

## PAPER

# A variant of multifocal motor neuropathy with acute, generalised presentation and persistent conduction blocks

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**Objective:** Multifocal motor neuropathy with persistent conduction blocks is classically described as a chronic neuropathy with progressive onset, and acute forms have not previously been characterised. We report four cases of severe motor impairment with acute and generalised onset and with persistent motor conduction blocks.

**Patients and results:** An acute tetraparesis with diffuse areflexia but little or no sensory disturbance was the clinical picture. Serial electrophysiological tests showed persistent multifocal motor conduction blocks with absent F waves in most tested motor nerves. No or minor abnormalities of the sensory nerve action potentials were observed. Cerebrospinal fluid contained normal or mildly increased protein levels (<1 g/l) without cells. *Campylobacter jejuni* serology was negative in three patients and consistent with past infection in one patient. Anti-ganglioside antibodies were positive in three patients. A five day course of intravenous immunoglobulins produced nearly complete symptom resolution in three patients and was ineffective in one patient.

**Conclusion:** Because of the persistence of multifocal motor conduction blocks for several weeks or months as the isolated electrophysiological feature, these cases could not be consistent with Guillain-Barré syndrome or chronic inflammatory demyelinating polyneuropathy. They suggest an original variant of multifocal motor neuropathy with an acute and generalised initial presentation and persistent motor conduction blocks affecting all four limbs.

**M**ultifocal motor neuropathy with persistent conduction blocks (MMNCB) is an immune-mediated neuropathy characterised by distal, asymmetric, chronic motor deficits that generally predominate in the upper limbs.<sup>1–4</sup> Some patients have fasciculations and cramps mimicking anterior horn disease,<sup>1</sup> but electrophysiological studies show persistent multifocal motor conduction blocks without significant slowing of motor nerve conduction outside the blocks.<sup>5–6</sup>

In this study, we describe the cases of four patients who presented with pure motor deficits and persistent multifocal motor conduction blocks without abnormalities outside the blocks. Conduction blocks were defined as an amplitude ratio of responses from proximal to distal stimulation of less than 0.5, which has been reported to be the most specific and sensitive criterion for defining the conduction blocks in MMNCB.<sup>7</sup>

However, these four cases of MMNCB exhibited two unusual features, which were the acute onset and the generalised involvement of all four limbs. Thus, they suggest that MMNCB could present as an acute and generalised disease. We will discuss the nosological boundaries that separate this original variant of MMNCB from Guillain-Barré syndromes (GBSs), either acute motor axonal neuropathy (AMAN) or acute inflammatory demyelinating neuropathy (AIDP), and from chronic inflammatory demyelinating polyneuropathies (CIDPs) with either an acute onset or a relapsing course.

## CASE REPORTS

### Patient one

A 32 year old woman presented with a history of relapsing weakness in all four limbs, starting in 1985. In 1994, she experienced an episode of diffuse ascending paralysis affecting all four limbs and the face and requiring 24 hours of assisted ventilation. An electrophysiological study dis-

closed multiple motor conduction blocks with normal nerve conduction velocities outside the blocks. Cerebrospinal fluid (CSF) examination showed an increased protein concentration (0.6 mg/l) with no cells. GBS was diagnosed. A 5 day course of intravenous immunoglobulins (IIGs) was given and the patient recovered within a few days. She then experienced relapsing motor deficits in all four limbs, predominating in the distal right upper limb and the left lower limb. Onset was acute, with no precipitating events. At each episode the symptoms improved transiently after intravenous Ig therapy.

At admission, the physical examination showed motor deficits predominating in the right upper limb (extension of the fingers, 3/5) and left lower limb (dorsal flexion of the foot, 4/5). She had difficulty walking on her heels and standing up from the squatting position. All deep tendon reflexes were abolished. There was no evidence of sensory or autonomic system involvement.

An electrophysiological study disclosed motor conduction blocks in both median and ulnar nerves and in the left tibial nerve, as well as prolonged F wave latencies (table 1). Other electrophysiological findings, including sensory nerve conduction parameters, were within the normal range.

