LETTERS TO THE EDITOR

Multiple sclerosis and hypertrophic demyelinating neuropathy

Exceptionally demyelinating lesions may occur in spinal roots and in peripheral nerves,[1–5] in multiple sclerosis (MS). A patient who satisfied criteria for clinically definite MS also developed hypertrophic demyelinating polyneuropathy identified by sural nerve biopsy.

A 24 year old white male mechanic with no personal or family history of relevant disease was admitted to hospital in June 1985 with diplopia, weak, numb legs and a sensation of oppression radiating girdlewise at the midthoracic level. He recovered without treatment within four weeks, but three months later again had numbness on the right side. On this occasion he was treated with adrenocorticotrophic hormone (ACTH) and the symptoms disappeared.

In March 1986 he was admitted to our centre with weakness of the legs, accompanied by an urge to urinate. Clinical examination revealed horizontal nystagmus, asymmetrical paraparesis affecting chiefly the left leg, superficial hypoaesthesia on the right side below the level of dermatome T5, profound hypoaesthesia in both legs, enhanced knee reflexes and bilateral Babinski's sign. Examination showed normal CSF and CT scans, brainstem evoked potentials with waves IV and V missing bilaterally and visual evoked potentials with bilaterally increased latencies. ACTH treatment brought about almost complete recovery from leg weakness and profound hypoaesthesia.

He was again admitted to our centre in November 1988 after six weeks of progressive paraparesis with Lhermitte's sign. Examination revealed vertical nystagmus, asymmetrical paraparesis with marked weakness in dorsiflexion of the right foot, absence of the right knee reflex, right and left Achilles tendon reflexes, and bilateral Babinski's sign. T2 weighted MRI showed several areas of increased signal in the periventricular white matter of both cerebral hemispheres. Treatment for two weeks with intravenous methylprednisolone showed a marked improvement. He was sent home, and the following year took 150 mg oral azathioprine a day. During this time he had transitory reduction of visual acuity in the left eye and right hemifacial numbness from which he recovered in less than a week.

In May 1990, after five months without medication, he was admitted to our hospital for the third time with intense tetraparesis preventing eating and locomotion, and hypoaesthesia in both hands and feet. Clinical examination revealed predominantly distal tetraparesis, total lack of osteotendon reflexes and persistent Babinski's sign. No abnormality was detected by blood analyses (serotests were carried out for: syphilis, HIV, HTLV-1, Lyme disease, antinuclear antibodies, antiphospholipid antibodies; determination of B12 vitamin, folic acid, porphyrin metabolism, adrenal function and lead) or by urine tests for metachromatic bodies. HLA-A3 and HLA-B7 were negative. The protein content of CSF was 680 mg/l, with 100 mg/l of IgG, but the cell count was normal. Visual and brainstem evoked potentials and MRI were similar to those recorded previously. Electroneuromyography revealed slow motor nerve conduction in all four limbs: right median was 41 m/s (normal 50–70), right ulnar 43 m/s (normal 50–70), left tibial 29 m/s (normal 40–60) and an absence of evoked response in the right common peroneal nerve; sensory conduction velocities and action potentials amplitudes were decreased: right median 45 m/s (normal 50–70) and 6·5 μV (normal > 8), left sural 32 m/s (normal 50–70) and 2·5 μV (normal > 5). A right sural nerve biopsy revealed that some fascicles exhibited slight fibre loss, with early onion bulb formation in occasional fibres, whereas others showed prominent hypertrophic neuropathy with abundant large bulbs and thin myelin sheaths (fig).

Demyelination was confirmed by examination of teased fibres, and a number of fibres with axonal degeneration ovoids were also observed. There was no vasculitis, amyloid or metachromatic material. The patient was treated with intravenous methylprednisolone and subsequently with oral prednisone. In May 1991 he maintained an acceptable condition and led an independent life with 30 mg a day prednisone.

This patient fulfilled the criteria for clinically definite MS. At the same time, histopathological examination of the sural nerve revealed demyelinating neuropathy. Nukada *et al*[6] have described a similar case of hypertrophic neuropathy with no inflammatory infiltrate and with different degrees of affectation among the fascicles of the same nerve.

The combination of central and peripheral demyelination has previously been reported.[2 3] In 1987 Rubin *et al*[3] described two cases very similar to our patient, referring to them as cases of combined central and peripheral myelinopathy. CNS demyelination of the kind associated with MS has also been found in Guillain-Barré syndrome.[1 4 5] CNS myelin plaques like those produced by MS were observed, together with the demyelination and inflammatory infiltration of spinal roots, such as found in the postmortem examination of another patient with idiopathic acute demyelinating polyradiculoneuropathy.[7]

The chronology of our patient's case history suggests that the first bouts of symptoms were caused by CNS myelin lesions, but that the peripheral nervous system has been most affected in the past two years. The observed hypertrophic demyelinating neuropathy is quite different from neuropathies caused by compression or nutritional problems, and also from the subclinical neuropathies revealed by electrophysiological examination in a larger number of patients with MS.[8 9] It resembles chronic idiopathic demyelinating polyneuropathy, which can evolve either progressively or in recurrent bouts but generally responds well to corticotherapy. It has also been associated with subclinical signs of CNS white matter involvement on MRI.[10 11]

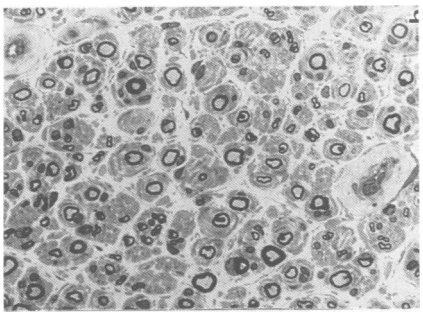

Figure Sural nerve biopsy, loss of myelinated fibres, thin myelin sheaths and presence of abundant onion bulbs (1μm toluidine blue stained, × 400).

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Chlorambucil fails to improve patients with motor neuropathies and antibodies to gangliosides

Evidence that an autoimmune mechanism may play a role in the pathogenesis of motor neuron syndromes has been emphasised by the presence of anti-gangliosides antibodies in some of these patients.[1 2] Recent data suggest that "high" levels of serum anti-GM1 antibodies are commonly found in some patients with a predominantly motor neuropathy that can mimic a motor neuron disease: the interest in identifying patients with such antibodies and progressive motor neuron syndromes lies in the fact that they may improve following immunotherapy.[2] We report three patients with multifocal motor neuropathy and serum antibodies to gangliosides. Immunosuppressive treatment with