Table 1 Summary of characteristics

Patient	Eye	Age† (years)	Sex	Duration of RA‡ (years)	Sjögren's disease	Nodules	RF	ANA	Duration of melt¶ (weeks)	IV Cyclophosphamide (total dose in mg)
1	Left	89	F	22	No	Yes	+	+	6	2000
2	Both	71	F	7	Yes	Yes	+	−	9	4500
3*	Right	64	M	10	No	No	+	+	3	1000
4	Left	87	F	20	Yes	No	−	+	2	500
5	Right	50	F	2	No	Yes	+	+	6	3000
6	Right	67	F	2	Yes	No	−	+	2	1000
7*	Left	75	M	11	Yes	Yes	−	+	4	750

*1 g methylprednisolone given; †mean (SD) age 71 (13) years; ‡mean (SD) duration of RA 10.5 (8) years; ¶mean (SD) duration of melt 4.2 (2.5) weeks.

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Therapeutic use of infliximab in sight threatening uveitis: retrospective analysis of efficacy, safety, and limiting factors

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Anti-tumour necrosis factor (TNF) molecules have become a valuable addition to the therapeutic armamentarium for patients with severe uveitis.[1–7] A retrospective study was conducted from June 2001 to June 2003 including patients with a refractory uveitis, resistant to corticosteroids and conventional immunosuppressive drugs. Patients were screened for infectious conditions. Informed consent was obtained in all cases. Treatment was given if patients were suffering. Infliximab was initially given at a dose of 5 mg/kg, renewed at weeks 2, 6, and every 8 weeks, and then every 10–12 weeks when uveitis had been controlled for more than 6 months. Prednisone and immunosuppressive drugs were tapered progressively if there was no evidence of ocular inflammation. Dose escalation (10 mg/kg) was proposed when relapse or secondary resistance occurred.

Twelve patients (21 eyes) were included in this study (mean age of 35 years). Uveitis was bilateral in 10/12 (83%) cases. Mean duration of disease before starting infliximab was 7 years (range 2–20). Rapid control of uveitis was achieved in all cases. Improvement by six lines of vision and three lines of vision was obtained respectively in five and 10 patients at the end of follow up (table 1). Systemic disease was controlled in all cases. Mean follow up was 17.4 months (range 8–30). Relapses occurred in four (33%) cases after a mean period of 57.3 weeks (range 14–108). Of these four patients, two had Behçet's disease (fig 1), one had ankylosing spondylitis, and one idiopathic panuveitis. Relapses occurred when infusions were performed less frequently than every 8 weeks (between 10 and 12 weeks). Finally, immunosuppressive drugs were discontinued and corticosteroids were tapered in four (33%) cases; methotrexate and low dose corticosteroids were continued in five (42%) cases. Azathioprine or mycophenolate mofetil were necessary in three patients. No serious adverse event occurred in this series.

The 5 mg/kg dose of infliximab is effective and has been used in most of the previous studies on uveitis. Although his study was not controlled, choosing patients refractory to a combination of high dose steroids and immunosuppressive drugs, rules out an overestimation of the benefit of the drug. The use of anti-TNFα after failure of other drugs is a promising alternative, but long term efficacy of infliximab must be discussed. Its high cost still limits its use. Potential adverse effects need close monitoring before and during treatment.[8–10] Long term effects of the treatment are still unknown. Meanwhile, we recommend the use of anti-TNF agents after the failure of conventional immunosuppressive drugs (fig 2). The effect of infliximab on acute inflammatory ocular lesions is spectacular. As a rescue strategy, its use may be discussed in severe forms of retinal necrosis associated

Table 1 Demographic, clinical, and therapeutic characteristics of patients before anti-TNF treatment and at the end of follow up