The following laboratory tests were negative or normal: blood cell counts, serum electrolyte levels, antinuclear antibodies, rheumatoid factor, and complement fractions. Serological tests were negative for *Campylobacter jejuni*,

**Abbreviations:** MMNCB, multifocal motor neuropathy with persistent conduction blocks; GBS, Guillain-Barré syndrome; AMAN, acute motor axonal neuropathy; AIDP, acute inflammatory demyelinating neuropathy; CIDP, chronic inflammatory demyelinating polyneuropathy; CSF, cerebrospinal fluid; Ig, immunoglobulin; CMAP, compound muscle action potential; HNPP, hereditary neuropathy with susceptibility to pressure palsies; AMM NCB, acute multifocal motor neuropathy with persistent conduction blocks

**Table 1** Electrophysiological findings at admission (M0) and 1.5 or 3 months later (M1.5, M3) in the four patients who had acute multifocal motor neuropathy with persistent conduction blocks

	Case 1				Case 2				Case 3				Case 4					
	Symptomatic M0		Symptomatic M3		Symptomatic M0		Symptomatic M1.5		Symptomatic M0		Symptomatic M1.5		Asymptomatic M3		Symptomatic M0		Symptomatic M1.5	
	Right	Left	Right	Left	Right	Left	Right	Left	Right	Left	Right	Left	Right	Left	Right	Left	Right	Left
Median nerve motor nerve conduction amplitude, thenar (mV)	12	11	11	10	13	10	17	20	11	9	13	10	11	10	13	17.5	12	13
distal latency (ms)	2.6	2.7	3.1	3.3	2.8	2.9	3.2	3.5	2.9	2.9	3.5	2.8	2.9	2.8	3.6	3.5	4	3.8
conduction velocity, forearm (m/s)	67	64	62	67	55, block: 60%	56, block: 60%	54, block: 60%	53, block: 60%	56	54	60	56	60	56	52	55	51	50
conduction velocity, arm (m/s)	70	68	74	74	67	67	60	60	60, block: 65%	ND, block: >90%	67	58, block: 65%	60, block: 65%	67	65	65	60	62
conduction velocity, Erb/axillary (m/s)	ND, block: >90%	ND, block: >90%	ND, block: >90%	ND, block: >90%	29.7	29.6	30	30	31.5	33.7	32.2	34.7	32	34.7	31.6	55, block: >90%	ND, block: >90%	ND, block: >90%
F wave latency (ms)	33	37	31	41														33
Median nerve sensory nerve conduction amplitude (µV)	74	68	84	92	65	64	70	60	50	54	47	62	56	105	89	89	95	98
conduction velocity, wrist (m/s)	56	57	56	53											57	57	45	49
Ulnar nerve motor nerve conduction amplitude, hypothenar (mV)	7	7	9	9	12	8	12	12	11	6	12	9	12	9	11	11	10	11
distal latency (ms)	2.2	2.3	2.8	2.4	2.7	3.5	3	3.3	2.7	2.7	2.7	2.6	2.7	2.6	3	3	2.8	2.9
conduction velocity, forearm (m/s)	67	67	63	63	80%	57, block: 60%	56, block: 60%	48, block: 50%	57	60	66	68	66	68	54	48	50	48
conduction velocity, arm (m/s)	65	64	75	71	63	63	60%	60%	ND, block: 88%	ND, block: >90%	54, block: 55%	45, block: 80%	58	48	48	50	50	48
conduction velocity, Erb/axillary (m/s)	ND, block: >90%	ND, block: >90%	ND, block: >90%	ND, block: >90%	A	A	A	A	33.7	36.5	34.5	35.7	34.5	35.7	43, block: >90%	40, block: >90%	48, block: >90%	
F wave latency (ms)	35	38	33	40											34	37	37	
Ulnar nerve sensory nerve conduction amplitude (µV)	23	20	20	20	69	65	57	60	24	20	22	15	25	25	25	25	28	28
conduction velocity, wrist (m/s)	56	56	50	48	56	57	60	55	50	50	60	58	51	49	49	54	54	52
Radial nerve motor nerve conduction amplitude, forearm (mV)					3	2									6			
distal latency (ms)					3.5	5									3.2			
conduction velocity, arm (m/s)					50, block: 50%	50									50, block: 90%			
First interosseous muscle electromyography					A	A	A	A	A	A	A	A	A	A	A	A	A	A
spontaneous activity	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R
interference pattern																		

ND, not determined; A, absent; R, reduced.

