Reply

Anti-IL1 blocking agents in drug-resistant Behçet's syndrome: our *little* case series

Sirs,

We really thank Dr Caso *et al*. for their comments to our article and for their case report, which further confirm the good response to anakinra in refractory Behçet syndrome (BS), in this case complicated with sacroiliitis involvement. Cantarini *et al*. in a recent larger case series (1) also reported the efficacy and safety of anakinra in 9 patients with BS. In our experience the IL-1 receptor antagonist anakinra showed efficacy in another patient with a different disease phenotype (muco-cutaneous, articular and intestinal), while the human monoclonal anti-IL-1β antibody – canakinumab – was successfully used for BS patient with severe ocular involvement. Notably, both patients, who presented a BS diagnosis according to the International Study Group Criteria, had previously been treated with several immunosuppressive and biological therapies.

In the first case we describe a 26-year-old woman with BS diagnosis for the presence of recurrent oral ulcers, pseudofolliculitis, erythema nodosum and positive pathergy test. She also had complained abdominal pain with diarrhoea (with non-specific signs of inflammation at colonscopy) and hands, wrists and knees arthritis with elevation of inflammatory markers. At our first evaluation the patient had already been treated with azathioprine (AZA, 2 mg/kg/day), cyclosporine A (CSA, 3 mg/kg/day) and methotrexate (15 mg/week), all discontinued due to gastrointestinal symptoms. Infliximab (IFX) had also been used at a dose of 3–5 mg/kg with improvement of all symptoms, but after 12 months this treatment had been interrupted due to the occurrence of intense fatigue and switched to adalimumab (ADA, 40 mg every 2 weeks). However, also this biological drug had been interrupted early, since the patient had experienced generalised malaise, occurring soon after injections. The patient had also been already treated with intravenous pulse corticosteroid therapy and then with an oral regimen. For the control of muco-cutaneous, articular and intestinal symptoms and systemic inflammation, anakinra was started at a dose of 100 mg/day, with a rapid clinical improvement and normalisation of acute phase reactants; at 8 months of follow-up the patient maintains a good response with no serious adverse reactions.

In the second case we present a 39-year-old man fulfilling BS criteria for the presence of recurrent oral aphthosis, erythema nodosum, bilateral retinal vasculitis with reduced visual acuity. The patient had been previously treated with AZA (2 mg/kg/day) and CSA (3–5 mg/kg/day), interrupted for inefficacy, and later with IFNα-2a (3MU/day), not tolerated for intense flu-like symptoms. The patient had started infliximab therapy (5 mg/kg) with an initial good response in visual acuity. However after a few months the drug had been stopped because of loss of efficacy and switched to adalimumab, which determined only a poor improvement of the ocular manifestations; fluorescein angiography subsequently confirmed the presence of residual active vasculitis at the right eye with reduced visual acuity. Due to the refractoriness to conventional immunosuppressive and biological agents, the patient was treated with canakinumab (150 mg/8 weeks) with good control of eye symptoms, considering that no flares during the 6-month follow-up period were observed.

Recently, a 33-year-old BS patient with severe muco-cutaneous manifestations, recurrent balanitis and prostatitis (without underlying infectious causes) and abdominal pain with diarrhoea, resistant to traditional treatment, has started anakinra therapy (100 mg/day), however clinical and laboratory data are not yet available.

As mentioned by Caso *et al*., BS is a systemic inflammatory disease with protean manifestations (2) and so the treatment can be different on the basis of the district predominant involved; the discovery of new immunopathological pathways underlying BS pathogenesis can partly explain the efficacy of the new biologic agents (3). In particular, anti-TNF-α agents proved to be effective in controlling all the manifestations of BS, particularly muco-cutaneous, neurological, ocular and vascular (3, 4); recently, growing evidence is coming from different case reports (6-10), case series (1) and from an open-label study (5), suggesting that IL-1 blocking agents might be alternative therapies to anti-TNFs, particularly useful for refractory BS patients, with or without severe ocular involvement.

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