Letters to the Editors

CD25 blockade for refractory polymyositis

Sirs,

Polymyositis (PM) remains a potentially disabling disorder (1). There is thus an unmet need for novel medications. We report a patient with refractory PM treated with the high-affinity interleukin-2 receptor (CD25) blocker basiliximab.

In 2002 a 42-year-old woman developed proximal muscle weakness. Past medical history revealed Raynaud's phenomenon, photosensitivity, and Hashimoto thyroiditis. Muscle strength was tested in 12 proximal and distal muscle groups by manual muscle test and graded according to the Medical Research Council (MRC) scale translating + and – symbols in decimals as described elsewhere (2). The global MRC score (obtained by dividing the sum of scores of the individual muscles by the number of muscles tested) was 4.32. Creatine kinase (CK) was 6,137 U/l (normal range 25–140), while ANA and extractable nuclear antigens (ENA) were negative. Electromyography demonstrated a myopathic pattern with fibrillations and small, brief motor unit potentials. Muscle biopsy disclosed endomysial lymphocytic infiltration with muscle fibre necrosis and regeneration as well as positive HLA-I staining of muscle fibers, but negative staining for endothelial membrane attack complex and normal dysferlin, cytochrome-c-oxidase and succinate dehydrogenase reactivity.

PM was diagnosed and treatment with prednisone 50 mg/day tapering and methotrexate 20 mg/week commenced. The patient responded well to her treatment, but repeatedly flared upon prednisone tapering. Attempts to control disease activity with low-dose glucocorticoids and combined methotrexate (20 mg/week) plus cyclosporine (3 mg/kg/day) therapy, later replaced by methotrexate plus mofetil mycophenolate (2 g/day), provided only partial benefit. Therefore, after obtaining the patient's written informed consent and Ethics Committee approval, we decided to treat her with adjunctive basiliximab (20 mg iv/monthly for 6 months). Concomitant methylprednisolone 4 mg/day, mofetil mycophenolate 2 g/day, and methotrexate 20 mg/week were left unchanged.

Before treatment, MRC score was 4.37, CK 1196 U/l, and health assessment questionnaire (HAQ) score 0.625. Basiliximab infusions were well-tolerated.

Five months after the onset of basiliximab therapy, MRC score was 4.21, CK 1,354 and HAQ score 0.875. Because of the lack of response (or possibly slight worsening of disease activity), basiliximab was withdrawn before the scheduled sixth infusion.

PM is characterised by endomysial infiltration of cytotoxic CD3+CD8+ and CD3+CD4+ lymphocytes expressing CD25 (3, 4). Interleukin-2 is required in humans to sustain *in vitro* $CD8^+$ lymphocyte expansion (5). Thus, blocking CD25 may theoretically abrogate cytotoxic lymphocyte activity. Also, a patient with systemic sclerosis-associated myositis responded favorably to basiliximab (6). However, basiliximab therapy did not improve muscle strength in our patient. This lack of efficacy could be due to the fact that the CD25 antigen is expressed not only by myotoxic lymphocytes, but also by the T-regulatory cells. CD25-positive T-regulatory cells infiltrate inflamed muscles in myositis and dampen inflammation (7). Therefore, the inhibition of myotoxic lymphocytes by basiliximab might be offset by the concomitant inhibition of T-regulatory cells. Alternatively, blockade of CD25 alone might not suffice to block myotoxic lymphocytes, perhaps because little interleukin-2 is detectable in muscles from patients with active PM (8), and other cytokines such as IL-15 are probably more important in driving the inflammatory response (9). This case suggests that targeting T cell antigens other than CD25, or other immunological pathways, may be required to treat refractory PM. However, more data is required to arrive at a more conclusive judgment on the role of basiliximab in PM.

N. PIPITONE, *MD, PhD*
C. SALVARANI, *MD*

Rheumatology Unit, Department of Internal Medicine, Azienda Ospedaliera ASMN, Istituto di Ricovero e Cura a Carattere Scientifico, Reggio Emilia, Italy.

Address correspondence to:
Dr Carlo Salvarani, Dipartimento di Reumatologia, Arcispedale Santa Maria Nuova, Viale Risorgimento 80, 42123 Reggio Emilia, Italy.
E-mail: salvarani.carlo@asmn.re.it

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