**Table 1 Continued**

	Case 1				Case 2				Case 3				Case 4			
	Symptomatic M0		Symptomatic M3		Symptomatic M0		Asymptomatic M1.5		Symptomatic M0		Asymptomatic M3		Symptomatic M0		Symptomatic M1.5	
	Right	Left	Right	Left	Right	Left	Right	Left	Right	Left	Right	Left	Right	Left	Right	Left
Peroneal nerve motor nerve conduction amplitude – foot (mV)	7	9	7	8	4	4	4	4.5	3.5	3.5	4.5	3	1.3	4	1.7	2
distal latency (ms)	3.8	4.2	4	3.6	5	4.6	5	5.5	5	4.3	4.3	4	4.6	4	5.5	4.9
conduction velocity – leg (m/s)	50	48	50	53	47	45	37	44	n.d., block: 85%	45	45	36	n.d., block: 90%	40	34	40
conduction velocity – popliteal fossa (m/s)	50	48	60	58	47	45	40	60%	45	45	45	75%	90%	43	90%	
conduction velocity – thigh (m/s)					47									n.d., block: 90%		
F wave latency (ms)	57	50	59	53	absent	absent	absent	absent	absent	absent	59	absent	absent	59	absent	absent
Peroneal nerve sensory nerve conduction amplitude (µV)	biopsy	13	biopsy	15	26	27	16	15	14	15	15	15	biopsy	8	biopsy	6
Tibial nerve motor nerve conduction amplitude – foot (mV)	6	8	6	6	1	2	3.5	4.5	5.5	5.5	7	8	5	12	1	11
distal latency (ms)	4.4	4.2	5.9	5.1	5.2	4.5	5.8	6.3	6	6	5.2	5.6	6.5	6.2	6.5	6
conduction velocity – leg (m/s)	47	44	48	45	49	45	44	44	42	46	40	42	n.d., block: >90%	42	n.d., block: >90%	40
conduction velocity – thigh (m/s)		88%		82%	40%	40%	70%	70%	75%	73%	80%	80%	>90%	n.d., block: 90%	>90%	
F wave latency (ms)	66	54	65	56	absent	absent	66	65	absent	64	64	60.5	absent	54	absent	55
Sural nerve sensory nerve conduction amplitude (µV)	biopsy	18	biopsy	25	42	40	26	32	29	32	32	30	24	24	biopsy	15
conduction velocity – ankle (m/s)	62	62	62	45	52	55	40	50	40	44	44	45	40	42	40	48
Tibialis anterior muscle Electromyography spontaneous activity interference pattern	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A
	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R

ND, not determined; A, absent; R, reduced.

cytomegalovirus, HIV 1 and 2, and hepatitis B and C viruses. There was a polyclonal increase in IgG (26.8 g/l) and IgM (3.34 g/l) levels with a normal IgA level (2.3 g/l). Thin layer chromatography detected IgM anti-GM1 antibodies.

The motor deficit improved within a few days after a five day course of intravenous Igs (0.4 g/kg/d). A relapse occurred four weeks later with motor deficits at the same sites and with the same intensity as the previous event. An electrophysiological control study was performed three months later and showed persistent multifocal motor conduction blocks (table 1). Following examinations (four and five months after admission) showed the same abnormalities with persistent conduction blocks.

### Patient two

Acute tetraparesis developed within a week in this 29 year old man, who reported a mild episode of sore throat two weeks before motor symptom onset. He had a history of severe obsessive compulsive disorder. At admission three days after symptom onset, he had symmetric lower limb paresis that prevented him from climbing stairs. The weakness worsened rapidly until he was unable to get up from a chair, and then was unable to walk. Physical examination showed symmetrical proximal (2/5) and distal (4/5) motor impairment in the lower limbs, severe proximal (1/5) and distal (2/5) motor impairment in the upper limbs, and left sided facial paresis. Deep tendon reflexes were abolished. Sensory and autonomic functions were normal.

An electrophysiological study disclosed motor conduction blocks in the median, ulnar, peroneal, and tibial nerves on both sides, with absent F waves except in the median nerves (table 1). A block was also present in the right radial nerve at the arm. Sensory and other nerve conduction parameters were normal.

CSF examination showed a high protein level (0.54 mg/l) with a cell count of less than 1/mm<sup>3</sup>. Most biological findings were normal or negative: blood cell counts, serum electrolyte levels, standard immunological tests, such as tests for antinuclear antibodies and cryoglobulin, and serological tests for cytomegalovirus, Lyme disease, HIV 1 and 2, and hepatitis B and C viruses. *C jejuni* antibodies were positive in a titre of 1/128, with no increase eight days later. IgM anti-GM1 and IgG anti-GM2 antibodies were detected by thin layer chromatography.

