Multifocal motor neuropathy with conduction block: a study of 24 patients

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Abstract

Twenty four patients with pure motor neuropathy are reported. The chronic motor involvement associated with fasciculations and cramps, mainly in the arms, led, in most patients, to an initial diagnosis of motor neuron disease. In some patients (nine of 24), there was no appreciable muscle atrophy. Tendon reflexes were often absent or weak. The finding of persistent multifocal conduction block confined to motor nerve fibres raises questions about the nature and the importance of this syndrome. Segmental reduction of motor conduction velocity occurred at the site of the block, but significant slowing of motor nerve conduction was not found outside this site. The response to intravenous IVIg treatment seems to be correlated with the absence of amyotrophy. Patients with little or no amyotrophy had an initial and sustained response to IVIg, and did not develop amyotrophy during the follow up study. They could be considered to have a variant of chronic inflammatory demyelinating polyneuropathy. Patients with pronounced amyotrophy independent of the disease duration did not respond as well to IVIg treatment, suggesting the existence of a distinct entity. Among the patients treated about two thirds who had an initial good response to IVIg had high or significant antiganglioside GM1 (anti-GM1) antibody titres, but there was no correlation between the high titres before treatment and long lasting response to IVIg treatment.

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Keywords: motor neuropathy; conduction block; anti-GM1 antibodies; immunoglobulin treatment

Since the description, by Lewis *et al* in 1982,¹ of a multifocal chronic sensory-motor peripheral neuropathy with persistent conduction blocks, pure multifocal motor neuropathy with persistent conduction blocks has been widely reported.²⁻¹² The patients have multiple mononeuropathy with purely motor manifestations. There is asymmetric weakness with various degrees of amyotrophy, cramps, fasciculations, and preserved or abolished tendon reflexes. Most patients were initially diagnosed as having motor neuron disease. In some cases, the presence of a high serum anti-

GM1 antibody titre^{5 10 13-19} and the response to immunosuppressive treatment²⁰⁻²⁶ suggested an immunopathological mechanism. This was supported by the fact that anti-GM1 antibodies bind at the node of Ranvier,²⁷ and that demyelination occurs at the site of the conduction block.²⁸

Although some authors²⁹ suggest that multifocal motor neuropathy may be a variant of a chronic inflammatory demyelinating polyneuropathy, many questions persist concerning the nature of the underlying process, the natural history, the homogeneity of the syndrome,^{19 30-33} and its response to treatment. We report here the clinical, electrophysiological, histological, and biological findings and response to treatment in 24 patients with pure multifocal motor neuropathy and persistent conduction block.

Patients and methods

PATIENTS

Most patients were referred with a diagnosis of motor neuron disease, although they lacked signs of upper motor neuron or bulbar involvement. Patients were considered to have multifocal motor neuropathy if they had had progressive weakness in at least one limb for at least six months without sensory loss, and multifocal conduction block in at least two nerves.

CLINICAL EXAMINATIONS

The patients were assessed using: (a) the Medical Research Council (MRC) rating scale for muscle strength; five muscle groups corresponding to proximal and distal upper and lower limbs were examined and tested according to the MRC scale. (b) A modified Rankin disability scale: 0 = asymptomatic; 1 = non-disabling symptoms that do not interfere with lifestyle; 2 = minor disability symptoms that lead to some restriction to lifestyle, but do not interfere with the patients' capacity to look after themselves; 3 = moderate disability symptoms that significantly interfere with lifestyle or prevent totally independent existence; 4 = moderately severe disability symptoms that clearly prevent independent existence although the patient does not need constant attention day and night; 5 = severely disabled, totally dependent, requiring constant attention day and night.

ELECTRODIAGNOSTIC STUDIES

Electrodiagnostic studies were performed with a Viking Nicolet electromyograph.