Patient No	Sex	Age (years)	Duration of uveitis (years)	Clinical presentation	Aetiology/anatomical localisation	Treatment before infliximab	F	Evolution/ *Initial/final VA*	Treatment at last examination
1	M	33	7	OD: macular oedema and vitritis OS: macular necrosis	BD/panU	Prednisone, pentoxifylline, cyclophosphamide, interferon α2a, azathioprine	28	OD: Rapid regression of macular oedema and vitritis OS unchanged. Relapses at weeks 82 and 108 *OD 20/200 OS 20/400* *OD 20/25 OS 20/400*	Prednisone, MTX, infliximab
2	F	38	4	OD: macular oedema OS: macular necrosis	BD/PU	Prednisone, pentoxifylline, interferon α2a, azathioprine, cyclophosphamide	30	Regression of right macular oedema *OD 20/200 OS LP* *OD 20/20 OS LP*	Prednisone, infliximab
3	F	21	8	OD: enucleated OS: macular necrosis	BD/PU	Prednisone, cyclophosphamide, interferon α2a, azathioprine	29	Regression of inflammatory signs *OS 20/40* *OS 20/20*	Prednisone, infliximab
4	M	30	2	Bilateral vasculitis, haemorrhagic retinitis, vitritis, macular oedema	BD/panU	Prednisone, interferon α2a	16	Initial improvement but relapses at weeks 14 and 40 *OD 20/60 OS 20/40* *OD 20/25 OS 20/25*	Infliximab (10 mg/kg), mycophenolate mofetil, MTX, prednisone
5	M	20	2	Bilateral vasculitis, haemorrhagic retinitis, vitritis, macular oedema	BD/panU	Prednisone, azathioprine, interferon α2a, rifampin	8	Efficacy but still receiving prednisone and methotrexate *OD 20/100 OS 20/200* *OD 20/20 OS 20/20*	Infliximab, MTX, prednisone
6	M	45	9	OD: vision lost due to chronic inflammation and glaucoma OS: inflammation and ocular hypertension	Ankylosing spondylitis, HLA-B27+/panU	Prednisone, MTX, cyclophosphamide, azathioprine	24	Relapse at week 54 Restarted immunosuppressive treatment *OD NLP OS 20/40* *OD NLP OS 20/20*	Prednisone, azathioprine
7	M	38	6	Unilateral non-granulomatous anterior uveitis and refractory glaucoma	Ankylosing spondylitis, HLA-B27+/AU	Prednisone, MTX, ciclosporin A	9	Control of ocular and articular inflammation *OD 20/50 OS 20/20* *OD 20/20 OS 20/20*	Infliximab, MTX, prednisone
8	F	42	4	OD: Normal. OS: anterior chamber inflammation, macular oedema, epiretinal membrane, secondary glaucoma	Psoriasis/panU	Prednisone, MTX	16	No relapse Low dose prednisone, cataract surgery *OD 20/20 OS 20/60 V*	Infliximab, prednisone
9	F	57	16	Bilateral non granulomatous panuveitis with posterior synechiae, secondary glaucoma, vitritis, macular oedema	Psoriasis/panU	Prednisone, MTX	12	No relapse Cataract surgery, trabeculectomy OD and OS *OD 20/60 OS 20/80* *OD 20/20 OS 20/30*	Infliximab, prednisone, azathioprine
10	F	34	4	Bilateral panuveitis, bilateral macular oedema Seronegative ankylosing spondylitis	B27− spondyloarthropathy /panU	Prednisone, MTX	9	Regression of inflammatory signs and macular oedema *OD 20/50 OS 20/40* *OD 20/30 OS 20/25*	Infliximab, MTX, prednisone
11	M	43	20	Right eye lost through neovascular glaucoma Left eye, papillitis, macular oedema, vitritis, retinal necrosis	Idiopathic panU	Prednisone, azathioprine, cyclophosphamide	16	Regression of inflammatory signs and macular oedema Relapse at week 46 *OD NLP OS CF* *OD NLP OS 20/40*	Infliximab, MTX, prednisone
12	F	16	7	OD: papillitis, macular oedema, vitritis OS: macular oedema, vitritis, optic atrophy	Idiopathic panU	Prednisone, azathioprine, interferon α2a	12	Regression of inflammatory signs and macular oedema Cataract surgery *OD 20/400, 0S CF* *OD 20/40 OS 20/200*	Infliximab, prednisone

OD, right eye; OS, left eye, BD, Behçet's disease; panU, panuveitis; PU, posterior uveitis; AU, anterior uveitis; F, follow up (months); CF, counting fingers; MTX, methotrexate.

