Efficacy of infliximab and adalimumab in the treatment of a patient with severe neuro-Behçet's disease

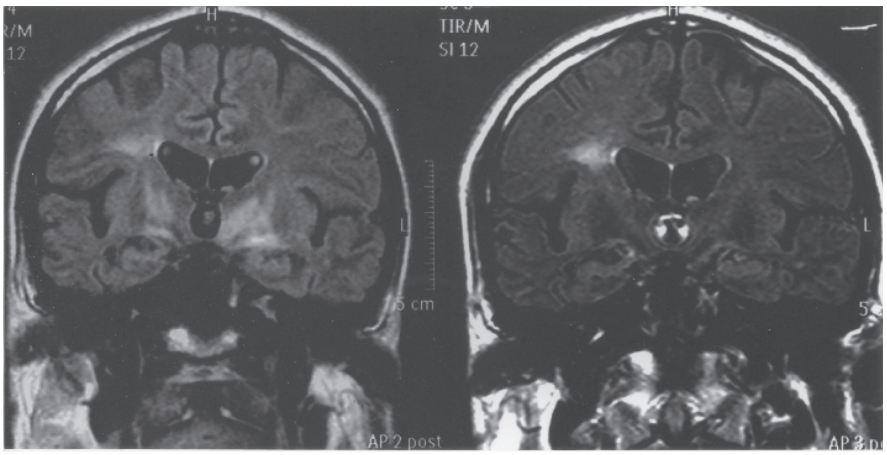
Sirs,

The use of anti-TNF drugs is increasing as part of the strategy for the treatment of systemic vasculitis (1). We present the case of a young man with neuro-Behçet's disease resistant to steroids, cyclophosphamide and azathioprine, who was successfully treated, first with infliximab and, one year later following new complications, with adalimumab.

The patient was a 36-year-old man who had been diagnosed 10 years earlier as having Behçet's disease (BD) on the basis of recurrent oral ulcers, cutaneous folliculitis and bilateral anterior and posterior uveitis. He received treatment with cyclosporine for 10 years. After this period of time (while receiving cyclosporine 200 mg/day) he was admitted to hospital because of progressive difficulty in walking. On exploration left hemiparesis and a positive left Babinski's sign were present. Magnetic resonance imaging (MRI) showed a high-signal intensity right hemispherical lesion on T2-weighted images. Cerebral vasculitis was suspected and he was treated with corticosteroids (3 bolus of 1 g methylprednisolone followed by oral prednisone 60 mg/day for one month, with gradual scheduled tapering thereafter) and a monthly bolus of cyclophosphamide (1 g). Hemiparesis and the hemispherical lesion on MRI remained stable.

After 6 boluses of cyclophosphamide the patient was re-admitted with spastic paraparesis. A new MRI showed persistence of the right hemispherical lesion and several new lesions in the cervical and dorsal spinal cord. Intravenous cyclophosphamide plus oral corticosteroids were considered ineffective and a regimen of 4 doses of infliximab (3 mg/kg at weeks 0, 2, 4 and 8) was empirically administered with good results and disappearance of the spinal lesions. No adverse reactions were seen. After this the patient received maintenance therapy consisting of steroids (similar doses with scheduled tapering) and azathioprine (2.5 mg/kg/day).

One year later he was re-evaluated because of progressive difficulty in walking that had been increasing over the last 4 weeks. On physical examination new spastic right hemiparesis with positive bilateral Babinski's sign were identified. MRI showed 2 new bilateral hemispherical areas of high signal intensity (Fig. 1A). Because delayed infusion reactions (myalgia, arthralgia, fever, rash, pruritus, facial edema, dysphagia, urticaria, sore throat and headache) have been described in patients receiving a second course of infliximab, we decided to treat him instead with adalimumab (40 mg every other week). Three months later, the patient had clearly improved and only one residual right hemispherical lesion was observed on MRI (Fig. 1B). To date, 2 years later, a standard regimen of adalimumab is being administered with stabilization of the neurological manifestations. New MRI have failed to detect any lesions apart from the one previously mentioned.



A **B**

Fig. 1. Magnetic resonance imaging on T2-weighted images showing 3 hemispherical areas of high signal intensity (**A**). After 6 doses of adalimumab only one residual lesion persisted (**B**).

Neurological involvement is a serious complication of BD and affects 5% of patients. Focal parenchymal lesions and complications of vascular thrombosis are the most common abnormalities. Aseptic meningoencephalitis, arterial vasculitis and psychiatric complications may also develop. These have been reported more frequently in patients receiving cyclosporine, although the reasons for this are unclear (2).

Potentially life-threatening neurological complications of BD should be treated as posterior uveitis. In these cases, in addition to high-dose corticosteroids a second drug – anti-TNF agents, cyclophosphamide, cyclosporine or azathioprine – is usually needed. The selection of one of these over the others remains empirical due to the lack of comparative studies. There have been few reports analysing the efficacy of anti-TNF agents in the treatment of BD. The majority of these are isolated cases, generally involving the use of infliximab in patients with ocular involvement with good results (3). Few cases of the treatment of neurological manifestations with infliximab have been reported (4-6). Only anecdotal reports mention the use of etanercept (7) or adalimumab (8) in BD, and none of these have involved the nervous system.

A review report stemming from an expert panel meeting has recently been published. It includes recommendations on the use of anti-TNF agents for this condition. According to the authors, infliximab can be considered as the drug of first choice in patients with severe unilateral or bilateral posterior uveitis. Referring to the nervous system, they recommend its use in parenchymal central nervous system involvement when manifestations are refractory to pulse cyclophosphamide and corticosteroids, or in patients who relapse while on maintenance therapy with azathioprine and prednisolone (9).

Interestingly, although autoantibodies have been detected in patients with BD on infliximab therapy, its pathogenic role has not been yet elucidated (10).

In our case, the lack of response to pulse cyclophosphamide and corticosteroids, as well as the severity of the clinical picture, led us to empirically try infliximab. This therapy was followed by excellent initial results. It should be pointed out that due to the low dose administered (4 infusions of 3 mg/kg/day each) the risk of a secondary attack was possible. After stopping infliximab new brain lesions did develop. A regimen of adalimumab was introduced and these lesions disappeared. For this reason treatment with adalimumab has been continued.

In conclusion, the blockade of TNF-α with either infliximab or adalimumab could offer a good treatment option in patients with BD and severe neurologic complications that are resistant to other immunomodulatory drugs.

J. Belzunegui
L. López
I. Paniagua
J.J. Intxausti
O. Maíz

Rheumatology Department, Hospital Donostia, San Sebastián, Spain.

Address correspondence to:
Dr. Joaquín Belzunegui, Rheumatology Department, Hospital Donostia, 20013 San Sebastián, Spain.
E-mail: belzunegui@chdo.osakidetza.net

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