A five day course of intravenous Igs (0.4 g/kg/d) was followed by stabilisation within 24 hours and then recovery to independent walking within three weeks, while conduction blocks persisted. To our knowledge, this patient has not experienced any recurrences.

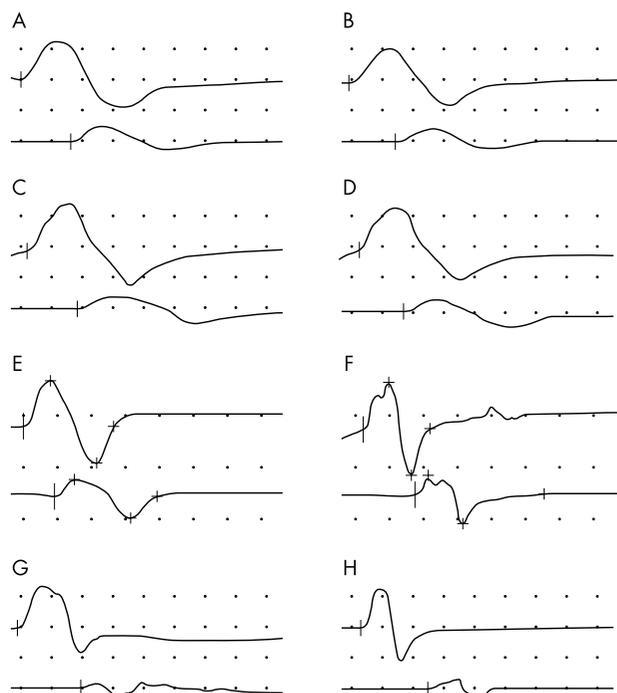
### Patient three

A 38 year old man was referred to our institution for acute motor impairment in all four limbs, which occurred during a chemotherapy course. He had had diphtheria at 7 years of age. He was taking stavudine, lamivudine, and nelfinavir for HIV 1 infection diagnosed six years earlier. His CD4+ count was 420/mm<sup>3</sup> and his viral load was 3470 copies/ml. Non-Hodgkin's lymphoma developed. During the first chemotherapy course, which combined adriamycin, cyclophosphamide, bleomycin, and methylprednisolone, he experienced an acute episode of tetraparesis that required intensive care unit monitoring. GBS was considered. The neurological manifestations resolved promptly after intravenous Ig therapy. The second course of chemotherapy was followed by diffuse severe motor impairment predominating in the left upper limb (3/5) and right lower limb (2/5). There was diffuse areflexia, but no evidence of sensory, autonomic, or cranial nerve dysfunction.

**Table 2** Features of acute multifocal motor neuropathy with persistent conduction blocks in the four patients from the literature and the four patients in the present series

	Abbruzzese et al	White et al	Wohrle et al	Sugie et al	patient one	patient two	patient three	patient four
Age (years)	52	63	83	25	32	29	38	60
Sex	Male	Male	Female	Male	Female	Male	male	male
Preceding events	Diarrhoea	Diarrhoea	Not reported	Diarrhoea	No	Sore throat	corticosteroids	no
Deficit onset time	Two weeks	A few days	A few days	A few days	A few days	A few days	A few days	A few days
Motor deficit distribution	Distal, asymmetric, in all four limbs	Distal, asymmetric, in all four limbs	Asymmetric, in all four limbs	Distal, asymmetric, in all four limbs	Distal, asymmetric, in all four limbs	Global, symmetric, in all four limbs	Distal, asymmetric, in all four limbs	Asymmetric, in all four limbs
Sensory signs	No	No	No	No	No	No	No	Yes
Motor relapses	Yes	No	No	No	Yes	No	Yes	Yes
Persistent motor conduction blocks	Bilateral median n. and left peroneal n.	Bilateral ulnar n. and left median n.	Bilateral ulnar n.	Multifocal and distal	Bilateral median and ulnar n.; left tibial n.	Bilateral median, ulnar, peroneal, and tibial n.	Bilateral median and ulnar n.; right tibial and left peroneal n.	Bilateral median, ulnar, peroneal, and tibial n.
Other electrophysiological abnormalities	Reduced distal motor potential amplitudes	No	Reduced distal motor potential amplitudes	No	No	No	No	Reduced distal motor potential amplitudes
CSF protein (mg/l)	normal	not done	0.42	0.66	0.6	0.54	0.44	0.55
<i>Campylobacter jejuni</i> Anti-ganglioside antibody	positive (recent) IgM anti-GM1, then IgG anti-GM1	positive in stool culture IgG anti-GM1	Not done	positive anti-GM1, anti-GalNAc-GD1a	negative IgM anti-GM1	positive (not recent) IgM anti-GM1, IgG anti-GM2	negative IgM anti-GM1	negative
Disease evolution	recovery after intravenous Igs but relapses	recovery within a few weeks after intravenous Igs	spontaneous recovery within 3 weeks	spontaneous recovery within 7 weeks	recovery after intravenous Igs but relapses	recovery within a few weeks after intravenous Igs	recovery within a few days after intravenous Igs	no improvement after intravenous Igs

