

# Proximal motor neuropathy, IgA paraproteinaemia and anti-myelin-associated glycoprotein reactivity

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**Summary:** We report a case with proximal motor neuropathy associated with benign IgA lambda paraproteinaemia. Immunoblot demonstrated reactivity to myelin-associated glycoprotein and not to P<sub>2</sub> protein of peripheral nerve. Dramatic improvement of the polyneuropathy was observed with steroid treatment alone within 4 weeks.

## Introduction

Peripheral neuropathy in association with monoclonal gammopathy, especially that of IgM, has been increasingly recognized since the reports of Latov<sup>1</sup> and Braun.<sup>2</sup> The most prevalent IgM antibody activity is directed against myelin-associated glycoprotein (MAG).<sup>2,3</sup> Other target antigens, such as glycolipids, gangliosides and chondroitin sulphate have also been defined.<sup>4–7</sup> Immuno-suppressive therapy directed at lowering the anti-MAG M-protein concentration did not always result in improvement of the neuropathy.<sup>8–11</sup> Plasmapheresis in these patients may be beneficial when performed on a weekly basis for prolonged periods.<sup>12</sup>

We report a patient with proximal motor neuropathy with benign IgA lambda paraproteinaemia and MAG reactivity. Dramatic clinical improvement was observed with steroid treatment alone.

## Case report

A 69 year old Thai monk presented with a 2-month history of progressive weakness of both arms and legs which worsened so that he became chairbound prior to admission. He denied symptoms of numbness or difficulty in urination. There was no history of hexacarbon abuse, glue sniffing, porphyria, diphtheria, or lead exposure.

On examination, he was alert and coherent. There was generalized weakness of the axial and limb musculature with no wasting or fasciculations. Weakness was most severe in muscles of the shoulder girdle, upper arms, and pelvic girdle (III/V, MRC) with relative sparing of distal muscles (IV/V). Deep tendon reflexes were absent. The plantar responses were flexor, and results of the sensory examination were normal including joint position and vibratory sense. Results of the general examination were normal. There was no lymphadenopathy or hepatosplenomegaly.

Laboratory data revealed a haemoglobin of 11.9 g/dl, packed cell volume of 36% and leucocyte count of  $6.5 \times 10^9/l$ . Other laboratory tests included normal fasting plasma glucose, creatinine, electrolytes, and liver function tests. Serum protein electrophoresis showed a monoclonal band (M-spike) at the beta-globulin region. This was characterized as IgA lambda by immunoelectrophoresis and also confirmed by immunofixation. The level of IgA was 0.87 g/dl (normal:  $0.316 \pm 0.129$ ). The IgG and IgM levels were within normal range. Urine Bence Jones protein was not detected nor was serum cryoglobulin. A bone marrow aspirate revealed 4% plasma cells. A skeletal survey showed no osteolytic or sclerotic lesions. The level of cerebrospinal fluid (CSF) protein was 1.1 g/l and there were no cells in the CSF. Nerve conduction studies revealed a reduction of motor-nerve-conduction velocities of the median nerve (32 m/s) and of the common peroneal nerve (30 m/s) (normal value, above 46 and 40 m/s for median and common peroneal nerve respectively). A sural nerve biopsy specimen showed segmental demyelination.

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Serum was assayed for the presence of antibody against MAG, and P<sub>2</sub> protein by immunoblot as previously described.<sup>13,14</sup> Banked serum from 5 patients with other neurological diseases including sporadic Guillain-Barré syndrome (GBS), thiamine polyneuropathy and Semple vaccination-induced polyneuritis served as controls. Antibody to MAG, not to P<sub>2</sub> protein, could be demonstrated in serum of this patient. Five control patients had no antibody to MAG or P<sub>2</sub> protein.

Therapy with prednisolone 60 mg/day resulted in dramatic clinical improvement. After one month, he could walk a distance of 15 metres without support and climbed stairs with the aid of a railing. On examination, muscle strength had improved by one grade in the proximal muscles. Two months after starting prednisolone, muscle strength returned to normal. There was no limitation in functional activity. Deep tendon reflexes, however, were still absent. Clinical improvement coincided with a decrease in the IgA level which fell to 0.67 g/dl and the M band declined to an undetectable level. Improvement was also confirmed by motor-nerve-conduction velocities of median and common peroneal nerves which rose to 40 m/s. Four months after initiation of treatment with prednisolone, at which time the dosage was tapered to 20 mg daily, there was a subjective deterioration in strength. A further skeletal survey showed no changes.

## Discussion

Monoclonal gammopathy is reported in 10% of patients with polyneuropathy.<sup>15</sup> Particular attention

has been focused on IgM M-protein due to its more common prevalence and its specificity to unique antigen such as MAG.<sup>8,16-18</sup> There seem to be no reports of neuropathy with MAG reactivity and immunoglobulins other than IgM proteins.<sup>8,10</sup> Generally, anti-MAG reactivity indicates an unsatisfactory response to apheresis, chemotherapy, or steroids in patients with IgM monoclonal gammopathy.<sup>8-10,17</sup>

The patient described herein had benign IgA lambda monoclonal gammopathy with reactivity to MAG. Immune responses to P<sub>2</sub> protein had been detected in some studies of patients with sporadic GBS<sup>19-22</sup> but not in all<sup>14,23</sup> and have not been reported in patients with neuropathy and paraproteinaemia. Failure to detect antibody to P<sub>2</sub> protein confirmed, unique specificity of this entity. The clinical pattern of proximal demyelinating motor neuropathy was somewhat atypical, since neuropathies found in association with paraproteinaemias, with or without MAG reactivity, are usually distal sensorimotor or pure sensory neuropathies.<sup>8-10,16,17,24</sup> A case of proximal motor neuropathy, dermato-endocrine syndrome associated with IgG kappa paraproteinaemia has been reported.<sup>25</sup> However, it was not known whether these antibodies reacted against MAG. Good response to steroid treatment was another atypical feature. This patient, without any adjunct chemotherapy or plasmapheresis, improved with the use of steroids alone and his clinical status was still maintained with only low dose. We feel that MAG reactivity alone may not be a poor indicator for treatment outcome in polyneuropathy associated with paraproteinaemia.

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