Recalcitrant Ulcers Associated with Anti-SAE-Positive Dermatomyositis Treated with Surgery Followed by Intravenous Immunoglobulin

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Cutaneous ulcers are seen in approximately 26% of patients with dermatomyositis (DM)[1]. Though the exact pathophysiology remains elusive, these ulcers are thought to be associated with vasculopathy, vasculitis or severe interface dermatitis[1]. The treatment-resistant nature of these ulcers poses significant challenges to management. We report a case of recalcitrant DM-related ulcers treated successfully with surgery, followed by intravenous immunoglobulin (IVIg).

A 41 year-old Caucasian woman with biopsy-proven DM developed multiple painful punched-out ulcers involving the dorsal hands, fingers and thighs whilst on immunosuppressive therapy (Figure 1). She first presented to our clinic with characteristic skin manifestations of DM including heliotrope erythema, shawl sign, holster sign and Gottron's papules. She later developed upper limb myositis with creatinine kinase levels peaking at 2299. The diagnosis of DM was confirmed with skin and muscle biopsies. Her other previous investigations were unremarkable (including extractable nuclear antigen, anti-double stranded DNA and malignancy screening), except for a positive anti-nuclear antibody of 1:80 speckled.

Histopathology from an ulcer on her dorsal hand revealed an ulcerated epidermis with surface acute inflammatory cells, underlying dermal fibrin within superficial vessels with a presumed secondary vasculitis (Figure 2). No true vasculitis, vasculopathy, calcification, granuloma, malignancy or fungus was identified. Her myositis autoantibody panel revealed anti-small ubiquitin-like modifier activating enzyme (anti-SAE)-positivity, while prothrombotic screen was negative.

Her myositis was well-controlled although ulcers remained unresponsive to multiple treatments, including prednisolone (50 mg/day step down), hydroxychloroquine (400mg/day), methotrexate (20mg/week), topical tacrolimus and topical betamethasone dipropionate. Due to lack of response, methotrexate was changed to cyclosporin (4.5mg/kg).

Despite multiple treatments, the ulcer over her right second metacarpophalangeal joint deteriorated rapidly resulting in tendon exposure. Due to imminent risk of extensor tendon rupture and difficulties accessing IVIg within the ideal timeframe, she underwent urgent surgical closure for that ulcer. She subsequently received IVIg (2g/kg) immediately post-surgery. The surgical repair was successful and all other ulcers healed completely within two weeks after IVIg. Six months post commencement of IVIg, she was started on a three-monthly IVIg regime (2g/kg). She remained ulcer-free for 18 months since commencement of IVIg. She is currently stable on hydroxychloroquine (400mg/day), quinacrine (100mg/day) and three monthly IVIg (2g/kg). Cyclosporin was ceased due to hypertension.

Surgical intervention is generally reserved for DM-related ulcers associated with calcinosis[2]. Although medical treatments are preferred for ulcers unrelated to calcinosis, surgery may be considered under exceptional circumstances[2]. Our patient underwent surgical intervention due to high-risk clinical deterioration. She recovered well postoperatively despite concerns about possible pathergy.

The efficacy of IVIg on DM-related ulcers is generally supported by the limited case reports available on this topic[3,4]. We report another case demonstrating the efficacy of IVIg for these ulcers, specifically in a post-surgical context. The rapid response of her other ulcers to IVIg supports the early use of IVIg for these ulcers.

DM-related ulcers are associated with anti-melanoma differentiation-associated gene (anti-MDA5) antibody[1]. Conversely, although multiple studies have demonstrated the association between anti-SAE antibodies and cutaneous involvement in DM, its correlation with

cutaneous ulcers has not been specifically established[5]. A case of anti-SAE-positive DM associated with cutaneous ulcers has been described in the literature[5].

This case highlights the potential role of surgical management for DM-related ulcers that are generally treated medically. IVIg should be considered early for recalcitrant DM-related ulcers. Further studies are required to clarify the association between anti-SAE antibodies and these ulcers.

References

[1] Fiorentino D, Chung L, Zwerner J et al. The mucocutaneous and systemic phenotype of dermatomyositis patients with antibodies to MDA5 (CADM-140): a retrospective study. J Am Acad Dermatol. 2011; 65(1): 25-34.

[2] Fujimoto M, Asano Y, Ishii T et al. The wound/burn guidelines – 4: guidelines for the management of skin ulcers associated with connective tissue disease/vasculitis. J Dermatol. 2016; 43: 729-757.