n., nerve; Igs, immunoglobulins.



**Figure 1** Conduction block. (A) and (B), for the right median nerve, patient three. (C) and (D), for the left ulnar nerve between elbow and Erb point sites of stimulation, patient four. (E) and (F), for the left peroneal nerve, patient two. (G) and (H), for the left tibial nerve between ankle and knee sites of stimulation, patient one. Electrophysiological findings at admission (A, C, E, and G) and 1.5 or three months later (B, D, F, H): sweep 5 ms/division; gain 5 mV/division (A–D) or 2–3 mV/division (E–H).

An electrophysiological study disclosed motor conduction blocks on the right and left median and ulnar nerves, the left peroneal nerve, and the right tibial nerve, with absent F waves in the lower limbs (table 1). Sensory nerve action potentials and other electrophysiological values in the four limbs were normal.

CSF examination showed a normal protein level (0.44 mg/l) with a cell count of less than  $1/\text{mm}^3$ . In the blood, the leukocyte count was  $2600/\text{mm}^3$  (neutrophils,  $1300/\text{mm}^3$ ; lymphocytes,  $1100/\text{mm}^3$ ), the platelet count was  $391\,000/\text{mm}^3$ , and the haemoglobin level was 10.4 g/l. Serum electrolyte levels were normal, and the C-reactive protein level was less than 5 mg/l. No antinuclear antibodies were detected. Serological tests were negative for *C jejuni* and cytomegalovirus. IgM anti-GM1 antibodies were found by thin layer chromatography.

The patient recovered completely within two days after initiation of a five day course of intravenous Igs (0.4 g/kg/d). There were no recurrences during the period after the end of chemotherapy during which conduction blocks persisted (according to electrophysiological examinations three, five, and nine months after the initial event).

#### Patient four

This 60 year old man was referred for diffuse proximal motor weakness predominating in the right upper limb and both lower limbs. The symptoms had set in within one week. He was taking treatment for diabetes mellitus and for non-Hodgkin's lymphoma. He had a history of multiple episodes of motor impairment. The first occurred in 1997 and resolved spontaneously within a few weeks. In 1999, a pure motor deficit occurred in the right lower and upper limbs, associated

with fever and weight loss of 12 kg. Bone marrow examination established the diagnosis of B large cell lymphoma. A biopsy of the right superficial peroneal nerve showed myelinated fibre loss and small perivascular polyclonal inflammatory infiltrates with no visible lymphoma cells. Four courses of chemotherapy were followed by complete remission of the lymphoma and complete resolution of the motor deficit.

The episode that led to referral to our department was characterised by motor impairments in the right upper limb predominating in the radial nerve territory (1/5); in the entire right lower limb predominating distally (2/5); and in the left lower limb predominating proximally (2/5). Deep tendon reflexes were absent in the lower limbs and right upper limb. Tingling and painful paraesthesia were present in the right lower limb in a radicular distribution.

An electrophysiological study disclosed motor conduction blocks in the median, ulnar, peroneal, and tibial nerves on both sides, with absent F waves in the right lower limb (table 1). In the left lower limb, proximal magnetic stimulation showed a motor conduction block at the thigh. Another conduction block was present in the right radial nerve at the arm. The amplitude of the distal compound muscle action potentials (CMAPs) was reduced in the right lower limb. In addition, the amplitude of distal sensory nerve action potentials was mildly reduced in the left superficial peroneal nerve, while the right one was impossible to examine because of the previously performed nerve biopsy.

