European Journal of Ophthalmology / Vol. 14 no. 5, 2004 / pp. 445-448

SHORT COMMUNICATION

Infliximab for the treatment of posterior uveitis with retinal neovascularization in Behçet disease

F. GIANSANTI[1], M.L. BARBERA[1], G. VIRGILI[1], B. PIERI[1], L. EMMI[2], U. MENCHINI[1]

[1]Eye Clinic, Department of Oto-Neuro-Ophthalmological Surgical Sciences
[2]Immunoallergology Service, Department of Internal Medicine, University of Firenze, Firenze - Italy

PURPOSE. *To report a case of posterior uveitis with retinal neovascularization in a patient with Behçet disease treated with infliximab.*
METHODS. *A 50-year-old man with a history of recurrent relapses of ocular inflammation despite immunosuppressive therapy developed retinal neovascularization near the optic disk. The patient was treated with infliximab and followed up for 12 months.*
RESULTS. *Retinal neovascularization regressed 8 months after the first anti–tumor necrosis factor (TNF) treatment and with six infusions of infliximab. The ocular inflammation resolved almost completely.*
CONCLUSIONS. *The result suggests that anti-TNF therapy may be effective in the treatment of retinal neovascularization caused by panuveitis in Behçet disease. (Eur J Ophthalmol 2004; 14: 445-8)*

KEY WORDS. *Behçet disease, Infliximab, Retinal neovascularization, Uveitis*

Accepted: May 23, 2004

INTRODUCTION

Behçet disease is a recurrent inflammatory disorder with systemic and ocular manifestations. Recent reports have indicated that anti-tumor necrosis factor (TNF) therapy may be effective in the management of refractory panuveitis associated with Behçet disease (1-4). Previous reports included no cases of retinal neovascularization. We describe a case of panuveitis with retinal neovascularization associated with Behçet disease treated with infliximab.

Case report

A 38-year-old man was diagnosed with Behçet disease in 1996. He was treated with cyclosporine 3 mg/kg/die and prednisone 50 mg/die tapered. While receiving this treatment, he experienced multiple relapses of intraocular inflammation, recurrent oral and genital aphthous ulcers, and erythema nodosum. In 2001, he was diagnosed with diabetes mellitus type 1. After diagnosis of diabetes a therapy with insulin was started and glycemic control obtained. New relapses of ocular inflammation occurred in 2002 in both eyes. During ophthalmic examination a diagnosis of macular hole was made in left eye and of impending macular hole and retinal neovascularization in right eye. Despite treatment with cyclosporine (4 mg/kg/die) and prednisone (15 mg/die) his ocular inflammation and retinal neovascularization remained stable (Fig. 1, top left and top right). We decided to treat the patient with infliximab according to the protocol used for therapy of rheumatoid arthritis (5).

