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Conduction block in acute motor axonal neuropathy

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Guillain–Barré syndrome is divided into two major subtypes, acute inflammatory demyelinating polyneuropathy and acute motor axonal neuropathy. The characteristic electrophysiological features of acute motor axonal neuropathy are reduced amplitude or absence of distal compound muscle action potentials indicating axonal degeneration. In contrast, autopsy study results show early nodal changes in acute motor axonal neuropathy that may produce motor nerve conduction block. Because the presence of conduction block in acute motor axonal neuropathy has yet to be fully recognized, we reviewed how often conduction block occurred and how frequently it either reversed or was followed by axonal degeneration. Based on Ho's criteria, acute motor axonal neuropathy was electrodiagnosed in 18 patients, and repeated motor nerve conduction studies were carried out on their median and ulnar nerves. Forearm segments of these nerves and the across-elbow segments of the ulnar nerve were examined to evaluate conduction block based on the consensus criteria of the American Association of Electrodiagnostic Medicine. Twelve (67%) of the 18 patients with acute motor axonal neuropathy had definite ($n = 7$) or probable ($n = 5$) conduction blocks. Definite conduction block was detected for one patient (6%) in the forearm segments of both nerves and probable conduction block was detected for five patients (28%). Definite conduction block was present across the elbow segment of the ulnar nerve in seven patients (39%) and probable conduction block in two patients (11%). Conduction block was reversible in seven of 12 patients and was followed by axonal degeneration in six. All conduction blocks had disappeared or begun to resolve within three weeks with no electrophysiological evidence of remyelination. One patient showed both reversible conduction block and conduction block followed by axonal degeneration. Clinical features and anti-ganglioside antibody profiles were similar in the patients with ($n = 12$) and without ($n = 6$) conduction block as well as in those with ($n = 7$) and without ($n = 5$) reversible conduction block, indicating that both conditions form a continuum; a pathophysiological spectrum ranging from reversible conduction failure to axonal degeneration, possibly mediated by antibody attack on gangliosides at the axolemma of the nodes of Ranvier, indicating

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that reversible conduction block and conduction block followed by axonal degeneration and axonal degeneration without conduction block constitute continuous electrophysiological conditions in acute motor axonal neuropathy.

Keywords: anti-ganglioside antibody; acute motor axonal neuropathy; acute motor conduction block neuropathy; conduction block; Guillain–Barré syndrome

Abbreviations: AIDP = acute inflammatory demyelinating polyneuropathy; AMAN = acute motor axonal neuropathy; CMAP = compound muscle action potential; GBS = Guillain–Barré syndrome; IgG = immunoglobulin G

Introduction

Guillain–Barré syndrome (GBS) has two major subtypes, acute inflammatory demyelinating polyneuropathy (AIDP) and acute motor axonal neuropathy (AMAN) (McKhann *et al*., 1993). GBS is a post-infectious autoimmune disease prototype, AMAN being associated with antecedent *Campylobacter jejuni* enteritis and immunoglobulin G (IgG) autoantibodies against gangliosides (Ogawara *et al*., 2000, 2003). Autopsy study results of advanced AMAN cases show Wallerian-like degeneration of motor fibres in the spinal nerve roots and peripheral nerves but with little lymphocytic inflammation or demyelination (McKhann *et al*., 1993). Electrophysiological studies have been important in the diagnosis and classification of these GBS subtypes (Ho *et al*., 1995; Hadden *et al*., 1998). Characteristic features of AMAN include reduced amplitude or absence of distal compound muscle action potentials (CMAPs), which suggest axonal degeneration.

Although most demyelination criteria include conduction block as a physiological finding—indicative of segmental demyelination—the phenomenon is not always related to demyelination (Lewis, 2007). For instance, conduction block is also a local anaesthetic mechanism caused by sodium channel function blockage at the nodes of Ranvier without segmental demyelination. Electron microscopy studies have shown that the earliest and mildest changes in AMAN consist of complement deposits at the nodes of Ranvier, lengthening of the nodes with distortion of paranodal myelin and in some instances, breakdown of the outermost myelin terminal loops (Griffin *et al*., 1996; Hafer-Macko *et al*., 1996). This arrangement appears to be stable for some time, but in many fibres the axon subsequently undergoes Wallerian-like degeneration. Nodal and paranodal changes may cause the paralysis seen in some pathologically mild cases by interfering with impulse conduction. In the early phase these changes may be reversible, accounting for the rapid recovery of some severely paralysed patients with AMAN (Ho *et al*., 1997). In other words, motor conduction block may occur at an early AMAN stage and may be followed by axonal degeneration or rapid resolution. There have been no comprehensive studies showing conduction block in AMAN, but reversible conduction failure has been reported in GBS associated with preceding *C. jejuni* infection or IgG anti-ganglioside antibodies (Kuwabara *et al*., 1998, 1999, 2004; Hiraga *et al*., 2005*a*). Here we retrospectively report on the frequency of conduction block in patients with AMAN and how often it is reversible or leads to axonal degeneration.

Materials and methods

Patients

At Dokkyo Medical University Hospital between April 1999 and December 2008, one of the authors (NK) performed nerve conduction studies on 54 patients who fulfilled the clinical criteria for GBS (Asbury and Cornblath, 1990). Features reviewed included antecedent infection, clinical symptoms and signs, number of days to nadir, Hughes functional grade scores (Hughes *et al*., 1978) at nadir and clinical outcome. Patients with acute-onset chronic inflammatory demyelinating polyneuropathy (Ruts *et al*., 2010) were excluded.

Electrophysiological studies

Nerve conduction studies were done with a Nicolet VIKING IV EMG machine (CareFusion Japan, Tokyo, Japan). As described elsewhere (Oh, 2003), CMAPs were recorded from the abductor pollicis brevis muscle after stimulation of the median nerve at the wrist, elbow and axilla; the abductor digiti minimi muscle after stimulation of the ulnar nerve at the wrist, below the elbow, above the elbow and axilla; the extensor digitorum brevis muscle after stimulation of the peroneal nerve at the ankle and fibular head; the abductor hallucis muscle after stimulation of the tibial nerve at the ankle and popliteal fossa. For CMAP recordings the EMG filter was set at 20 Hz to 20 kHz. Amplitude, area and duration of the initial negative phase were the CMAP measurements used. The patients with GBS were divided into two subtypes, namely AIDP and AMAN, based on Ho's electrodiagnostic criteria (Ho *et al*., 1995). We were careful to avoid misdiagnosis caused by Martin-Gruber anastomosis or other technical failures.

The CMAP parameters determined to evaluate conduction abnormalities in the forearm segment and across the elbow segment were amplitude decrement (%), calculated as (distal CMAP amplitude – proximal CMAP amplitude) × 100/(distal CMAP amplitude); area decrement (%), calculated as (distal CMAP area – proximal CMAP area) × 100/(distal CMAP area); and temporal dispersion (%), calculated as (proximal CMAP duration/distal CMAP duration) × 100. Based on the consensus criteria of the American Association of Electrodiagnostic Medicine (Olney, 1999), definite partial conduction block was defined as an amplitude decrement of more than 50% with <30% temporal dispersion. Probable partial conduction block was defined as an amplitude decrement of 40–49% with <30% temporal dispersion. These criteria were applied only to a nerve in which the distal CMAP amplitude was 20% or more of the lower limit of normal. Furthermore, based on changes in serial recordings, conduction blocks were classified into two groups; reversible conduction failure and length-dependent conduction failure. Reversible conduction failure was defined as conduction block being resolved quickly with no development of excessive temporal dispersion or other demyelination features (Kuwabara *et al*., 1998, 1999). Length-dependent conduction

failure was defined as the disappearance of conduction block due to progressive reduction of distal CMAP amplitude.

