protein content of 0.7 g/l but no cells. Once again, the symptoms began to improve 3 to 4 weeks from the onset and within 2 months the patient had almost fully returned to normal.

As noted above, relapse among patients with the Guillain-Barré syndrome is well recognised. For the Miller Fisher syndrome, the only previous relevant reports of which we are aware are those of Barontini *et al*⁴ and Kaplan *et al*⁵. Barontini *et al*⁴ described a patient suffering from a Miller-Fisher type disorder who had a history of a similar event 19 years earlier, but the first illness was not observed and, during the second, CSF and EMG studies were normal. Kaplan *et al*⁵ have recently documented two cases of relapsing sensory neuropathy accompanied by ophthalmoplegia that were considered to represent a variant of relapsing inflammatory neuropathy, similar in some respects to the Miller Fisher syndrome.

The first phase of our patient's biphasic illness demonstrated features not only of the Miller Fisher syndrome, manifested by ophthalmoplegia, ataxia and tendon areflexia, but also some minor changes consistent with the Guillain-Barré syndrome (limb weakness and distal paraesthesiae). The relapse, however, was characterised by features more compatible with a pure Miller Fisher syndrome. This single case, therefore, demonstrates an overlap between these two syndromes occurring sequentially in the same patient and would thus suggest a similar pathogenesis underlying both disorders. Arnason² has commented on the presence of limb weakness in some cases of the Miller Fisher syndrome, indicating a link with the Guillain-Barré syndrome.

The pathological findings in the Guillain-Barré syndrome consist of multifocal infiltrates of inflammatory cells in the spinal roots and peripheral nerves associated with segmental demyelination and variable axonal destruction.² The pathological changes in the Miller Fisher syndrome are so far poorly delineated. Phillips *et al*⁶ reported the postmortem findings in a case diagnosed as the Miller Fisher syndrome. The patient had a combination of bilateral external ophthalmoplegia, facial and bulbar weakness, limb weakness and ataxia, tendon areflexia and sensory loss in the arms and legs. Nerve conduction velocity was considerably reduced. Necropsy revealed demyelination in the peripheral nerves, spinal roots and lower cranial nerves, with sparse inflammatory infiltrates. No abnormalities were detected in the third, fourth or sixth cranial nerves, but only the proximal portions were examined. Other patients with an acute

inflammatory polyneuropathy have been described in which there was a combination of limb weakness and an internal and external ophthalmoplegia but in which limb ataxia was not a feature.^{7,8}

Al-Din *et al*⁹ reported a series of cases with clinical features similar to those of the Miller Fisher syndrome but which were considered to have brainstem encephalitis, some on the basis of computed tomography and postmortem examination. It was suggested that a spectrum might exist ranging between cases with pure brainstem involvement at one end, through mixed cases, to those with pure peripheral nerve involvement at the other. The present patient showed no evidence of CNS involvement apart from some delay in the SSEPs. The consensus opinion, however, is that the Miller Fisher syndrome represents a peripheral nerve disorder. Nevertheless, it is often difficult to demonstrate abnormalities of nerve conduction in the syndrome. Cases with relatively minor changes in motor nerve conduction and more obtrusive changes in sensory conduction have been documented.¹⁰ Those in the present case were modest but definite.

The mechanism of tremor in the Miller Fisher syndrome is unknown but a peripheral disturbance is generally assumed.² It may involve a mismatch between afferent proprioceptive signals from muscle spindles and those from Golgi tendon organs.¹¹ A central disturbance, related to a disruption of central cerebellar connections is not excluded, but lacks pathological substantiation.

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Primary amyloidosis in a patient with myotonic dystrophy

Sir: Several immunoglobulin abnormalities have been described in myotonic dystrophy, a hereditary progressive muscle disorder transmitted as an autosomal dominant trait. These include hypogammaglobulinaemia,¹ shortened half life of ¹³¹I-labelled gammaglobulin,² increased catabolism of IgG,³ and diminished antibody production to certain antigens.⁴ We describe the hitherto unreported occurrence of amyloidosis in patient with myotonic dystrophy and hypogammaglobulinaemia.

