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Successful treatment of refractory mononeuritis multiplex secondary to rheumatoid arthritis with the anti-tumour necrosis factor α monoclonal antibody infliximab

Sir, There is enough evidence to show that single or combined therapies are able to modify rheumatoid arthritis (RA) [1]. However, many patients do not have an adequate response because of toxicity or lack of efficacy. Continuing research into the pathogenesis of RA will lead to the identification of more effective therapeutic approaches for the management of this disease [2]. In a recent article in *Rheumatology* [3], Richter *et al*. showed a successful response to etanercept of mononeuritis secondary to RA. We would like to describe our experience in the treatment of refractory mononeuritis multiplex secondary to RA with infliximab, a monoclonal antibody to tumour necrosis factor α (TNF-α).

A 70-yr-old white woman was admitted to hospital for weakness in both lower extremities. One year previously, she had been referred to our rheumatology out-patient clinic because of a 2-month history of symmetrical polyarthritis involving the elbows, wrists, the metacarpophalangeal and proximal interphalangeal joints of the hands and knees and the metatarsophalangeal joints of the feet, and morning stiffness lasting more than 1 h. She was positive for rheumatoid factor and negative for antinuclear antibodies (ANA), and plain radiographs of her hands and feet did not show cortical bone erosions. She fulfilled the 1987 revised American College of Rheumatology classification criteria for RA [4]. She was treated initially with non-steroidal anti-inflammatory drugs, a low dose of prednisone, and chloroquine (250 mg/day) for 4 months, without significant improvement. Consequently, methotrexate (10 mg/week orally) was added. The methotrexate dose was increased to 15 mg/week orally 4 months later because of inadequate control of RA. Three weeks before admission she had noticed weakness of her right foot, and later she also complained of weakness of her left foot. Physical examination revealed paresis of dorsiflexion and eversion of both feet. Her erythrocyte sedimentation rate was 40 mm in the first hour. The concentration of rheumatoid factor was 98 IU/ml (normally <20 IU/ml). Creatinine, glucose, hepatic function tests, ANA, anti-native DNA, C3, C4, anticardiolipin antibodies, HIV antibody, serology for *Borrelia* and lues, and the urine biochemistry profile were negative or normal. Her chest radiograph was also normal. Electromyography (EMG) showed axonal neuropathy with spontaneous activity, and was consistent with mononeuritis multiplex involving the peroneal, tibial, radial and ulnar nerves. Biopsy of the left sural nerve showed focal and segmental necrotizing arteritis of small and medium-sized arteries with fibrinoid necrosis, and neutrophils as well as lymphomononuclear cells in the artery wall, loss of the thick fibres, and axonal degeneration. Joint space narrowing and cortical bone erosions in the metacarpophalangeal joints of the hands were observed. She was diagnosed as having polyarteritis nodosa related to RA. Therapy with methotrexate was discontinued and she was started on treatment with intravenous boluses of methylprednisolone (1 g/day) for three consecutive days, followed by oral prednisone (initially a dose of 20 mg three times daily). A monthly intravenous bolus of cyclophosphamide for six consecutive months was also prescribed (1 g/m^2 of body surface area), without improvement in the neurological features. Consequently, methotrexate was reinitiated and therapy with anti-TNF-α monoclonal antibody (infliximab) was considered. Infusion of infliximab at a dose of 3 mg/kg body weight was administered according to a previous protocol, at weeks 0, 2, 6 and 14 and then every 8 weeks [5]. Six weeks after the first dose of infliximab the motor dysfunction had regressed markedly. Twenty-two weeks after the start of therapy with infliximab, a new EMG showed only mild signs of residual axonal neuropathy.

Although the underlying cause of RA is unknown, TNF is believed to contribute to the pathogenesis of synovitis and joint destruction [6]. This cytokine has emerged as a promising therapeutic target on the basis of experimental studies employing specific biological inhibitors, such as monoclonal antibodies. Both etanercept and infliximab bind TNF potently and block inflammation by inhibiting the downstream effects of this cytokine [5, 7]. However, there are still deficiencies in our knowledge of this new anticytokine therapy [8]. On the basis of this case report, we wish to emphasize the possibility of considering anti-TNF-α monoclonal antibody therapy in cases of refractory mononeuritis multiplex secondary to RA.

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