The CSF protein level was elevated (0.55 mg/l), with a cell count of less than  $1/\text{mm}^3$ . Blood cell counts were normal and the erythrocyte sedimentation rate was 50 mm/h. Blood glucose was 6.7 mmol/l. No B cell clonality was found. Bone marrow examination was normal. Findings from a right sural nerve biopsy were similar to those from the first biopsy, with myelinated fibre loss and no lymphocytic infiltrates. No antinuclear antibodies or cryoglobulin were found. Serological tests were negative for *C jejuni*, cytomegalovirus, HIV 1 and 2, and hepatitis B and C viruses. Thin layer chromatography showed no anti-ganglioside antibodies.

The patient did not recover from motor deficits despite successive courses of intravenous Ig, corticosteroids and rituximab: the motor conduction blocks were persisting.

#### DISCUSSION

The presenting clinical picture in all four patients was a pure, severe and diffuse motor impairment with an acute or rapidly progressive onset and areflexia. Only patient four presented with some sensory symptoms (tingling and pain in one limb), but he had no loss of sensation. In addition, three patients had a CSF protein level elevated above 0.45 mg/l. We therefore could suggest that all four patients met the classical diagnostic criteria for GBS.<sup>8</sup> However, the recurrent episodes of motor impairment observed in three patients raised the possible diagnostic of CIDP, given that relapsing AIDPs can be considered as CIDP variants.<sup>9</sup>

In contrast, the electrophysiological abnormalities presented by the four patients were characterised by multifocal persistent motor conduction blocks, and fulfilled the criteria for MMNCB.<sup>5</sup> The conduction blocks were found in almost all tested nerves of all four limbs, distally or proximally. Additional conduction blocks may have been present on untested nerves and may have contributed to the generalised and severe presentation of the motor impairment. No motor conduction slowing was noted outside the blocks, but some F waves were delayed or absent, as usual in MMNCB. The amplitude of the distal CMAPs and the sensory nerve conduction parameters were normal except in patient four. In this patient, the reduction in CMAP amplitudes together with the distribution of the paraesthesia in the right lower

limb could be related to the existence of a lumbar radiculopathy. In all four patients, the persistence of multifocal conduction blocks without any decrease in distal CMAP amplitude, during more than one month as assessed by serial electrophysiological testing, was not consistent with the figures of "pseudo-conduction blocks" described in vasculitic neuropathy.<sup>10</sup>

Conduction blocks and motor deficits occur in various conditions, and the nosological boundaries separating GBS (in its AIDP or AMAN variants), relapsing CIDP, hereditary neuropathy with susceptibility to pressure palsies (HNPP), and MMNCB deserve discussion.

In favour of the diagnoses of GBS, our cases demonstrated acute pure motor deficit, which could suggest AMAN<sup>11-13</sup>; but they also showed isolated motor conduction blocks, which could be possibly observed in the early phase of AIDP.<sup>14-16</sup> However, AMAN can be ruled out because this syndrome is electrophysiologically characterised by a marked reduction in distal CMAP amplitude with no conduction block or evidence of segmental demyelination,<sup>13</sup> and the finding of persistent conduction blocks on serial electrophysiological tests without any additional conduction abnormality is not consistent with long term follow up descriptions of AIDP.<sup>17-21</sup>

Regarding causes of relapsing-remitting neuropathy, CIDP could be invoked, but in CIDP conduction blocks are never observed alone without any other features of demyelination, such as prolonged distal motor latency or slowing of motor nerve conduction in two or more nerves.<sup>22-25</sup> Relapsing-remitting neuropathies have also been described in non-Hodgkin's lymphoma.<sup>26</sup> These cases were histologically characterised by the presence of diffuse lymphoma cell infiltration within the endoneurium. In two successive sensory nerve biopsies, patient four showed some perivascular but no endoneurial infiltration. To be exhaustive, the diagnosis of HNPP should be discussed, because HNPP has been described as a relapsing diffuse motor disorder in rare cases.<sup>27</sup> However, the conduction blocks in this condition are always located at entrapment sites and are associated with various sensory nerve conduction abnormalities.

Regarding the persistence of pure motor conduction blocks, the four present cases suggest a variant of MMNCB with an acute and generalised initial presentation. Therefore, we suggest that this acute variant of MMNCB (AMMNCB) should be differentiated from GBS, AMAN, and relapsing CIDP.