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Table 1 Summary of techniques A and B for anti-GM1 antibody determination in human serum by enzyme linked immunosorbent assay (ELISA)

	Technique A	Technique B
Plates	Polystyrene (Dynatech)	Immulon (Dynatech)
GM1 for coating	GM1 (Fidia) 1 mg	GM1 (Fidia) 0.5 mg
Blocking solution	PBS + 0.05% Tween 20	PBS + 1% BSA
Blocking duration	30 min	6 h overnight
Blocking temperature	RT	RT + 4°C
Test serum dilution	1: 20	1: 100
Incubation time with test serum	2 h	overnight
Incubation temperature	4°C	4°C
Washing solution	PBS + Tween 20	PBS
Secondary antibody (SA)	Goat	Goat
IgG or IgM	HRP	HRP
Incubation time with SA	2 h	1 h
Incubation temperature	4°C	RT
Substrate	OPD	OPD

BSA = bovine serum albumin; PBS = phosphate buffered saline; RT = room temperature; HRP = horseradish peroxidase conjugate; OPD = *o*-phenylene diamine.

Needle EMG examination was performed in all patients. The incidence of spontaneous activity at rest (fibrillation potentials and positive sharp waves) was recorded. The size of motor unit potentials (MUPs) and the pattern of recruitment during maximal effort were also analysed.

Motor nerve conduction studies were performed with supramaximal percutaneous nerve stimulation, whereas compound muscle action potentials (CMAPs) were recorded with surface electrodes. For all patients, median, ulnar, and peroneal nerves were examined on both sides. The median nerve was stimulated at the wrist, elbow, axilla, and Erb's point. The ulnar nerve was stimulated at the wrist, below and above the elbow, on the axilla, and at Erb's point. At Erb's point, the nerve was stimulated with monopolar electrodes. We did not systematically search for conduction block in the radial nerve, as this was considered unreliable. The peroneal nerve was stimulated at the ankle, below and above the fibular head. For all nerve conduction studies skin temperature was maintained at 36°C. Distal latencies, conduction velocity, evoked motor response amplitudes (baseline to negative peak), and areas under the negative phase and its duration were measured. In upper limbs, the nerves were stimulated at five sites, corresponding to four segments. No segments exceeded 25 cm in length. Variation in the proximal/distal amplitude and area ratio and conduction velocity were measured for each segment. Latencies for F waves were measured after distal supramaximal stimulation (at least 16 stimuli) in the median, ulnar, and peroneal nerves.

Sensory nerve conduction and amplitude were measured in the median, ulnar, superficial peroneal, and sural nerves with surface recording and stimulating electrodes. The nerves were stimulated by orthodromic techniques in the upper limbs and antidromic techniques in the lower limbs. Amplitudes were measured peak to peak.

To determine if the reduction in amplitude was due to conduction block, or temporal dispersion, or both, we analysed the amplitude,

area, and duration of the negative phase of the CMAP elicited from each site of stimulation. Between Erb's point and the axilla, a loss of 50% of the CMAP amplitude and area after proximal stimulation suggested a possible partial conduction block. More distally a loss of 30% was considered sufficient to confirm the block. The reduction of CMAP amplitude was considered to be due to temporal dispersion if the duration of the CMAP increased by more than 30% and the corresponding loss of area did not exceed 50%. The amplitude and area changes occurred abruptly over each nerve segment rather than as gradual losses along the length of the nerve.

HISTOLOGICAL EXAMINATIONS

Morphological examination of a sensory nerve (radial cutaneous), including teased fibre studies, was performed in 12 patients under local anaesthesia. The nerve specimens were fixed in 3.6% glutaraldehyde. The fragments were postfixed in osmium tetroxide. One nerve fragment was studied by teasing the endoneurial content. Another was embedded in epon and thionin stained 1 μ thick sections were examined.

