

Case report

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Remission of Behcet's disease with anti-tumor necrosis factor monoclonal antibody therapy: a case report

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Published: 28 August 2003

Received: 18 March 2003

BMC Musculoskeletal Disorders 2003, 4:19

Accepted: 28 August 2003

This article is available from: <http://www.biomedcentral.com/1471-2474/4/19>

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Abstract

Background: Behcet's disease (BD) is a chronic relapsing multisystem inflammatory disorder with mucocutaneous, ocular, articular, vascular, gastrointestinal and central nervous system manifestations. Tumor necrosis factor (TNF)-alpha is believed to play a pivotal role in BD. Therapeutic blockade of the activity of TNF has been successfully given in a short course of therapy with favorable effects in patients with BD refractory to conventional immunosuppressive drugs. We aimed to find out whether a 12-month treatment with infliximab, a chimeric monoclonal antibody to TNF-alpha, had any beneficial effect in reducing relapses of a patient with long-standing BD refractory to conventional immunosuppressive drugs.

Case presentation: A 54 year-old-woman with a 35-year history of BD with orogenital ulcerations, arthritis in the right knee and retinal lesions compatible with vasculitis received infliximab, 5 mg/kg by a two-hour intravenous infusion. Symptoms improved within 24 hours and eight days later the genital and oral ulcers healed as well as the arthritis in the right knee subsided. The retinal infiltrates completely resolved within 10 days. The infusions were repeated at weeks 2, 6, 14, 22 and then every 8 weeks. The patient was able to return to her domestic daily life. No exacerbation of the mucocutaneous ocular or arthritic symptoms occurred during the treatment period.

Conclusions: Previous studies have suggested that infliximab given in a short course of treatment is effective in inducing remission of severe mucocutaneous, gastrointestinal and ocular manifestations of BD. Our patient received a 12-month infliximab treatment showing a favorable effect on remission of BD manifestations.

The long-term infliximab treatment appears as a new therapeutic option for patients with active BD who failed to respond to conventional immunosuppressive agents.

Background

Behcet's disease (BD) is a chronic relapsing multisystem inflammatory disorder that causes orogenital ulcerations, skin lesions, intraocular inflammation (uveitis and retinal vasculitis) and less commonly arthritic, vascular, gastrointestinal and neurologic manifestations [1,2].

The enhanced inflammatory reaction in BD appears to be mediated by cytokines derived from T helper type I lymphocytes, including tumor necrosis factor (TNF)-alpha [3].

TNF-alpha is produced by monocytes as part of the inflammatory cascade in BD and concentrations of TNF and soluble TNF receptors are increased in the serum of patients with the active disease [4].

It has been demonstrated that the T lymphocytes expressing the gammadelta receptor in BD are activated in vivo and produce increased amounts of TNF-alpha and interferon-gamma compared with healthy controls [5].

TNF-alpha and interleukin-8 might increase the expression of the CD11b-CD18 constitutively present on the polymorphonuclear neutrophils membrane and facilitate their rolling and diapedesis through the vascular endothelial wall [2,6].

Therapeutic blockade of the activity of TNF has been successfully employed to treat Crohn's disease and rheumatoid arthritis, two other Th-1 mediated disorders [7].

Recently a short-term anti-TNF treatment was given with favorable effects in patients with BD refractory to conventional immunosuppressive drugs [8-10].

We aimed to find out whether a 12-month treatment with infliximab, a chimeric monoclonal antibody to TNF-alpha, had any beneficial effect in reducing relapses of a patient with long-standing BD.

Case presentation

A 54-year-old woman with a 35-year history of BD was admitted to our Unit. The patient fulfilled the International Study Group criteria for diagnosis of BD [1]. She had a history of recurrent genital and oral aphthous ulcers. Thirty years ago she was diagnosed retinal lesions compatible with vasculitis which lead a few years later to a decrease in visual acuity and blindness in the right eye.

