

Treatment of Recalcitrant Dermatomyositis with Efalizumab

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Sir,

Dermatomyositis (DM) is an auto-immune disease that primarily affects muscles and skin. Muscle weakness appears in the shoulders and hips in particular. Skin symptoms include a diffuse violaceous erythema and oedema, predominantly of the upper face including the orbita, and violaceous-red papules of the finger (Gottron papules). The pathogenesis of DM is unclear, but recent studies suggest a central role of auto-aggressive lymphocytes and type I interferons (1–4), as has been proposed earlier for cutaneous lupus erythematosus (5–7).

Corticosteroids are the established first-line treatment for DM. However, their use is limited because of side-effects. Unfortunately, recalcitrant courses exist that respond poorly to corticosteroids and to other immunomodulatory and immunosuppressive drugs (8).

CASE REPORT

An 82-year-old woman presented with peri-orbital violaceous-red oedema and erythema extending to the chest with proximal muscle weakness (Fig. 1a). She suffered from dysphagia and 6 kg weight loss during the last 4

months. Histology of lesional skin biopsy, taken from the chest, revealed an interface dermatitis associated with sparse lymphocytic infiltration in a perivascular distribution and mucin depositions. Electromyographic investigations confirmed a pathological reaction pattern in the biceps brachii muscle, indicating myositis. Muscle biopsy was denied. She had slightly elevated antinuclear antibodies (1:80, granular pattern), but blood count, liver enzymes, and serum creatinine kinase were within normal limits. No malignancy could be found.

Initial treatment with 60 mg prednisolone per day did not improve the clinical picture. Additional intravenous administration of 15 mg methotrexate per week for 8 weeks also had no effect.

This prompted us to initiate a subcutaneous treatment with efalizumab (Raptiva®, Serono) 1 mg/kg body weight per week, combined with 40 mg prednisolone per day. This therapy led to a prominent reduction of the facial oedema and the thoracic erythema. The violaceous-red erythemas of the eyelid showed only a minor response (Fig. 1b).

During the following month efalizumab treatment was increased to 1.8 mg/kg per week. Prednisolone



Fig. 1. (a) The patient presented initially with a pronounced violaceous-red facial oedema predominantly involving the peri-orbital region and erythema of the chest, which did not respond to oral corticosteroids and methotrexate. (b) Additional application of efalizumab led to a prominent reduction of the facial oedema and the thoracic erythema. After a follow-up period of 12 months the clinical picture has remained stable.

application was reduced to 10 mg/day. A low dose of azathioprine of 50 mg/day was initiated.

After a follow-up period of 12 months the clinical picture has remained stable. The patient feels well and has gained 12 kg body weight.

DISCUSSION

Efalizumab is a monoclonal antibody against CD11a, the alpha-subunit of LFA1 (leukocyte-function-associated antigen 1). The molecule blocks the interaction between LFA1 and ICAM1, which is important for the firm attachment of lymphocytes to endothelial cells during lymphocyte skin homing, which promotes recruitment of T lymphocytes into the skin (9, 10). Efalizumab was developed for treatment of psoriasis, but has been reported to be effective in allergen-induced airway responses and airway inflammation in subjects with atopic asthma (11) and has been shown in a phase I trial to be potentially effective in renal transplantation (12, 13).

Recent studies have provided evidence that treatment with monoclonal anti-B-cell antibodies (rituximab) might also be effective in DM (14), others have found that the selective blockage of tumour necrosis factor alpha with infliximab is effective in DM (15). This supports the assumption that DM is probably a complex type I interferon driven disease in which the recruitment of B- and T lymphocytes and the induction of pro-inflammatory cytokines plays a central role (4, 16).

REFERENCES

1. Tezak Z, Hoffman EP, Lutz JL, Fedczyna TO, Stephan D, Bremer EG, et al. Gene expression profiling in DQA1*0501+ children with untreated dermatomyositis: a novel model of pathogenesis. *J Immunol* 2002; 168: 4154–4163.
2. Uzel G, Pachman LM. Cytokines in juvenile dermatomyositis pathophysiology: potential and challenge. *Curr Opin Rheumatol* 2003; 15: 691–697.
3. Caproni M, Torchia D, Cardinali C, Volpi W, Del Bianco E, D'Agata A, et al. Infiltrating cells, related cytokines and chemokine receptors in lesional skin of patients with dermatomyositis. *Br J Dermatol* 2004; 151: 784–791.
4. Wenzel J, Scheler M, Bieber T, Tuting T. Evidence for a role of type I interferons in the pathogenesis of dermatomyositis. *Br J Dermatol* 2005; 153: 462–463.
5. Ronnblom L, Alm GV. The natural interferon-alpha producing cells in systemic lupus erythematosus. *Hum Immunol* 2002; 63: 1181–1193.
6. Wenzel J, Worenkamper E, Freutel S, Henze S, Haller O, Bieber T, et al. Enhanced type I interferon signalling promotes Th1-biased inflammation in cutaneous lupus erythematosus. *J Pathol* 2005; 205: 435–442.
7. Farkas L, Beiske K, Lund-Johansen F, Brandtzaeg P, Jahnsen FL. Plasmacytoid dendritic cells (natural interferon-alpha/beta-producing cells) accumulate in cutaneous lupus erythematosus lesions. *Am J Pathol* 2001; 159: 237–243.
8. Sontheimer RD. The management of dermatomyositis: current treatment options. *Expert Opin Pharmacother* 2004; 5: 1083–1099.
9. Sun YN, Lu JF, Joshi A, Compton P, Kwon P, Bruno RA. Population pharmacokinetics of efalizumab (humanized monoclonal anti-CD11a antibody) following long-term subcutaneous weekly dosing in psoriasis subjects. *J Clin Pharmacol* 2005; 45: 468–476.
10. Dedrick RL, Walicke P, Garovoy M. Anti-adhesion antibodies efalizumab, a humanized anti-CD11a monoclonal antibody. *Transpl Immunol* 2002; 9: 181–186.
11. Gauvreau GM, Becker AB, Boulet LP, Chakir J, Fick RB, Greene WL, et al. The effects of an anti-CD11a mAb, efalizumab, on allergen-induced airway responses and airway inflammation in subjects with atopic asthma. *J Allergy Clin Immunol* 2003; 112: 331–338.
12. Vincenti F. New monoclonal antibodies in renal transplantation. *Minerva Urol Nefrol* 2003; 55: 57–66.
13. Kuypers DR, Vanrenterghem YF. Monoclonal antibodies in renal transplantation: old and new. *Nephrol Dial Transplant* 2004; 19: 297–300.
14. Levine TD. Rituximab in the treatment of dermatomyositis: an open-label pilot study. *Arthritis Rheum* 2005; 52: 601–607.
15. Hengstman GJ, van den Hoogen FH, van Engelen BG. Treatment of dermatomyositis and polymyositis with anti-tumor necrosis factor-alpha: long-term follow-up. *Eur Neurol* 2004; 52: 61–63.
16. Greenberg SA, Pinkus JL, Pinkus GS, Burleson T, Sanoudou D, Tawil R, et al. Interferon-alpha/beta-mediated innate immune mechanisms in dermatomyositis. *Ann Neurol* 2005; 57: 664–678.