Letters to the editor

Successful treatment of recalcitrant genital ulcers of Behçet's disease with adalimumab after failure of infliximab and etanercept

Sirs,

Tumor necrosis factor α (TNF-α) antagonists have been the most significant advancement in the management of Behçet's disease (BD) (1, 2). All three available anti-TNF-α blockers have been shown to be effective on ocular (3, 4), neurological (5-7) and severe mucocutaneous manifestations (8-12). Severe, recalcitrant and therapy-resistant orogenital ulceration is a challenging problem in BD (8-10, 12). We have successfully treated a case of severe and recalcitrant orogenital ulceration by switching among the anti-TNF-α blockers.

A 47-year-old man suffering from HLA-B51 positive BD for 6 years was referred to us in February 2006 due to severe oral and genital ulcers which had not responded to traditional therapy including colchicine, thalidomide, cyclosporine, azathioprine and high doses of corticosteroids. Each drug was given alone or in combination at therapeutic doses and for a sufficiently long period of time. His disease was characterized by exclusive muco-cutaneous lesions including recurrent major apthosis, large and painful genital ulcerations and papulo-pustolosis.

Physical examination showed large oral apthae involving the gengivae, the internal surfaces of the lips and cheeks and the ventral surface of the tongue, papulo-pustular lesions on the chest and large painful genital ulcers involving the majority of scrotal skin together with penile skin and glans penis. The pain was so severe that the patient had difficulty in walking.

Laboratory evaluation was unremarkable except for a mild increase of C-reactive protein (CRP) to 12.5 mg/L (normal <5).

After obtaining his informed consent, we began intravenous infliximab therapy at a dose of 5 mg/kg at weeks 0, 2 and 6 and every two months subsequently. After the first three infusions, the mucocutaneous lesions disappeared completely. Unfortunately the disease flared after the fifth infusion so that the sixth infusion was anticipated by a month. No results were obtained. In October 2006, the patient was given etanercept at a dose of 50 mg/week subcutaneously. The drug was ineffective also after the increase of the dose to 100 mg/week. In February 2007, we switched to adalimumab at a dose of 40 mg every other week subcutaneously. The genital ulcers and the oral apthae were of the same severity as one year before (Fig. 1A). There was an important improvement of the lesions after the first injection and the complete resolution after the second one (Fig. 1B). So far, the disease has remained in complete remission.

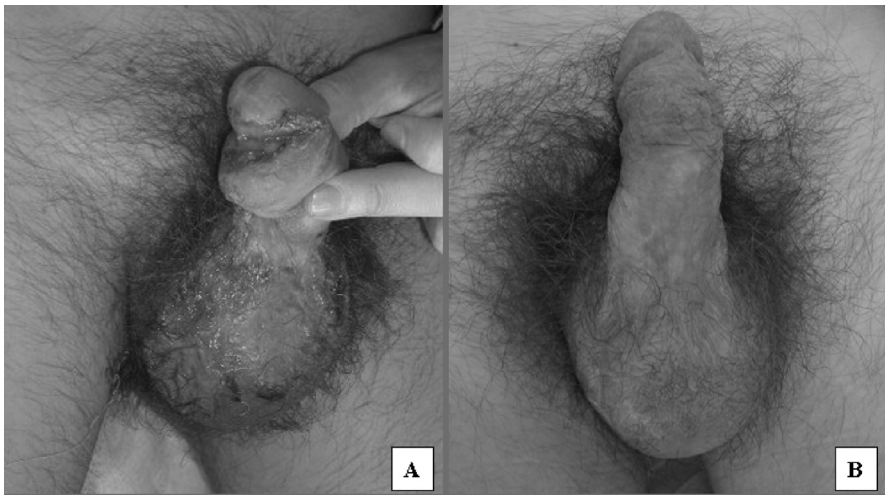

Fig. 1. Genital ulcers of the scrotal and penile skin and glans penis. **A.** Before the first injection of adalimumab. **B.** After the second injection, 4 weeks from the beginning of therapy.

