Efficacy of anakinra in refractory Behçet's disease sacroiliitis

Response to: Anakinra for resistant Behçet uveitis: why not?

EMMI G, SILVESTRI E, CAMELI AM *et al*.: *Clin Exp Rheumatol* 2013; 31 (Suppl. 77): S152-3.

Sirs,

We read with great interest the article by Emmi G *et al*. (1) describing the case of a 27-year-old woman with Behçet's disease (BD): the patient showed recurrent aphthosis, skin lesions, and severe bilateral retinal vasculitis. She also complained of musculoskeletal involvement, abdominal pain, and diarrhoea. The authors reported the early withdrawn of both azathioprine and the tumour necrosis factor (TNF)-α neutralizing agent infliximab due to the onset of adverse events. In addition, corticosteroids, the anti-TNF-α agent adalimumab, and the anti-CD20 monoclonal antibody rituximab failed to induce a good control of disease activity. Later on, this patient started treatment with the recombinant form of human interleukin (IL)-1 receptor antagonist anakinra, at the dose of 100 mg/daily subcutaneously, which allowed her to achieve a prompt stable remission of all clinical manifestations, maintained at the 12-month follow-up visit with no adverse events. Following these intriguing results, the authors advocated further studies on a large number of patients in order to confirm the efficacy and safety of anakinra in treating BD. To this end, we would like to present our additional data on anakinra efficacy in managing BD-related sacroiliitis.

A 36-year-old male was admitted to our Unit for recurrent oral and genital ulcerations, pseudofolliculitis, severe bilateral panuveitis with retinal vasculitis and sacroiliitis. At admission, laboratory investigations revealed increased inflammatory markers. Homocysteinaemia, antithrombin III, protein C, protein S, and factor V were normal. The HLA-B51 allele was positive. The patient fulfilled the International Study Group Criteria and was diagnosed with BD (2).

Over the past years he had been treated with cyclosporine A (3–5 mg/kg/day), several cycles of pulsed intravenous methylprednisolone, non-steroidal anti-inflammatory drugs (NSAIDs), and prednisone (PDN) (up to 50 mg/daily). Each of these drugs failed to induce an adequate clinical remission. Infliximab had been also administered (at a dose of 5 mg/kg/monthly), resulting in an initial satisfying disease control, but was withdrawn after 5 years due to loss of efficacy with several flares of sacroiliitis. Magnetic resonance imaging (MRI) showed subchondral bone marrow oedema involving both sacroiliac joints, with associated sclerosis and erosions. NSAIDs were resumed and PDN dosage increased (to 50 mg daily), but no remission was obtained. Anakinra (at a dose of 100 mg/day) was then started, and a few days later the patient became symptom-free, while acute phase reactants returned to normal. PDN was gradually tapered (to 5.0 mg/daily) and NSAIDs were interrupted. The improvement of symptoms was maintained for six months, and no adverse events occurred. In addition, MRI performed 8 months after starting anakinra showed the complete resolution of sacroiliac subchondral bone marrow oedema.

The aim of BD treatment is to prevent irreversible multi-systemic damage, and an ideal therapy should be tailored according to the extent and severity of different clinical manifestations (3). Multiple cytokines likely contribute to the pathological scenery of BD, and it is doubtful that blocking a single cytokine will resolve all of protean disease manifestations (4). Convincing evidence for a role of IL-1β in BD derives from a trial of the monoclonal anti-IL-1β antibody gevokizumab in patients with multi-resistant uveitis: following a single dose of gevokizumab there was a sustained reduction of uveal inflammation with improvement in visual acuity (5). Recently, two reports (one from our group) have been published on the successful treatment of BD with canakinumab (6, 7). Also anakinra recently showed to induce a significant remission in BD (1, 8-10). We recently reported a case series of 9 BD patients, in whom 7 out of 9 patients responded to 100 mg/day of anakinra (10); one of the remaining 2 patients showed a complete clinical remission by increasing the dose to 150 mg/day, with no adverse event. In conclusion, our additional case of BD-related sacroiliitis responding to anakinra demonstrates the usefulness of IL-1 antagonists in the management of BD. Nevertheless the number of published reports is still low, making difficult to draw firm and definite conclusions. Therefore, in agreement with Emmi *et al*., we believe that further investigation involving a wider population with BD with a longer-term follow-up and a control group are needed to corroborate these recent observations.

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