Letters

Sensory neuropathy as the initial manifestation of primary biliary cirrhosis

Sir: Primary biliary cirrhosis (PBC) is a chronic progressive disorder characterised by cholestasis, liver destruction and circulating mitochondrial antibodies.¹ Neurological complications of PBC are unusual. In a previous report a pure sensory neuropathy was described in a patient with PBC.² This study describes a second case of pure sensory neuropathy as the initial manifestation of PBC.

A 62 year old woman was admitted to hospital with a one year history of progressive numbness and clumsiness in her right hand and unsteadiness of gait. She denied pruritus, or gastrointestinal symptoms. General examination was normal. Neurological examination demonstrated normal muscular strength. Deep tendon reflexes were absent. Position and vibration senses were absent in the right hand and severely decreased in the left hand and legs. Loss of the other sensory modalities was found in the same distribution but to a lesser degree. Pseudoathetotic movements were present in the right hand. Gait was ataxic with a positive Romberg's sign. The rest of the neurological examination was normal.

Routine laboratory analyses were normal except for a serum alkaline phosphatase level of 1530 U/l (N < 279) and gamma-glutamyl transpeptidase of 552 U/l (N < 65). There was an elevation of the levels of IgG to 2960 mg/100 ml (N: 600–1800) and IgM to 1560 mg/100 ml (N: 50–150). Rheumatoid factor, anti-DNA, Sm, RNP, Ro and La antibodies were negative. Antimitochondrial antibodies were positive at 1:10, 240. Serum electrophoresis, CSF examination, serum B₁₂ and folate levels, and Schilling's test were normal. Schirmer's and Rose Bengal tests and a minor salivary gland biopsy were negative. Liver biopsy specimen revealed a reduced number of normal bile ducts surrounded by infiltrates of lymphocytes and the presence of small atypical bile ducts with mild portal fibrosis consistent with stage II PBC.¹

Indirect immunofluorescence on frozen sections of normal human dorsal root ganglia and peripheral nerve incubated with the serum of the patient (1:500) demonstrated staining of the axons with a fine granular pattern. Nuclear membrane of all cell types was also positive. An identical pattern of staining was obtained with the serum of five patients with PBC without sensory neuropathy and high titres of antimitochondrial antibodies. Serum of ten normal controls was negative.

Electrophysiological studies disclosed

normal motor nerve conduction velocities and distal latencies. Central and peripheral sensory evoked potentials were absent in the four extremities. Needle EMG did not show denervation. A sural nerve biopsy demonstrated a 50% reduction in the number of myelinated fibres. The density of unmyelinated fibres was normal. There were some clusters of small myelinated fibres indicative of regeneration. Teased preparations of 50 myelinated fibres did not demonstrate acute axonal degeneration or primary demyelination. Fourteen fibres had all the internodes of short length suggesting axonal regeneration. Inflammatory or xanthomatous infiltrates. Immunoglobulin or amyloid deposits or abnormalities in the blood vessels were not found.

The patient was discharged on azathioprine and colchicine. Seven months later the neuropathy has progressed while the liver disease remains asymptomatic.

The association of a sensory neuropathy with PBC was previously reported in a patient who also presented the neuropathy as the initial manifestation of PBC.² The sural nerve biopsy taken from the right ankle demonstrated a severe axonal degeneration while the biopsy of the left sural nerve at the calf level was normal. It was concluded that the neuropathy was due to a dying-back type of axonal degeneration. However, like our patient, she presented with an asymmetric neuropathy mainly involving the right arm and leg so that we cannot rule out the possibility that the right sural nerve was more damaged than the left only because the neuropathy was asymmetric. Biopsies should have been done at different levels of the same nerve to support the hypothesis of a dying-back type of axonal degeneration. The histological findings in the nerve biopsy of our patient are either consistent with a neuronopathy or a distal axonopathy. Although the dorsal root ganglia was not studied to definitively prove a sensory neuronopathy, the clinical and electrophysiological features of our patient and the one previously reported² are more consistent with a sensory neuronopathy than with a distal axonopathy.

The pathophysiology of the neuropathy is unclear. A mild sensory, mostly dysaesthetic, neuropathy has been described in patients with PBC and generalised cutaneous xanthomata secondary to xanthomatous infiltrates in the nerve.³ These features were not observed in our patient and the symptoms of the neuropathy were also different. We did not find any specific antibody directed against antigens of the peripheral nerve or sensory neurons. Antimitochondrial antibodies could have been internalised by

the sensory axons to cause the neuropathy but there is no experimental evidence that they interfere with the metabolism of mitochondria.¹ PBC is characterised by widespread inflammatory infiltrates in the liver and sometimes other organs and there is some evidence to consider the liver damage is mediated by cytotoxic T lymphocytes.¹ Similar infiltrates in the dorsal root ganglia could be the cause of the neuropathy as it has been suggested in the sensory neuronopathy associated with Sjogren's syndrome.⁴

This case report emphasises the idea that a pure sensory neuropathy may be associated with different autoimmune diseases.⁵ Patients presenting with a sensory neuropathy should be studied for the presence of antimitochondrial antibodies to rule out an otherwise asymptomatic PBC.

We thank Dr J Rodes for his advice and criticism on the review of the manuscript and Ms MJ Iranzo for her excellent technical assistance in the immunofluorescence studies.

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