Safety and efficacy of TNF α blockade in relapsing vasculitis

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B lockade of tumour necrosis factor alpha (TNF α) using infliximab, a chimeric monoclonal antibody against TNF α , is an effective treatment in rheumatoid arthritis and Crohn's disease.¹² Sifikakis reported success using infliximab in sight threatening Behçet's disease.³ A preliminary study has also reported clinical improvements in the primary systemic vasculitis, Wegener's granulomatosis, with the soluble TNF α receptor etanercept.⁴ The benefit of lenercept, a soluble p55 TNF α receptor fusion protein, on digital vasculitis in rheumatoid arthritis has also been reported.⁵

We report the compassionate treatment of six patients with refractory vasculitis using infliximab. Diagnoses were Wegener's granulomatosis in three and microscopic polyangiitis in three. Three patients were positive for proteinase-3 antineutrophil cytoplasmic antibodies (PR3-ANCA) and one for myeloperoxidase (MPO)-ANCA. Four were female, with a mean age of 58 years (range 23–77) and mean disease duration of 3.5 years. All had had at least three clinical relapses and had received prolonged treatment with corticosteroids and at least four immunosuppressive drugs. At the time of infliximab treatment the eyes were affected in four patients and the lung in three; in addition, five had profound constitutional symptoms. The mean prednisolone dose was 17 mg.

Three intravenous doses of infliximab 200 mg were given at monthly intervals for three months. One patient complained of fatigue, myalgia, and blurred vision 24 hours after the first infusion, which did not recur on rechallenge. Infliximab was otherwise well tolerated. Five patients had remission of their disease, four within two weeks of treatment. This allowed steroid withdrawal in three and reduction by more than 50% in two. Disease activity assessed by the Birmingham Vasculitis Activity Scores (BVAS) improved from a mean of 6.3 to 0.8 at three months (fig 1).⁶ One patient receiving continued infliximab for six months relapsed when the treatment interval was extended to two months. Mean falls in erythrocyte sedimentation rate and C reactive protein were 17 mm/1st h and 13 mg/l, respectively. The ANCA status was unchanged.

Anti-TNF α treatment heralds a new wave of specifically targeted biological interventions of potential value in the treatment of vasculitis. It offers the hope of improved therapeutic efficacy over current agents and the possibility of reducing exposure to steroids and immunosuppressive drugs. Further studies are warranted to confirm these observations and explore the role of infliximab as a component of initial protocols.

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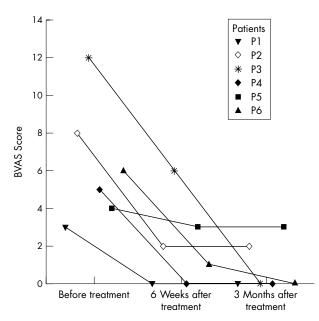


Figure 1 BVAS scores for the six patients treated with infliximab.

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REFERENCES

- Maini R, St Clair EW, Breedveld F, Furst D, Kalden J, Weisman M, 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. Lancet 1999;354:1932–9.
- 2 Present DH, Braakman T, DeWoody KL, Schaible TF, Rutgeerts PJ. A short-term study of chimeric monoclonal antibody cA2 to tumour necrosis factor alpha for Crohn's Disease cA2 Study Group. N Engl J Med 1997;337:1029–35.
- 3 Sifikakis PP, Theodossiadis PG, Katsiari CG, Kaklamanis P, Markomichelakis NN. Effect of infliximab on sight-theatening panuveitis in Behçet's disease. Lancet 2001;358:295–6.
- 4 Stone JH, Uhlfelder ML, Hellmann DB, Crook S, Bedocs NM, Hoffman GS. Etanercept combined with conventional treatment in Wegener's granulomatosis: a six-month open-label trial to evaluate safety. Arthritis Rheum 2001;44:1149–54.
- 5 Den Broeder AA, van den Hoogan FHJ, van de Putte LBA. Isolated digital vasculitis in a patient with rheumatoid arthritis: good response to tumour necrosis factor α blocking treatment. Ann Rheum Dis 2001;60:538–9.
- 6 Luqmani RA, Bacon PA, Moots RJ, Janssen BA, Pall A, Emery P, et al. Birmingham vasculitis activity score (BVAS) in systemic necrotizing vasculitis. Q J Med 1994;87:671–8.

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