MRI guided muscle biopsy confirmed polymyositis diagnosis in a patient with interstitial lung disease

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Abstract

Idiopathic inflammatory myopathies, such as polymyositis (PM), may present with general symptoms such as fever and fatigue and only minimal muscle weakness, making it difficult to make a definite diagnosis and provide adequate treatment. Here a case is described in which interstitial lung disease was the first and most prominent manifestation of PM. Later, when muscle weakness became apparent and inflammatory muscle disease was suspected the first muscle biopsy was non-diagnostic. However, magnetic resonance imaging (MRI) scans of the clinically weak thigh muscles showed high signal on T₂ weighted images, suggesting muscle inflammation more proximal to the first biopsy site. A second biopsy at this site disclosed typical histopathological findings for myositis. After treatment with prednisolone in combination with cyclophosphamide both pulmonary and muscle function improved.

Conclusion—MRI scans of muscles may be helpful in selection of a site for muscle biopsy in patients with suspected inflammatory myopathy when a first muscle biopsy turns out to be negative. Additionally, patients with interstitial lung disease of unknown cause should be tested for muscular function to exclude an associated inflammatory muscle disorder.

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Polymyositis (PM) is a subgroup of the idiopathic inflammatory myopathies (IIM), which are all characterised by symmetrical, proximal muscle weakness, decreased muscle endurance, and chronic inflammation in muscle tissue.¹ Systemic features and other organ manifestations are not uncommon.²

Diagnosis is based upon symmetric proximal muscle weakness, an increase of serum levels of muscle enzymes, abnormal electromyogram, and the presence of an inflammatory infiltrate in muscle biopsy.³ A muscle biopsy is preferred to confirm diagnosis and to exclude other causes of muscle disorders. The typical histopathology of PM is the presence of degenerating and regenerating muscle fibres with inflammatory cells in and surrounding non-necrotic muscle cells. However, in some cases a muscle biopsy is negative.⁴ This might be due to a focal distribution of the inflammatory infiltrates, and some authors have advocated magnetic resonance imaging (MRI) as a routine investigation

to select a biopsy site in order to increase the accuracy of a muscle biopsy.⁵ The diagnostic value of MRI in myositis is unknown, however, and only a limited number of cases have been reported in which MRI has been useful in selecting a muscle biopsy site.⁵ After MRI guided biopsy one case of treatment resistant IIM turned out to have an inclusion body myositis (IBM).⁵ In another case MRI was helpful for diagnosis of PM.⁶

Here we describe a case in which a pulmonary manifestation was the first and most prominent symptom of the underlying inflammatory muscle disorder and in which muscle biopsy guided by MRI findings was helpful in establishing diagnosis.

Case report

A 60 year old man, previously healthy except for an old injury in the plexus brachialis, presented in November 1997 at a primary care unit with muscle and joint pain, fever, and weight loss. Erythrocyte sedimentation rate (ESR) was 65 mm/1st h and C reactive protein (CRP) 45 µcat/l (normal value <7). Lactate dehydrogenase (LDH) was 15.8 µcat/l (normal value <8 µcat/l). A chest radiograph disclosed an interstitial infiltrate in the left lung. Pneumonia was suspected and the patient was treated with antibiotics for some weeks without effect.

During the following months he became dyspnoeic and a slight impaired pulmonary function was noted (total lung capacity (TLC) 74% of normal value and the transfer factor of the lung for carbon monoxide (TLCO) was reduced to 57% of the predicted value). Bronchoalveolar lavage showed a number of infiltrating inflammatory cells within the normal range. Polymerase chain reaction for *Pneumocystis carinii* from the lavage was positive and the patient was treated for three weeks with trimetoprim sulfamethoxazole in combination with 10 mg prednisolone daily, with some reduction of the joint pain but without effect on the dyspnoea. At this time he had also developed severe muscle weakness and was referred to our rheumatology department in May 1998. On physical examination a symmetrical proximal and distal muscle weakness was evident. The patient could barely hold his head upright and while standing up from sitting he had to support himself with his arms. The hands displayed hyperkeratosis, hyperpigmentation and he had then also developed arthritis with swelling of the metacarpophalangeal joints.