BIOLOGICAL EXAMINATIONS

Serum enzymes and conventional biological variables were assayed. Protein immunoelectrophoresis was performed and CSF was examined. In all cases, the patients were sampled before immunosuppressive treatment. Anti-GM1 antibody titres were measured by enzyme linked immunosorbent assay (ELISA) according to two techniques previously described.^{18,34} Table 1 summarises these and they have been evaluated previously.³⁵ The results of the assays were expressed differently. In technique A, serum was considered to contain anti-GM1 antibodies when, at a 1:20 dilution, the optical density (OD) was more than 2 SD above the mean obtained with 10 internal standards (ODX). The titre was defined as the reciprocal of the serum dilution required to obtain the ODX. Thus in technique A, a titre ≥ 20 was considered to be significant (+) and a titre ≥ 100 was considered to be high (++). In technique B, serum was considered to contain anti-GM1 antibodies when, at a 1:100 dilution, the optical density was three times the mean of the normal controls at the same dilution. As reported by Sadiq *et al*,¹⁷ anti-GM1 antibodies were found in normal serum up to a 1:400 dilution. The titre was considered significant (+) when antibodies were detected at 1:800 dilution, and high (++) when detected at $\geq 1:3200$. In technique B, all positive cases were confirmed by immunodetection on thin layer chromatography as described by Mailly *et al*³⁶ with serum at a 1:100 dilution. When positivity was not confirmed by thin layer chromatography the sample was considered to be negative. Controls consisted of patients with chronic inflammatory demyelinating polyneuropathy and normal subjects of the same age groups.

Table 2 Clinical characteristics

	All patients (n = 24)	Group 1 (n = 15)	Group 2 (n = 9)
Sex ratio M/F	20/4	14/1	6/3
Age at onset (y) (mean (SD))	49.8 (9.5)	50.3 (8.8)	47.3 (11.2)
Disease duration (y) (mean (SD))	9.2 (6.3)	12.06 (6.8)	6.7 (2.6)*
Limb onset (No of patients):			
Upper	21	13	8
Lower	3	2	1
Cramp (No of cases)	14	9	5
Fasciculation (No of cases)	17	11	6
Myokymia (No of cases)	2	1	1
Tendon reflex (No of cases):			
Normal	6	3	3
Absent or weak	17	12	5
Brisk	1	—	1

Group 1 = patients with amyotrophy; group 2 = patients without amyotrophy.

* $P < 0.05$, group 1 *v* group 2.

Results

CLINICAL CHARACTERISTICS (TABLE 2)

Twenty four patients, 20 men and four women, were selected on the basis of persistent multifocal conduction blocks in motor fibres. The mean age (SD, range) at onset of symptoms was 49.8 (9.5, 32–70) years. The mean duration of the disease was 9.2 (6.3, 3–28) years.

Onset occurred in one distal upper limb in 21 of 24 patients. In three patients, onset was unilateral in the lower limbs. There were no particular circumstances surrounding the onset, except in two patients with proximal pain in an upper limb. Painful cramps were a usual complaint in 14 of 24 patients. There were no sensory symptoms and the motor deficit was isolated. The disease usually had a very slow progression.

When the deficit was fully developed, upper limb involvement was present in all patients: motor weakness was distal and unilateral in nine patients, distal and bilateral in 13, and affected the proximal and distal parts of the limbs in two patients. In the lower limbs, motor weakness, when it occurred (in 12 cases), was always distal and was unilateral in six cases. The motor deficit therefore affected the distal muscles in the median and ulnar distribution in the upper limbs, although in one third of patients, the deficit mainly affected the wrist and finger extensors in a radial distribution. In six patients, the motor deficit was limited to one upper limb, without amyotrophy in five. Overt muscle atrophy was present in 15 of 24 patients and was usually located at the site of maximal motor deficit. In nine patients no appreciable muscle atrophy was found. One of them with radial motor weakness had hypertrophy of the extensor carpi radialis longus and brevis. A significant difference in the duration of the disease occurred in these two categories of patients: in patients with amyotrophy the mean duration was 12 (SD 6.7) years *v* 6.6 (SD 2.5) years in the non-atrophied group ($P = 0.033$). In the first group the onset of amyotrophy always appeared during the first year of evolution.

Fasciculations were seen in 17 of 24 patients, usually in the involved limb, whereas myokymia occurred in only two patients. The tendon reflexes were weak or abolished in the

involved territories in 17 of 24 patients. They were brisk without Babinski's sign in only one patient, who spontaneously improved and whose deficit was localised in the right distal upper limb.

