Concise Report

Mycophenolate mofetil treatment in resistant myositis

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Objectives. To assess the efficacy and tolerability of mycophenolate mofetil (MMF) in six patients with myositis refractory to conventional immunosuppressive therapy.

Methods. Six patients were identified from hospital notes. All had previously failed to respond to other immunosuppressive treatments. Efficacy was measured as changes in muscle strength, creatine kinase (CK) levels and prednisolone dose.

Results. The mean age of the group was 49.8 ± 9.1 yrs, 6 (100%) were female and Caucasian. Patients had failed to respond to a median of 3 (range 1–3) immunosuppressive drugs. They received MMF for a mean of 22.3 ± 18.9 months with a mean MMF dose of 1.6 ± 0.5 g/day. The mean initial prednisolone dose was 13.7 ± 7.7 mg and the mean follow up dose was 8.5 ± 4.9 mg/day (P = 0.03). CK levels were reduced from mean 2395 IU/l ± 1202.8 to 746.6 ± 555.8 IU/l (P = 0.03).

Conclusion. Our data demonstrate that MMF may be effective in myositis, previously unresponsive to conventional immunosuppressive drugs.

KEY WORDS: Myosistis, Mycophenolate mofetil, Treatment.

Introduction

Studying the natural course and treatment of inflammatory myopathies has been difficult because of the rarity of the disorders and the variability of the clinical outcome.

The current management of inflammatory myopathy is mainly empirical, with only azathioprine and intravenous immunoglobulin (IVIG) being evaluated in randomized clinical trials [1, 2].

Despite the lack of randomized controlled clinical trials, steroids are the standard first-choice therapy of all patients with myositis. Patients who fail to improve muscle strength or require high doses of steroids to achieve remission are considered treatment failures. For treatment failures, a variety of immunosuppressors have been used, most commonly methotrexate and azathioprine. Patients not responding to these medications are currently treated with IVIGs, cyclosporine A, tacrolimus and cyclophosphamide. There are case reports of patients treated successfully with anti-tumour necrosis factor, B-cell depletion (rituximab) and mycophenolate mofetil (MMF) [3–5].

MMF is an immunossuppressive agent widely used in organ transplantation and currently used to treat a variety of autoimmune conditions [6]. The greatest experience is in systemic lupus erythematosus (SLE), particularly lupus nephritis. In addition, patients with systemic vasculitis, myasthenia gravis, pemphigus vulgaris, bullous pemphigoid, epidermolysis bullosa acquisita and psoriasis have successfully been treated with MMF [7–10].

The purpose of this study is to assess the efficacy and tolerability of MMF in six patients with myositis refractory to conventional immunosuppressive therapy.

Patients and methods

Six patients with myositis treated with MMF were identified from hospital notes. Five patients fulfilled Bohan and Peter’s criteria for idiopathic inflammatory myositis (two patients had dermatomyositis, three polymyositis) and one patient fulfilled clinical criteria for SLE and developed myositis [11, 12].

Patient records were retrospectively reviewed to identify previous therapies, details of MMF therapy and clinical outcome. For data collection related to MMF treatment, patient records were reviewed from commencement of the drug until the final time point, defined as last follow-up or withdrawal of the drug. Starting dose, maximum dose and duration of treatment with MMF were available for analysis. All prior treatments were documented, including steroid dose and previous immunosuppressive therapies.

Efficacy was measured as changes in muscle strength following the Medical Research Council grading, creatine kinase (CK) levels and prednisolone dose pre- and post-MMF treatment [13].

Adverse event information and reasons for MMF discontinuation were obtained from physician evaluations noted in the records from baseline to final time point.

