Refractory Generalised Morphea in Association with Reactive Hypereosinophil Syndrome Successfully Managed with Abatacept

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Dear Editor,

Morphea, or localised scleroderma, is an inflammatory condition causing sclerosis of skin and subcutaneous tissues. Its generalised variant can be associated with systemic complications.[1] While eosinophilia is observed in morphea,[2] it rarely reaches levels indicating potential organ damage. Among the therapeutic interventions for morphea, abatacept, a T-cell modulating CTLA-4 fusion protein, is under investigation with encouraging outcomes.[3]

A 38-year-old man with generalised morphea affecting deep tissues developed multiple polymorphous pruritic lesions, which persisted for 3 months. These lesions were unresponsive to treatment with high-potency topical corticosteroids and oral antihistamines [Figure 1]. The diagnosis of deep and generalised morphea had been confirmed by imaging and histopathologic studies; in 2006, progressive eosinophilia was observed in 2009, when the disease progressed. In 2019, aortitis not attributable to any immune, infectious, or neoplastic condition was also diagnosed. His eosinophil count consistently exceeded 1.5 × 10^9/L, coinciding with morphea and aortitis exacerbations. Various therapies were tried, including corticosteroids, phototherapy, methotrexate, mycophenolate mofetil, cyclophosphamide, photopheresis, rituximab and tocilizumab, but only a transient response to methylprednisolone boluses was detected, improving cutaneous symptoms and peripheral eosinophilia temporarily. Physical examination of the new pruritic lesions revealed erythematous papules, eczematous plaques, hives and indurated morphea plaques, causing joint contractures [Figure 1]. Comprehensive laboratory and imaging, including PET-CT scan, confirmed persistent eosinophilia (7.4 × 10^9/L) and ruled out other malignancies or infections. Genetic abnormalities and primary hematologic disease were excluded using next-generation sequencing of myeloid neoplasms-related genes and tyrosine kinase gene fusions. Cutaneous biopsies from two distinct lesions (one from a corticosteroid-resistant eczema plaque and another from an itchy papule) revealed moderate perivascular and interstitial eosinophil infiltrate in the dermis [Figure 2]. The clinical findings suggested a reactive hypereosinophilic syndrome (HES) potentially associated with his morphea. His symptoms stabilised after starting abatacept at a dose of 750mg/28d combined with tapering methylprednisolone until discontinuation, and eosinophilia reduced over 15 months, reaching an average count. The morphea lesions stabilised, softened and became hyperpigmented, with the patient reporting improved mobility and reduced tightness and pruritus.

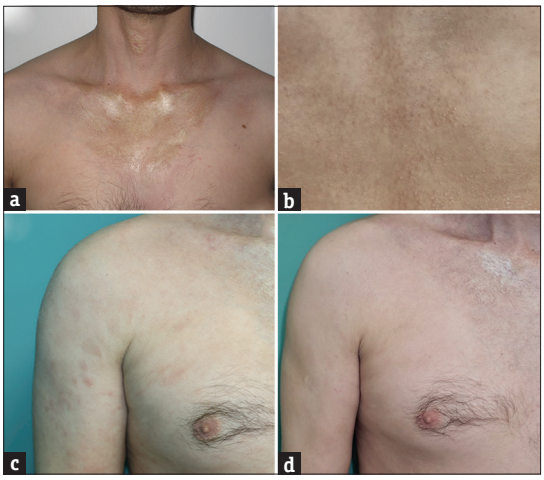

Figure 1: (a) Indurated, thick plaques of active morphea in the neck and upper thorax. (b) Pruritic papules in the lower back. (c) Eczematous pruritic plaques in right arm and chest before abatacept treatment. (d) Improvement of previously mentioned lesions 2 months after abatacept treatment

Hypereosinophilia (HE) has been defined as a persistent eosinophilia exceeding >1.5 × 10^9/L in the context of eosinophilic disorders. When associated with organ damage, it is termed HES. Three subtypes are distinguished: idiopathic, primary (neoplastic) and secondary (reactive or HESr), with the latter arising from an underlying nonclonal disease.[4] Treatment of the root cause is deemed essential for HESr.

HE has been reported in patients with severe morphea being extreme in some cases[2]; however, organ damage attributable to HE is exceptional. A notable case linked eosinophilic fasciitis, which is classically considered analogous to deep morphea,[1] with HES and demonstrated management success using corticosteroids and cyclophosphamide.[5] In our presented case, we

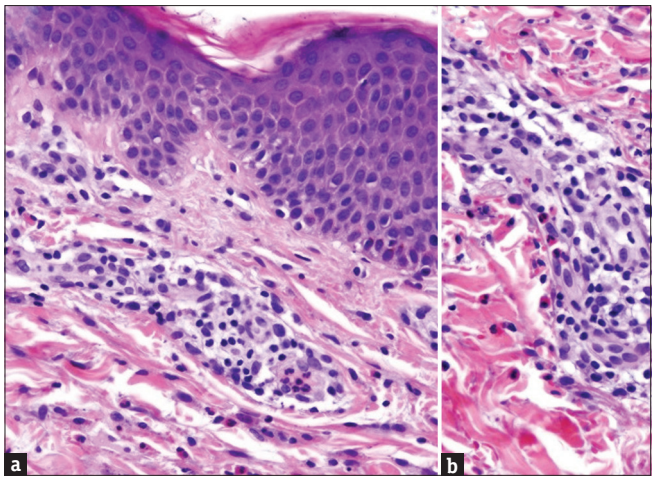

Figure 2: (a) Hematoxylin and eosin (H/E) stained biopsy of an eczematous plaque show mild spongiosis and superficial perivascular infiltration of lymphocytes and histocytes. Moderate perivascular and interstitial eosinophil infiltrate is observed (X200 magnification). (b) H/E: Detailed perivascular eosinophil infiltrate (X400 magnification)

thought a potential association between HES and morphea. After the diagnosis of morphea, a progressive eosinophilia was observed. Elevated eosinophil counts correlated with morphea exacerbations and systemic symptoms. Skin manifestations of HES include therapy-resistant eczema, angioedema, atypical urticarial lesions and pruritic papules. Interestingly, our patient showed all these signs, barring angioedema. Histological findings from skin biopsies further reinforced this association. In addition, the stability of clinical symptoms and eosinophil levels during morphea management with abatacept further reinforced our tentative diagnosis. Nonetheless, definitive attribution of HES to morphea remains challenging. Comprehensive diagnostic evaluations effectively ruled out differential diagnoses, such as systemic sclerosis, toxic oil syndrome and hematologic conditions.

This case illustrates the complexities of morphea management, highlighting systemic complications in severe forms and the potential of abatacept for recalcitrant cases. The insights advocate for a collaborative approach, necessitating expertise from both rheumatology and dermatology for an optimised patient outcome.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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