

Use of cyclosporin in the management of steroid dependent non-necrotising scleritis

K N Hakin, J Ham, S L Lightman

Abstract

Many patients with non-necrotising scleritis can be treated adequately with non-steroidal anti-inflammatory drugs or steroids. But, as many of them are young, treatment may present problems if they require high doses of steroids to control the scleral inflammation and then relapse when the dosage is reduced. Five such patients were treated with a combination of steroids and low-dose cyclosporin therapy, and in all cases the scleritis remained under control on a much lower dose of steroids than when steroids were used alone. Cyclosporin is therefore a useful drug in the management of younger patients dependent on high-dose steroids to control their scleral inflammation.

Anterior scleritis can be diffuse, nodular, or necrotising.¹ In many patients non-steroidal anti-inflammatory drugs (NSAIDs), such as flurbiprofen, can be used to control diffuse or nodular scleritis, whereas high-dose steroids, often with other potent immunosuppressives such as cyclophosphamide, are necessary for the treatment of necrotising scleritis.²

Cyclosporin, which is used extensively in the treatment of posterior uveitis, has previously been described in the treatment of necrotising disease, which usually occurs in older patients.³

We here present five patients with severe anterior diffuse scleritis in whom systemic prednisolone was effective only at high dosage or could not be tolerated at such doses. Any attempt at steroid reduction resulted in severe recurrence of the scleral inflammation. These patients received low-dose cyclosporin (5 mg/kg/day) in addition to the controlling steroid dose, and in all cases the steroid dosage could then be reduced to a more acceptable level while the scleral inflammation remained under control.

Patients and methods

The patients were recruited from the Scleritis Clinic at Moorfields Eye Hospital. The scleritis was classified as anterior diffuse, nodular or necrotising, or posterior, according to Watson.¹ Investigations including a full blood count, erythrocyte sedimentation rate, autoimmune screen, urea, electrolytes, creatinine, and chest x ray were performed to exclude an underlying systemic disease.

Patients with non-necrotising disease were started on an NSAID, usually flurbiprofen or indomethacin, which if ineffective, was then changed to high-dose systemic corticosteroid, prednisolone 60-80 mg per day. After one or two weeks at this high level a slow reduction of the daily dose was attempted, eventually to be

stopped completely. If the disease relapsed as the steroids were reduced, then NSAID were sometimes combined with the steroids to attempt disease control. If the inflammation could not be controlled on a satisfactorily low steroid level, the steroids were increased back to or above the controlling dose, and cyclosporin A added, at 5 mg/kg/day, in two divided doses, after the serum creatinine was checked and found to be within the normal range. After one or two weeks on the combination therapy slow steroid reduction was attempted.

The cyclosporin dose was monitored by two-weekly serum creatinine measurements and adjusted if the creatinine started to rise. If relapse occurred while treatment was being reduced, the prednisolone dose was increased and then again slowly tapered off. The cyclosporin was also increased, if thought necessary, but to a maximum dose of 7.5 mg/kg/day for up to a week, before being reduced back to 5 mg/kg/day.

Results

Five patients with non-necrotising scleritis received cyclosporin. Their ages ranged from 21 to 64 years, average 32. Systemic investigations revealed Crohn's disease with primary sclerosing cholangitis in one patient and nasal cartilage collapse in another (possibly indicative of relapsing polychondritis). The others were healthy. In four patients satisfactory control of the ocular inflammation was achieved with high-dose steroids, but the disease relapsed when the treatment was reduced. The ocular inflammation was said to be controlled when the patient no longer experienced pain and the slit-lamp examination showed resolution of oedema, with minimal dilatation of the episcleral vessels. The fifth patient immediately developed intolerable side effects from the steroids, and thus required alternative therapy. Four received NSAID/steroid combination therapy to try to control the relapses, and one of these was also treated with azathioprine.

In all five patients the concurrent use of cyclosporin with prednisolone allowed the daily dose of prednisolone to be reduced. Three patients did relapse again (one on three occasions) but are now well controlled on a low daily steroid dose after the steroid dose had been temporarily increased to greater than 40 mg/day to re-establish control. Two patients managed to stop all treatment, one after seven weeks, the other after eight months, of cyclosporin therapy. There were no detectable renal complications from the use of cyclosporin as judged by the serum creatinine. Hirsutism, in one patient, was the only side effect.

Moorfields Eye Hospital,
City Road, London
EC1V 2PD
K N Hakin
J Ham
S L Lightman

Correspondence to:
Professor S Lightman,
Moorfields Eye Hospital,
City Road, London
EC1V 2PD.

