Intravenous immunoglobulin for the treatment of morphea: A retrospective review of 2 academic medical centers

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Background
• Morphea is a rare, inflammatory disease characterized by sclerosis and atrophy of the skin and subcutaneous tissues.
• First-line systemic therapies include steroids, methotrexate, and mycophenolate mofetil.1
• Some patients may not tolerate, have refractory disease or contraindications to these medications.
• Intravenous immunoglobulin (IVIg) has demonstrated efficacy in other fibrosing diseases including eosinophilic fasciitis2 and systemic sclerosis.3
• Only a few case reports describe the use of IVIg for morphea.4-6

Objectives
• The primary objective was to retrospectively evaluate the response of patients with morphea to IVIg.

Methods
• Adult patients seen at Massachusetts General Hospital and Brigham and Women’s Hospital from January 2000 to January 2023 with a diagnosis of morphea and treated with IVIg were eligible for inclusion.
• Medical records were retrospectively reviewed to assess demographic data, clinical phenotype, indications for IVIg, treatment course, and clinical response.
• Clinical response was defined as: complete (resolution of erythema and softening of lesions with no disease progression), partial (incomplete improvement of erythema and/or softening of lesions with no disease progression) or no response (continued disease progression).

Results

<table>
<thead>
<tr>
<th>Pt</th>
<th>Age/sex/ethnicity</th>
<th>Morphea subtype</th>
<th>Indication for starting IVIg</th>
<th>Medication changes with IVIg</th>
<th>Clinical response</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>26/F/White (non-Hispanic)</td>
<td>Linear morphea</td>
<td>Failed MTX and MMF</td>
<td>None</td>
<td>Unable to fully assess*</td>
</tr>
<tr>
<td>2</td>
<td>38/F/Hispanic</td>
<td>Linear morphea (ECDS and early facial hemiatrophy overlap)</td>
<td>Breastfeeding</td>
<td>None</td>
<td>No response</td>
</tr>
<tr>
<td>3</td>
<td>37/F/Hispanic</td>
<td>Linear morphea (ECDS)</td>
<td>Plans for pregnancy, pregnancy and breastfeeding</td>
<td>None</td>
<td>No response</td>
</tr>
<tr>
<td>4</td>
<td>35/F/White (non-Hispanic)</td>
<td>Linear morphea (ECDS)</td>
<td>Plans for pregnancy</td>
<td>None</td>
<td>Partial response</td>
</tr>
<tr>
<td>5</td>
<td>61/M/White (non-Hispanic)</td>
<td>Generalized morphea</td>
<td>Contraindications to other medications</td>
<td>None</td>
<td>No response</td>
</tr>
<tr>
<td>6</td>
<td>76/F/White</td>
<td>Generalized morphea with LSetaR overlap</td>
<td>Infections on MMF and MTX</td>
<td>None</td>
<td>Partial response (stopped early)</td>
</tr>
<tr>
<td>7</td>
<td>65/F/White (non-Hispanic)</td>
<td>Pansclerotic morphea/EF overlap</td>
<td>Failed MMF and MTX</td>
<td>None</td>
<td>Complete response</td>
</tr>
<tr>
<td>8</td>
<td>61/F/White (non-Hispanic)</td>
<td>Generalized morphea</td>
<td>Failed MMF and solumedrol, MTX contraindicated</td>
<td>Tapered off prednisone and MPA, started tocilizumab</td>
<td>No response</td>
</tr>
<tr>
<td>9</td>
<td>75/F/White (non-Hispanic)</td>
<td>Radiation-induced pansclerotic morphea</td>
<td>MMF not approved by insurance</td>
<td>None</td>
<td>Complete response</td>
</tr>
<tr>
<td>10</td>
<td>52/F/White (non-Hispanic)</td>
<td>Generalized morphea/EF overlap</td>
<td>Failed steroids, MTX, MMF</td>
<td>Tapered MMF</td>
<td>Complete response</td>
</tr>
<tr>
<td>11</td>
<td>63/M/White (non-Hispanic)</td>
<td>EF/pansclerotic morphea overlap</td>
<td>Failed MTX, MMF, prednisone</td>
<td>Tapered off prednisone, decreased MTX</td>
<td>Complete response</td>
</tr>
<tr>
<td>12</td>
<td>59/M/White (non-Hispanic)</td>
<td>EF/morphea overlap</td>
<td>Failed MMF, lung toxicity from MTX, side effects of prednisone</td>
<td>None</td>
<td>Complete response</td>
</tr>
<tr>
<td>13</td>
<td>67/M/White (non-Hispanic)</td>
<td>EF/morphea/myositis overlap</td>
<td>Severity of disease, muscle weakness</td>
<td>Upitted MMF, tapered off MTX and steroids</td>
<td>Complete response</td>
</tr>
<tr>
<td>14</td>
<td>42/F/White (non-Hispanic)</td>
<td>Generalized pansclerotic morphea/EF/deep morphea overlap</td>
<td>Breastfeeding, plans for pregnancy</td>
<td>None</td>
<td>Complete response</td>
</tr>
</tbody>
</table>

*Lost to follow-up thus could not be fully evaluated

ECS, en coup de sabre; LSetaR, lichen sclerosus et atrophicus; MTX, methotrexate; MMF, mycophenolate mofetil; MPA, mycophenolic acid. Standard dosing for IVIg was 2g/kg divided over 2 days every 4 weeks. Some patients received 1g/kg every 2 weeks (generally due to side effects).

• 7 patients (50%) had complete response, 2 (14.3%) had partial, and 4 (28.6%) had no response. One patient was lost to follow-up.
• Of the 10 patients with generalized or pansclerotic disease, 70% had complete response.
• 50% of linear morphea patients had no response, and none had complete response.
• Indications for IVIg included failure of or contraindications to first- and second-line morphea treatments and pregnancy or breastfeeding-related concerns.
• 75% of linear morphea patients started IVIg due to pregnancy or breastfeeding-related concerns.
• Common adverse effects included headaches, nausea, and vomiting.

Discussion
• Clinical response to IVIg appeared to be more robust for pansclerotic and generalized morphea than linear morphea.
• Disease refractory to systemic steroids, MTX, and MMF can be responsive to IVIg.
• Treatment options may be limited in patients who are pregnant, breastfeeding or planning to become pregnant, and IVIg is generally accepted as safe in these cases. Thus, despite relatively poorer clinical responses in linear morphea, IVIg may still be an important therapeutic option.
• Prospective studies are needed to further examine the efficacy of IVIg for morphea as well as the difference in response between various morphea subtypes.
• Study limitations include small sample size, retrospective methodology, and lack of validated outcome measures for morphea.

Conclusion
• To our knowledge, this is the largest study reporting the use of IVIg for treating morphea.
• IVIg can be effective for refractory cases, particularly generalized or pansclerotic disease.
• Efficacy may be limited for linear morphea, though it is a safe steroid-sparing option when contradictions to other systemic medications exist, such as pregnancy.
• More research is needed to evaluate the use of IVIg for morphea and its subtypes.

References