Figure 1 (A) Coronal MRI illustrating the approximate level of biopsy sites. (B) T_2 weighted axial images soon after admission to the rheumatology department. The upper slice displays symmetrically distributed signal increase, indicating inflammation in almost all muscles. The arrow depicts the approximate location of the second biopsy. In the lower slice only a slight signal increase is evident. The arrow denotes the approximate location of the first biopsy.

Laboratory investigations showed serum creatine kinase $>76.9 \mu\text{cat/l}$ (normal value $<3 \mu\text{cat/l}$). Other serum muscle enzymes, aspartate

aminotransferase, alanine aminotransferase, LDH, and myoglobin, were also increased. The ESR was 40 mm/1st h , CRP $23 \mu\text{cat/l}$, haemoglobin 116 g/l , leucocyte count $20.4 \times 10^9/\text{l}$, platelet count $503 \times 10^9/\text{l}$, creatinine $90 \mu\text{mol/l}$ (normal value $<120 \mu\text{mol/l}$). High resolution computed tomography (HRCT) scan of the lungs displayed peripheral interstitial infiltrates.

A muscle biopsy from the vastus lateralis muscle disclosed minor pathological findings with occasional degenerating and regenerating fibres. An electromyogram displayed no changes related to muscle disease, but a discrete neuropathic pattern. However, the severe clinical symptoms still made IIM a likely diagnosis. MRI showed an increased signal on T_2 weighted images most prominent in the proximal thigh muscles, indicating pronounced proximal inflammation (fig 1). Distally, where the first biopsy specimen had been taken, only discrete signs of inflammation were evident (fig 1).

A second muscle biopsy more proximal in the vastus lateralis muscle showed tissue changes typical of inflammatory myopathy, including inflammatory infiltrates of mononuclear cells in the endomysium and with non-necrotic fibres surrounded and invaded by inflammatory cells (fig 2). At the same time anti-Jo-1 antibodies were detected. A diagnosis of polymyositis with pulmonary involvement was made according to the criteria suggested by Bohan and Peter.³ The patient was initially treated with prednisolone 0.75 mg/kg/day and because of the severe pulmonary disease, cyclophosphamide 150 mg/day .

Clinical improvement was already noticed after one week with subjectively decreased dyspnoea. One month later muscle function measured by a myositis index⁷ had improved.

Figure 2 The second muscle biopsy from the left lateral vastus muscle. (A) Immunohistochemical staining of major histocompatibility complex class I expressed in many muscle fibres (arrow). In this section prominent changes with numerous degenerating, some regenerating, and also many atrophic muscle fibres with a perifascicular distribution are seen. Note the infiltrates consisting of T lymphocytes and macrophages in the perimysial connective tissue. (B) Occasional non-degenerating muscle fibres with invading mononuclear inflammatory cells.

Figure 3 Symptoms and investigations over time. HRCT = high resolution computed tomography.

Three months after starting treatment HRCT showed regression of the interstitial lung changes. After six months of treatment the muscle function was further improved, but pulmonary function tests were not changed (TLC 82% and TLCO 61% of predictive value). Figure 3 presents an overview of the clinical course.

Discussion

To our knowledge this is the first reported case in which MRI was useful in selection of a muscle biopsy site to confirm the diagnosis of polymyositis in a patient with a severe interstitial lung disease. In this case fatigue, general symptoms, and dyspnoea initially predominated over the muscular symptoms. When muscle weakness progressed and an IIM was suspected the first muscle biopsy sample, although taken from the clinically weak thigh muscle, was non-diagnostic for IIM. However, a second biopsy taken proximally, the site being selected with guidance from the MRI, displayed typical histopathological findings for PM and the diagnosis was confirmed.

