Idiopathic myositis: a rheumatological view

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Abstract

Twenty five patients with idiopathic myositis attended this department for long term follow up from 1980 to 1989. Twelve patients had primary polymyositis (four men, eight women) and six had primary dermatomyositis (three men, three women); five women had an overlap syndrome. Two patients had a malignant condition associated with the myositis.

The mean age at diagnosis was 40 years. All of the patients had proximal muscle weakness, 18/25 had a raised creatine kinase value (mean 2325 IU/l), 19/20 had an abnormal electromyogram, and 19/24 had positive muscle biopsy samples. Of the disease specific antibodies, anti-Jo-1 was detected in only 1/21 patients tested (three patients with fibrosing alveolitis were negative for this antibody), but the 56 kDa antibody was detected in 12/17 patients. The HLA data analysed in the white patients (17/25) showed that 6/8 of those tested were HLA-DR3 positive.

All patients were treated with prednisolone and azathioprine was used for 14/25 patients. Only three deaths occurred during the eight year follow up, but there was a substantial morbidity, which may reflect the referral pattern. Muscle strength tests and creatine kinase levels were useful in recording the response to treatment in some patients.

These data emphasise that careful long term follow up of patients with myositis is mandatory and that although the present treatment strategy has substantially reduced the death rate, morbidity associated with the disease remains a major problem.

Myositis is an autoimmune rheumatic disease characterised by chronic inflammation of skeletal muscle. Myositis has been recognised as a disease for over 100 years.¹ The disease remains a serious clinical problem with a significant morbidity and mortality. After much discussion, most authorities have agreed to use the criteria of Bohan and Peter for diagnosis.²

There remain a number of disputed areas, notably the range of clinical features, prognosis, treatment, autoantibody associations, and immunogenetic associations. There have been few studies analysing clinical and laboratory data with specific antibody tests, HLA typing, prognosis, and survival.³⁻⁸ The aim of this study was to provide an insight into patients with myositis as they have presented to a rheumatology department with a particular interest in the disease. The patients in the study

have been followed up for a longer period of time than in other surveys. Among the clinical aspects we have put particular emphasis on assessing the morbidity of these patients rather than the mortality.

We now present detailed information on the clinical features, serology, immunology, treatment, and outcome of 25 patients with myositis who presented to this department with some form of myositis from 1980 to 1989 and who have been followed up for at least one year. Patients were only included if they satisfied three or more of the criteria of Bohan and Peter.²

Patients and methods

Twenty five patients who first presented from 1980 to 1989 to our rheumatology department with a diagnosis of polymyositis or dermatomyositis, and who satisfied three out of four criteria described by Bohan and Peter, were evaluated retrospectively.² All were seen regularly by one or two doctors (MLS or DAI). Patients were classified into four subgroups: group 1, primary polymyositis; group 2, primary dermatomyositis; group 3, polymyositis or dermatomyositis associated with another autoimmune rheumatic disease or some features of such a disease; group 4, polymyositis or dermatomyositis associated with a malignant disease. Patients who were identified as having an overlap syndrome had to satisfy the revised criteria of the American Rheumatism Association for systemic lupus erythematosus⁹ and/or the criteria for the diagnosis of Sjogren's syndrome.¹⁰ Measurements of creatine kinase were performed by the biochemical department using an NADP/NADPH system (Durazyne), routine autoantibodies (antinuclear antibodies using HEP-2 cells as a substrate and anti-Ro/La/Sm/RNP by counterimmunoelectrophoresis) were detected by the immunology department. Details of the assays for the specific antibodies,

Figure 1 Subgroups of patients examined in this study.

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i.e. Jo-1 antibody and 56 kDa antibody are described elsewhere.^{11 12} Histocompatibility typing was performed as described previously.¹³ Data were evaluated by demographic features, clinical features, electromyogram, and muscle biopsy data, serological parameters, and clinical outcome. Muscle tissue was obtained for analysis by needle biopsy.

STATISTICS

Fisher's exact test with two tailed probability or χ^2 with Yates's correction was used as appropriate.

