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To the Editor:

Ocular cicatricial pemphigoid (OCP) is a functionally dangerous disorder that typically warrants long-term systemic therapy. While corticosteroids’ adverse effects can preclude their prolonged use, mycophenolate mofetil (MMF) may be effective.

Institutional Review Board approval was obtained to review medical records of patients evaluated at Wake Forest’s dermatology clinic who received MMF for OCP between 2010-2020. Diagnoses were established by ophthalmologists’ slit-lamp examinations; disease was staged according to Foster’s classification (stage 3: symblepharon, trichiasis, entropion; stage 4: ankyloblepharon). All patients were followed by their cornea specialist who performed ophthalmologic exams. Outcomes were categorized as complete response (asymptomatic, no active inflammation on ophthalmologists'/dermatologists’ exam [“quiet”, white eyes]), partial response (symptomatic relief with active, reduced inflammation [on ophthalmologists’ exam]), and no response. Flares were defined as signs/symptoms of worsening inflammation - either patient-reported (increased pain, erythema, subjectively declining vision) or observed on ophthalmologists’ exam.

Patients were primarily White (95%), females (63%), mean age 67 years, with bilateral (82%) Foster’s stage 3 (89%) disease at baseline. Many patients (56%) underwent conjunctival (45%) and buccal mucosal (11%) biopsies. Medications failed before MMF included: dapsone (2 anemia, 2 inefficacy, 1 unspecified), azathioprine (transaminitis), hydroxychloroquine (inefficacy), methotrexate (inefficacy), and cyclosporine (unspecified). Supplementary Table 1 contains patient-level data (available via Mendeley at http://dx.doi.org/10.17632/mx5bn8tcbc.1).
Twenty-nine patients received initial concomitant prednisone (median maximum dose 27.5 mg); 28 underwent tapers (median minimum dose 2.5 mg) and 13 weaned off completely (Table 1). Patients remained controlled on their lowest prednisone dosages for a mean 21.8 ± 25.6 months (time from start of lowest dose of prednisone to last follow-up, discontinuation of MMF [if applicable], or flare [if applicable]). Five patients flared during prednisone tapering. Two patients experienced Foster’s stage progression (5, 15 months after MMF initiation).

Nine patients with mild baseline disease underwent MMF monotherapy (89% response rate at 12-month evaluation) (Table 2). Of the 38 overall patients (29 MMF + initial concomitant prednisone, 9 MMF monotherapy) with evaluations at 3, 6, 12 months’ follow-ups, response rates were: 65%, 70%, 74% respectively (mean response duration 29.3 ± 28.8 months [time from response to flare or last follow-up evaluation, if no flares]). Monotherapy response rates were higher possibly due to milder baseline disease. The non-responders who remained on MMF, despite failing to improve on their ophthalmologic exams, reported less frequent flares. Seven patients discontinued MMF due to side effects (4 gastrointestinal upset, 1 fatigue, 1 thrombocytopenia, 1 “decreased urination”). Laboratory monitoring was generally performed every 3 months; subclinical anemia was detected in five patients (all continued therapy).

Therapies with comparable/slightly higher response rates to MMF have limitations. Cyclophosphamide is typically reserved for severe cases due to its toxicity. The costs of rituximab and IVIG may preclude routine administration.

Although we present several diagnoses without biopsies, immunohistologic findings are frequently negative in OCP. Several monotherapy patients improved and response rates generally trended
favorably during prednisone dose reductions. Consistent with previous studies, MMF appears effective for late stage, mild-moderately actively inflamed OCP; however, cicatrization can progress despite control of inflammation.²,⁵
References:


Table 1. Outcomes in 29 ocular cicatricial pemphigoid patients managed with mycophenolate mofetil and prednisone

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Starting regimen</th>
<th>~3 month (1.7-4.4) follow-up (n=26)</th>
<th>~6 month (4.5-8.9) follow-up (n=28)</th>
<th>~12 month (9.1-14.0) follow-up (n=25)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Outcome, n (%)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Complete response</td>
<td>2 (8%)</td>
<td>6 (21%)</td>
<td>4 (16%)</td>
<td></td>
</tr>
<tr>
<td>Partial response</td>
<td>14 (54%)</td>
<td>12 (43%)</td>
<td>13 (52%)</td>
<td></td>
</tr>
<tr>
<td>No response</td>
<td>10 (38%)</td>
<td>8 (29%)</td>
<td>7 (28%)</td>
<td></td>
</tr>
<tr>
<td>Flare at visit</td>
<td>0 (0%)</td>
<td>2 (7%)</td>
<td>1 (4%)</td>
<td></td>
</tr>
<tr>
<td>MMF dose, mg daily</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean ± SD</td>
<td>1362 ± 498</td>
<td>1680 ± 690</td>
<td>1558 ± 605</td>
<td>1533 ± 732</td>
</tr>
<tr>
<td>Prednisone dose, mg daily</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean ± SD</td>
<td>24.2 ± 11.5</td>
<td>17.3 ± 11.8</td>
<td>10.2 ± 7.6</td>
<td>7.0 ± 5.4</td>
</tr>
<tr>
<td>Median [range]</td>
<td>27.5 [5-40]</td>
<td>15.0 [0-45]</td>
<td>8.75 [0-25]</td>
<td>5 [0-15]</td>
</tr>
</tbody>
</table>

*in calculating percentages, non-responders who were not evaluated during a follow-up evaluation time window due to discontinuation (before the follow-up evaluation time window) were categorized as non-responders; patients who flared at visits were categorized as non-responders for response rate calculations

MMF: mycophenolate mofetil, SD: standard deviation

Table 2. Outcomes in 9 ocular cicatricial pemphigoid patients managed with mycophenolate mofetil monotherapy

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Starting regimen</th>
<th>~3 month (1.7-4.4) follow-up (n=8)</th>
<th>~6 month (4.5-8.9) follow-up (n=9)</th>
<th>~12 month (9.1-14.0) follow-up (n=9)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Outcome, n (%)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Complete response</td>
<td>2 (25%)</td>
<td>3 (33%)</td>
<td>7 (78%)</td>
<td></td>
</tr>
<tr>
<td>Partial response</td>
<td>4 (50%)</td>
<td>5 (56%)</td>
<td>1 (11%)</td>
<td></td>
</tr>
<tr>
<td>No response</td>
<td>2 (25%)</td>
<td>1 (11%)</td>
<td>1 (11%)</td>
<td></td>
</tr>
<tr>
<td>Flare at visit</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td></td>
</tr>
<tr>
<td>MMF dose, mg daily</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean ± SD</td>
<td>1389 ± 333</td>
<td>1214 ± 393</td>
<td>1219 ± 411</td>
<td>1313 ± 530</td>
</tr>
</tbody>
</table>

*in calculating percentages, non-responders who were not evaluated during a follow-up evaluation time window due to discontinuation (before the follow-up evaluation time window) were categorized as non-responders; patients who flared at visits were categorized as non-responders for response rate calculations

MMF: mycophenolate mofetil, SD: standard deviation