Initial examinations were made on the day of admission and follow-up studies between 2 and 14 weeks after disease onset. Stimulus duration was 0.2 ms in all the examinations, with intensity ranging from 20–100 mA to obtain supramaximum stimulation. Skin temperature was maintained above 32°C. Normal values were obtained from 48 healthy subjects, mean age 42 years (range 19–81 years). For distal motor latency, CMAP duration and conduction velocity, any value falling outside 2.5 standard deviations (SD) of the control mean was considered abnormal. CMAP amplitude abnormality was taken to be a value <2.5 SD of the mean of the logarithmically transformed amplitude of the controls.

Electrophysiological demyelination features were a distal motor latency of more than 4.8 ms (or more than 5.3 ms if the distal CMAP amplitude was <2.4 mV) in the median nerve and more than 4.0 ms (or more than 4.3 ms if the distal CMAP amplitude was <2.0 mV) in the ulnar nerve. For conduction velocity, it was a value <45 m/s (or <43 m/s if the distal CMAP amplitude was <2.4 mV) in the median nerve and <46 m/s (or <44 m/s if the distal CMAP amplitude was <2.0 mV) in the ulnar nerve. Based on Ho's criteria (Ho *et al*., 1995), axonal degeneration was defined as a distal CMAP amplitude of <80% of the lower normal limit, and <3.8 mV in the median nerve and 3.3 mV in the ulnar nerve. Distal nerve demyelination was defined as a distal CMAP duration of more than 6.6 ms in the median and 6.7 ms in the ulnar nerve (Isose *et al*., 2009).

Serological studies

Serum IgG and IgM antibodies to the gangliosides GM1, GM1b, GD1a, GalNAc–GD1a, GD1b, GT1a and GQ1b were measured by an enzyme-linked immunosorbent assay, as described elsewhere (Yuki *et al*., 1997). In the present study, serum was considered positive when the optical density was 0.5 or more at a 1:500 dilution. IgG antibodies to at least one combination of two of the seven gangliosides (GM1, GM2, GD1a, GD1b, GT1a, GT1b and GQ1b, each 5 pmol/well) were determined. Anti-ganglioside complex antibodies were judged positive when the optical density was 0.5 greater than the sum of the antibodies against each ganglioside.

Statistical analyses

Differences in medians were examined by the Mann-Whitney U-test using statistical software (SPSS 12.0J; SPSS Inc, Chicago, Illinois). Differences in frequencies between groups were compared by the χ^2 or Fisher exact test (two-tailed). A difference of $P<0.05$ was considered statistically significant.

Results

Electrodiagnostic classification

This classification was based on conventional motor nerve conduction studies of the median, ulnar, peroneal and tibial nerves. The 54 patients with GBS underwent the first electrophysiological study 2–16 days (median 6 days) after onset of symptoms. Test results showed 19 AIDP (35%), 13 AMAN (24%) and 22 equivocal (13 unclassifiable and nine normal) patients (Fig. 1). Follow-up study results however, reclassified them as 14 AIDP (26%) and 31 AMAN (57%) patients. Five of nine patients who finally were classified

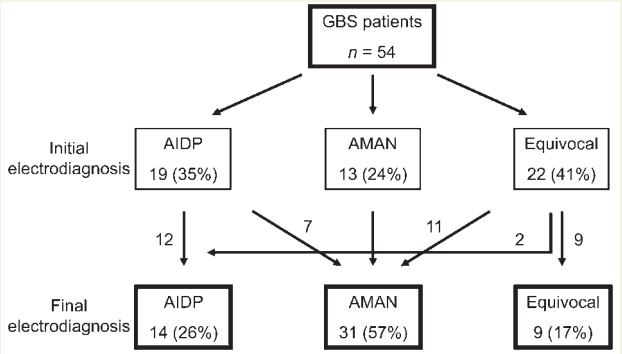

Figure 1 Serial electrodiagnostic subtype changes in 54 patients with GBS. Arrows indicate direction of change from one subtype to another. Numbers indicate the patients changing group. Equivocal refers to electrodiagnostically normal and unclassifiable groups. Initially 22 patients were classified as equivocal. Eleven were later re-classified as having AMAN. Seven patients with GBS who, at first had prolonged distal motor latencies, eventually developed AMAN.

'equivocal' did not undergo follow-up studies at the appropriate times. Sensory nerve conduction studies were normal in all AMAN patients but one who had diminished sensory nerve action potentials (Patient 18), for whom acute motor sensory axonal neuropathy was the diagnosis.

Because 18 of the 31 patients with AMAN had undergone conduction studies of both the forearm and elbow segments, further electrophysiological recordings were reviewed selectively. The 18 patients received two or more examinations during the 2 months after disease onset. Neither the clinical nor serological features differed significantly for these 18 and the other 13 patients with AMAN.

Distal compound muscle action potential

Nerve conduction studies were done on 16 of the 18 patients within 7 days of disease onset. During week 1, distal CMAP amplitudes were within the normal range in eleven patients (69%, Patients 1, 2, 4, 6, 8, 9, 10, 11, 12, 13 and 14), in the median nerve and in nine patients (60%, Patients 1, 2, 3, 6, 8, 9, 10, 13 and 17) in the ulnar nerve (Fig. 2A). Axonal degeneration was present in only five patients in the median nerve and in four patients (27%) in the ulnar nerve. At disease nadir (median 7 days, range 3–13 days), decreases in CMAPs were observed in all patients as compared with earlier study or recovery stage data.

In the early disease stage, prolonged distal motor latencies in the median nerve that fulfilled demyelination criteria were present in five of the 18 patients (Patients 2, 8, 9, 11 and 17); whereas distal motor latencies in the ulnar nerve were normal in all 18 patients (Table 1). Four of those five patients had prolonged distal motor latency in one median nerve, and one had it bilaterally (Patient 9). Serial nerve conduction studies showed rapid recovery without prolonged distal CMAP duration in Patient 9 and rapid improvement in distal motor latency with only residual minimal prolongation in