ELECTROPHYSIOLOGICAL CHARACTERISTICS

In the upper limbs, conduction blocks were found at proximal sites between Erb's point and the axilla, at intermediate sites between axilla and elbow, and at distal sites below the elbow. In lower limbs, the conduction blocks were located only below or in the area of the fibular head on the peroneal nerve. Conduction blocks were always found in the upper limbs. In the lower limbs conduction blocks were only found in six patients. The location of conduction blocks was similar in both nerves and there were no predominant sites in the distribution of the conduction blocks. In all cases, the degree of the conduction block exceeded 50%, which excluded a reduction of the CMAP area due to an interphase cancellation.³⁷ Motor nerve conduction velocities were usually normal outside the site of the blocked segments. Across the blocked segments, the motor conduction velocity was sometimes greatly reduced. In one patient, a pronounced slowing of proximal conduction without associated conduction block was initially found, but distal amplitude was very low. After IVIg treatment, an improvement in distal CMAP amplitude was found and a proximal conduction block could therefore be demonstrated. Motor distal latencies were slightly prolonged in most patients: for the median nerve, 19 of 24 patients had latencies of more than 3.6 (mean (SD) 4.2 (0.7)) ms; for the ulnar nerve, 15 of 24 patients had latencies of more than 3 (mean 3.5 (0.9)) ms; for the peroneal nerve, and 12 of 24 had latencies of more than 5 (mean 5.3 (1.1)) ms.

Distal CMAPs were considerably reduced in some blocked nerves, although in other blocked nerves in the same patient they were normal. In most patients, the reduction in CMAP amplitude was correlated with the degree of muscle atrophy. In a few patients however, despite some degree of clinical atrophy, the reduction in CMAP amplitude was less than expected. In the case of a large reduction in distal CMAP amplitude (less than 1 mv), conduction block was mostly difficult to demonstrate. Only one patient had normal F wave latencies in all nerves. Some patients had normal F wave latencies even in the presence of blocks, but a prolonged or absent F wave latency was found in at least one of the nerves examined. In some patients, an F wave was not obtained or its latency was prolonged even in the absence of conduction blocks. In nine cases, an intermediate wave with electrophysiological characteristics of an axonal reflex was found in the upper limbs: in the median nerve in four patients, in the ulnar nerve in three patients and in both nerves in two patients.

Sensory potential was usually normal or slightly altered: in the median nerve, it was below 15 μ v in eight of 21 patients (mean 23.5 (SD 17.1) μ v); in the ulnar nerve, it was

Table 3 Biological and histological characteristics

	All patients (n = 24)	Group 1 (n = 15)	Group 2 (n = 9)
Serum immunoelectrophoresis (23/24):			
Normal	17	11	6
Polyclonal gammopathy	5	3	2
Hypogammaglobulinaemia	1		1
Serum anti-GM1 IgM activity (technique A) (24/24):			
Negative < 20	7	3	4
Significant ≥ 20	7	5	2
High titres ≥ 100	10	7	3
Serum anti-GM1 IgM activity (technique B) (23/24):			
Negative or low titres	11	7	4
Significant ≥ 1:800	4	2	2
High titres ≥ 1:3,200	8	6	2
Nerve biopsy (12/24):			
Normal	5	3	2
Clusters	4	1	3
Demyelination and remyelination	2	1	1
Active axonal lesion + clusters	1	—	1

Group 1 = patients with amyotrophy; group 2 = patients without amyotrophy.

below 10 μ v in nine of 21 patients (mean 12.2 (SD 7.9) μ v); in peroneal nerve it was below 10 μ v in five of 22 patients (mean 17.6 (SD 11.7) μ v).

Needle EMG showed fibrillation potentials in distal muscles in five of 20 patients in the upper limbs and in six of 24 patients in the lower limbs. The interference pattern was reduced but no giant units were detected.

LABORATORY EXAMINATIONS (TABLE 3)

The CSF was examined in 19 of 24 patients, and was normal in all. Serum immunoelectrophoresis was performed in 23 of 24 patients; no monoclonal peaks were found. A polyclonal profile was found in five patients (three IgM, two IgG), one patient had hypogammaglobulinaemia. The other biological variables were normal.

