Anakinra for resistant Behçet uveitis: why not?

Sir,

Behçet syndrome (BS) is a systemic vasculitis characterised by mucocutaneous and articular manifestations, recurrent thrombosis/thrombophlebitis, central nervous system and gastrointestinal involvement. Panuveitis and retinal vasculitis are among the major and more frequent manifestations of disease, occurring in 60–80% of patients, and often result in blindness over a few years if untreated; of note, up to 20% of patients may loose useful vision despite a correct and early treatment. Local or systemic corticosteroids associated with traditional immunosuppressive drugs have been the main therapeutic choice for years. Recently, some new evidence has suggested that biologic therapy may be effective in refractory cases, especially in those with ocular manifestations (1, 2).

We describe the case of a 27-year-old woman with a BS diagnosed in 2006 according to the 1990 ISGC criteria for the presence of recurrent oral and genital ulcers and pseudofolliculitis of the trunk, arthtritis/arthralgia of knees, ankles and wrists and abdominal pain with diarrhoea. Since 2007 she also presented a severe ocular involvement with bilateral retinal vasculitis and reduced visual acuity and, in another hospital, she had been already treated with intravenous pulse corticosteroid therapy (then orally tapered at an intermediate dosage of prednisone 0.5 mg/kg/day) and azathioprine (2 mg/kg/day), which after a few months the patient had discontinued due to deep fatigue and nausea. Infliximab had been then started at a dose of 5 mg/kg with improvement of ocular, gastrointestinal and articular symptoms, but after 3 months it had been interrupted due to adverse reaction (diffuse urticaria with angioedema). Infliximab had been switched to adalimumab (40 mg every 2 weeks), with recurrence of uveitis and visual loss after 6 months; due to resistance to anti-TNF-α, rituximab had been finally started, with improvement of joint symptoms but persistent uveitis.

At our first evaluation in May 2012 the patient had recurrent oral ulcers and pseudofolliculitis with arthralgia of the wrist and diarrhoea. Laboratory data showed a mild microcytic anaemia and an increased erythrocyte sedimentation rate. The ophthalmologic evaluation showed a 2+ vitritis, an hyperaemic optic nerve head and diffuse peripheral retinal vasculitis in the right eye (RE) and 1+ vitritis and mild peripheral retinal vasculitis in the left eye (LE). Best corrected visual acuity (BCVA) was 20/50 in RE and 20/32 in LE. Due to multiple resistances/ineffectiveness to other immunosuppressive/biologic therapy, anakinra was started at the dosage of 100 mg/day, with rapid and persistent disappearance of joint pain, mucocutaneous and bowel manifestations; after 3 months a new ophthalmological evaluation with fluorescein angiography demonstrated a regression of ocular inflammation with complete clearing of the vitreous opacity and restoration of the retinal-blood barrier in both eyes (OU). Retinal vessels, previously characterised by vasculitic leakage of the fluorescein die, showed pigmentary and fibrotic changes of the perivascular tissues but no residual active inflammation (Fig. 1). BCVA appeared restored to 20/20 in OU.

Interleukin-1 (IL-1) is an active pro-inflammatory cytokine and blocking his activity in rheumatoid arthtritis (RA) and autoinflammatory syndromes results in a reduction of disease severity. Anakinra is a recombinant form of human IL-1 receptor antagonist, that is approved for the treatment of RA in combination with methotrexate, which acts by competitively inhibiting the local inflammatory effects of IL-1 (3). Nowadays many immunomodulating drugs can be useful in BS for refractory patients or to taper corticosteroids; anti-TNF-α drugs have been used succesfully in recent years, especially for neurological and ocu-