On admission she had orogenital ulcerations, and arthritis in the right knee. The ulcers on the buccal mucosa and tongue were painful with a diameter ranging from 2 to 6 mm. The right knee was swollen with severe functional limitation. She had retinal infiltrates in the left eye. Previ-

ous treatment with prednisolone, colchicine, azathioprine and cyclosporin was ineffective and the symptoms recurred periodically.

Erythrocyte sedimentation rate (ESR) was 18.5 mm/h and C-reactive protein (CRP) was markedly elevated (+++). CRP levels were measured semiquantitatively and graded negative (-), detectable (+), elevated (++) and markedly elevated (+++). PPD Mantoux test was negative.

Infliximab (Remicade, Centocor Inc, Malvern, PA, Schering Plough SpA, Italy), 5 mg/kg, was administered by a two-hour intravenous infusion.

The patient was observed for 1 hour after stopping infusion and no adverse effects occurred.

An improvement in symptoms was reported within 24 hours after the first infusion. Eight days later the ulcers healed and the arthritis subsided as well. The retinal infiltrates completely resolved within 10 days. A detailed ophthalmological examination was done before and 1, 2, 4, 7, 10, 14, 21, 28 days after the beginning of the treatment; then every 14 days for three months and every 28 days for other eight months.

The infusions were repeated at weeks 2, 6, 14, 22 and then every 8 weeks for 12 months. No other immunosuppressive agent was administered together with infliximab infusions.

After 4 weeks ESR was 15.5 mm/h and CRP elevated (++)

The patient was able to return to her domestic daily life.

No exacerbation of the mucocutaneous ocular or arthritic symptoms occurred during the treatment period. After 12 months ESR was 7.5 mm/h and CRP detectable (+). Neither serious infections nor development of autoantibodies against double-stranded DNA were observed.

Previous studies have suggested that BD can be treated effectively with TNF blocking therapy. Infliximab given in a short course of treatment has been reported to be effective in inducing and maintaining remission of BD. Infliximab was successfully administered for treating severe mucocutaneous [10-12], gastrointestinal [13-15] and ocular [16-18] manifestations of BD, with a prompt improvement of long-lasting symptoms which disappeared within a few weeks. The efficacy of infliximab after the failure of etanercept was also reported [19]. Infliximab is a chimeric monoclonal antibody directed against TNF-alpha. The antibody binding to soluble TNF-alpha is responsible of the initial dramatic improvement in symptoms after infliximab infusions.

The longer-lasting effects are related to infliximab binding to transmembrane TNF-alpha expressed on the surface of activated T cells and macrophages, resulting in lysis of these cells via complement fixation or antibody-dependent cellular toxicity [20].

Conclusions

It is well known that conventional therapy for BD relies on available anti-inflammatory and immunomodulatory agents, and in view of the scarcity of controlled clinical trials, it is to a large extent empirical [8].

Several case series and single reports have suggested that infliximab given in a short course of treatment is effective in inducing remission of the various manifestations of BD [9-18]. Our patient received a 12-month treatment with a good therapeutic response.

When given in a long-term use infliximab seems to be a useful therapeutic approach for preventing relapses in patients with this disease. In particular the long-term infliximab treatment appears a promising new option for patients with active BD who failed to respond to conventional immunosuppressive agents.

List of abbreviations used

BD, Behcet's disease; TNF, tumor necrosis factor; ESR, erythrocyte sedimentation rate; CRP, C-reactive protein.

Competing interests

None declared.

Authors' contributions

SG participated in the design of the study and drafted the manuscript.

CA participated in the systemic examination and collecting data.

LB participated in the systemic examination and collecting data.

LM participated in the systemic examination and performed laboratory findings.

DS participated in the systemic examination and follow-up visits.

IC carried out the detailed ophthalmological assessment.

GFB conceived of the study, and participated in its design and coordination.

All authors read and approved the final manuscript.

Acknowledgements

Written consent was obtained from the patient for publication of study.

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Pre-publication history

The pre-publication history for this paper can be accessed here:

<http://www.biomedcentral.com/1471-2474/4/19/prepub>

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