 1120-6721/445-04$15.00/0

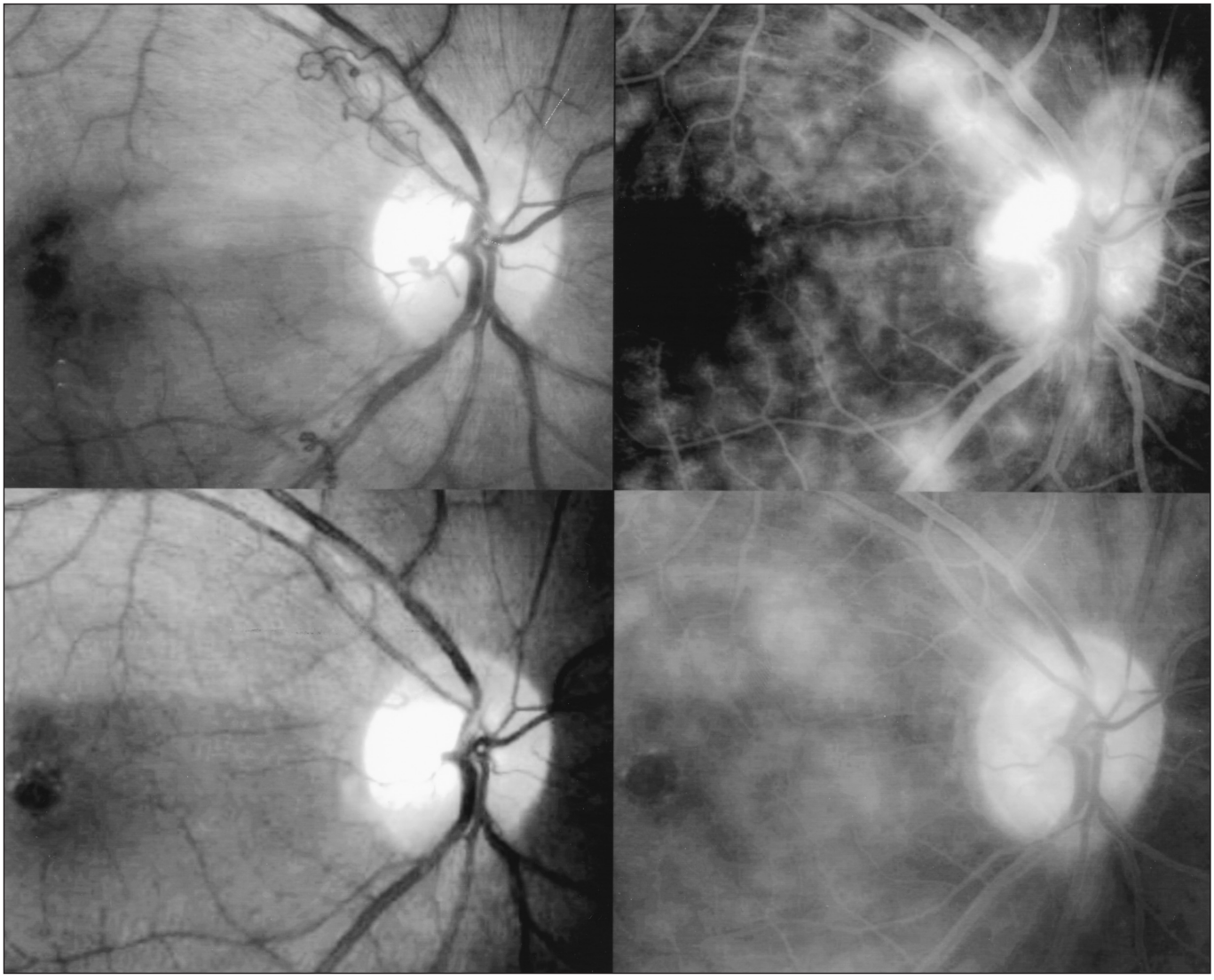

Fig. 1 - *Top left: Red free photograph reveals the retinal new vessels near the optic disk. Top right: Fluorescein angiography shows the fluorescein leakage from the new vessels near the optic disk. Bottom left: Red free photograph shows the regression of the new vessels 8 months after the first infusion of infliximab. Bottom right: Fluorescein angiography confirms the absence of the new vessels 8 months after first infusion of infliximab.*

Before administering the anti-TNF therapy, screening for latent tuberculosis was done. The patient was positive to purified protein derivative skin testing, but repeated chest radiographs did not reveal any evidence of tuberculosis. Prophylaxis for tuberculosis with rifampicin and isoniazid was performed for 3 weeks before treatment with infliximab.

The intravenous dosage of infliximab was 3 mg/kg; a second and a third dose were given at 2 and 6 weeks and then treatment was given every 8 weeks. Overall, the patient received six infusions of infliximab. Methotrexate 10 mg weekly was co-prescribed to reduce immunogenicity of infliximab. The patient was followed up with systemic and ocular examination. The degree of inflammation in the anterior chamber and vitreous was evaluated according to the standard scoring system to assess the anterior chamber cells on a scale of 0 to 4 (6) and vitreous haze on a scale of 0 to 4 (7). Fluorescein angiography was performed before treatment and at

fourth and eighth month follow-up visits. Before infusion of infliximab, visual acuity was 20/100 in right eye and 20/200 in left eye; the score of vitreous haze was 1 out of 4 and the score of the anterior chamber cells was 2 out of 4. No signs of diabetic retinopathy, such as hemorrhages, hard exudates, or cotton wool spots, were seen by fundus examination in both eyes. The fluorescein angiography showed a tuft of retinal neovascularization near the optic disk (Fig. 1), a peripheral retinal perivenous exudation, and no microaneurysms. Two weeks after the first dose of infliximab the score of vitreous haze decreased to trace and the score of the anterior chamber cells was 1. Visual acuity improved to 20/50 in 12 weeks in the right eye and remained at 20/200 in the left eye because of the macular hole. After 4 months the score of anterior chamber cells was 1 and no vitreous haze was detected but retinal neovascularization was still present. Visual acuity was 20/40 in the right eye and 20/200 in the left eye. Eight months after the beginning of treatment with infliximab, he had no retinal neovascularization in right eye, no peripheral retinal perivenous exudation, and visual acuity was 20/30 (Fig. 1, bottom left and bottom right). Optical coherence tomography performed during the follow-up did not show posterior vitreous detachment over the macular area.