ANTI-GM1 ANTIBODIES

Table 3 summarises anti-GM1 antibody titres. All the significant or high antibody titres were of the IgM class. In one patient,

anti-GM1 antibodies were not titred with technique B. When examined with technique A, 10 of 24 patients (42%) and eight of 23 (35%) with technique B had high titres. With technique A seven of 24 (29%) and with technique B four of 23 (17%) had significant titres. Thus with technique A, 17 of 24 (71%) of the patients and with technique B 12 of 23 (52%) had significant or high antibody titres. Assayed by technique A, 17.5% normal subjects had low levels of anti-GM1 antibodies. By technique B, they were excluded as the titres were always below or equal to 1:400.¹⁸ With both techniques, 13% of patients with CIDP without conduction blocks had low but significant anti-GM1 antibody titres.

NERVE BIOPSIES (TABLE 3)

Twelve patients had nerve biopsies. In five patients, no abnormalities were detected. In four patients, the density of nerve fibres was preserved, and there were no abnormalities on teased fibre preparations, but several clusters of regenerating fibres were present on semithin sections (figure). In one patient, we found signs of active axonal lesions in one fascicle associated with regeneration in other fascicles (clusters). In two patients, signs of demyelination and remyelination on teased fibre preparations and semithin sections were seen for a few fibres.

TREATMENT (TABLES 4 AND 5)

Five patients were not treated. The other 19 had IVIg (0.4 g/kg/day during five days every month for at least six months). All patients have been followed up for at least two years and were evaluated every three months. IVIg was repeated every two or three months if there was improvement at the end of the six month period. Improvement was correlated with at least a one point gain in muscle strength (MRC scale), and one point gain in

Cross section (1 μ) of a biopsy specimen of the superficial radial nerve from a patient with motor neuropathy and multifocal conduction block. The density of nerve fibres is normal. Several clusters (arrows) of small regenerating fibres are present, indicating that lesions of axons have occurred proximally, likely at the site of conduction block. Thionin staining, bar = 10 μ m.

Table 4 Response to treatment

	All patients (n = 24)	Group 1 (n = 15)	Group 2 (n = 9)
Treatment:			
None	5	2	3
Intravenous IVIg	19	13	6
Response to IVIg treatment (19/24):			
Absent	2	2	—
Transient	11	10	1
Sustained	6	1	5
Follow up study:			
Without treatment:			
Improvement	1	—	1
Stabilisation	4	2	2
IVIg treatment:			
Improvement	6	1	5
Stabilisation	12	12	—
Worsened	1	—	1

Group 1 = patients with amyotrophy; group 2 = patients without amyotrophy; transient = transient response to IVIg lasting no longer than six months; sustained = response to IVIg lasting longer than six months; follow up study = follow-up study after six months (mean duration = three years).

the score of the functional activity scale. Two patients showed no response to IVIg, but one was recently stabilised by an immunosuppressive drug (azathioprine). Six patients had a very good initial and sustained response that started after the first infusion. Five of them who had no muscle atrophy, had a one to two point gain on the MRC scale and two points or more on the functional activity scale, which persisted after six months. They were essentially those with radial involvement. Some of them totally recovered their wrist extension. The last one, with muscle atrophy, had a two point gain on the functional activity scale. The others (11 patients) had a good initial response that did not last more than six months. Most patients showed a dramatic change in their daily living due to improved hand skill only during the first IVIg treatments, although the MRC scale did not show significant variation. Ten of the 11 patients with a transient response to IVIg treatment had pronounced distal upper limb amyotrophy. In the group of patients who had long term improvement, repetition of the treatment did not have the same response. Nevertheless, motor weakness remained better than their original state. Of the 19 treated patients who had significant or high anti-GM1 antibodies (13 (68%) with technique A and 11 (58%) with technique B) were associ-

ated with an initial good response to IVIg. Four patients with technique A and five with technique B with an initially good clinical response had low or negative values (one of the 17 patients who initially responded to IVIg was not titred with technique B). One of the patients who did not respond to the IVIg treatment had no anti-GM1 antibodies with both techniques, and the other had significant titres with technique A only. Of the five patients who were not treated, one improved spontaneously and had negative titres. Among the four others, who all stabilised, three had high or significant titres with technique A and one with technique B. Of the 19 treated patients, during the follow up study six improved, four had high or significant titres with technique A and five with technique B. Twelve stabilised, nine had high or significant titres with technique A and six with technique B. Therefore, of the 18 patients who stabilised or improved with IVIg treatment, 13 (72%) had high or significant titres with technique A or technique B. The patient who worsened had high titres with technique A.