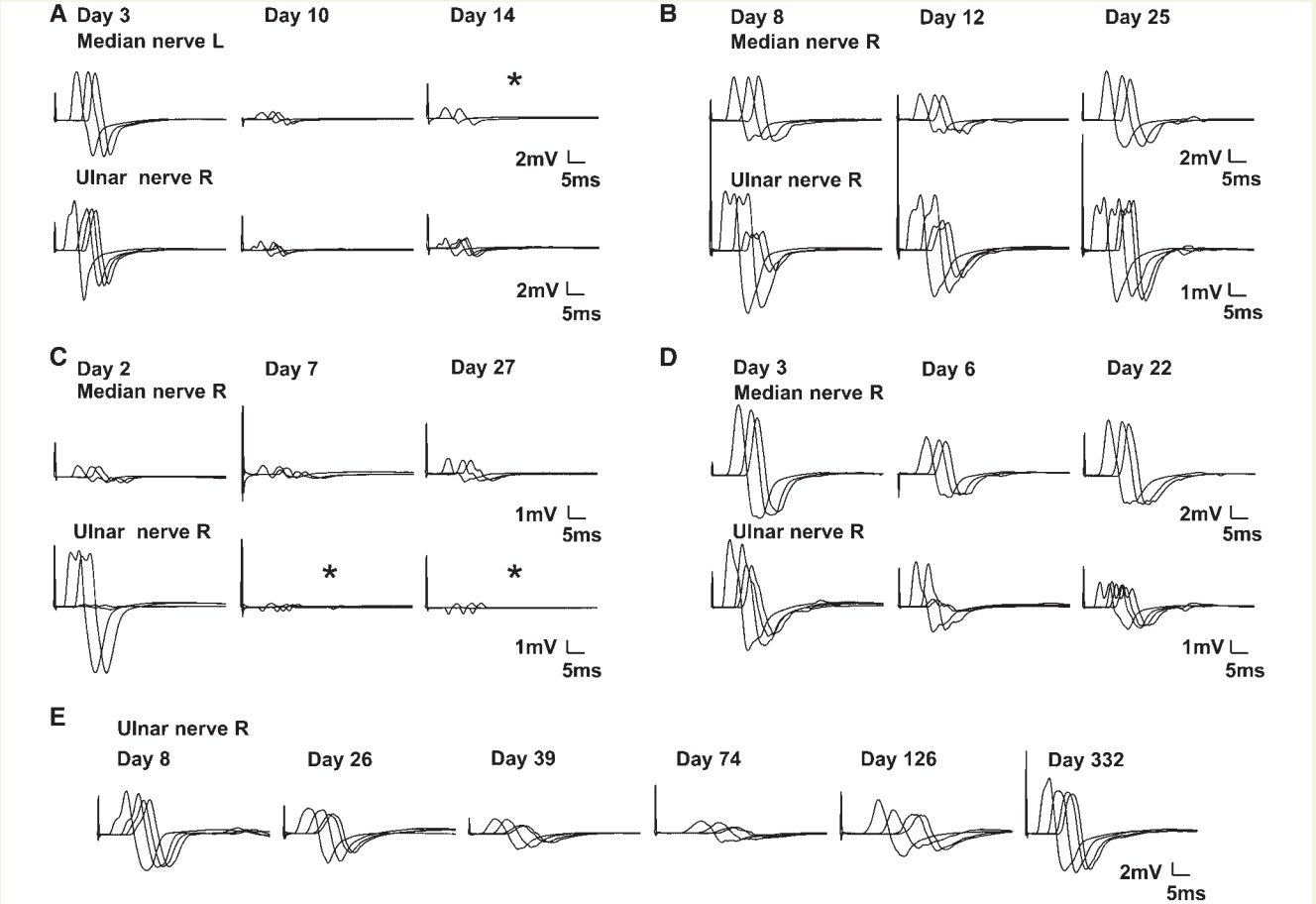

Figure 2 Serial changes in motor conduction abnormalities. Recordings show superimposed CMAPs from the abductor pollicis brevi stimulated at the wrist, elbow and axilla in the median nerve, and from the abductor digiti minimi at the wrist, below the elbow, above the elbow and axilla in the ulnar nerve. (**A**) Typical AMAN (Patient 13). On Day 3 CMAPs have normal amplitudes. A progressive decrease in CMAP amplitude is present at follow-up. (**B**) AMAN with reversible conduction failure (Patient 15). On Day 8 definite conduction block is present across the elbow segment of the ulnar nerve but CMAP amplitudes in the median nerve are within normal limits. Subsequently, conduction block has been resolved rapidly with no excessive temporal dispersion. CMAP amplitudes in the median nerve are decreased transiently on Day 12 and restored on Day 25. (**C**) AMAN with length-dependent conduction failure (Patient 3). On Day 2 a marked CMAP amplitude decrease is seen in the median nerve, and definite conduction block is present across the elbow segment of the ulnar nerve. A subsequent, progressive decrease in distal CMAPs is seen at follow-up. (**D**) AMAN with reversible and length-dependent conduction failure (Patient 1). On Day 3 CMAPs in the median and ulnar nerves are within the normal range but with mild amplitude reduction of CMAP across the elbow segment of the ulnar nerve. On Day 6 CMAPs are decreased in the median nerve and definite conduction block is present in the ulnar nerve. On Day 22 CMAPs have recovered in the median nerve but decreased progressively in the ulnar nerve. Conduction block in the ulnar nerve is lessened because of the proximal CMAP increase and distal CMAP amplitude decrease. (**E**) AIDP. On Day 8, slight amplitude reduction of proximal CMAP is present across the elbow segment. Although clinical symptom nadir occurred on Day 10, conduction abnormalities worsened over 2 months. Distal motor latency was 8.1 ms and distal CMAP duration 10.1 ms on Day 74. CMAPs gradually improved with marked prolongation of distal motor latencies, conduction slowing and excessive temporal dispersion, especially across the elbow segment. Asterisk denotes nerves not stimulated at the axilla; L = left; R = right.

Patients 2, 8, 11 and 17 at follow-up. None had prolonged distal CMAP durations that fulfilled the criteria for distal demyelination in either nerve during the course of the illness.

Compound muscle action potential amplitude decrement

Twelve of the 18 patients (67%) had probable or definite conduction block. With respect to the forearm segments, conduction block was definite for one patient (6%, Patient 14) in the median nerve, probable for two patients (11%, Patients 12 and 17) in the median nerve and for three patients (16%, Patients 2, 7 and 8) in the ulnar nerve. A common entrapment site (across the elbow segment of the ulnar nerve) showed definite conduction block in seven patients (39%, Patients 1, 3, 7, 9, 14, 15 and 18) and probable conduction block in two patients (11%, Patients 11 and 17). In four (Patients 1, 9, 14 and 15) of these seven patients, bilateral definite conduction blocks were observed. The time from disease onset in the first study of the 12 patients with AMAN who

Table 1 Clinical features of and nerve conduction study results for 18 patients with AMAN

Patient number	Age	Sex	Antecedent symptom	Sensory sign		Nerve conduction study results												Hughes grade at		Weeks to discharge
						Distribution and time course of conduction block														
						Forearm segment							Elbow segment							
						Prolonged median distal motor latency	Median nerve	Decrement		Time course	Ulnar nerve	Decrement		Time course	Ulnar nerve	Decrement		Time course	Nadir	Discharge	
								Amplitude	Area			Amplitude	Area			Amplitude	Area				
1	31	M	Diarrhoea and pyrexia*	No	L	No	No				No				Definite CB	78%	75%	Reversible	4	2	4
					R	No	No				No				Definite CB	84%	80%	Reversible			
2	51	M	Diarrhoea	Yes	L	NE	NE				NE				NE				2	2	5
					R	Yes	No				Probable CB	48%	43%	Followed by AD	No						
3	31	M	Diarrhoea and pyrexia	No	L	NE	NE				NE				NE				4	3	5
					R	No	No				No				Definite CB	96%	96%	Followed by AD			
4	41	M	Running nose, cough	No	L	NE	NE				NE				NE				2	2	2
					R	No	No				No				No						
5	18	F	Diarrhoea and pyrexia	No	L	No	No				No				No				2	2	4
					R	No	No				No				No						
6	37	M	Sore throat	Yes	L	NE	NE				NE				NE				3	2	4
					R	No	No				No				No						
7	33	M	Diarrhoea	No	L	No	No				No				No				4	4	3
					R	No	No				Probable CB	47%	34%	Followed by AD	Definite CB	57%	59%	Followed by AD			
8	53	F	Diarrhoea and pyrexia*	No	L	NE	NE				NE				NE				4	3	8
					R	Yes	No				Probable CB	48%	46%	Followed by AD	No						
9	52	F	Diarrhoea and pyrexia	No	L	No	No				No				Definite CB	72%	65%	Reversible	4	2	5
					R	Yes	No				No				Definite CB	52%	56%	No follow-up			
10	44	M	Diarrhoea and sore throat	No	L	NE	NE				NE				NE				3	2	3
					R	No	No				No				No						
11	31	F	Diarrhoea and pyrexia	No	L	NE	NE				NE				NE				4	2	8
					R	Yes	No				No				Probable CB	41%	48%	Reversible			
12	73	M	Diarrhoea and pyrexia	Yes	L	No	Probable CB	49%	31%	Reversible	No				No				3	1	3
					R	No	No				No				No						
13	55	M	Sore throat	Yes	L	No	No				No				No				4	3	5
					R	No	No				No				No						
14	35	M	Diarrhoea and pyrexia	Yes	L	No	Definite CB	96%	97%	Reversible	No				Definite CB	74%	71%	Reversible	2	1	7
					R	No	No				No				Definite CB	77%	85%	Reversible			
15	32	F	No	Yes	L	No	No				No				Definite CB	67%	68%	Reversible	2	2	4
					R	No	No				No				Definite CB	69%	71%	Reversible			
16	61	M	Diarrhoea and pyrexia	No	L	No	No				No				No				4	2	6
					R	No	No				No				No						
17	77	F	Sore throat	No	L	NE	NE				NE				NE				5	5	8
					R	Yes	Probable CB	47%	46%	Followed by AD	No				Probable CB	48%	49%	Followed by AD			
18	38	F	Sore throat	Yes	L	No	No				No				No				3	2	4
					R	No	No				No				Definite CB	51%	42%	Reversible			