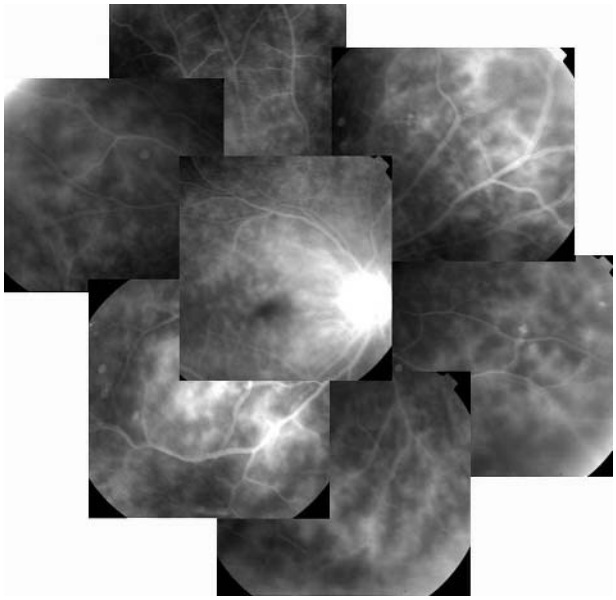

Figure 1 Early relapse of posterior uveitis in a patient with Behçet's disease, 6 weeks after the third infusion of infliximab. Fluorescein angiography showing diffuse retinal choriocapillaropathy, macular oedema, and papillitis.

with Behçet's disease, to control the acute phase of the inflammatory process. It will be possible to discuss a further shift to standard immunosuppressive drugs when the acute phase of the disease has been controlled. Furthermore, association of infliximab and other standard immunosuppressive drugs allows the anti-TNF dosage to be decreased. This should be taken into consideration to prevent immunogenicity against the drug, inducing secondary resistance. Tapering of corticosteroids and discontinuation of immunosuppressive drugs must be achieved cautiously, in order to prevent further relapses.

It is difficult to consider infliximab as a chronic long term monotherapy. Owing to the rapidity of action, it has to be administered earlier in the course of the disease, to spare steroids and to facilitate the action of other immunosuppressive drugs. Induction treatment with infliximab has an increased likelihood of a sustained response over a long term period if infusions are continued every 8 weeks. However the optimal dose, rhythm, and duration of infliximab infusions need to be standardised. Our data indicate the need for larger controlled trials before drawing up further adapted guidelines.

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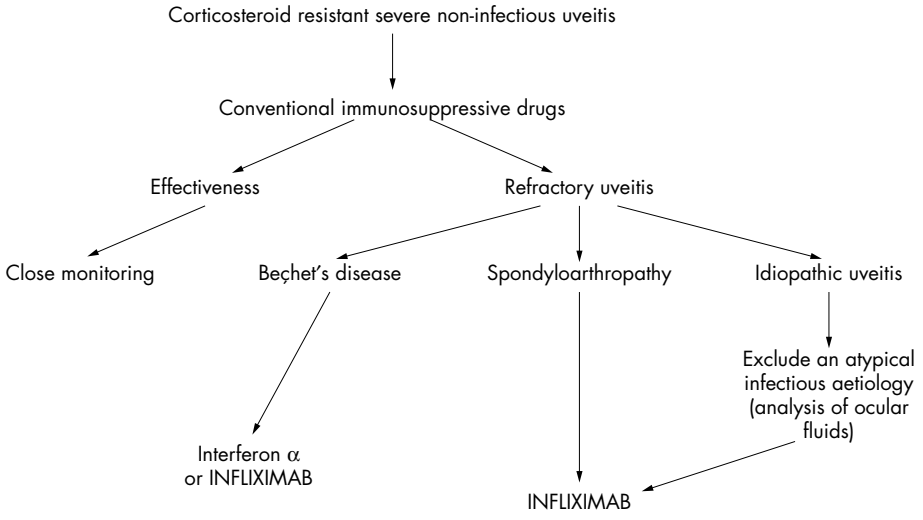

Figure 2 Therapeutic escalation in patients with severe refractory uveitis.