[3] Kuwano Y, Ihn H, Yazawa N et al. Successful treatment of dermatomyositis with high dose intravenous immunoglobulin. Acta Derm Veenreol. 2006; 86: 158-159.

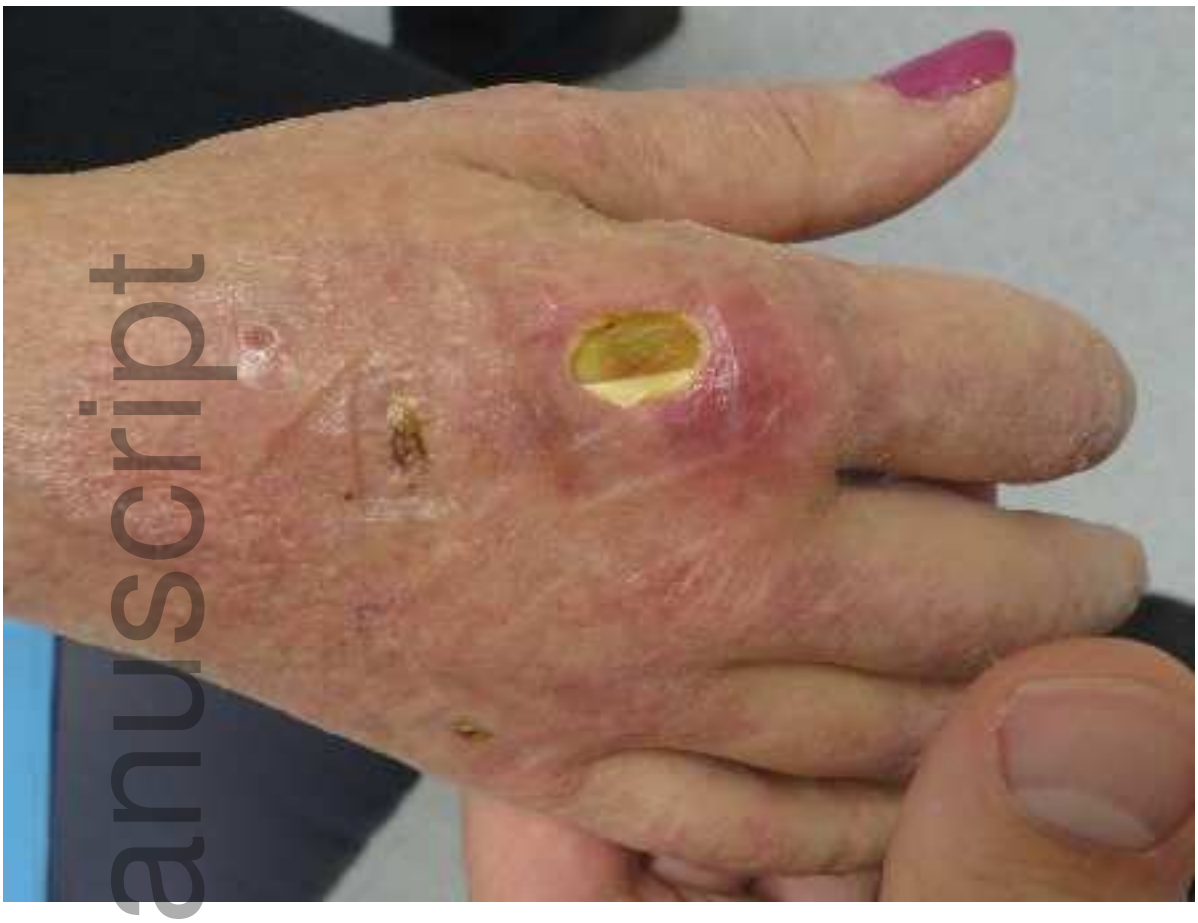
[4] Cafardi JM, Sami N. Intravenous immune globulin in amyopathic dermatomyositis – report of two cases and review of the literature. Open Rheumatol J. 2015; 9: 77-81.

[5] Bodoki L, Nagy-Vincze M, Griger Z et al. Four dermatomyositis-specific autoantibodies – anti-TIF1Ɣ, anti-NXP2, anti-SAE and anti-MDA5 – in adult and juvenile patients with idiopatic inflammatory myopathies in a Hungarian cohort. Autoimmun Rev. 2014; 13: 1211-1219.