AD = axonal degeneration; Amplitude (Area) decrement = reduction (%) of the amplitude (area) of the CMAP on proximal versus distal stimulation; CB = partial conduction block; F = female; M = male; L = left; R = right; * = positive *Campylobactor jejuni* in stool culture; NE = Not examined.

had conduction block (median 3 days, range 2–8 days) was similar to that in the six who did not (median 5 days, range 3–11 days, $P = 0.207$).

On sequential evaluation, rapid resolution was found in seven (58%, Patients 1, 9, 11, 12, 14, 15 and 18) of the 12 patients who had probable or definite conduction block (Table 1 and Fig. 2B). No excessive temporal dispersion of proximal CMAPs was found during the recovery period. Conduction block was resolved after intravenous immunoglobulin therapy or plasma exchange in six of the seven patients and in one (Patient 15) who refused immunotherapy and showed spontaneous recovery. These patients' conditions fulfilled the definition of reversible conduction failure.

In five patients (42%, Patients 2, 3, 7, 8 and 17), distal CMAP amplitudes decreased, becoming comparable to those of proximal CMAPs with the disappearance of conduction block, but without development of excessive temporal dispersion or other features of demyelination (Fig. 2C). Those patients' conditions fulfilled the definition of length-dependent conduction failure. All the abnormal CMAP amplitude decrements were detected during the 3 weeks after disease onset. Reversible conduction failure and length-dependent conduction failure patterns were present in the ulnar nerve of Patient 1 (Fig. 2D). Table 1 shows the area decrement (%) and amplitude decrement (%) in the patients who showed conduction block.

Conduction velocities

The initial study of one patient (Patient 12) showed conduction slowing in forearm segments of the median (43 m/s) and ulnar (46 m/s) nerves, fulfilling demyelination criteria, but which on follow-up quickly returned to the normal range. Abnormal amplitude decrements were present in these segments. The across-elbow segment of the ulnar nerve showed conduction slowing in 13 of the 18 patients with AMAN with and without conduction block (mean 45 m/s; range 31–68 m/s). In the follow-up study, slight conduction slowing still remained in nine patients.

Clinical features

Table 2 shows clinical profiles of the 14 AIDP and 31 AMAN patients. Age distribution did not differ significantly between the groups. Females predominated in AIDP, males in AMAN, but the difference did not reach statistical significance. In contrast, diarrhoea preceded AMAN significantly more often than it did AIDP [$P = 0.004$; odds ratio (OR) 9.5; 95% confidence interval (CI) 1.80–50.08]. Facial weakness ($P = 0.007$; OR 0.14; 95% CI 0.03–0.57) and sensory signs ($P = 0.028$; OR 0.20; 95% CI 0.05–0.85) were less common in AMAN. Median number of days to nadir was significantly shorter in AMAN ($P = 0.015$). Patients who required endotracheal intubation ($P = 0.049$; OR 0.20; 95% CI 0.04–0.89) or mechanical ventilation ($P = 0.007$; OR 0.09; 95% CI 0.02–0.55) were significantly fewer in the AMAN than AIDP group.

Age distribution, sex ratio, antecedent diarrhoea, progression period and the Hughes grade score at nadir did not differ significantly between the AMAN subgroups with and without conduction block (Table 2). Nor did they differ between the AMAN subgroups with reversible conduction failure and length-dependent conduction failure. Hughes grade scores at discharge for patients with AMAN with reversible conduction failure were significantly milder than for the group with length-dependent conduction failure ($P = 0.010$; OR 20.0; 95% CI 1.42–282.45). None of the 31 patients with AMAN showed treatment-related fluctuations (Ruts *et al.*, 2010), but two of the patients (Patients 4 and 17) received additional intravenous immunoglobulin therapy because of poor recovery.

Serological studies

Of the 31 patients with AMAN, 29 (94%) had one or more anti-ganglioside IgG antibodies tested and 6 (19%) had IgM antibodies tested. The IgG anti-ganglioside antibodies frequently present were against GM1 (61%), GM1b (52%) and GD1b (42%). Frequencies of the anti-ganglioside antibody did not differ between the AMAN subgroups with and without conduction block or between those with reversible and length-dependent conduction failure. The presence of IgG antibodies against ganglioside complex was examined in the 18 patients with AMAN who underwent detailed follow-up studies. There were no significant differences between the presence of conduction block or reversible conduction failure and any of the anti-ganglioside complex antibodies (Table 3). Antibodies to the GM1/GalNAc–GD1a complex were detected in two patients with AMAN who had conduction block (Patients 1 and 7). One showed reversible conduction failure, the other length-dependent conduction failure.

Discussion

The term AMAN originates from pathology studies but currently it is diagnosed by electrophysiological testing. Autopsy studies show deposits of IgG and complement at the nodal and internodal axolemma in patients with AMAN, which produce minimal nodal changes to severe axonal degeneration (McKhann *et al.*, 1993; Hafer-Macko *et al.*, 1996). In contrast, electrodiagnostic criteria for this GBS subtype are based on the assumption that AMAN causes only axonal degeneration (Ho *et al.*, 1995; Hadden *et al.*, 1998). In the early disease phase some patients with anti-ganglioside antibodies have nerves with reduced distal CMAP amplitudes and prolonged distal motor latencies and nerves with conduction block at common entrapment sites mimicking demyelination features (Kuwabara *et al.*, 1998, 1999). At follow-up some patients showed persistently reduced or distal CMAP absence; whereas others showed rapid normalization of their distal CMAP amplitudes, distal motor latencies and conduction block recovery without development of temporal dispersion or increased latency. These findings were thought to be incompatible with demyelination and remyelination, indicating that AMAN is characterized not only by axonal degeneration but also by reversible conduction failure, possibly induced by anti-ganglioside antibodies at the axolemma of the Ranvier nodes (Kuwabara *et al.*, 1998, 1999). These studies and hypotheses prompted us to

