

Switching to adalimumab is effective in a case of neuro-Behçet's disease refractory to infliximab

Sirs,

In the last years, several reports have suggested the efficacy of anti-tumour necrosis factor- α (TNF- α) chimeric antibody infliximab in the management of the neurological manifestations of Behçet's disease (BD) (1-5). Recently, a patient of ours developed neuro-Behçet's disease (NBD) while in therapy with infliximab and was cured with the human anti-TNF- α antibody adalimumab. The patient, a 40-year-old man, came to the outpatient clinic of the Rheumatology Department of Lucania in March 2007. The disease had begun three years before with recurrent oral aphthosis, erythema nodosum like-lesions and symmetrical arthritis involving wrists and knees. After one year, papulopustular eruption, recurrent epididymitis and genital ulceration had appeared. In September 2005, he developed bilateral posterior uveitis and was treated with oral steroids until February 2006, when the diagnosis of BD was made and cyclosporine (3mg/Kg/day) was added. In October 2006, because he was a poor-responder to the treatment, the cyclosporine dosage was increased to 3.5mg/Kg/day with partial improvement of the ocular and the mucocutaneous symptoms and signs. Due to a mild increase of serum creatinine, the cyclosporine dose was reduced to 3 mg/Kg/day. Physical examination showed diffuse papulopustular lesions, minor oral aphthae involving the internal surfaces of the lips and the ventral surface of the tongue together with genital scars. Ophthalmological evaluation revealed posterior uveitis in his left eye. The pathology test was negative. HLA typing was positive for the B51 antigen. In September 2007, we added infliximab therapy (5mg/kg) at weeks 0, 2 and 6 and subsequently every 2 months, after obtaining his informed consent. There was such a rapid improvement of symptoms and signs that we decided to stop steroid treatment after the fifth infusion. Unfortunately, seven weeks later, the patient developed a headache of increasing intensity, loss of strength in his legs and subsequently mental confusion together with slight dysarthria. Magnetic resonance

imaging (MRI) showed high signal lesions in thalamus, right mesencephalon and the right frontal subcortical white matter. Cerebrospinal fluid analysis showed 20 white blood cells/mm³ and normal glucose and protein levels. An infectious complication, including tuberculosis, in an immunocompromised patient was excluded. NBD was diagnosed, cyclosporine was stopped and the patient was treated with an infusion of intravenous methylprednisolone at a dose of 1000 mg per day for three consecutive days and, subsequently, with 25mg/die of oral prednisone. Intravenous infliximab was continued at a dose of 5 mg/kg and repeated every five weeks. Cerebral MRI, performed 3 months later, showed only a partial regression of the acute lesions and neurological examination revealed mild left hemiparesis, action tremor and dystonic posture of his left hand. Six months after the initial episode, the disease worsened with oral aphthosis, erythema nodosum like-lesions and genital ulcers, so we decided to switch the anti-TNF- α therapy to adalimumab at a dose of 40 mg subcutaneously every other week, with the resolution of the mucocutaneous manifestations after the first injection. After 2 months of adalimumab therapy, there was an unexpected improvement of the neurological symptoms with the resolution of action tremor, a significant regression of left hemiparesis and the dystonic posture of his left hand. A new MRI showed the complete regression of the active lesions. This case report shows the efficacy of adalimumab in NBD unresponsive to infliximab. The neurological disease of our patient began when he was in a combination treatment with cyclosporine and infliximab. Cyclosporine is well known to be potentially neurotoxic (6). There is also the possibility that the neurological manifestations of our patient are due to cyclosporine toxicity. However, BD patients with more severe ocular disease, as in our case, are at greater risk of developing an usual NBD (7). The efficacy of adalimumab in NBD given after infliximab was suggested by Belzunegui and co-workers in 2008 (2). However, their patient was treated with adalimumab because the disease relapsed one year after the end of a successful course of infliximab therapy and because delayed infusion reactions have been reported in patients receiving a second course of infliximab. Although infliximab is an effec-

tive and promising drug for the treatment of neuro-Behçet's disease in patients with an insufficient response to corticosteroids (1-5), some patients could have an inadequate response. A secondary failure to infliximab could be explained by the development of anti-infliximab antibodies. Our case suggests that a probable lack of efficacy during the treatment with infliximab could be associated to a neurological involvement and, as for other clinical manifestations of BD (5), also in NBD there is place for the switching from one TNF- α blocker to another.

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