may be 50 times the upper limit of normal or higher (may be in excess of 10,000 units/litre). In IBM the CK is normal or shows only a mild elevation.

Electromyography may be indistinguishable between PM, DM and IBM. Myopathic motor units are seen with increased insertional activity and fibrillations indicative of active disease. Non-specific complex repetitive discharges may be seen suggesting chronicity. All changes may be patchy and fibrillation potentials (often most reliably detected in the paraspinal muscles) may be the only abnormality.

Muscle biopsy provides histological confirmation of disease. Again, findings may be patchy and several levels need to be examined. Small biopsy samples may not include foci of disease. In PM and sporadic IBM the inflammatory infiltrate is endomysial and predominantly CD8+ve T cells and macrophages. Invasion and necrosis of individual muscle fibres is seen (Figure). In DM there is perifascicular atrophy and perimysial infiltration with predominantly CD4+ve T cells and B cells. Micro infarcts may be seen. MHC class I is unregulated only on perifascicular cells in DM but on all mature muscle fibres in PM. In IBM, MHC class I tends only to be expressed on those fibres that show partial invasion by the inflammatory infiltrate.

Focal myositis may have distinct, more benign pathological features⁴.

Treatment

As mentioned in the introduction, only PM and DM respond to treatment. IBM does not and will not be discussed further.

Steroids are the mainstay of treatment, but not without side effects. Some cases will fail to respond to steroids alone and in other cases avoidance of steroids might be desirable (e.g. brittle diabetes).

Treatment is largely empirical in the absence of adequate trials. A typical regime will commence with between 60 and 100mg of oral prednisolone per day depending on weight (approximately 1mg/kg). Occasionally intravenous methyl prednisolone (1g/day for 3 days) is used to get on top of aggressive disease. The patient is usually embarking on long-term therapy and appropriate bone prophylaxis should be instituted. This initial dose is continued for 4 weeks or until CK has normalised. The prednisolone is then gradually reduced by 5 mg/day at weekly intervals until the patient is taking 20mg per day at which time further reductions may be made more slowly. Some authors

prefer alternate day steroids. There is probably no difference in efficacy but there is some suggestion that it may lessen certain side effects but others, in particular impaired glucose tolerance, are more difficult to manage. Certainly, prednisolone should be taken in a single morning dose. Obviously, the exact details of a drug regime need to be tailored to the individual patient.

Addition of a 'steroid sparing' agent from the onset is a matter of clinical preference. Azathioprine (1.5-3mg/kg as tolerated) is the normal used. It does, however, take some time for the full effects of azathioprine to kick in and hence the preference of many clinicians to prescribe it from the outset. Azathioprine is usually well tolerated but an impairment of liver function necessitates discontinuation. A small degree of anaemia or drop in white cell count may be accepted.

Other immunosuppression

There is evidence from a single, randomised controlled trial in adults and from one uncontrolled trial in children supporting the use of intravenous immunoglobulin (IVIg) in DM (reviewed in 5). There are no controlled trials of IVIg in PM. Based on this the Association of British Neurologists' guidelines on the use of IVIg state that '*IVIg has a role in dermatomyositis in adults and children which is refractory to other treatments. There is insufficient evidence supporting use as primary or long-term treatment. In severe refractory polymyositis there may also be a place for IVIg but this is not substantiated and in these cases reinvestigation should first consider the possibility of inclusion body myositis*'⁶. In the same document it is highlighted that randomised controlled trials have failed to demonstrate a benefit in IBM, therefore IVIg is not recommended for treatment of IBM^{5,6}.

Methotrexate has a faster mode of action than azathioprine and may have a role in severe or steroid resistant disease. A usual oral regime commences with 7.5mg weekly adjusted according to response increasing in 2.5 mg increments per week to a total of 15 mg as required and tolerated. Occasionally 20mg per week may be required. Bloods must be monitored closely (see BNF). A complicating factor

when using methotrexate is methotrexate pneumonitis that resembles the interstitial lung disease associated with some inflammatory muscle disease described above.

In non-responsive disease, other agents including cyclophosphamide, cyclosporin and chlorambucil have been tried with varying results.

The important issues with regard to treatment are that one must treat the patient and not the CK. CK may fall in response to treatment prior to clinical improvement. Also, patients who fail to respond completely to long-term steroid therapy may be developing a steroid myopathy. Their weakness will, of course, only be exacerbated by the further use of steroids. This can be a confusing clinical scenario and may only be resolved by a repeat biopsy.

Acknowledgements

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References

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