Discussion

We have studied 24 patients with a pure motor syndrome resulting from persistent multifocal conduction blocks. Some patients had minor sensory symptoms, such as shoulder pain or slight distal paraesthesiae, but none had sensory loss. Tendon reflexes were normal, decreased, or abolished in all cases but one. There were no signs of upper motor neuron involvement or bulbar signs. In most, onset was in the distal upper limbs, usually asymmetrically. Upper limbs were always affected. Onset was always insidious, although in two patients it was preceded by proximal pain in the upper limbs. The syndrome usually progressed over several years. In some patients there was a clear multifocal pattern affecting several limbs, primarily distally. In others, the distribution was more confined to one limb, mimicking the motor involvement seen at the onset of motor neuron disease. The pattern of muscle wasting varied. In some patients it was pronounced, whereas in others

Table 5 Response to treatment in relation to the titre of anti-GM1 activity

	All patients n = 24	High titres		Significant titres	
		Technique A n = 24	Technique B n = 23	Technique A n = 24	Technique B n = 23
Treatment:					
None	5	1	1	2	—
Intravenous IVIg	19	9	7	5	4
Response to IVIg treatment (19/24):					
Absent	2	—	—	1	—
Transient	11	6	4	3	2
Sustained	6	3	3	1	2
Follow-up study:					
Without treatment:					
Improvement	1	—	—	—	—
Stabilisation	4	1	1	2	—
IVIg treatment:					
Improvement	6	3	3	1	2
Stable	12	5	4	4	4
Worsened	1	1	—	—	—

Transient = transient response to IVIg lasting no longer than six months; sustained = response to IVIg lasting longer than six months; follow-up study = follow-up study after six months (mean duration = three years).

it was absent, even after five years of evolution. It was, therefore, possible to distinguish two groups of patients according to the presence or absence of muscle atrophy. The duration of the disease was significantly longer in the patients with atrophy, although the amyotrophy did not depend on the duration. The amyotrophy was always present during the first year of the disease. Cramps and fasciculations were present in most patients, mainly at the onset of the symptoms.

Motor involvement usually interfered with daily living, but in most cases, less than expected from the intensity of the motor deficit and wasting. Patients did not have the same pattern of evolution: most, after an initial worsening, were stable, and motor involvement did not show the progression usually found in motor neuron disease. A few patients progressively worsened. One patient improved spontaneously.

Conduction blocks were found constantly in the upper limbs in all patients. These were usually multifocal with no site predominance, although in three patients who presented with monomelic upper limb involvement, conduction blocks were located proximally. In some cases, conduction blocks occurred without corresponding clinical motor deficit in the nerve territory, although in most of the patients there was a good correlation between conduction block and motor deficit.

A segmental reduction of motor nerve conduction velocity was found at the sites of blocks, contrasting, in proximal blocks, with normal or slightly reduced distal velocities, except in one case. It is difficult, however, to interpret the importance of the conduction failure because the type and size of fibres in which conduction velocity was measured were not the same. Conduction velocities through, and distal to, the site of block cannot therefore be compared.

F waves were altered in most of the nerves with conduction blocks, as already reported.⁹ Abnormal F waves in the absence of conduction blocks suggest more proximal involvement. In these patients, spinal cervical stimulation is thought to be helpful,⁹ but not in the six patients in whom it was performed in our series. In patients with motor neuron disease, F waves are never altered to the same degree.³⁸ Altogether, alteration of F waves seemed to be a reliable electrophysiological variable in this type of neuropathy.

