

Remission of Behçet's syndrome with tumour necrosis factor α blocking therapy

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A 40 year old man presented in 1986 with painful noduli and skin ulcers on his foot. Based on a deep skin biopsy, showing obliteration of the vascular lumen with necrosis and infiltration of lymphocytes in the vascular wall, a diagnosis of polyarteritis nodosa was made. Treatment with prednisone (40 mg daily) was started, but because of persistent disease activity azathioprine (150 mg/day) and, subsequently, cyclophosphamide (100 mg/day) was added. Despite this treatment, the symptoms recurred periodically. In subsequent years he became steroid dependent and neither cyclophosphamide pulse treatment nor thalidomide induced a remission.

In September 1999 the patient developed ulcers of the mouth, anus, and praeputium (fig 1). At that time he was treated with prednisone 15 mg/day and methotrexate 15 mg/week. The skin of the left foot showed ulcerations and the ophthalmologist observed retina lesions compatible with vasculitis. Based on these findings, a diagnosis of Behçet's syndrome was made. Because the patient did not respond to conventional treatment and the disease course was progressive, it was decided to treat the patient with infliximab, a chimeric IgG1 monoclonal antibody directed against tumour necrosis factor (TNF) (Remicade; Schering Plough BV, Maarsse, The Netherlands). He received two doses of 700 mg (10 mg/kg) with an interval of one month. Two weeks after the first injection the ulcers of the penis, anus, mouth, and skin were considerably smaller when he visited the outpatient clinic in January 2000, and had disappeared at the time of the second injection. The patient is still in remission 12 months after the last infusion with infliximab.

Behçet's syndrome is a systemic necrotising vasculitis affecting arteries and veins of all sizes, and treatment requires the use of immunosuppressive drugs.¹ The cause of the vasculitis is unknown, but a pathogenic role of Th1 mediated immune response has been proposed.² Because high serum levels of TNF and soluble TNF receptor have been found in Behçet's syndrome,³ we treated this patient with infliximab. Infliximab, now registered for the treatment of rheumatoid arthritis and



Figure 1 Ulcers on the penis before the first infusion with infliximab.

Crohn's disease, is an antibody neutralising the biological activity of TNF by binding with high affinity to the soluble and transmembrane forms of TNF. The prompt improvement of longstanding symptoms directly after the infusion of infliximab strongly suggests a causal relation and indicates a central role of TNF in the pathogenesis of Behçet's syndrome. In conclusion, this case suggests that Behçet's syndrome can be treated effectively with TNF blocking therapy.

- 1 Wolfgang LG. New concepts in treatment protocols for severe systemic vasculitis. *Curr Opin Rheumatol* 1999;11:41-6.
- 2 Turan B, Galatti H, Erdi H, Gürler A, Michel BA, Villiger PM. Systemic levels of the T cell regulatory cytokines IL-10 and IL-12 in Behçet's diseases; soluble TNFR-75 as a biological marker of disease activity. *J Rheumatol* 1997;24:128-32.
- 3 Sayinalp N, Özcebe OI, Özdemir O, Haznedaroglu IC, Dündar S, Kirazli S Cytokines in Behçet's disease. *J Rheumatol* 1996;23:321-2.

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