Results

The mean age of the group was 49.8 ± 9.1 yrs; six (100%) were female and Caucasian. Patients had failed to respond to a median of 3 (range 1–3) immunosuppressive drugs (Table 1). None of the immunosuppressive drugs were used in combination; prior immunosuppressive drugs were discontinued when MMF...
was started. They received MMF for a mean of 22.3 ± 18.9 months with a mean MMF dose of 1.6 ± 0.5 g/day. The mean initial prednisolone dose was 13.7 ± 7.7 mg and the mean follow-up dose was 8.5 ± 4.9 mg/day, \( P = 0.03 \) (Table 1). Mean CK levels were reduced from 2395 ± 1202.8 IU/l to 746.6 ± 555.8 IU/l, \( P = 0.03 \) (Table 2). Table 2 gives details of muscle strength in upper and lower limbs pre- and post-MMF treatment. One patient (patient number 3) required IVIG pulses due to persistent weakness and elevated CK levels.

All the patients were receiving MMF at the time of the last assessment. Two patients developed mild side effects: nausea and headaches, which did not require MMF withdrawal.

### Discussion

The majority of patients with myositis are adequately controlled with steroids alone or in combination with immunosuppressive drugs. Of all the patients, 20–30% remain active despite immunosuppressive therapy (methotrexate, azathioprine, cyclosporine A and cyclophosphamide), and other options such as IVIG should be considered [14].

MMF is a potent immunosuppressive agent widely used in organ transplantation and has been shown to be useful to treat lupus and lupus nephritis in several uncontrolled and randomized studies [6–10]. MMF inhibits both B- and T-lymphocyte proliferation. Lymphocytes are dependent on the de novo synthetic pathway of purine nucleotides, in contrast to other eukaryotic cells. Mycophenolate acid (MPA) is the active agent of MMF, which has higher oral bioavailability. MPA is a reversible and non-competitive inhibitor of inosine monophosphate dehydrogenase (IMP-DH), which catalyses a rate-limiting step in this synthetic pathway, consequently a relatively lymphocyte-specific effect. MMF inhibits more strongly the type II isoform of IMP-DH, which is expressed in stimulated rather than in resting lymphocytes [15]. MMF reduces antibody production, and can affect glycosylation of adhesion molecules and their \textit{in vitro} expression. The exact mechanism leading to an improvement of myositis is uncertain but might be related to the effects of MMF on lymphocyte and on the expression of adhesion molecules between others.

This study describes our observations regarding the use of MMF in six patients with myositis. Our results showed a good clinical response in all patients with increased muscle strength measured objectively using the Medical Research Council scale. The CK levels were significantly reduced, and prednisolone dose was significantly lower after MMF was introduced. Although 2/6 patients developed side effects, there was no need to discontinue the medication. At the last follow-up, all patients continued with the medication.

The experience of MMF use in myositis is scarce, but our results agree with the experience of other authors. Majithia et al. [5] described seven patients with inflammatory myositis successfully treated with MMF. They showed improvements in muscle strength and reduction of CK levels, inflammatory markers and prednisolone dose.

### References


### Table 1. Previous immunosuppressive treatments and prednisolone doses

<table>
<thead>
<tr>
<th>Patient number</th>
<th>Previous immunosuppressive drugs</th>
<th>Prednisolone dose (initial)</th>
<th>Prednisolone dose (follow-up)</th>
</tr>
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<tr>
<td>1</td>
<td>HCQ, AZA</td>
<td>20</td>
<td>10</td>
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<td>2</td>
<td>IVIG</td>
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<tr>
<td>3</td>
<td>MTX, IVIG, AZA</td>
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<tr>
<td>4</td>
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<tr>
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<td>MTX, IVIG, AZA</td>
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</tr>
<tr>
<td>6</td>
<td>CYC, AZA, MTX</td>
<td>20</td>
<td>10</td>
</tr>
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</table>

HCQ, hydroxychloroquine; AZA, azathioprine; IVIG, intravenous immunoglobulin; MTX, methotrexate; CYC, cyclophosphamide.

### Table 2. Muscle power and CK levels

<table>
<thead>
<tr>
<th>Patient number</th>
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<th>CK levels (UI/l) initial</th>
<th>CK levels (UI/l) follow-up</th>
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<tr>
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<td>1558</td>
<td>859</td>
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</tbody>
</table>

UL, upper limbs; LL, lower limbs.