A 47-year-old garage manager known to have myotonic dystrophy since 1947, was referred in September, 1981 with exertional left inframammary chest pain and paraesthesia in the left arm refractory to glyceryl trinitrate, metoprolol and nifedipine. On examination he had generalised muscle wasting with sternomastoid atrophy, frontal balding, testicular atrophy and early bilateral cataracts. Tendon reflexes were diminished, he had difficulty relaxing handgrip and myotonic contraction could be elicited by percussion of thenar eminences. His ECG, exercise ECG, echocardiograph and coronary angiogram were normal although left ventricular end diastolic pressure was 12 mm Hg. In January, 1982 he developed a nephrotic syndrome. Investigations in

cluded: creatinine clearance 90 ml/min; urinary protein 5G/24 h (non-selective) serum albumin, 20 g/l; ESR 108 mm in 1 h; ANF and anti double-stranded DNA, negative; ASO titre < 200 Todd units/ml; and serum complement normal. Serum IgA and IgM were normal but IgG was reduced (1.39 g/l). Plasma and urine electrophoresis and immunoelectrophoresis showed no monoclonal bands. Renal biopsy showed a mild mesangial-proliferative glomerulonephritis with granular IgM and scanty deposits of C₃, C1q and fibrin in the mesangium. Congo red stain showed amyloid in the glomeruli (fig). Amyloid fibrils were seen on electron microscopy.

Between January and November, 1982 he was readmitted four times with left inframammary pain, oedema and increasing muscle weakness. Upper gastrointestinal endoscopy, oesophageal manometry, barium swallow and acid provocation test showed a hypotonic upper gastrointestinal tract. Most ECGs during chest pain were normal, a few showed ischaemia, and twice an arrhythmia was noted (supraventricular tachycardia and atrial fibrillation). In December, 1982 he died following the development of left hemiparesis and bronchopneumonia.

At necropsy the heart was slightly enlarged, stiff and waxy in texture; the major coronary arteries were normal. Lungs showed lower lobe pneumonia with oedema. Kidneys were slightly enlarged with pale, smooth cortices. Microscopy showed perivascular amyloid in the lungs, spleen, liver, oesophagus, stomach, duodenum, thyroid, aorta, testes and brain. In the kidney, amyloid was deposited in the glomeruli and larger blood vessels. Perivascular and intramural amyloid was found in small vessels in the myocardium but luminal narrowing was slight. The individual myocytes and capillaries were surrounded by amyloid and electron microscopy revealed muscle fibres being replaced by amyloid fibrils. Unfortunately skeletal muscle was not examined. The cerebral arteries were normal. A recent infarct in the right basal ganglia and insular cortex was attributed to hypotension preceding admission. Immunoperoxidase staining of amyloid was positive for lambda light chains.

Although cardiac abnormalities interfering with conduction, and minor abnormalities of cardiac muscle on electron microscopy, are well recognised features of myotonic dystrophy,^{5,6} we are unable to find any previous report of amyloidosis. The amyloidosis gave rise to ischaemic cardiac pain, as has been previously described,⁷ but this could not be diagnosed during life by

Fig Renal biopsy specimen showing glomerular deposits of amyloid seen as spiky protrusions on the epithelial aspect of glomerular basement membrane. (Congo red viewed under polarised light $\times 200$).

coronary angiography because the major coronary arteries and their larger branches were patent. Refractoriness of the angina to drug treatment may have resulted from ischaemia caused by the thick layer of amyloid fibrils that surrounded the muscle cells and capillaries.

The distribution of amyloid was similar to that found in the primary form of the disease and immunoperoxidase studies were in keeping with this being light chain in type. This type of amyloidosis occurs in myelomatosis but in a proportion of patients no cause is found and the condition is classified as primary amyloidosis.^{8,9} Although the bone marrow was not examined in our case, the presence of myeloma is virtually excluded by the absence of monoclonal abnormalities on immunoelectrophoresis of serum and urine. In the rare type of "non-secretory myeloma",^{10,11} where monoclonal abnormalities are found in the plasma cell but not in the serum or urine, amyloidosis has only been reported in one case¹¹; moreover renal involvement is unusual in this form of myeloma.¹² The absence of serum and urine abnormalities in the case of non-secretory myeloma associated with amyloid was explained by the authors as perhaps representing secretion of incomplete protein fragments not identifiable as immunoglobulins or Bence-Jones proteins.¹¹ It seems unlikely that the present case had non-secretory myeloma in view of the lack of bone involvement and otherwise normal haematology. In patients with primary amyloidosis in whom the usual diagnostic criteria for myelomatosis are absent, it seems probable that immunoglobulin components are released from a dyscratic plasma cell clone.¹² While the hypogammaglobulinaemia in this case may be attributed to the nephrotic syndrome, immunoglobulin abnormalities have been

reported in patients without proteinuria in myotonic dystrophy.¹⁻⁴ The relation between the previously described immunoglobulin abnormalities in myotonic dystrophy and primary amyloidosis in the present case is unclear.

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