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Letter to the Editor

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Short-term efficacy of abatacept in the treatment of refractory ocular and cutaneous Behçet's disease

Key message

- Abatacept may be effective for different manifestations of Behçet's disease.

Sir, Behçet's disease (BD) is a chronic systemic vasculitis characterized by recurrent oral and genital ulcers, skin lesions and uveitis [1]. Treatment of cases refractory to conventional treatment is a challenging task and biologic treatments are arising as promising therapies, particularly anti-TNF agents [2]. However, cases unresponsive to anti-TNF therapy are also observed and new treatments must be chosen among the plethora of available biologic therapies based on case reports or a physiopathological basis.

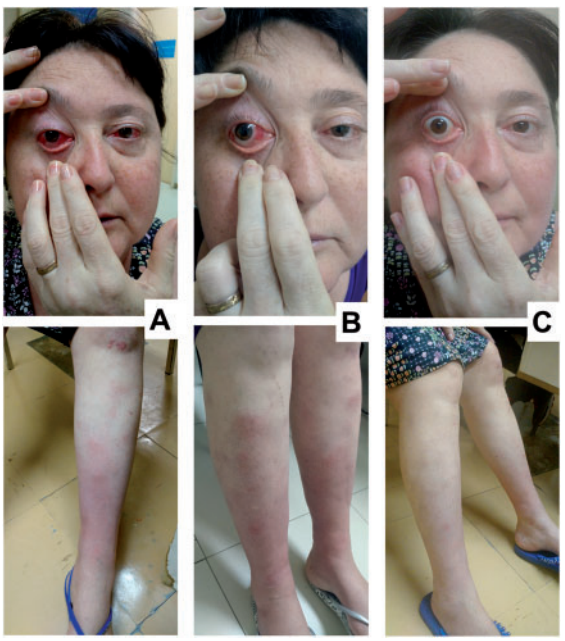
There are reports of therapeutic success with anti-IL-1β (anakinra and canakinumab), anti-IL-6 (tocilizumab), anti-IL-23 (ustekinamb) and anti-CD20 (rituximab) agents [3, 4]. In this report we describe treatment with abatacept of a refractory case of BD with ocular and skin manifestations.

A 47-year-old woman was diagnosed with BD based on the recurrence of oral ulcers, genital ulcers and erythema nodosum. She also had major vessel involvement with subclavian and renal arteries stenosis. She was treated with corticosteroids, which reduced the frequency and severity of symptoms but contributed to uncontrolled diabetes mellitus. Azathioprine, cyclosporin and etanercept were not effective in controlling the disease. She had a severe infusional reaction to infliximab, precluding its use. When she was on methotrexate 20 mg/week and prednisone 40 mg/day she complained of ocular pain and diffuse conjunctival and scleral hyperaemia in both eyes. On biomicroscopic examination there was no anterior chamber reaction or any signs of anterior, intermediate or posterior uveitis. There were no complaints of low visual acuity and she had normal pupillary reflexes. The diagnosis of diffuse anterior scleritis was defined and attributed to BD activity, as extensive painful erythema nodosum (confirmed by biopsy showing septal panniculitis) was also present. The C reactive protein (CRP) serum level was 92 mg/l (Fig. 1A). Because diabetes was uncontrolled (haemoglobin A1c 9.8%), the prednisone dosage was not increased. Ocular dexamethasone was used for 4 weeks without improvement. Tocilizumab was considered, but due to the severity of symptoms and immediate availability of abatacept, the patient agreed to receive it as infusions.

She received 750 mg i.v. of abatacept. After 2 weeks, CRP decreased to 7.5 mg/l and there was partial improvement of scleritis and erythema nodosum (Fig. 1B). She then received 500 mg i.v. of abatacept and after 2 weeks there was complete resolution of her symptoms (Fig. 1C). She remained free of symptoms for 4 weeks after the last infusion of abatacept, when a sudden flare of disease occurred with the same manifestations and similar CRP levels as before abatacept treatment (96 mg/l). After that, the patient started therapy with tocilizumab and a similar response was obtained.

TNF, IL-1β, IL-6 and IL-23 are all reported to be involved in BD physiopathology [5]. However, it is important to note that there are also reports of therapeutic failure in blocking these cytokines. Because tocilizumab was reported to be efficacious in uveitis but not in mucocutaneous BD, it was proposed that there are different pathogenic mechanisms involved in different clusters of clinical expression of BD, each one with its specific pattern of

Fig. 1 (**A**) Presentation with diffuse anterior scleritis and extensive erythema nodosum. C reactive protein (CRP) was 92 mg/l. Patient received an infusion of 750 mg of abatacept. (**B**) Two weeks after the first infusion, the patient returned with partial improvement of symptoms. CRP was 7.5 mg/l. The patient received a second infusion of 500 mg of abatacept. (**C**) Two weeks after the second infusion, there was complete resolution of symptoms.



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effector cytokines [6]. A connection between different effector mechanisms in BD could be the relation of disease flares with microbial triggering [7]. We hypothesize that interfering with antigen presentation could be a valid therapeutic approach for several BD manifestations if they depend on the presentation of microbial antigens to T cells. Abatacept prevents the delivering of the second signal to T cells, which is necessary to activate them after antigen presentation. As far as we know, this is the first report of abatacept use in BD. Its efficacy in anti-TNF refractory uveitis was described in JIA [8].

There is some evidence of causality between abatacept infusion and the evolution of our case: there was a close temporal relation between the start of therapy and disease improvement, with a dose–response relationship (partial improvement after the first infusion, complete improvement after the second infusion) and a new exacerbation exactly 4 weeks after the last infusion. Although this was not a case of uveitis (usually the most severe ocular manifestation of BD), this patient was refractory to all other tested therapies. Thus we suggest that abatacept may be effective for treatment of BD, including different manifestations such as ocular and cutaneous disease.

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