A case of overlap syndrome successfully treated with tocilizumab: a hopeful treatment strategy for refractory dermatomyositis?

Sir, DM and PM are characterized by chronic inflammation of striated muscles and sometimes of the skin (DM). Options for treating these diseases normally include high-dose glucocorticoid therapy, immunosuppressants and IVIG. Tocilizumab is used to treat RA, Castleman’s disease, SLE, Takayasu’s arteritis and other conditions with excellent results [1]. We treated a patient with concomitant DM, SSc and RA using tocilizumab and report that it was effective not only for RA but also for DM.

A 32-year-old Japanese woman was affected by generalized myalgia and sclerema of the palms in 2002. The patient also noticed RP on the hands and ulceration on the fingertips. Physical examination showed proximal limb muscle weakness, heliotrope rash and Gottron’s sign. Sclerema from the fingers to the upper arm, trismus and fingertip ulceration were also observed. Laboratory examination found increased serum myogenic enzymes [creatine kinase (CK) 336 U/l (normal range 36–216 U/l)], aldolase 18.2 U/l (normal range 0.5–3.1 U/l)]. EMG showed a low-voltage myogenic pattern. ANA measurement at 80× (diffuse) and RF at 19 IU/ml (normal value ≤13.5 IU/ml) were increased slightly; however, antibodies against histidyl-tRNA synthetase, topoisomerase I, centromere and U1-RNP were negative. Muscle biopsy showed lymphocyte infiltration surrounding blood vessels and invasion of the perimysium, consistent with DM. We diagnosed the patient with overlap syndrome involving SSc and DM. High-dose prednisolone therapy improved the patient’s muscle weakness and CK elevation. Because the CK level increased and the muscle manifestation worsened further, ciclosporin, i.v. CYC, IVIG and tacrolimus were prescribed, but were ineffective or effective only temporarily. In 2009 the joint of the right wrist was swollen and tender and the CRP level increased to 0.45 mg/dl (normal value <0.2 mg/dl). No abnormalities were observed on X-ray, whereas MRI of the hands showed thickness of the synovium and bone marrow oedema as well as bone erosions in the right carpal bones. Anti-CCP antibody was positive [≥100 U/ml (normal value <4.5 U/ml)]. The patient’s symptoms fulfilled seven points of the ACR/European League Against Rheumatism (EULAR) classification criteria for RA [2]. We diagnosed the patient’s condition as complicated with RA.

MTX and adalimumab were prescribed, but were discontinued because of coughing and CK elevation, respectively. The patient’s heliotrope rash, Gottron’s sign and muscular weakness all gradually worsened. In July 2012 both the RA and DM were judged to be active. The 28-joint DAS with ESR (DAS28-ESR) showed a moderate value of 4.54. We decided to treat the patient with tocilizumab. Her skin symptoms resolved and the swelling and tenderness of the right wrist joint began to improve 1 month after initiating tocilizumab treatment. The DAS28-ESR attained remission, the serum CK level decreased to within the normal range and her muscle weakness improved gradually. Tocilizumab therapy allowed tapering of the glucocorticoid without exacerbation of the patient’s condition (Fig. 1).

Differences in cytokines involved in DM and PM have been reported as well as differences in clinical symptoms and histopathology. In PM and DM patients, Th2/Th1 and Th2/Th17 are increased compared with controls, and this is greater in DM [3]. Ishii et al. [4] also reported Th2 predominance in the peripheral blood of patients with active DM compared with those with PM or healthy controls. Moreover, serum IL-6 level is increased in both diseases, but it is higher in DM compared with PM. While in DM the elevated serum IL-6 level is reversed significantly after treatment, this is not significant in PM [3]. IL-6 mRNA is also elevated in tissue with local inflammation in DM and PM, with IL-6 levels shown to correlate with DM disease activity [5, 6]. These findings suggest that IL-6 plays an important role in inflammatory muscle diseases, particularly DM. While the efficacy of tocilizumab has been reported in two patients with PM showing inadequate
responses to conventional treatments, this was lacking for DM patients [7]. To our knowledge, this is the first report of the efficacy of tocilizumab against DM. Tocilizumab may be effective against DM for which conventional treatment is inadequate.

**Rheumatology key message**

- Tocilizumab may be effective against DM for which conventional treatment is inadequate.

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**References**