Inflammatory cell infiltrates and non-necrotic muscle fibres invaded by mononuclear inflammatory cells are typical histopathological findings of PM and are regarded as a prerequisite for diagnosis of this condition.⁸ A diagnosis of possible or probable PM can still be made without typical changes in the muscle biopsy specimen according to the suggested criteria by Bohan and Peter.³ Normal muscle biopsies have been reported in 10–20% of patients with IIM. Sampling error due to skip lesions has been suggested as one possible explanation for

negative biopsies.⁴ Another reason for a negative biopsy, at least in some cases, may be treatment with corticosteroids before the biopsy sampling. In our case both explanations were considered as the cause of the first negative muscle biopsy. From the MRI scans, however, it was obvious that the earlier 10 mg prednisolone regimen had not suppressed the muscle inflammation and that the negative biopsy was rather a result of the local distribution of the inflammation. Both the first and second biopsies were made within a period of two days, and therefore the contribution of a general disease progression as an explanation for the findings must be considered marginal.

MRI of muscle with T₁ and T₂ weighted images has been reported as a sensitive diagnostic tool in patients with myositis. Muscle changes in IIM as detected with MRI include oedema within and around muscles, muscle calcification, fatty infiltration, and fibrosis.⁹ The inflammatory lesions detected by MRI also correlate with disease activity,⁹ which makes MRI a possible tool for follow up studies.

In the recently suggested revised classification criteria of IIM, positive MRI scans have been suggested for inclusion.¹⁰ The drawback of this technique as a routine diagnostic tool, however, is primarily the high costs that prevent the use of MRI scans as a screening tool for muscle inflammation. Furthermore, the inflammatory changes recorded are not specific for IIM and may therefore not replace a muscle biopsy in the diagnostic investigation. Besides, a muscle biopsy is still required to subclassify the IIM on histopathological grounds.⁸

In this case general and pulmonary symptoms preceded the muscular weakness and careful diagnostic procedures for the pulmonary disease were undertaken, though without conclusive results. The patient was even treated with antibiotics for a suspected *Pneumocystis carinii* infection, which could later be excluded. Interstitial lung disease in PM or dermatomyositis occurs in about 5–30% of the cases,¹¹ and in patients with anti-Jo-1 antibodies fibrosing alveolitis has been reported in as many as 50–100%.¹² The prognosis of these patients is generally poor with a five year survival of 40%.¹³ Fibrosing alveolitis has also been reported as an isolated lung disease in a limited number of patients with anti-Jo-1 antibodies and as the initial symptom in patients eventually developing myositis.¹⁴ An open lung biopsy was actually planned in our case when the muscular symptoms became prominent and an increased serum creatine kinase level made IIM a likely diagnosis. To our surprise the muscle biopsy showed only slight non-specific findings. Although the observation of hyperkeratosis and hyperpigmentation of the hands, clinical signs typical of “mechanic’s hands”, together with the positive anti-Jo-1 antibody would suffice for a diagnosis of Jo-1 positive PM with interstitial lung disease, we still thought it to be of clinical importance to have a positive biopsy. Therefore we pursued the diagnostic procedures with MRI of the thigh

muscle after the first biopsy turned out negative.

This case illustrates how muscle inflammation with moderate clinical muscle symptoms can be easily overlooked in patients with pronounced pulmonary disease. Thus a higher incidence of muscle inflammation in association with fibrosing alveolitis than hitherto reported may not be excluded, and clinical examination of muscle function should be included in these patients.

The presence of the anti-Jo-antibody seems to be a sensitive marker for lung disease,¹⁴ and should in patients with primary interstitial lung disease raise the question of a possible underlying inflammatory muscle disorder.

Our conclusion from this case is that in a patient with severe muscle symptoms and a negative muscle biopsy MRI should be performed in order to locate the inflammatory tissue changes.

We find it important to pursue the diagnostic procedures in order to get a histopathological confirmation of diagnosis. Firstly, because a delay in diagnosis due to a negative biopsy may result in a poor functional outcome. Secondly, a distinction between PM and IBM is not always evident on clinical grounds. Furthermore, we recommend that patients with interstitial lung disease of unknown cause should be tested for muscle function to exclude an associated inflammatory muscle disorder.

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