Legends

Figure 1 Multiple punched out ulcers with surrounding erythema involving the dorsum of the right hand. The ulcer on her right second metacarpophalangeal joint had exposed her extensor tendon.

Figure 2 An ulcerated epidermis with surface acute inflammatory cells, underlying dermal fibrin within superficial vessels and an adjacent arteriole showing some inflammatory cells within the wall, without fibrinoid necrosis. Adjacent dermis shows a mixed inflammatory infiltrate (H&E x100).



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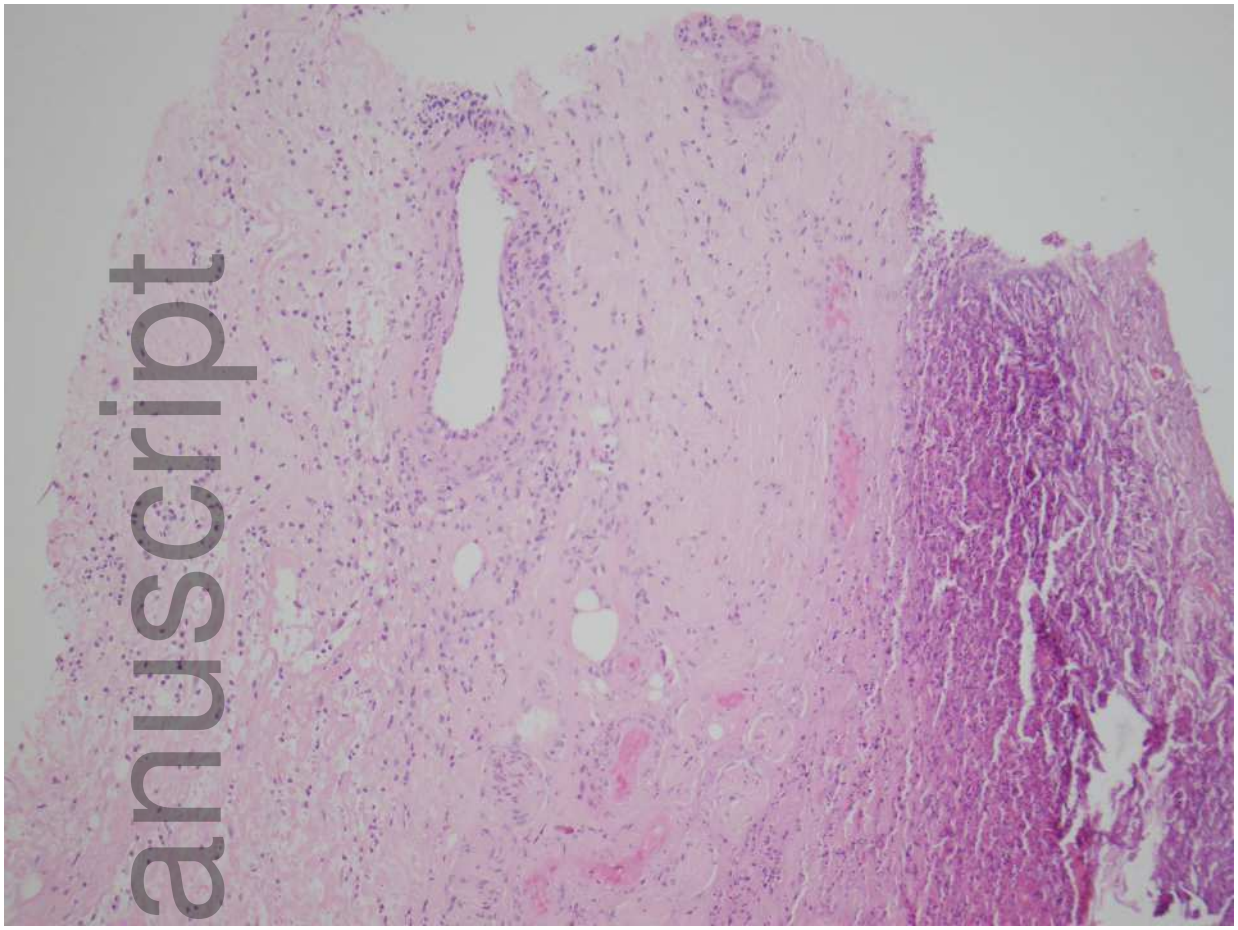

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