MMNCB is usually an indolent, chronic, distal, multifocal disease that causes limited disability.<sup>3-4,6</sup> To our knowledge, only three cases of MMNCB leading to severe quadriplegia have been reported.<sup>28-30</sup> MMNCB could also include some sensory disorders, in its Lewis-Sumner variant.<sup>31</sup> This variant may be subacute, but the motor deficit is associated with pain, affecting the upper limbs first and the lower limbs only a few months or years later. Thus, acute and generalised motor impairment is a very unusual presentation of MMNCB. In the literature, we found only five cases compatible with the diagnosis of AMMNCB.<sup>32-36</sup> Table 2 illustrates the most striking features in these five patients and in the four patients reported in the present study. The conduction blocks recovered within six weeks, in parallel with the improvement in strength in three patients<sup>33-34,36</sup> but not in the two other published patients and in the four present cases. An additional case of probable AMMNCB can be found in an older series of "acute relapsing GBS".<sup>37</sup> In this series of five patients with relapsing diffuse motor deficits, three patients had "normal motor nerve conduction velocities", a feature taken by the authors to distinguish their condition from relapsing CIDP. Interestingly, one of these three patients "had conduction blocks in several nerves three years after a second acute episode of GBS", which was reported as a

"purely motor syndrome" with onset within one week after an episode of diarrhoea.

The pathophysiological mechanisms of AMMNCB probably overlap those of chronic MMNCB. MMNCB is usually associated with anti-GM1 antibodies and may be related to *C jejuni* infection.<sup>2,38</sup> The same is true of AMAN.<sup>39</sup> In the present series of AMMNCB, the serological profile of one patient was consistent with past colonisation with *C jejuni*, and anti-GM1 and anti-GM2 antibodies were found in three patients. In the five previous cases of probable AMMNCB found in the literature, *C jejuni* enteritis was present in four patients, and anti-ganglioside antibodies in three patients.

Regarding the treatment, a relapsing course and a good response to repeated intravenous Ig administration are classically described in MMNCB.<sup>40,41</sup> In contrast, abrupt motor deficit may result from the use of corticosteroids.<sup>42</sup> In the present series of AMMNCB, three patients recovered following intravenous Igs, as did three patients in the literature, whereas corticosteroids seemed to have caused the relapses of motor deficit in our patient three. Thus the usual, chronic form of MMNCB and AMMNCB have similar profiles of response to treatment.

To conclude, AMMNCB may be considered a variant of MMNCB that should be differentiated from GBS, AMAN, relapsing GBS, and CIDP. Typical features of AMMNCB may include diffuse, severe motor impairment with an acute or rapidly progressive onset, usually affecting all four limbs, often in an asymmetric distribution, and with electrophysiological evidence of pure, generalised motor conduction blocks without any other motor or sensory nerve conduction abnormalities. Additional features may include a relapsing course, a slightly increased CSF protein concentration, various anti-ganglioside antibodies, and a response to intravenous Ig therapy, while motor conduction blocks persist.

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## ECHO

### Eye traits identify coma types



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In future, comatose patients—the bulk of those seen in emergency departments—could have the cause of their coma identified by simple eye tests. A prospective probabilistic study has for the first time confirmed loss of light reflex and unequal pupil size as important diagnostic criteria.

These two criteria independently predicted coma with a structural cause in multivariate analysis corrected for age, sex, and level of consciousness (odds ratio 11.02 (95% confidence interval 3.9 to 30.9) for loss of light reflex and 7.5 (1.4 to 39.4) for unequal pupil size). The likelihood ratio of a positive result in structurally caused coma was 9.0 for unequal pupil size and 3.59 for loss of light reflex. The results were based on tests in 115 patients, 113 of whom had a final diagnosis of structurally (40%) or metabolically (60%) caused coma. The precise cause was also ascertained. The results for the cohort matched probability estimates quoted in textbooks but not rigorously evaluated until now.

Comatose patients aged  $\geq 15$  years seen in the emergency department of a community teaching hospital during a year were recruited consecutively. All had initial eye tests, full physical and neurological examinations, basic biochemical tests, and imaging tests, if clinically necessary. They were followed up as inpatients, and their medical records were reviewed after a year. One clinical researcher, two if there was disagreement, reviewed the likely cause of the coma.

Usefulness of these two criteria in differential diagnosis of coma has been poorly described before. Differential diagnosis is usually based on clinical experience.

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