Results

Twelve patients had primary polymyositis (four men, eight women) and six had primary dermatomyositis (three men, three women); five women had an overlap syndrome (three systemic lupus erythematosus and two Sjogren's syndrome). Two patients had a malignant condition; one patient with polymyositis had Hodgkin's disease and one had dermatomyositis with a monoclonal gammopathy (fig 1).

Of the 25 patients, 17 were white, five Asian, two West Indian, and one Chinese. The mean age at diagnosis was 40 years (range 15–68

Figure 2 Relations between muscle strength, creatine kinase level, and treatment with prednisolone in four patients.

years) and the duration of symptoms prior to diagnosis was seven months (range 3–12 months). Three of the patients had fibrosing alveolitis and one had a cardiomyopathy. All of the patients had proximal muscle weakness, 21/25 had an increased creatine kinase value (mean 2325 IU/l), 19/20 had an abnormal electromyogram, and 19/24 had positive muscle biopsy samples. Antinuclear antibodies were positive in 17/25 patients, mostly low titre (1:40 to 1:80, speckled pattern) except in the patients with concurrent systemic lupus erythematosus whose titres were much higher. Antibodies to ribonucleoprotein were present in four patients. Of the disease specific antibodies, anti-Jo-1 was detected in only 1/21 patients tested (three patients with fibrosing alveolitis were negative for this antibody), but the RNP 56 kDa antibody was detected in 13/19 patients tested. Specifically, the 56 kDa antibody was positive in 4/5 patients with dermatomyositis, 8/11 patients with polymyositis, but only 1/4 patients with an overlap syndrome. HLA data analysed in the white patients (17/25) revealed that 3/8 patients were HLA-A1, B8, DR3 positive and 6/8 patients with polymyositis were HLA-DR3 positive.

These 25 patients have been followed up for a mean of eight years (range 3–21 years). All patients were treated with prednisolone (60 mg was the usual starting dose). Figure 2 shows the observed correlation between muscle strength, creatine kinase level, and prednisolone dose in four patients. As muscle strength is regained, the creatine kinase level and prednisolone dose decreases. We found that comparisons of muscle strength between patients were not useful.

The most common treatment in addition to prednisolone was azathioprine, used in 14/25 patients. Only three deaths occurred, one from a recurrence of Hodgkin's disease, one from a dilated cardiomyopathy (not conclusively shown to be related to the myositis), and the other from a fractured skull incurred in a fall. Figure 3 shows the clinical outcome based on an assessment of activities of daily living and muscle strength testing.

Discussion

Myositis varies considerably in its clinical

Figure 3 Clinical outcome of patients examined in this study.

presentation and severity, and selection bias by different doctors produces various results and conclusions. We have given an insight into patients who presented to a rheumatology department with a particular interest in the disease.

The division into diagnostic categories was broadly similar to other series, except that fewer malignancies were seen.^{3–8} The female to male ratio was 2.2:1. All five of the overlap patients were women, which agrees with the ratio of 8:1 found by Hochberg *et al.*⁴ In addition, these patients were more likely to have polymyositis than dermatomyositis.

The creatine kinase level, electromyogram and muscle biopsy samples form the basis of investigations in patients with myositis. The creatine kinase level was increased in 21/25 patients and correlated with disease activity in some, as has been found by other workers. The creatine kinase level was helpful in assessing the response of myositis to treatment in those patients whose initial levels were high. Figure 2 shows four patients who illustrated this well. Figure 2 shows that muscle strength testing can be a useful objective measure of morbidity, although it requires the patients to make the maximum effort. A normal creatine kinase value can occur in up to 20% of patients,¹⁴ but in this study it did not imply any less serious disease. We found the creatine kinase value to be helpful in assessing the response of myositis to treatment in those patients whose initial levels were high. The occurrence of a normal electromyogram and muscle biopsy (needle biopsy) samples, noted in 5 and 20%, respectively, of patients in our series has been noted before.⁴ This phenomenon could be attributed to a focal or variable intensity of lymphocytic infiltration¹⁵ or, more simply, a sampling error. Needle biopsies can be performed in numerous sites which can resolve this problem, although we found that occasionally the specimen was too small to make a definitive diagnosis. However, Devere and Bradley found completely normal muscle biopsy samples in 17% of patients using an open muscle biopsy technique; this is not significantly less than our false negative rate.³ Open muscle biopsy is considerably more traumatic than needle biopsy.

