SHORT REPORT

Treatment of chronic inflammatory demyelinating polyneuropathy with cyclosporin-A

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Abstract

Chronic inflammatory demyelinating polyneuropathy (CIDP) is an immune mediated polyneuropathy for which there are effective therapies. However, not all patients improve with these treatments. Eight patients with CIDP, two with IgG monoclonal gammopathies, were treated with cyclosporin-A (3 to 5 mg/kg/day). In three, this treatment was successful. It was unsuccessful in four patients who were resistant to other treatments and in one who had initially received cyclosporin-A. There were no serious side effects. In selected patients with CIDP, cyclosporin-A is a potentially useful treatment.

(*J Neurol Neurosurg Psychiatry* 1996;60:185-187)

Keywords: cyclosporin-A; inflammatory demyelinating polyneuropathy

Chronic inflammatory demyelinating polyneuropathy (CIDP) is an immune mediated neuropathy most often treated with prednisone, plasma exchange, or human immunoglobulin (Hlg).¹ Because many patients either fail to respond to these standard treatments, become refractory to them, or develop intolerable side effects, other treatments have been tried. We report eight patients with CIDP treated with cyclosporin-A, which has been given previously with mixed results.²⁻⁸

Patients and methods

Three men and five women, ranging in age from 17 to 68 years, received cyclosporin-A

for CIDP (table), which was diagnosed by standard criteria.⁹ Two had IgG monoclonal gammopathies of undetermined significance (MGUS). Cyclosporin-A was started at 3-5 mg/kg/day in divided doses with dose adjustments based on monitoring of trough concentrations, blood pressure, haematology, and biochemical profiles.

Results

Most patients had been given other treatments before starting cyclosporin-A (table). In three (1, 3, and 6), treatment with cyclosporin-A was successful. Patient 1, who had not improved while on prednisone for three months (during which time plasma exchange and Hlg had also been given) improved within two weeks of starting cyclosporin-A (figure). Four years later, weakness returned as the drug was reduced. A more detailed account is given later. Patient 3, who had responded initially to prednisone but had significant side effects, continued to improve on cyclosporin-A and was able to reduce prednisone without relapsing. Patient 6 previously responded to prednisone, plasma exchange, and Hlg, but each treatment became less effective with time and was associated with appreciable side effects. Eight years into her illness, during a period of decreasing response to Hlg and no response to high dose prednisone, plasma exchange was initiated and was successful, but was required every two weeks. After starting cyclosporin-A, plasma exchange was no longer necessary. Two years later, with weaning off cyclosporin-A, weakness returned. In all three, prednisone was gradually reduced and finally stopped. Two recently relapsed during

Clinical features of patients treated with cyclosporin-A

Patient	Age	Sex	CSF		Para-protein	Nerve biopsy results			Treatment	
			Protein (mg/dl)	Cells (No/ μ l)		Inflammation	Demyelination	Axonal loss	Prior	Concurrent
1	40	F	321	2	None	1	2	1	Hlg, PE	Pred
2	39	F	202	0	None	0	2	3	Hlg, PE	Pred
3	17	F	43	0	None		Not done		None	Pred
4	43	M	83	0	IgG λ	0	1	1	Hlg	Pred, AZA
5	55	M	168	0	IgG λ	1	2	2	None	None
6	17	F	53	1	None	0	2	2	Hlg	Pred, PE
7	68	M	40	2	None		Not done		Hlg, AZA	Pred
8	56	F	51	1	None	0	0	2	Pred, Hlg, PE	None

AZA = Azathioprine; Hlg = human immune globulin; PE = plasma exchange; Pred = prednisone. Nerve biopsy results have been assigned arbitrary values from 0 (none) to 3 (severe).

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Received 6 June 1995
and in revised form
21 September 1995
Accepted 29 September 1995

Clinical course of patient 1. PE = plasma exchange; Hlg = human immunoglobulin.

cyclosporin-A reduction, and one remains well on cyclosporin-A alone at the original dose.

In the five other patients, there was no clear response to the drug.

Patient 5 received cyclosporin-A as initial treatment but it failed to stop the progression of his weakness, which rapidly reversed with prednisone. In four patients resistant to treatment, cyclosporin-A was also unsuccessful. Two of these later responded: one to cyclophosphamide (patient 7) and one to plasma exchange (patient 8). The other two patients did not improve on any other treatments, and CIDP progressed. One patient with an IgG paraprotein later developed a plasmacytoma, and the other died of respiratory failure related to CIDP.