Table 2 Clinical profiles of 45 patients with GBS

	AIDP (*n* = 14)	Total AMAN (*n* = 31)	AIDP versus AMAN Two-tailed *P*-value	AMAN with CB (*n* = 12)	AMAN without CB (*n* = 6)	AMAN with CB versus without CB Two-tailed *P*-value	AMAN with RCF (*n* = 7)	AMAN with LDCF (*n* = 5)	AMAN with RCF versus LDCF Two-tailed *P*-value
Mean age [range], years	43 [5–81]	46 [13–86]	0.680	45 [31–77]	42 [18–61]	0.707	42 [31–73]	49 [33–77]	0.462
Male to female sex ratio	6:8	22:9	0.100	6:6	5:1	0.316	3:4	3:2	>0.99
Antecedent infection									
Diarrhoea	2 (14)	19 (61)	0.004	9 (75)	3 (50)	0.344	5 (71)	4 (80)	>0.99
Upper respiratory tract infection	7 (50)	8 (26)	0.310	2 (17)	4 (67)	0.107	1 (14)	1 (20)	>0.99
Initial symptoms									
Limb weakness	7 (50)	22 (71)	0.200	8 (67)	3 (50)	0.627	3 (43)	5 (100)	0.081
Sensory symptoms	9 (64)	11 (36)	0.110	3 (25)	3 (50)	0.344	3 (43)	0 (0)	0.205
Diplopia	0 (0)	1 (3)	>0.99	1 (8)	0 (0)	>0.99	1 (14)	0 (0)	>0.99
Neurological findings (during illness)									
Ophthalmoparesis	0 (0)	4 (13)	>0.99	2 (17)	0 (0)	0.529	1 (14)	1 (20)	>0.99
Facial weakness	10 (71)	8 (26)	0.007	5 (42)	1 (17)	0.600	3 (43)	2 (40)	>0.99
Upper limb weakness	14 (100)	31 (100)		12 (100)	6 (100)		7 (100)	5 (100)	
Lower limb weakness	14 (100)	30 (97)		12 (100)	6 (100)		7 (100)	5 (100)	
Sensory sign	11 (79)	13 (42)	0.028	5 (42)	2 (33)	>0.99	4 (57)	1 (20)	0.293
Autonomic nerve dysfunction	1 (7)	2 (7)	>0.99	2 (17)	0 (0)	0.529	0 (0)	2 (40)	0.152
CSF albuminocytological dissociation	8 (73)	17 (65)	>0.99	6 (67)	3 (60)	>0.99	3 (75)	3 (60)	>0.99
Endtracheal intubation	6 (43)	4 (13)	0.049	2 (17)	0 (0)	0.529	1 (14)	1 (20)	>0.99
Therapy									
Intravenous immunoglobulin	12 (86)	27 (87)		11	6		6	5	
Plasma exchange	2 (14)	6 (19)		0	1		0	0	
None	0 (0)	1 (3)		1	0		1	0	
Median No. [range] of days to nadir	11 [6–16]	8 [3–16]	0.015	4 [2–5]	3 [2–4]	0.135	4 [2–4]	4 [2–5]	0.315
Hughes grade at symptom nadir									
Grade 3 or more	13 (93)	22 (71)	0.137	9 (75)	4 (67)	>0.99	5 (71)	4 (80)	>0.99
Grade 4 or more	12 (86)	19 (61)	0.165	8 (67)	1 (17)	0.131	4 (57)	4 (80)	0.576
Grade 5 or more	6 (43)	2 (7)	0.007	1 (8)	0 (0)	>0.99	0 (0)	1 (20)	0.417
Hughes grade at discharge									
Grade 2 or less				8 (67)	5 (83)	0.615	7 (100)	1 (20)	0.010

CB = partial conduction block; LDCF = length-dependent conduction failure; RCF = reversible conduction failure. Data are given as number (percentage) unless otherwise indicated.

Table 3 Anti-ganglioside complex antibodies in 18 patients with AMAN

IgG antibodies to	AMAN with CB ($n=12$)	AMAN without CB ($n=6$)	AMAN with CB versus without CB Two-tailed *P*-value	AMAN with RCF ($n=7$)	AMAN with LDCF ($n=5$)	AMAN with RCF versus LDCF Two-tailed *P*-value
GM1/GM1b	2 (17)	0 (0)	0.529	1 (14)	1 (20)	>0.99
GM1/GM2	3 (25)	0 (0)	0.515	1 (14)	2 (40)	0.523
GM1/GalNAc–GD1a	2 (17)	0 (0)	0.529	1 (14)	1 (20)	>0.99
GM1/GT1a	2 (17)	0 (0)	0.529	0 (0)	2 (40)	0.152
GM1/GT1b	3 (25)	0 (0)	0.515	2 (28)	1 (20)	>0.99
GM1/GQ1b	3 (25)	0 (0)	0.515	2 (28)	1 (20)	>0.99
GM1b/GM2	2 (17)	0 (0)	0.529	2 (28)	0 (0)	0.470
GQ1b/GT1b	3 (25)	1 (17)	>0.99	2 (28)	1 (20)	>0.99

CB = partial conduction block; LDCF = length-dependent conduction failure; RCF = reversible conduction failure. Data are given as number (percentage) unless otherwise indicated.

investigate the frequency of conduction block and its time course in AMAN.

Of our 18 patients whose final classification was AMAN, 12 (67%) had definite or probable conduction block. Six patients had conduction block in their forearm segments and nine across their elbow segments. Conduction block is the term used to describe the condition in which saltatory conduction is stopped but the axon remains intact. In practice, it is recognized by an abnormal amplitude/area CMAP reduction on proximal stimulation as compared with CMAP on distal stimulation. Conduction block is usually considered to be the electrophysiological correlate of segmental demyelination. In the early disease stage and based on only one recording, no electrodiagnostical distinction between demyelinating conduction block and other causes of abnormal amplitude reduction of proximal CMAP, such as reversible conduction failure and length-dependent conduction failure, is possible. Observation of serial electrophysiological changes is important for determining the pathophysiological origin of abnormal CMAP amplitude reduction in GBS subtypes. The concept of reversible conduction failure encompasses the rapid recoveries of prolonged distal motor latencies, reduced distal CMAP amplitudes and conduction block, none of which are explained by remyelination (Kuwabara *et al*., 1998, 1999). In contrast, resolution of demyelinative conduction block in AIDP is usually associated in serial recordings with conduction slowing and increased CMAP duration with remyelinating slow components (Albers and Kelly, 1989) (Fig. 2E). At follow-up, 7 of 12 patients with AMAN and conduction block had a reversible conduction failure pattern and six had a length-dependent conduction failure pattern. None had features characteristic of a remyelinating pattern. Length-dependent conduction failure may be caused by one or more mechanisms: Wallerian degeneration that has reached the proximal stimulus site but not the distal site; conduction block that occurred at first, followed by axonal degeneration; or conduction block that came first and adjunctive axonal degeneration that occurred in the distal nerve terminals. As any distinction between these conditions is impossible, we have defined them all as length-dependent conduction failure and consider this pattern to be an expression of axonal damage (Uncini *et al*., 2010*b*).