Of the specific antibodies that are found in patients with myositis the Jo-1 antibody was found in only 1/25 patients compared with 30% found by Yoshida *et al.*¹⁶ The Jo-1 antibody has been shown to be more frequent when the pulmonary function is affected, but was negative in the three patients in this study with associated lung disease. There is no explanation for this discrepancy, though it may, in part, reflect differences in the population studied. The 56 kDa antibody was found more frequently than the Jo-1 antibody ($p < 0.001$). Although it did not distinguish between patients with polymyositis and dermatomyositis, being positive in 80 and 73% of patients, respectively, the 56 kDa antibody was significantly less frequent ($p < 0.05$) in the group with myositis and another autoimmune disorder. Other studies have confirmed that this antibody is rarely found in patients with any other autoimmune

rheumatic disorder and is thus the most specific and sensitive antibody related to myositis. In addition, the semiquantitative densitometry levels of this antibody have been shown to correlate with disease activity in some patients.¹⁷

Like many other immune disorders, there is a predominance of HLA-B8 and DR3 in patients with polymyositis. Hirsch *et al* found no association with dermatomyositis and suggested that polymyositis and dermatomyositis are pathogenetically different disorders.¹³ Our HLA data indicate that 75% of white patients with polymyositis have the HLA-DR3 haplotype. This compares with a frequency of 27% found in a survey of 20% of kidney donors performed by the UK Transplant Service ($p < 0.02$).¹⁸ The numbers were too small to draw statistically significant conclusions about other subgroups. HLA-DR3 is also known to correlate with myositis in white patients with the Jo-1 antibody,¹⁹ though no association has previously been sought with the 56 kDa antibody.

All patients were treated with steroids. The mean highest dose of 60 mg is very similar to that used by other workers. Unusually, over half of the patients were treated with immunosuppressive agents, in this instance azathioprine, which is a much higher frequency compared with other workers.^{4,7,8} We believe that this allowed us to reduce the dose of steroids more quickly. A prospective double blind trial using azathioprine and prednisolone compared with placebo and prednisolone showed no real difference in outcome, though the trial period was only three months.²⁰ However, three years later it was noted that the patients in the trial who were given prednisolone and azathioprine had performed better than the patients treated with prednisolone alone, and these patients required a lower dose of prednisolone.²¹

The present study shows a low death rate, which is in accord with some other surveys. Hochberg *et al* quote a cumulative survival rate of 73% after eight years among 76 patients with adult onset myositis.⁴ This compares favourably with the figures of Medsger *et al*,²² who showed a 53% cumulative survival after seven years, and Steiner, who, before the availability of steroids, reported that 17 out of 28 patients died.²³

Other series do not comment on the morbidity associated with myositis, an outcome indicator that has become increasingly more important now that the death rate is decreasing. We used a simple scale to assess morbidity, but more complex assessments need to be developed to monitor the response to treatment. In this study there was significantly morbidity in over half the patients, who were left with marked residual weakness. The group of patients described were often referred by other hospitals and this may lead to a higher proportion of chronic and more severe cases of myositis. Experience in a rural hospital has shown that the patients seen tend to have milder disease, a low death rate, and require less aggressive

treatment.⁸ The overall low death rate may be explained by the advances in general medicine. The significant morbidity could be attributed to the limited success of the drugs used to treat the myositis itself.

This study indicates that in a group of patients biased towards a rheumatology practice, the death rate, is low but the morbidity remains a problem. This is reflected by the high proportion of patients receiving immunosuppressive drugs. Patients with myositis should continue to be looked after by doctors with experience and an interest in the subject.

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