LETTERS TO THE EDITOR

Progressive systemic sclerosis with CNS vasculitis and cyclosporin A therapy

Progressive systemic sclerosis is a multisystem disorder characterised by inflammatory, vascular and fibrotic changes of skin and a variety of internal organs. Most reports describing neurological complications of PSS have focused on damage to the peripheral nervous system. CNS dysfunctions are rare and are thought to result from uraemia, hypoxaemia, and severe hypertension. This is the first trial of cyclosporin A (CyA) in a patient with CNS vasculitis secondary to PSS.

A 67 year old woman was admitted with difficulty in walking and with speech. She had been in good health until December 1985, when she noted that her hands turned white in a cold environment. Subsequently, she developed a nonproductive cough. In February 1986 she experienced occasional dizziness. In July 1990 she began to walk with a waddle.

On admission, her blood pressure, pulse, body temperature, and respiration were normal. The skin of her face was so taut that she was unable to open her mouth fully; her lips were thin and shortened. She had telangiectasis on the chest. Auscultation of the chest disclosed fine crackles on the lower fields of both lungs. The skin of her fingers and hands was firm and thickened and tightly bound to underlying subcutaneous tissue. The skin changes spread from her hands to the chest. Calcinosis cutis was not found. Raynaud's phenomenon could be induced by cold stimuli.

She had dysarthria; left hemiparesis with slight rigidity and spasticity; and mild incoordination. Deep tendon reflexes were normal and pathological reflexes were absent.

The ESR, blood count, and biochemical tests, were normal. The C-reactive protein was negative; rheumatoid factor positive; antinuclear antibody present in a 1:320 dilution; anti-Scl-70 antibody (antiscleroderma antibody) was positive in a 1:16 dilution. Electrocardiogram showed first-degree atrioventricular block with a prolonged PR interval of 0·24 second. Pulmonary function tests revealed a slightly restrictive ventilatory defect; the ratio of FEV1/FVC was 0·96 and the ratio of FVC observed/FVC predicted was 0·73. Cold water (10°C) immersion test on the skin of the hand showed a delay in regaining the initial temperature, which was compatible with Raynaud's phenomenon. CSF was normal. Radiograph of the chest showed fine fibrotic strands in the lower portions of both lungs. Barium-meal revealed a dilated oesophagus with decreased peristalsis. MRI scan of the head disclosed ischaemic lesions in the right occipital region, the right middle cerebellar peduncle, and the basilar part of the pons. Digital subtraction angiogram (DSA) showed localised severe stenosis and poststenotic dilation, a "string of beads" appearance, from the distal end of the right vertebral to the proximal portion of the basilar arteries (fig). There was no definite stenosis in other arteries. Skin biopsy specimen showed proliferation of thickened collagen fibres in the dermis.

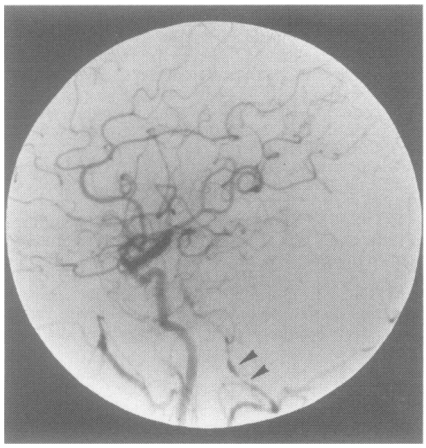

Figure Digital subtraction angiogram shows localised stenosis and post-stenotic dilation. There was no definite stenosis in other arteries.

Based on these findings, we diagnosed PSS, following the scleroderma criteria of the American Rheumatism Association, and we attributed the abnormal angiogram findings to vasculitis. Treatment was started with CyA 8 mg/kg a day. Two months later, urinalysis disclosed an increase in urinary β_2-microglobulin, a sign of renal damage caused by CyA. Immediately the dose was reduced to 6 mg/kg, and during the next month it was reduced by 1 mg/kg every week, to 3 mg/kg.