Early reversible conduction failure in AMAN is thought to be induced by anti-GM1 antibodies, possibly due to sodium channel damage, but this is controversial (Takigawa *et al*., 1995; Hirota *et al*., 1997). An immunohistochemical study of AMAN rabbits developed by sensitization with GM1 has shown sequential pathological changes starting with IgG deposits at the nodes of Ranvier (Susuki *et al*., 2007). The bound antibodies activate complement resulting in the formation of a membrane attack complex at the nodal axolemma, disruption of the nodal sodium channel cluster, lengthening of the nodal region and detachment of paranodal myelin terminal loops, as detected in patients with AMAN (Griffin *et al*., 1996; Hafer-Macko *et al*., 1996). The last feature mimics paranodal demyelination, but the primary pathology is on the axonal side. All these changes lower the safety factor for impulse transmission which induces potentially reversible conduction failure. If autoimmune attack progresses, axonal damage and Wallerian degeneration develop. Interestingly, reversible conduction failure and length-dependent axonal degeneration patterns coexisted in the same nerve of one of our patients with AMAN (Patient 1) (Fig. 2D). In this patient, CMAPs in the median nerve were reduced on Day 6 but had recovered by Day 22, which suggests early reversible conduction failure at the distal nerve terminal. In contrast, distal CMAP in the ulnar nerve decreased progressively during the follow-up period, which suggests length-dependent conduction failure and, at the same time, conduction block and rapid resolution of conduction block occurred across the elbow segment. Moreover, the majority of patients with reversible conduction failure also had slightly reduced distal CMAPs in the early stage compared with values at follow-up (which may be considered distal reversible conduction failure) (Fig. 2D). These findings indicate that the pathophysiological process in AMAN varies from mild axonal functional involvement expressed as a reversible conduction failure pattern to axonal degeneration expressed as length-dependent conduction failure or distal CMAP reduction and that these conditions are on a continuous spectrum.

Conduction blocks were present more often across the elbow segment of the ulnar nerve than across the forearm segments. Since the majority of our patients with conduction block could

Table 4 Acute motor conduction block neuropathy/acute multifocal motor neuropathy in the literature

Authors and patient number	Age	Sex	Antecedent illness	Motor deficits distribution	Cranial nerve involvement	Sensory sign	Relapse	Distribution of CB		Time course of CB	Anti-ganglioside antibody		Disease evolution
								Forearm segment	Elbow segment		Isotype	Ganglioside	
White *et al*. (1996)	63	M	*C. jejuni* enteritis	Distal, asymmetric	No	No	No	Yes	Not reported	Resolved rapidly	IgG	GM1	Recovery within 6 weeks after IVIg
Abbruzzese *et al*. (1996)	52	M	*C. jejuni* enteritis	Distal leg, symmetric	No	No	Yes	Yes	Not reported	Not reported	IgM and IgG	GM1	Recovery within a month, but two relapses
Wöhrle *et al*. (1996)	83	F	Not reported	Proxymal, asymmetric	No	No	No	No	Yes	Resolved rapidly		Negative	Spontaneous recovery within a few weeks
Sugie *et al*. (1998)	25	M	*C. jejuni* enteritis	Distal, asymmetric	No	No	No	Yes	Not reported	Resolved gradually	IgM	GM1and GalNAc–GD1a	Spontaneous recovery within 7 weeks
											igG	GM1, GalNAc-GD1a, GD1a and GD1b	
Susuki *et al*. (2001)	22	M	Diarrhoea	Distal, symmetric	No	No	No	No	Yes	Resolved rapidly	IgG	GM1b	Recovery within a few weeks after IVIg
Lefaucheur *et al*. (2003)													
1	32	F	No	Distal, symmetric	No	No	Yes	Yes	Not reported	Persistent	IgM	GM1	Recovery after IVIg but relapses
2	29	M	Sore throat	Global, symmetric	VIIth	No	No	Yes	Not reported	Persistent	IgM	GM1	Recovery within a few weeks after IVIg
											IgG	GM2	
3	38	M	HIV and Hodgkin's Lymphoma	Distal, symmetric	No	No	Yes	Yes	Not reported	Persistent	IgM	GM1	Recovery within a few weeks after IVIg
4	60	M	No	Global, asymmetric	No	Yes	Yes	Yes	Not reported	Persistent		Negative	No improvement after IVIg
Cappaso *et al*. (2003)													
1	41	M	Enteritis	Global, symmetric	No	No	No	Yes	Yes	Resolved rapidly	IgG	GM1 and GD1a	Recovery after PE
2	26	F	*C. jejuni* enteritis	Distal, symmetric	No	No	No	Yes	Yes	Resolved rapidly	IgG	GD1b, GD1a and GM1	Recovery within a few weeks after IVIg
Rajabally *et al*. (2006)	50	F	*C. jejuni* enteritis	Distal, symmetric	No	Yes	No	Yes	Not reported	Followed by AD	IgM and IgG	GM1	No improvemant after IVIg
Fernandez-Torre *et al*. (2008)	31	F	No	Proxymal legs, symmetrc	No	Yes	No	Yes	Yes	Resolved gradually		Negative	Recovery after IVIg
Kaida *et al*. (2008)	72	M	No	Distal, symmetric	No	No	No	Yes	Not reported	Resolved gradually	IgG	GM1/GalNAc-GD1a	Recovery after IVIg
Manganelli *et al*. (2009)	21	M	No	Distal, symmetric	No	No	No	No	Yes	Resolved rapidly	IgM	GD1a and GQ1b	Recovery after IVIg
Ogawa *et al*. (2009)	38	M	Sore throat	Distal, symmetric	No	No	No	Yes	No	Resolved gradually	IgG	GM1/GalNAc–GD1a and GD1b/GalNAc–GD1a	Recovery after IVIg

AD = axonal degeneration; CB = partial conduction block; *C. jejuni* = *Campylobactor jejuni*; F = female; M = male; IVIg = intravenous immunoglobulin therapy; PE = plasma exchange.

move their arms freely, it is unlikely that all the conduction blocks were due to nerve compression. Several investigators have reported that the conduction abnormalities in GBS tend to be present at the distal nerve terminals, nerve roots and common entrapment sites of the peripheral nerves, where the blood-nerve barrier is thought to be relatively deficient or weak (Brown and Snow, 1991; Kuwabara *et al*., 1998, 1999). In addition, conduction blocks across the elbow segment were present in the majority of the patients with GBS in Table 4 when the examinations including the elbow segment were done. Our study confirmed these results and showed that the conduction abnormalities at the common entrapment sites are a characteristic neurophysiologic feature observed in AMAN.

