The successful use of subcutaneous abatacept in refractory anti- human transcriptional intermediary factor 1-gamma dermatomyositis skin and oesphagopharyngeal disease

**Rheumatology key message**

- Subcutaneous abatacept may be an effective treatment in dermatomyositis patients with refractory skin and oesphagopharyngeal disease.

Sir, Successful management of dermatomyositis (DM) requires suppression of immune-driven inflammatory disease in the skin as well as striated, oesophageal and cardiac muscle. Control of all manifestations of this disease can be difficult, and in a recent series only 38% of DM patients achieved clinical skin remission over 3 years despite active treatment [1]. We report the efficacy of subcutaneous abatacept in a patient with resistant skin and oesphagopharyngeal disease.

A 70-year-old Peruvian woman presented in 2013 with an erythematous rash, joint pains, dysphagia and proximal muscle weakness. She had extensive cutaneous DM features—a periorbital heliotrope rash, widespread erythematos scaling of the scalp, arms and upper back in a shawl distribution, and V-sign on the anterior chest. On the hands there were Gottron’s papules, periangual erythema and ragged nailfolds. Video fluoroscopy confirmed oesophagopharyngeal dysmotility. Peak serum creatinine kinase (CK) was 2070 U/L (normal range 5–200), troponin I <17 ng/l, 25-OH vitamin D 53 nmol/l and thyroid function normal. ANA was positive 1/160–640 and ENA screen negative. Anti-human transcriptional intermediary factor 1 (TIF1)-γ antibody was weakly positive and anti-Jo-1, -PL7, -PL12, -OJ, -EJ, -MDA-5, -SAE, -Mi-2, -NXP-2, -SRP, -Ku and -PmScl were negative. EMG revealed proximal myopathic motor units and MRI of thighs showed oedema of both rectus femori and the left gracilis muscles. Biopsy showed interstitial and perivascular foci of lymphocytes and macrophages, and no necrosis. This phenotype of DM with severe cutaneous and oesophageal disease, no lung involvement and TIF1-γ antibodies prompted a thorough malignancy screen with normal CT chest, abdomen and pelvis, CEA, CA125, CA 19-9, αFP and fluorodeoxyglucose-PET scan.

Initial treatment with high-dose prednisolone (1 mg/kg) and IVIG resulted in rapid reduction of serum CK, and improvement of proximal muscle strength and cutaneous features. Dysphagia persisted and required gastrostomy feeding. Prednisolone reduction below 20 mg led to recurrent skin disease that was resistant to AZA 3 mg/kg and MTX 25 mg weekly. Rituximab (1 g × 2, 2 weeks apart) provided moderate cutaneous benefit, but this was not sustained following two further cycles over 12 months. Further courses of IVIG led to short-lasting cutaneous improvement for up to 3 months. Ciclosporin 2.5 mg/kg caused a significant deterioration in the rash, which then became refractory to IVIG (see supplementary Fig. S1 available at *Rheumatology* online). Over this 3-year period serum CK remained suppressed and muscle function was preserved, but dysphagia did not improve. Cutaneous Dermatomyositis Disease Area and Severity Index [2] total activity score was 32/97 and abatacept 125 mg weekly by subcutaneous injection was then commenced. After 6 months cutaneous features were markedly improved (see Fig. 1) and at 9 months Cutaneous Dermatomyositis Disease Area and Severity Index was 5/97. Between 6 and 9 months dysphagia improved significantly, enabling a safe swallow, and the patient started to feed orally again. At 6 months prednisolone was tapered below 10 mg for the first time in 2 years. This contrasts with IVIG, which had provided similar cutaneous improvement for a maximum of 3 months per course and had no effect on dysphagia.

Abatacept is a fully human fusion of cytotoxic T lymphocyte antigen-4 and the Fc portion of immunoglobulin. Cytotoxic T lymphocyte antigen-4 inhibits co-stimulation of T cell activation by blocking the binding of CD28 on T cells with CD80/86 on antigen-presenting cells. In patients with DM, B and CD4+ T cells predominate in the inflammatory infiltrate on muscle biopsy and CD28 has been found to be expressed on the cell surface of myocytes in patients with DM and PM, suggesting that these cells may take on a specialized antigen-presenting function in these diseases [3]. A role for abatacept in DM is also supported by the association with a plethora of myositisspecific antibodies, and the observation that in RA abatacept leads to a reduction in immunoglobulins and memory B cells [4]. Furthermore, clinical response to abatacept in RA correlates with ACPA titre [5].

A recent pilot study reported the effect of i.v. abatacept in 20 patients with idiopathic inflammatory myopathies who were resistant to conventional treatment agents. Of nine patients with DM, two were responders based on a core definition of improvement, focusing on muscle strength. Assessment of skin disease showed improvement, but did not reach statistical significance [6]. One case report concerning abatacept and the skin describes a patient with juvenile DM, extensive calcinosis cutis and ulceration, which responded to combination treatment with i.v. abatacept and topical sodium thiosulphate [7]. In mice, abatacept has been demonstrated to prevent the activation of immature dendritic cells in the skin, thereby promoting cutaneous immunological tolerance [8]. Skin histology has not been studied in humans and...
any effect that abatacept might have on dermal dendritic cells, inflammatory cell infiltrate and T cells is as yet undetermined.

We believe this is the first reported case in which subcutaneous abatacept has shown prolonged efficacy for DM cutaneous and oesophageal disease, in a patient with anti-TIF1-γ antibodies and severe cutaneous and oesophageal features refractory to conventional and anti-B cell treatment.

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Supplementary data
Supplementary data are available at Rheumatology online.

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References