Though the abnormal findings of serological tests were not improved, during this period the urinary β_2-microglobulin returned to normal. The patient's nonproductive cough subsided and Raynaud's phenomenon did not occur. The skin involvement gradually diminished, and the abnormal ECG findings and pulmonary function tests improved: PR interval, 0·20 second; FVC observed/FVC predicted ratio, 0·8. The neurological symptoms that resulted from multiple CNS infarction remained stable. Cold water immersion test showed a normal recovery to the initial temperature.

One year after the beginning of CyA treatment, the patient takes 150 mg/day (3 mg/kg/day) of CyA, her hands and fingers are still slightly firm and thick, but autoantibodies, including anti-Sc1-70 antibody, have normalised, except for a positive ANA in a 1:160 dilution.

The classical "string of beads" appearance on the angiogram is characteristic of vasculitis, but may be present in infection and arteriosclerosis. There have been three reports about PSS with CNS vasculitis.[1–3] In all the cases the authors diagnosed PSS based on angiograms, and in Lee's report, post mortem examination disclosed mononuclear cell infiltration into the left internal carotid artery.[1]

Recently, some researchers have emphasised the importance of vascular involvement in the pathogenesis of PSS, and have suggested that it was probably the initial event preceding abnormal fibrosis. Why our patient had CNS vasculitis without systemic vasculitis is unclear. We assume that there are unknown differences in antigenicity between arteries of the CNS and other organ systems.

Effective drug therapy in PSS has not been established. D-penicillamine has been reported to reduce skin thickening, but it does not change the clinical course of PSS. Corticosteroids are considered to aggravate symptoms of PSS. Some investigators have reported that CyA was effective against PSS.[4,5] Our first trial of CyA in PSS with CNS vasculitis appeared dramatically successful.

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1 Lee JE, Haynes JM. Carotid arteritis and cerebral infarction due to scleroderma. *Neurology* 1967;17:18–22.
2 Estey E, Lieberman A, Pinto R, Meltzer M, Ransohoff J. Cerebral arteritis in scleroderma. *Stroke* 1979;10:595–7.
3 Pathak R, Gabor AJ. Scleroderma and central nervous system vasculitis. *Stroke* 1991;22:410–3.
4 Zachariae H, Halkier-Sorensen L, Heickendroff L, Zachariae E, Hansen HE. Cyclosporin A treatment of systemic sclerosis. *Br J Dermatol.* 1990;122:677–81.
5 Gisslinger H, Burghuber OC, Stacher G, Schwarz W, Punzengruber C, Grainger W, Luger TA, Wolff K, Smolen JS. Efficacy of cyclosporin A in systemic sclerosis. *Clin Exp Rheumatol* 1991;9:383–90.

Ocular myasthenia: diagnostic value of single fibre EMG in the orbicularis oculi muscle

When myasthenia gravis is restricted to ocular muscles it can present a difficult diagnosis. Firstly, the response to Tensilon iv can be negative or ambiguous; secondly, repetitive nerve stimulation and titration of serum anti-acetylcholine receptor antibodies (anti-AChR abs) often give negative results.[1] Chronic progressive external ophthalmoplegia (CPEO) must be distinguished. Single fibre electromyography (EMG) has proved the most sensitive diagnostic test in patients with myasthenia gravis.[2] However, increased jitter and impulse blocking can also be found in nerve and muscle diseases[3,4] and abnormal findings have been reported in some patients with chronic progressive external ophthalmoplegia.[5,6]

In this study, we verified the diagnostic sensitivity of single fibre EMG of the orbicularis oculi muscle in patients with ocular myasthenia gravis and its usefulness in the distinction from chronic progressive external ophthalmoplegia.

We studied 14 patients with purely ocular myasthenia and 8 patients affected with chronic progressive external ophthalmoplegia. There were 7 male and 7 female patients with myasthenia gravis, aged 13–61, mean (SD) 41·4 (18·3), with duration of disease ranging from 1–40 years, mean (SD) 7 (10·1). The diagnosis of ocular myasthenia was based on history and clinical signs together with at least one of these features: unequivocal improvement after intravenous edrophonium; presence of serum antibodies to AChR; decremental response to repetitive nerve stimulation. Thirteen patients showed fluctuating ptosis and/or diplopia, while in one case, with long-standing disease, clear fluctuations were not evident. Twelve patients improved