Accepted for publication
29 November 1990

Table 1 Results

Age/ sex	Diagnosis	Duration of disease	Previous treatment	Minimum steroid prior to cyclosporin	Duration of cyclosporin treatment	Relapse?	Current therapy
64/M	Ant.scleritis/ limbitis	5 months	Flurbiprofen/pred	Pred 25 mg	6 months	Yes	Cyclosporin 200 mg/ pred 10 mg
23/F	Ant.scleritis	4 years	Flurbiprofen/pred	Side effects at pred 50 mg	18 months	Yes	Cyclosporin 200 mg/ pred 5 mg Flurbiprofen
28/M	Ant.scleritis	1 month	Indomethacin/pred	Pred 15 mg	7 weeks	No	Nil
21/F	Post.uveitis/ scleritis	6 years	Indomethacin/pred/ azathioprine	Pred 35 mg	13 months	Yes	Cyclosporin 150 mg/ pred 10 mg
26/M	Ant.scleritis	5 months	Flurbiprofen/pred	Pred 40 mg	8 months	No	Nil

Pred=prednisolone.

Discussion

Many patients with non-necrotising scleral disease can be controlled with systemic NSAIDs. Some require systemic steroids for control of the scleral inflammation (as judged by decreased pain and redness), and with slow steroid reduction many experience continued control of the disease on low-dose therapy. A minority require high-dose steroid therapy, and their disease process can become very steroid sensitive, so that any attempt at dose reduction results in relapse. The use of immunosuppressive drugs such as cyclophosphamide and chlorambucil is contraindicated in young patients,⁴ and in many patients with scleritis we have found azathioprine to be of little use in the short term in allowing significant steroid reduction.

Cyclosporin is now commonly used together with steroids in the management of posterior uveitis.^{5,6} Control of the disease is achieved with a lower dose of steroid than with steroids alone. In younger patients side effects such as tremor, hirsutism, gingival hypertrophy, and renal damage appear to be less common and the drug generally well tolerated.

Low-dose cyclosporin (less than 7.5 mg/kg/day) is now used, as at the higher dose of 10 mg/kg/day renal toxicity is common.⁷ At this lower dose cyclosporin must be used in combination with steroids to be effective in controlling the disease. The steroid dose may then be slowly reduced while the scleral disease is closely monitored.

Wakefield and McCluskey³ reported that cyclo-

sporin was a useful additional drug in the management of necrotising scleral disease. We have found that in combination with steroids it is also useful in treating non-necrotising disease, having a steroid-sparing effect.

Cyclosporin works by selectively inhibiting lymphokine secretion by activated T cells. Little is known about the pathogenesis of scleral inflammation, but a granulomatous inflammatory process is seen histologically.^{8,9} T lymphocytes, particularly of the CD4+ subtype, are involved in the delayed hypersensitivity response and may be involved in the inflammatory process in the sclera. The fact that cyclosporin is effective in the disease suggests that T cells are involved in the pathogenesis of the scleral inflammation, and this is under further investigation.

- 1 Watson PG. The nature and treatment of scleral inflammation. *Trans Ophthalmol Soc UK* 1982; 102: 257-81.
- 2 Foster CS. Immunosuppressive therapy for external ocular inflammatory disease. *Ophthalmology* 1980; 87: 140-50.
- 3 Wakefield D, McCluskey P. Cyclosporin therapy for severe scleritis. *Br J Ophthalmol* 1989; 73: 743-6.
- 4 Tabbara KF. Chlorambucil in Behçet's disease: a reappraisal. *Ophthalmology* 1983; 90: 906-8.
- 5 Nussenblatt RB, Palestine AG, Rook AH. Treatment of intraocular inflammatory disease with cyclosporin A. *Lancet* 1983; ii: 235-8.
- 6 Towler HMA, Whiting PH, Forrester JV. Combination low-dose cyclosporin A and steroid therapy in chronic intraocular inflammation. *Eye* 1990; 4: 514-20.
- 7 Palestine AG, Austin AH III, Barlow JE, et al. Renal histopathological alterations in patients treated with cyclosporin for uveitis. *N Engl J Med* 1986; 314: 1293-8.
- 8 Sevel D. Necrogranulomatous keratitis associated with Wegener's granulomatosis and rheumatoid arthritis. *Am J Ophthalmol* 1967; 63: 250-5.
- 9 Young RD, Watson PG. Microscopical studies of necrotising scleritis: I. Cellular aspects. *Br J Ophthalmol* 1984; 770-8.