During treatment with infliximab, cyclosporine was not administrated and steroids were tapered and discontinued. The patient received six infusions of infliximab at 0, 2, 8, 16, 24, and 32 weeks.

DISCUSSION

To our knowledge, this is the first report on the treatment of posterior uveitis with retinal neovascularization in Behçet disease with infliximab. Retinal neovascularization is an uncommon finding associated with Behçet disease. Neovascularization is associated in some cases with capillary closure on fluorescein angiography and an angiogenic factor produced by ischemic retina has been implicated in the pathogenesis. However, new vessels may also appear in the eye unassociated with capillary closure. In these cases it has been postulated that the neovascularization is a direct result of the inflammatory process (8). Angiogenesis is a hallmark of inflammatory disorders in many organs and monocytes, macrophages, platelets, mast cells, and other leukocytes release a myriad of angiogenic factors including VEGF and TNF-α (9).

Our patient developed retinal neovascularization 5 years after the first diagnosis of Behçet disease and 6 months after diagnosis of diabetes mellitus type I. Because no sign of diabetic retinopathy was seen, such as microaneurysms and hemorrhages, retinal neovascularization was caused by the inflammatory process. Furthermore, fluorescein angiography showed no areas of retinal nonperfusion. After treatment with infliximab ocular inflammation resolved almost completely and retinal neovascularization regressed 8 months after the first infusion. The last follow-up visit was performed at the 12th month and no ocular or systemic complications occurred.

In conclusion, our patient responded to infliximab treatment with a reduction of the ocular inflammation and regression of retinal neovascularization, but further investigations are necessary to evaluate the role of anti TNF-α in the ocular angiogenesis.

Reprint requests to:
Fabrizio Giansanti, MD
Eye Clinic
Department of Oto-Neuro-Ophthalmological Surgical Sciences
University of Firenze
Viale Morgagni 85
50134 Firenze, Italy
fabriziogiansanti@interfree.it

REFERENCES

1. Sfikakis PP, Theossidiadis PG, Katsiari CG, et al. Effect of infliximab on sight-threatening panuveitis in Behçet's disease [letter]. Lancet 2001; 358: 295-6.
2. Munoz-Fernandez S, Hidalgo V, Fernandez-Melon J, et al. Effect of infliximab on threatening panuveitis in Behçet's disease [letter]. Lancet 2001; 358: 1644.
3. Joseph A, Raj D, Dua HS, et al. Infliximab in the treatment of refractory posterior uveitis. Ophthalmology 2003; 110: 1449-53.

4. Triolo G, Vadala M, Accardo-Palumbo A, et al. Anti-tumor necrosis factor antibody treatment for ocular Behçet's disease. Ann Rheum Dis 2002; 61: 560-1.
5. Maini R, St Clair EW, Breedveld F, et al. Infliximab (chimeric anti-tumour necrosis factor alpha monoclonal antibody) versus placebo in rheumatoid arthritis patients receiving concomitant methotrexate: a randomised phase III trial. ATTRACT Study Group. Lancet 1999; 354: 1932-9.
6. Kimura SJ, Thygeson P, Hogan MJ. Signs and symptoms of uveitis. 1. Anterior uveitis. Am J Ophthalmol 1959; 47: 155-70.
7. Nussenblatt RB, Palestine AG, Chan CC, et al. Standardization of vitreal inflammatory activity in intermediate and posterior uveitis. Ophthalmology 1985; 92: 467-71.
8. Graham EM, Stanford MR, Shilling JS, et al. Neovascularization associated with posterior uveitis. Br J Ophthalmol 1987; 71: 826-33.
9. Carmeliet P, Jain RK. Angiogenesis in cancer and other diseases. Nature 2000; 407: 249-57.