There were no serious side effects of cyclosporin-A. Minor side effects included hypertension, transient headache, nausea, shortness of breath, sleep disturbances, cramps, and reversible increases in serum creatinine.

CASE REPORT

Patient 1

In March 1991, this 40 year old woman developed progressive weakness and paraesthesia in her limbs, and difficulty walking. Twelve weeks later, she was placed on prednisone (60 mg/day) and her decline stopped, but she did not improve. Plasma exchange and Hlg produced no clinical change. In July, cyclosporin-A was started at 5 mg/kg/day, and within two weeks she improved (figure). Prednisone was gradually reduced and discontinued in September 1992. She developed hypertension in November 1992. By December 1993, she had only minimal distal weakness and sensory deficit. Cyclosporin-A was tapered off slowly and by January 1995 her dose was 100 mg/day (1.5 mg/kg/day) but with a cyclosporin-A trough concentration of < 19 ng/ml. In April 1995, distal weakness and sensory loss reappeared, and so cyclosporin-A was reinstituted at 400 mg daily (5 mg/kg/day).

Discussion

Three patients with CIDP either improved or were able to discontinue prednisone after

starting treatment with cyclosporin-A. In the other five, cyclosporin-A had no effect. This parallels the results in the other studies of similar size,^{2,5} in which cyclosporin-A was useful mainly in patients who previously responded to prednisone. In addition, two patients relapsed during the clinical monitoring.

There are several past reports of cyclosporin-A being used in limited numbers of patients with CIDP.^{3,4,6-8} A clear conclusion was not evident from these reports. Tindall⁵ treated 10 patients with CIDP, all on concurrent prednisone, with cyclosporin-A starting at 5 mg/kg/day. After eight weeks, all patients were started on a fixed steroid taper. By six months, six had improved clinically and it was possible to lower the prednisone dose by amounts ranging from 12% to 100%. Four did not change appreciably. Long term follow up data are not available. Hodgkinson and colleagues² described eight patients with CIDP, five with MGUS, who received cyclosporin-A. All had received or were receiving other treatments. Cyclosporin-A was started at 10 mg/kg/day, tapering to a dose of 5 mg/kg/day after three months. Three patients went into complete remission. In the other five, the prednisone and plasma exchange requirements were reduced by cotreatment with cyclosporin-A.

The mechanism of action of cyclosporin-A is unclear but the drug is thought to suppress the response of T helper lymphocytes by inhibiting production of interleukin-2 and interferon- γ and preventing further recruitment of activated helper cells. Cyclosporin-A thus inhibits the response of T cells to antigens but has little effect on B lymphocytes. It has a rapid onset of action, usually within weeks. Its major side effects are nephrotoxicity and hypertension, both of which can be effectively managed by close clinical monitoring, use of a twice a day dosing regimen, employment of starting doses of 5 mg/kg or less, and frequent monitoring of serum cyclosporin-A and creatinine concentrations. In our study, there were no serious side effects of treatment with cyclosporin-A.

An important question is which clinical characteristics predict a favourable outcome with cyclosporin-A treatment. From previous reports, those patients already responsive to prednisone had the most favourable response to cyclosporin-A. Cyclosporin-A has rarely been effective either as the primary treatment or in patients resistant to other treatments; it has worked mainly as a steroid-sparing agent. This is similar to the clinical experience with azathioprine (AZA) in CIDP. Compared with AZA, cyclosporin-A has a more rapid onset of action and is less allergenic. Although cyclosporin-A can be more toxic than AZA, careful monitoring should increase its safety.

The limited data on patients with CIDP treated with cyclosporin-A make it difficult to evaluate its efficacy. At present, it should be reserved for those patients who are resistant to established treatments, or intolerant of their side effects. Caution must be taken when using cyclosporin-A in elderly patients with

raised creatinine concentrations or in patients with hypertension. Cyclosporin-A might be an ideal long term treatment for younger patients with relapsing CIDP, sparing them from the long term side effects of steroids.

This work was supported in part by Sandoz, USA and The James Dunn Fund for Neuromuscular Research.

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