Multifocal motor neuropathies are therefore in almost all cases associated with conduction blocks and segmental reduction of conduction velocity. In some cases, slowing of segmental conduction may precede the detection of a conduction block, as in one of our cases. It is more than likely that patients with multifocal motor neuropathy with segmental conduction slowing can be grouped together with patients with persistent conduction block.

In some patients an intermediate late response was found, which was considered to be an axon reflex.³⁹ This response is never found in motor neuron disease, but occurs

occasionally in patients with multifocal motor neuropathy and persistent conduction block.²

In some patients, we found a slight alteration of the SNAPs in the nerves tested, with or without motor conduction block, despite normal clinical examination of the different sensory modalities.

Minor abnormalities on biopsy specimens of the superficial radial nerve showed that sensory fibres were not completely spared. But these abnormalities were not predictive for response to immunosuppressive treatment as was reported by Sahenk *et al.*⁴⁰ In a few cases, subclinical involvement of sensory nerves was detected by electrophysiological examination. The slight electrophysiological abnormalities of SNAPs and the moderate morphological modifications of the radial cutaneous nerve in some patients could indicate that there is a continuum between purely motor neuropathies with conduction block and the sensory-motor neuropathies with conduction block of the type reported by Lewis *et al.*¹ Abnormal sensory potentials have also been described in motor neuron disease.^{41 42}

We found high titres of anti-GM1 antibodies in 42% of patients with technique A and 35% with technique B and in none of the control groups with CIDP or normal controls, confirming the specificity of high titres of anti-GM1 antibodies in this group.^{34 43} When using technique A and technique B, respectively 29% and 48% of the patients examined had no significant or detectable titres of anti-GM1 antibodies. It is known, however, that other autoantibodies can be found in this pathology and these should be assayed. In a previous study, Ben YOUNES-CHENNOUFI *et al.*¹⁸ found IgM reactivity against other glycolipids. The patients without anti-GM1 antibodies nevertheless had the typical clinical and electrophysiological features of multifocal motor neuropathy. Low concentrations of anti-GM1 antibodies, which are non-specific, can be encountered in other neurological diseases such as amyotrophic lateral sclerosis and stroke as well as in normal controls.^{16-19 30 34 44} Zielasek *et al.*³⁵ who evaluated those techniques and others, only found discrepancies for negative or low titres. The fact that there are natural antibodies with low titres in normal controls, however, does not negate the effect of high titres in autoimmune diseases.⁴⁵

All but five patients were treated by IVIg. Most of them improved initially, although only one third seemed to show a lasting response. Only one patient with amyotrophy who had an initial good response to IVIg treatment had a sustained response. The absence of amyotrophy therefore seemed to predict a good and prolonged response to IVIg treatment. The patients without amyotrophy, in our experience, did not develop muscle wasting during follow up. This finding seems to justify the separation of patients into two groups.

Among the patients treated, about two thirds with an initial good response to IVIg, whatever the subsequent responses, had high or significant anti-GM1 antibody titres, but

less than half of the patients had high titres. Only 50% of the patients with an initial good and sustained response had high titres. A correlation between the presence of high titres of anti-GM1 antibodies and the long lasting response to IVIg cannot therefore be confirmed, but no follow up study of the anti-GM1 antibody titre in relation to the patient's response was performed.

CONCLUSION

Two patterns of clinical presentation could be isolated—namely, patients with motor deficit without pronounced muscle wasting, with a good response to IVIg suggesting a demyelinating lesion on a motor nerve leading to a conduction block; and those with pronounced amyotrophy mimicking a spinal muscular atrophy with a predilection for upper limbs, and a lesser sensitivity to IVIg treatment. The homogeneity of the syndrome of multifocal motor neuropathy with persistent conduction blocks and underlying physiopathological mechanism is therefore uncertain. Although there was no obvious correlation between the long lasting response to IVIg treatment and the presence of high anti-GM1 antibody titres, further studies should be performed to detect antiglycolipid antibodies to other components of the nodes of Ranvier, and to evaluate the utility of the titres of these antibodies in determining the clinical response.

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