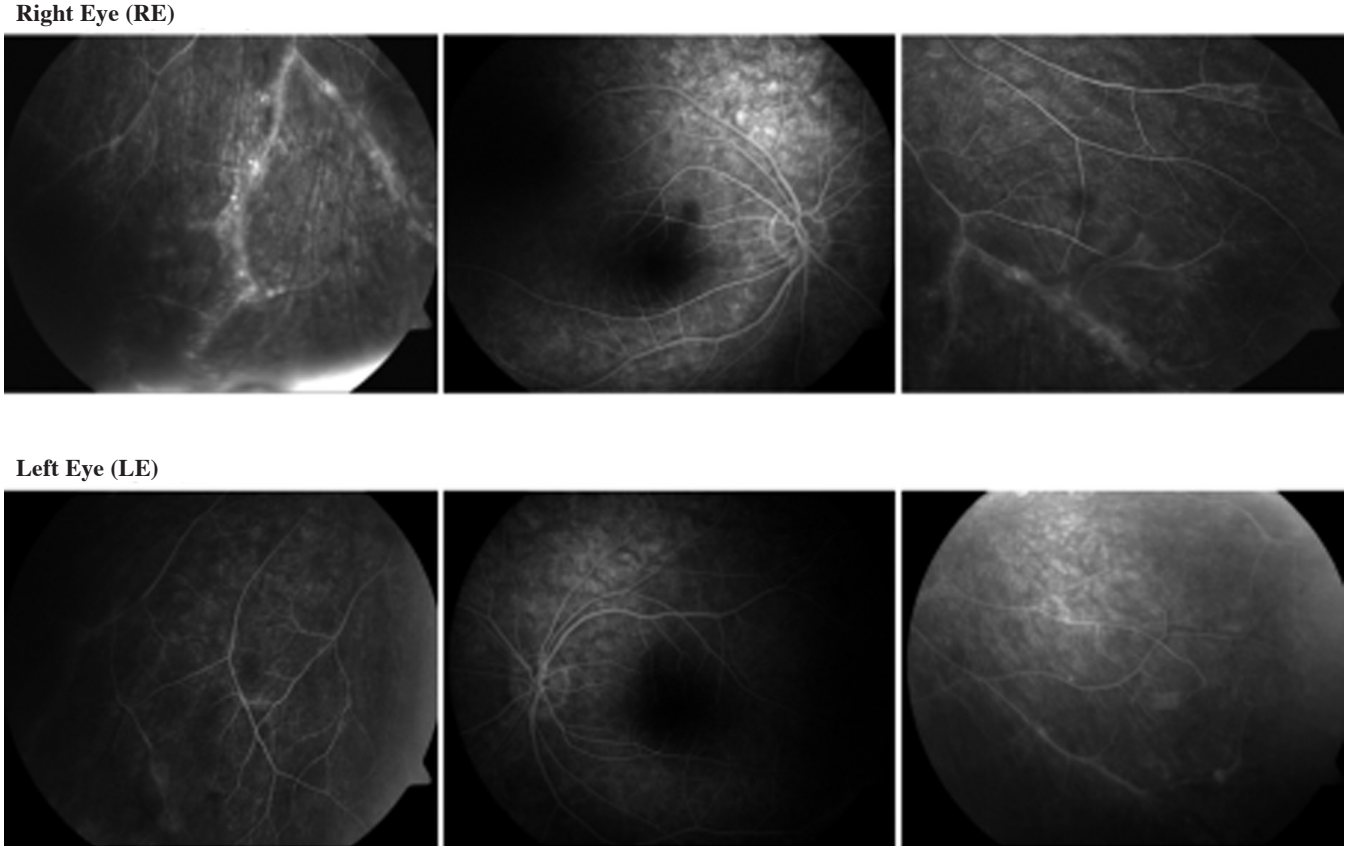

Fig. 1. Fluorescein angiography 3 months after therapy with anakinra.

lar manifestations (2). More recently IL-1 beta inhibition proved successful in ocular involvement in BS (7 patients with gevokizumab and 2 patients with canakinumab) (1, 4). Of note, anakinra had been successfully used only in a patient with a prevalent mucocutaneous involvement (5) and, to the best of our knowledge, this is the first description of its efficacy in ocular disease of BS.

After 12 months of treatment the patient no longer experienced flare of disease and especially no symptoms of uveitis or retinal vasculitis are currently present; moreover, there were no adverse drug reactions. Our patient had presented since the beginning of the disease a very severe ocular involvement, resistant to different therapies (in particular anti-TNF-α and anti-CD20), indicating a not self limiting course of disease. This case report suggests that anakinra may be an effective alternative for successful treatment in refractory BS eye involvement in those patients unresponsive to other immunosuppressive drugs or biological therapy. However, controlled trials on a larger number of patients will be necessary to confirm these observations and also a long-term evaluation of the optimal dosage and duration of treatment and of its long term possible side effects will be crucial.

G. EMMI[2]
E. SILVESTRI[1,2]
A.M. CAMELI[2]
D. BACHERINI[3]
L. VANNOZZI[3]
D. SQUATRITO[1,2]
L. EMMI[1]

[1]SOD Patologia Medica, Centre for Autoimmune Systemic Diseases – Behçet Centre and Lupus Clinic – AOU Careggi, Florence, Italy;
[2]Department of Experimental and Clinical Medicine, University of Florence, Italy;
[3]SOD Oculistica, Azienda Ospedaliero-Universitaria Careggi, Florence, Italy.

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Address correspondence to: Dr Giacomo Emmi, Dept. of Experimental and Clinical Medicine, University of Florence, L.go G. Brambilla 3, 50134 Firenze, Italy.
E-mail: giacomaci@yahoo.it

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