The clinical spectrum of anti-MAG neuropathies at the National Hospital for Neurology

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IgM paraproteins are commonly associated with peripheral neuropathies, most frequently demyelinating and inflammatory. The associated band is usually a gammopathy of uncertain significance, and more commonly with a kappa light chain. The IgM paraprotein may bind with anti-myelin-associated glycoprotein antibodies (anti-MAG) and this is thought to cause a slowly-progressive distal onset symmetrical demyelinating neuropathy with unsteadiness and tremor. We audited the clinical phenotype of 22 "strongly positive" (Bühlmann) anti-MAG patients at the National Hospital for Neurology. We describe their clinical phenotype, haematological diagnosis and response to treatment.

Patients were mildly affected at first consultation (month 0) (MRC score 66/70 ± 1.6 (mean ± SEM). There was a statistically insignificant progression of weakness over 10 years; at month 41 (± 11) the mean MRC score was 65 ± 2.4 and by month 113 (± 35) 62 ± 4.7. A 6 point sensory sum score increased from 5.4/24 ± 0.89 at month 0 to 6.5 ± 1.5 at month 41 but did not reach significance. Nine patients were documented to have a tremor at some stage during their disease and nine patients also developed unsteadiness of gait. There was no clear overlap between developing tremor and unsteadiness of gait.

21 of 22 patients had raised total IgM between 2.55 and 13.8 g/l (normal range 0.4 - 2.3) from which 18 patients had ≥ 1 IgM κ band detected on immunofixation. 19 patients had a diagnosis of MGUS. One patient progressed to chronic lymphocytic leukaemia after several years. Only 1 patient had a diagnosis of Waldenströms Macroglobulinaemia after initial assessment. There was no difference in clinical phenotype between any of the patients with different haematological diagnoses described above.

The indication for treatment in anti-MAG neuropathy with MGUS does not have clearly defined parameters, but most commonly it was worsening functional disability especially mobility. Twelve patients received immunomodulatory treatment. One patient received steroids and four intravenous immunoglobulin without effect. Seven patients received treatment with rituximab and, of these, four had no subjective improvement, one had an initial improvement in balance and then deteriorated, one patient had an objective improvement in sensation (sensory sum reduced from 7 to 2 within eight months of treatment) yet no actual improvement in tremor or balance, and one patient achieved stabilisation.

This cohort reflects that patients who present with a neuropathy strongly associated with anti-MAG antibodies have a slowly progressive mainly sensory neuropathy that is almost always associated with a haematological diagnosis of MGUS. Patients are usually refractory to common treatments and there was no consistent response to rituximab.