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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 fasciitis[2] 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

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

*Lost to follow-up thus could not be fully evaluated
ECDS, en coup de sabre; LSetA, 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 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

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