Use of Anti-Tumor Necrosis Factor Drugs in a Patient With Neurological Complications of Behçet's Disease

To the Editor: Anti-tumor necrosis factor (TNF) drugs are useful in the treatment of mucocutaneous, ocular, and intestinal complications of Behçet's disease (BD).[1-6] As far as we are aware of (MEDLINE search, descriptors Behçet, TNF, infliximab, and etanercept, between 1990 and 2005), only 2 published cases of BD with neurological complications have been treated with anti-TNF.[7,8] The case of a patient with serious and refractory ocular and neurological complications of BD and treated with anti-TNF is communicated in the lines below.

A 25-year-old woman, diagnosed with BD in 1995 after presenting oral and genital relapsing aphtosis, arthritis, erythema nodosum, and posterior uveitis. She was treated with glucocorticoids (GC, indicated during every flare of posterior uveitis at a dose of 60 mg/day deflazacort at the start of every cycle of treatment until its suspension), cyclosporine A (CsA, 5 mg/kg/day since 1996), and interpheron alfa-2b (6×10^6 U 3 times a week for 1 year) for uveitis. She was hospitalized in May of 1998 due to right hemihypoesthesia and instability, which resolved spontaneously after 72 h. The magnetic resonance (MR) was normal and the brain single photon emission computed tomography (SPECT) showed focal areas of low uptake in the frontotemporal lobes and left cerebellum (Figure 1). In January 2000 she was hospitalized again due to lymphocytic meningitis and posterior uveitis. The MR showed high uptake lesions in the bulboprotuberance region, as observed in T2 (Figure 2). GC was added (60 mg of deflazacort/day p.o., with a gradual reduction after improvement) as well as methotrexate (MTX, 7.5 mg/week) to the treatment based on CsA, with a resolution of symptoms. She was hospitalized again after a month with oral aphtous lesions, meningitis, vertigo, dyplopia due to left cranial nerve III and VI lesions as well as paresthesia and right hemiparesia. The cerebrospinal fluid was cloudy, with a pleocytosis of 1218 cells (95% polimorphonuclear), with 80 mg/dL of total protein, glucose 45 mg/dL and a negative culture for fungi and bacteria. MR once again evidenced confluent lesions in the bulboprotuberance region, similar to the ones seen a month earlier. A 1 g methylprednisolone/day pulse was administered for 5 days, but at the sixth day the patient fell into a coma. She improved progressively with bolus cyclophosphamide (CF, 750 mg/15 days) i.v. Nonetheless, she was hospitalized once again in April of the same year with tetraparesia and secondary respiratory failure that needed assisted mechanical ventilation. She improved after 5 i.v. steroid bolus and repeated doses of CF (6 doses every 15 days in total). At discharge, CF was substituted for chlorambucil (CB, 10 mg/day, p.o.), associated with CsA, for remission maintenance. Afterwards, CB was interrupted temporarily in several occasions due to pancytopenia, being substituted for tacrolymus (6 mg/12 h) due to recurrence of uveitis. In February 2002, after a new bout of optic neuritis and instability, she was treated

Figure 1. *Brain single photon emission computed tomography, which shows focal hypoperfusion in a left cerebellar and frontotemporal distribution (right of the image).*

Figure 2. *Magnetic resonance which shows high uptake T2 lesions in the bulboprotuberance area.*

with infliximab (IFX, 3 mg/kg on weeks 0, 2, 6, and every 8 weeks after that) associated to the previous treatment with GC, CB, and MTX. After a favorable response, all medication except IFX and MTX was suspended. The patient stayed in remission for 9 months and was hospitalized again for headache, instability and right hemiparesia that evolved into tetraparesia. MR was normal and SPECT detected a low uptake focal lesion in the pre-Rolandic left area. She was treated with GC (60 mg/day of deflazacort), i.v. CF (750 mg/month) and a new dose of IFX (5 mg/kg, 3 weeks after the last dose). Due to the persistence of symptoms, Mycophenolate Mophetyl was added (MFM, 2 g/day), reaching clinical remission. Since then (November 2002), the patient has been hospitalized 4 more times due to neurological symptoms (headache, dizziness, instability, and weakness associated to paresis in 1 or several extremities). In this interval, IFX (administered between December 2002 and November 2003) was substituted by etanercept (25 first ant then 50 mg, twice a week), that was started in January 2005 and was suspended in May of the same year, and multiple cycles of GC were administered (between 1 and 5 bolus dose in each internment, followed by the previously described oral treatment) and 2 6-monthly cycles of megadose i.v. CF (same dose as used previously, with an accumulated dose of 13.5 g).

The neurological complications of BD are among the most severe. Our group has dedicated special attention to them.[9] Licata et al[7] and Sarwar et al[8] treated several patients with neurological complications with IFX, having favorable responses in the short and median terms. The patient described above has been followed for 46 months after the start of treatment with anti-TNF medication. Though initially she showed some improvement, always with complex immunosuppressant doses, efficacy was eventually lost, and faced with the possibility that anti-TNF therapy could negatively influence the neurological symptoms, a circumstance that has been widely debated,[10] it was definitely suspended.

Francisco José García Hernández, Celia Ocaña Medina, Rocío González León, Rocío Garrido Rasco, and Julio Sánchez Román

Servicio de Medicina Interna, Unidad de Colagenosis, Hospitales Universitarios Virgen del Rocío, Sevilla, Spain

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