The present case permits us to make the following considerations: 1) recalcitrant and severe orogenital ulceration can successfully be treated with anti-TNF-α therapy. We confirm the observation by Robertson and Hickling (7) and Haugeberg *et al*. (9) who successfully treated similar cases with infliximab. 2) As suggested by Estrach et al. (8), who obtained good results on orogenital ulceration with infliximab after failing etanercept, the switch from one TNF-α blocker to another can also be useful in BD. 3) There can be a difference in the efficacy in BD between the soluble receptor etanercept and the monoclonal antibodies infliximab and adalimumab. Our patient responded temporarily to infliximab, had no response to etanercept and experienced a long-lasting remission with adalimumab. 4) Our patient was treated with anti-TNF-α therapy alone since he was resistant to conventional treatment. He had a complete remission with adalimumab. If the response had been partial we could have added azatioprin with the intention to enhance efficacy (2).

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References

1. HATEMI G, SILMAN A, BANG D et al.: EULAR recommendations for the management of Behçet's disease: report of a task force of the European Standing Committee for International Clinical Studies Including Therapeutics (ESCISIT). *Ann Rheum Dis* 2008 Jan 31; [Epub ahead of print].
2. SFIKAKIS PP, MARKOMICHELAKIS N, ALPSOY E *et al*.: Anti-TNF therapy in the management of Behçet's disease--review and basis for recommendations. *Rheumatology* (Oxford) 2007; 46: 736-41.
3. SFIKAKIS PP, KAKLAMANIS PH, ELEZOGLOU A, KATSILAMBROS N, THEODOSSIADIS PG, PAPAEFTHIMIOU *et al*.: Infliximab for recurrent, sight-threatening ocular inflammation in Adamantiades-Behçet disease. *Ann Intern Med* 2004; 140: 404-6.
4. MUSHTAQ B, SAEED T, SITUNAYAKE RD, MURRAY PI: Adalimumab for sight-threatening uveitis in Behçet's disease. *Eye* 2007; 21: 824-5.
5. PIPITONE N, OLIVIERI I, PADULA A *et al*.: Infliximab for the treatment of Neuro-Behçet's disease: a case series and review of the literature. *Arthritis Rheum* 2008; 59: 285-90.
6. VAN LAAR JA, MISSOTTEN T, VAN DAELE PL, JAMNITSKI A, BAARSMA GS, VAN HAGEN PM: Adalimumab: a new modality for Behçet's disease? *Ann Rheum Dis* 2007;66:565-6.
7. BELZUNEGUI J, LÓPEZ L, PANIAGUA I, INTXAUSTI JJ, MAÍZ O: Efficacy of infliximab and adalimumab in the treatment of a patient with severe neuro-Behçet's disease. *Clin Exp Rheumatol* 2008; 26 (Suppl. 50): S133-4.
8. ROBERTSON LP, HICKLING P: Treatment of recalcitrant orogenital ulceration of Behçet's syndrome with infliximab. *Rheumatology* (Oxford) 2001; 40: 473-4.
9. ESTRACH C, MPOFU S, MOOTS RJ: Behçet's syndrome: response to infliximab after failure of etanercept. *Rheumatology* 2002; 41: 1213-4.
10. HAUGEBERG G, VELKEN M, JOHNSEN V Successful treatment of genital ulcers with infliximab in Behçet's disease. *Ann Rheum Dis* 2004; 63: 744-5.
11. MELIKOGLU M, FRESKO I, MAT C *et al*.: Short-term trial of etanercept in Behçet's disease: a double blind, placebo controlled study. *J Rheumatol* 2005; 32: 98-105.
12. ALMOZNINO G, BEN-CHETRIT E: Infliximab for the treatment of resistant oral ulcers in Behçet's disease: a case report and review of the literature. *Clin Exp Rheumatol* 2007; 25 (Suppl. 45): S99-102.