Mycophenolate Mofetil for Chronic Inflammatory Demyelinating Polyradiculoneuropathy
An Open-Label Study
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Dear Sir,

Chronic inflammatory demyelinating polyradiculoneuropathy (CIDP), an immune-mediated heterogeneous progressive or relapsing disorder, is considered as the chronic variant of the Guillain-Barré syndrome that differs from the latter disease by its temporal evolution over at least 2 months, by its relative absence of cranial nerve implication or autonomic disorder, by its relative absence of previous infection and by treatment response to corticosteroids. There are several effective evidence-based therapies, but not all patients improve with these treatments. Around 30\% of patients do not respond to immunotherapy such as intravenous immunoglobulin (IVIg), plasma exchange, corticosteroids, azathioprine, cyclophosphamide or interferon-\textbeta \textsuperscript{1}.

Mycophenolate mofetil (MM), a non-competitive reversible inhibitor of inosine 5’-monophosphate dehydrogenase, is now widely used in transplantation medicine and in immune-mediated diseases. Its antiproliferative effect acts by inhibition of the de novo purine synthesis of activated T and B lymphocytes. MM can improve several neurological disorders such as myasthenia gravis, inflammatory myopathy or CIDP \textsuperscript{2–4}.

We conducted an open-label study in 7 patients with CIDP diagnosed according to common guidelines \textsuperscript{5}. Two women and 5 men with a mean age of 57.6 years (44–67 years), a mean disease duration of 9 years (2–23 years), 4 relapsing courses and 3 progressive courses were enrolled after oral informed consent because of insufficient response to previous therapies or because of a high frequency of IVIg therapy (at least every 4 weeks). Two patients had predominantly sensory signs, 2 predominantly motor signs and 3 motor and sensory signs. Superimposed axonal loss was demonstrated by electroneurography in 2 out of 7 cases. One gram of MM was administered twice daily, in 3 patients in association with prednisone and/or IVIg (table \textsuperscript{1}). Efficacy was defined as stability or improvement of disability after 6 months and/or reduction of IVIg dose within 12 months. The disability was measured by the disability grade (0–5 points; 0 = healthy, 1 = minor signs, 2 = able to walk without assistance but unable to run, 3 = able to walk 5 m only with help, 4 = chair/bed bound, 5 = death), the Neurological Disability Scale (NDS; 0–202 points; 0 = healthy, 202 = worst situation) \textsuperscript{6}, the Hammersmith Motor Ability Test (HMAT; 0–40 points; 0 = unable to move, 40 = normal) \textsuperscript{7} and the timed 10-meter walk test \textsuperscript{8}.

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patients responded after 4 months in one study [2]. In another study, 2 patients with additional IVIg or plasma exchange ‘rapidly’ recovered strength and sensation under MM, with a relapse after discontinuing and improvement after resuming MM [3]. Four patients had no benefit in another small study [4]. The dosage of IVIg in 2 other patients receiving simultaneously MM could be reduced by 50% [9]. Three out of 8 patients with idiopathic CIDP improved in a recently published study, whereas the 5 patients who had a secondary CIDP showed no response (4 associated with IgG or IgA monoclonal gammopathies of uncertain significance (MGUS), 1 with a POEMS syndrome) [10].

There might be subgroups of CIDP patients who respond to MM (e.g. relapsing course, CIDP without MGUS, predominantly sensory or motor-sensory signs). MM could be more effective if started early in the disease before axonal degeneration. A large prospective randomized trial is needed.

Table 1. Summary of clinical course

<table>
<thead>
<tr>
<th>Patient</th>
<th>Disease duration/years</th>
<th>Type/course</th>
<th>Previous treatments</th>
<th>Addition therapy</th>
<th>Follow-up months</th>
<th>Disability grade</th>
<th>NDS</th>
<th>HMAT</th>
<th>10-meter walk test</th>
<th>Reasons to stop MM</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>2</td>
<td>sensory/progressive, painful, demyelinating</td>
<td>IVIg</td>
<td>no</td>
<td>14</td>
<td>1/1</td>
<td>17/14</td>
<td>40/40</td>
<td>7.0/7.0</td>
<td>continued (relief of pain)</td>
</tr>
<tr>
<td>2</td>
<td>23</td>
<td>sensory/relapsing, demyelinating</td>
<td>prednisone, interferon-β, azathioprine, cyclophosphamide</td>
<td>IVIg</td>
<td>12</td>
<td>1/1</td>
<td>48/52</td>
<td>39/34</td>
<td>7.4/7.3</td>
<td>no benefit</td>
</tr>
<tr>
<td>3</td>
<td>7</td>
<td>motor/progressive, demyelinating</td>
<td>IVIg, azathioprine</td>
<td>no</td>
<td>12</td>
<td>2/2</td>
<td>55/72</td>
<td>22/19</td>
<td>18.2/19.0</td>
<td>no benefit</td>
</tr>
<tr>
<td>4</td>
<td>2</td>
<td>sensory-motor/relapsing, demyelinating</td>
<td>interferon-β, azathioprine, IVIg</td>
<td>prednisone</td>
<td>18</td>
<td>2/1</td>
<td>50/19</td>
<td>22/40</td>
<td>9.3/5.0</td>
<td>continued</td>
</tr>
<tr>
<td>5</td>
<td>14</td>
<td>motor/progressive, axonal-demyelinating</td>
<td>IVIg</td>
<td>no</td>
<td>6</td>
<td>2/2</td>
<td>46/46</td>
<td>24/24</td>
<td>–/8.0</td>
<td>no benefit, AE</td>
</tr>
<tr>
<td>6</td>
<td>14</td>
<td>sensory-motor/relapsing, axonal-demyelinating</td>
<td>prednisone, azathioprine, IVIg, cyclophosphamide, interferon-β</td>
<td>no</td>
<td>24</td>
<td>1/1</td>
<td>26/16</td>
<td>33/40</td>
<td>6.9/5.1</td>
<td>continued, AE</td>
</tr>
<tr>
<td>7</td>
<td>2</td>
<td>sensory-motor/relapsing, axonal-demyelinating</td>
<td>IVIg</td>
<td>prednisone 10</td>
<td>2/1</td>
<td>47/26</td>
<td>38/37</td>
<td>10.4/8.8</td>
<td>continuous</td>
<td></td>
</tr>
</tbody>
</table>

The 4 patients with an improvement are shown in bold (1 with relief of pain). AE = Adverse events; HMAT = Hammersmith Motor Ability Test; NDS = Neurological Disability Scale.

1 At baseline/at the end of follow-up.

References