In 2003, Capasso *et al*., reported two peculiar patients who developed acute symmetric weakness without sensory symptoms (Capasso *et al*., 2003). Both had experienced antecedent diarrhoea (*C. jejuni* was isolated from one) and had high IgG antibody titres to GM1, GD1a and GD1b. Electrophysiological studies showed reduced distal CMAP amplitudes, early partial motor conduction block in their forearm segments and normal sensory conduction, even across the motor conduction block sites. Distal CMAP amplitudes became normalized. Conduction block was resolved in 2–5 weeks, as was muscle weakness, without development of excessive temporal dispersion of distal or proximal CMAPs. Capasso *et al*. (2003) proposed the term 'acute motor conduction block neuropathy' as being another GBS variant. Similar cases have been reported as atypical GBS (Susuki *et al*., 2001; Fernández-Torre *et al*., 2008; Manganelli *et al*., 2009; Ogawa *et al*., 2009) or as an acute variant of multifocal motor neuropathy (White *et al*., 1996; Wöhrle *et al*., 1996; Abbruzzese *et al*., 1997; Sugie *et al*., 1998; Lefaucheur *et al*., 2003) (Table 4). Most of the patients with acute symmetrical presentation, who had a monophasic course with fast recovery as well as diarrhoea and evidence of *C. jejuni* and an IgG antibody isotype of an anti-GM1 antibody, should be classified as GBS subtypes (White *et al*., 1996; Susuki *et al*., 2001, Capasso *et al*., 2003; Rajabally *et al*., 2006; Kaida *et al*., 2008). Some patients, who had a more prolonged course or clinical relapses, presented persistent motor conduction block and had an autoantibody IgM isotype, possibly had acute presentation of multifocal motor neuropathy (Abbruzzese *et al*., 1997; Lefaucheur *et al*., 2003; Manganelli *et al*., 2009; Uncini *et al*., 2010*a*). In our study, two (11%) of the 18 patients with AMAN had reversible conduction block in the forearm segment, as in acute motor conduction block neuropathy. Four patients (22%) had conduction block followed by axonal degeneration, as in the case reported by Rajabally *et al*. (2006). The foregoing observations suggest that acute motor conduction block neuropathy and AMAN are correlated pathophysiologically and that acute motor conduction block neuropathy is a mild form of AMAN, characterized by reversible conduction failure in all nerves (Uncini and Yuki, 2009).

Patients with GBS associated with anti-GM1, -GM1b or -GalNAc–GD1a antibodies more frequently have had preceding *C. jejuni* infection and less frequently cranial nerve involvement and sensory disturbance than patients without anti-ganglioside antibodies (Jacobs *et al*., 1996; Ang *et al*., 1999; Yuki *et al*., 2000). In our study, as compared with AIDP, patients with AMAN more often had antecedent diarrhoea, but facial weakness and sensory signs were less common. We confirmed previous findings that patients with AMAN have a shorter disease progression, an earlier nadir and need artificial ventilation less often (Hiraga *et al*., 2003, 2005*a*). These clinical features did not differ between AMAN subgroups with and without conduction block or reversible conduction block. Moreover, anti-ganglioside antibody profiles did not differ between the subgroups. In summary, the similar clinical and serological features of the subgroups support the supposition that early reversible conduction failure, length-dependent conduction failure and axonal degeneration without conduction block constitute continuous conditions.

Of our 54 patients with GBS, 24% were classified as having AMAN in the initial studies. Recognition of the reversible conduction failure and length-dependent conduction failure patterns changed the classification to 57% at the follow-up. This confirms that repeated studies help in making an AMAN electrodiagnosis (Kuwabara *et al*., 2004; Hiraga *et al*., 2005*b*; Uncini *et al*., 2010*b*). Furthermore, 61% of those with the final AMAN diagnosis had the IgG anti-GM1 antibody and 94% had at least one of IgG anti-ganglioside antibodies tested. Our study confirms the close association of AMAN with antecedent diarrhoea and the IgG anti-GM1, -GM1b and -GD1b antibodies (Ogawara *et al*., 2000, 2003). Kaida *et al*. (2008) studied 10 patients with GBS who had IgG antibodies to the GM1/GalNAc–GD1a complex. Clinical findings for those 10 patients were characterized by a preserved sensory system and infrequent cranial nerve deficits. Based on Ho's criteria (Ho *et al*., 1995), four patients had the AIDP pattern, three the AMAN pattern, and five early motor conduction block in their forearm segments. Kaida *et al*. (2008) proposed that GM1 and GalNAc–GD1a form a complex in the axolemma at the nodes of Ranvier or the paranodes of the motor nerves and that the complex is a target antigen in pure motor GBS, especially in acute motor conduction block neuropathy. Two of our patients with AMAN with conduction block had IgG antibodies to the GM1/GalNAc–GD1a complex; whereas none of the patients with AMAN without conduction block had them. One of the two showed reversible conduction block, the other conduction block followed by axonal degeneration. These findings do not fully support the speculation that GM1/GalNAc–GD1a is a specific target for autoantibodies in acute motor conduction block neuropathy.

In conclusion, our study shows that AMAN often presents conduction block during the first 3 weeks of illness and frequently shows reversible conduction failure as well as length-dependent conduction failure. This may create confusion in making early electrodiagnoses of GBS subtypes lead to underestimation of AMAN diagnoses. Serial neurophysiological examinations are useful for understanding GBS pathophysiology and for obtaining a true AMAN electrodiagnosis.

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References

Abbruzzese M, Reni L, Schenone A, Mancardi GL, Primavera A. Multifocal motor neuropathy with conduction block after *Campylobacter jejuni* enteritis. Neurology 1997; 48: 544.

Albers JW, Kelly JJ Jr. Acquired inflammatory demyelinating polyneuropathies: clinical and electrodiagnostic features. Muscle Nerve 1989; 12: 435–51.

Ang CW, Yuki N, Jacobs BC, Koga M, van Doorn PA, Schmitz PIM, et al. Rapidly progressive, predominantly motor Guillain-Barré syndrome with anti-GalNAc-GD1a antibodies. Neurology 1999; 53: 2122–7.

Asbury AK, Cornblath DR. Assessment of current diagnostic criteria for Guillain-Barré syndrome. Ann Neurol 1990; 27 (Suppl): S21–4.

Brown WF, Snow R. Patterns and severity of conduction abnormalities in Guillain-Barré syndrome. J Neurol Neurosurg Psychiatry 1991; 54: 768–74.

Capasso M, Caporale CM, Pomilio F, Gandolfi P, Lugaresi A, Uncini A. Acute motor conduction block neuropathy. Another Guillain-Barré syndrome variant. Neurology 2003; 61: 617–22.

Fernández-Torre JL, Berciano J, Garcia-Gorostiaga I, Calleja J. Acute motor conduction block neuropathy pattern occurring in the course of an acute inflammatory demyelinating polyradiculoneuropathy. Neurophysiol Clin 2008; 38: 211–6.

Griffin JW, Li CY, Macko C, Ho TW, Hsieh ST, Xue P, et al. Early nodal changes in the acute motor axonal neuropathy pattern of the Guillain-Barré syndrome. J Neurocytol 1996; 25: 33–51.

Hadden RDM, Cornblath DR, Hughes RAC, Zielasek J, Hartung HP, Toyka KV, et al. Electrophysiological classification of Guillain-Barré syndrome: clinical associations and outcome. Plasma Exchange/Sandoglobulin Guillain-Barré Syndrome Trial Group. Ann Neurol 1998; 44: 780–8.

Hafer-Macko C, Hsieh S-T, Li CY, Ho TW, Sheikh K, Cornblath DR, et al. Acute motor axonal neuropathy: an antibody-mediated attack on axolemma. Ann Neurol 1996; 40: 635–44.

Hiraga A, Kuwabara S, Ogawara K, Misawa S, Kanesaka T, Koga M, et al. Patterns and serial changes in electrodiagnostic abnormalities of axonal Guillain-Barré syndrome. Neurology 2005a; 64: 856–60.

Hiraga A, Mori M, Ogawara K, Hattori T, Kuwabara S. Differences in patterns of progression in demyelinating and axonal Guillain-Barre syndromes. Neurology 2003; 61: 471–4.

Hiraga A, Mori M, Ogawara K, Kojima S, Kanesaka T, Misawa S, et al. Recovery patterns and long term prognosis for axonal Guillain-Barré syndrome. J Neurol Neurosurg Psychiatry 2005b; 76: 719–22.

Hirota N, Kaji R, Bostock H, Shindo K, Kawasaki T, Mizutani K, et al. The physiological effect of anti-GM1 antibodies on saltatory conduction and transmembrane currents in single motor axons. Brain 1997; 120: 2159–69.

Ho TW, Li CY, Cornblath DR, Gao CY, Asbury AK, Griffin JW, et al. Patterns of recovery in the Guillain-Barré syndromes. Neurology 1997; 48: 695–700.

Ho TW, Mishu B, Li CY, Gao CY, Cornblath DR, Griffin JW, et al. Guillain-Barré syndrome in northern China: relationship to *Campylobacter jejuni* infection and anti-glycolipid antibodies. Brain 1995; 118: 597–605.

Hughes RAC, Newsom-Davis JM, Perkin GD, Pierce JM. Controlled trial prednisolone in acute polyneuropathy. Lancet 1978; 2: 750–3.

Isose S, Kuwabara S, Kokubun N, Sato Y, Mori M, Shibuya K, et al. Utility of the distal compound muscle action potential duration for diagnosis of demyelinating neuropathies. J Peripher Nerv Syst 2009; 14: 151–8.

Jacobs BC, van Doorn PA, Schmitz PIM, Tio-Gillen AP, Herbrink P, Visser LH, et al. *Campylobacter jejuni* infections and anti-GM1 antibodies in Guillain-Barré syndrome. Ann Neurol 1996; 40: 181–7.

Kaida K, Sonoo M, Ogawa G, Kamakura K, Ueda-Sada M, Arita M, et al. GM1/GalNAc-GD1a complex: a target for pure motor Guillain-Barré syndrome. Neurology 2008; 71: 1683–90.

Kuwabara S, Mori M, Ogawara K, Mizobuchi K, Hattori T, Koga M, et al. Axonal involvement at the common entrapment sites in Guillain-Barré syndrome with IgG anti-GM1 antibody. Muscle Nerve 1999; 22: 840–5.

Kuwabara S, Ogawara K, Misawa S, Koga M, Mori M, Hiraga A, et al. Does *Campylobacter jejuni* infection elicit "demyelinating" Guillain-Barré syndrome? Neurology 2004; 63: 529–33.

Kuwabara S, Yuki N, Koga M, Hattori T, Matsuura D, Miyake M, et al. IgG anti-GM1 antibody is associated with reversible conduction failure and axonal degeneration in Guillain-Barré syndrome. Ann Neurol 1998; 44: 202–8.

Lefaucheur JP, Gregson NA, Gray I, von Raison F, Bertocchi M, Creange A. A variant of multifocal motor neuropathy with acute, generalised presentation and persistent conduction blocks. J Neurol Neurosurg Psychiatry 2003; 74: 1555–61.

Lewis RA. Neuropathies associated with conduction block. Curr Opin Neurol 2007; 20: 525–30.

Manganelli F, Pisciotta C, Iodice R, Calandro S, Dubbioso R, Ranieri A, et al. Case of acute motor conduction block neuropathy (AMCBN). Muscle Nerve 2009; 39: 224–6.

McKhann GM, Cornblath DR, Griffin JW, Ho TW, Li CY, Jiang Z, et al. Acute motor axonal neuropathy: a frequent cause of acute flaccid paralysis in China. Ann Neurol 1993; 33: 333–42.

Ogawa G, Kaida K, Shiozaki Y, Araki M, Kimura F, Kamakura K. Case of pure motor Guillain-Barré syndrome with motor conduction block and anti-GM1/GalNAc-GD1a antibody [In Japanese with English abstract]. Rinsho Shinkeigaku 2009; 49: 488–92.

Ogawara K, Kuwabara S, Koga M, Mori M, Yuki N, Hattori T. Anti-GM1b IgG antibody is associated with acute motor axonal neuropathy and *Campylobacter jejuni* infection. J Neurol Sci 2003; 210: 41–5.

Ogawara K, Kuwabara S, Mori M, Hattori T, Koga M, Yuki N. Axonal Guillain-Barré syndrome: relation to anti-ganglioside antibodies and *Campylobacter jejuni* infection in Japan. Ann Neurol 2000; 48: 624–31.

Oh SJ. Anatomical guide for common nerve conduction studies. In: Oh SJ, editor. Clinical electromyography. Nerve conduction studies. 3rd edn., Philadelphia: Lippincott Williams & Wilkins; 2003. p. 55–67.

Olney RK. Guidelines in electrodiagnostic medicine: consensus criteria for the diagnosis of partial conduction block. Muscle Nerve 1999; 8 (Suppl): S225–9.

Rajabally YA, Strens LH, Abbott RJ. Acute motor conduction block neuropathy followed by axonal degeneration and poor recovery. Neurology 2006; 66: 287–8.

Ruts L, Drenthen J, Jacobs BC, van Doorn PA. Dutch GBS Study Group. Distinguishing acute-onset CIDP from fluctuating Guillain-Barré syndrome. A prospective study. Neurology 2010; 74: 1680–6.

Sugie K, Murata K, Ikoma K, Suzumura A, Takayanagi T. A case of acute multifocal motor neuropathy with conduction block after *Campylobacter jejuni* enteritis [In Japanese with English abstract]. Rinsho Shinkeigaku 1998; 38: 42–5.

Susuki K, Johkura K, Yuki N, Hasegawa O, Kuroiwa Y. Rapid resolution of nerve conduction blocks after plasmapheresis in Guillain-Barré syndrome associated with anti-GM1b IgG antibody. J Neurol 2001; 248: 148–50.

Susuki K, Rasband MN, Tohyama K, Koibuchi K, Okamoto S, Funakoshi K, et al. Anti-GM1 antibodies cause complement-mediated disruption of sodium channel clusters in peripheral motor nerve fibers. J Neurosci 2007; 27: 3956–67.

Takigawa T, Yasuda H, Kikkawa R, Shigeta Y, Saida T, Kitasato H. Antibodies against GM1 ganglioside affect K^+ and Na^+ currents in isolated rat myelinated nerve fibers. Ann Neurol 1995; 37: 436–42.

Uncini A, Manzoli C, Capasso M. Acute motor conduction block neuropathy or acute multifocal motor neuropathy: an attempt at a nosological systematization. Muscle Nerve 2010a; 2: 283–5.

Uncini A, Manzoli C, Notturno F, Capasso C. Pitfalls in the electrodiagnosis of GBS subtypes. J Neurol Neurosurg Psychiatry 2010b; 81: 1157–63.

Uncini A, Yuki N. Electrophysiologic and immunopathologic correlates in Guillain-Barré syndrome subtypes. [Review] Experts Rev Neurother 2009; 9: 869–84.

White JR, Sachs GM, Gilchrist JM. Multifocal motor neuropathy with conduction block and *Campylobacter jejuni*. Neurology 1996; 46: 562–3.

Wöhrle JC, Amoiridis G, Heye N, Przuntek H. Acute multifocal motor neuropathy with early spontaneous recovery: a distinct syndrome from Guillain-Barré syndrome? Electromyogr Clin Neurophysiol 1996; 36: 37–41.

Yuki N, Ang CW, Koga M, Jacobs BC, van Doorn PA, Hirata K, et al. Clinical features and response to treatment in Guillain-Barré syndrome associated with antibodies to GM1b ganglioside. Ann Neurol 2000; 47: 314–21.

Yuki N, Tagawa Y, Irie F, Hirabayashi Y, Handa S. Close association of Guillain-Barré syndrome with antibodies to minor monosialogangliosides GM1b and GM1α. J Neuroimmunol 1997; 74: 30–4.