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Case Report

Reversible conduction failure in overlap of Miller Fisher syndrome and pharyngeal–cervical–brachial variant of Guillain-Barré syndrome in the spectrum of nodo-paranodopathies

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ABSTRACT

Patients with an overlap of the pharyngeal–cervical–brachial variant of Guillain–Barré syndrome and Miller Fisher syndrome (PCB/MFS) have rarely been reported. The electrophysiological findings in PCB/MFS are of great interest and may provide insight into the pathophysiology of the disorder. We report the clinical features and nerve conduction study findings in a patient with PCB/MFS with high titers of antiganglioside antibodies against GQ1b, GD1a, and GD1b. In serial nerve conduction studies, compound muscle action potential amplitudes normalised without development of temporal dispersion within 3 weeks, and absent median, ulnar, and sural sensory nerve action potentials became recordable within 4 months. These findings are consistent with reversible conduction failure in both motor and sensory fibres, and PCB/MFS could be classified in the recently described nodo-paranodopathy spectrum of acute neuropathies associated with anti-ganglioside antibodies.

1. Introduction

The pharyngeal-cervical-brachial variant (PCB) of Guillain–Barré syndrome (GBS) overlapped with Miller Fisher syndrome (PCB/MFS) has been described by Ropper as ophthalmoplegia, ataxia, and generalised areflexia accompanied by pharyngeal-cervical-brachial weakness [1]. The electrophysiological findings in PCB/MFS are of great interest and may provide insight into the pathophysiology of the disorder. Nodo-paranodopathy is a recently described pathophysiological subtype of immune mediated neuropathy and results in a pathophysiologic continuum from transitory nerve conduction failure to axonal degeneration [2,3]. We report the clinical features and serial nerve conduction study (NCS) findings in a PCB/MFS patient whose NCS findings were consistent with reversible conduction failure.

2. Case report

An 83-year-old woman was admitted with a 1 day history of diplopia and imbalance. On neurological examination, she had left-sided lateral gaze palsy and ataxia. Cranial MRI showed no abnormalities. There was no history of infections in the month prior to admission. Physical examination on the next day showed total ophthalmoplegia and progression of ataxia. Deep tendon reflexes were absent globally. Muscle strength (Medical Research Council [MRC] scale) was 3/5 in the left-sided upper limb proximal muscles (deltoid, biceps, and triceps), whereas muscle strength in the right-sided proximal muscles and the bilateral forearms and hands was 4/5. The patient exhibited full strength in the lower limbs bilaterally. NCS showed absent sensory responses, with slightly reduced compound muscle action potentials (CMAP) in the right median and right peroneal nerves with normal distal latencies and motor conduction velocities (Tables 1, 2). Partial conduction blocks were found in the right and left median nerves and the right peroneal nerve in intermediate segments. F wave latencies and persistencies were normal in the right median, bilateral ulnar and right tibial nerves. A diagnosis of MFS was established, and treatment with intravenous immunoglobulin (Ig) (0.4 g/kg/day for 5 days) was started. The following day, bilateral ptosis and swallowing difficulties developed. The muscle weakness progressed to MRC grade 1/5 in the upper limb proximal muscle groups bilaterally with no change in the MRC grades in the distal upper limb and lower limb muscles. Cerebrospinal fluid protein level was at the upper limit of normal at 0.45 g/L (normal, ⩽0.45 g/L), without cells. Repeated electrophysiological examination on day 10 showed absent sensory responses and further reduced CMAP in the bilateral median, ulnar, tibial, and peroneal nerves, which

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Table 1
Findings of serial motor nerve conduction studies

	Day 1	Day 10	Day 19	Day 120
Right median				
DML (ms)	2.4	2.3	2.9	2.9
CMAP amp (mV)	**4.3**	**3.4**	**4.4**	5.0
CV (m/s)	57	50	53	55
Left median				
DML (ms)	2.3	2.6	2.4	2.8
CMAP amp (mV)	5.3	**2.2**	**4.8**	5.6
CV (m/s)	57	51	55	53.6
Right ulnar				
DML (ms)	1.7	2.5	2.5	2.0
CMAP amp (mV)	6.4	**4.1**	6.3	8.0
CV (m/s)	56	57	50	61.8
Left ulnar				
DML (ms)	2.6	2.4	2.6	3
CMAP amp (mV)	5.8	**2.7**	5.8	6.6
CV (m/s)	64	68	54	51.4
Right tibial				
DML (ms)	4.4	5.9	4.8	4.7
CMAP amp (mV)	7.3	4	6	7.7
CV (m/s)	56	44	46	44.4
Left tibial				
DML (ms)	4.4	5.9	4.5	5.2
CMAP amp (mV)	7.8	4.5	7.4	7.8
CV (m/s)	52	48	47	50
Right peroneal				
DML (ms)	3.2	4.9	4	3.9
CMAP amp (mV)	**1.2**	**0.2**	**1.4**	**1.3**
CV (m/s)	52	38	41	44.4
Left peroneal				
DML (ms)	3.8	4.8	3.6	3.2
CMAP amp (mV)	2.8	2.2	2.9	2.5
CV (m/s)	57	44	44	50

The abnormal values have been highlighted in bold.
Amp = amplitude, CMAP = compound muscle action potential, CV = conduction velocity, DML = distal motor latency, SNAP = sensory nerve action potential, – = absent response.

were more pronounced in the upper limbs. F waves were absent in the right median, bilateral tibial and left peroneal nerves (Tables 1, 2). Needle electromyography examination revealed positive sharp waves and fibrillation potentials in the bilateral deltoids, biceps, and triceps muscles and reduced recruitment of motor units with normal configuration. Needle electromyography findings of the forearm and hand muscles were normal. The motor unit potentials with high amplitudes and long durations that were observed in the bilateral L5 and S1 innervated lower limb muscles can be explained by lumbar spondylosis revealed on the lumbar MRI. Serum contained high titers of IgG antibodies against GQ1b, GD1a, and GD1b, but not GM1 and GM2. At her follow-up visit on day 15, the patient's proximal upper limb strength had improved to MRC grade 3/5, she was able to swallow, and her ophthalmoplegia had improved slightly. NCS performed on day 19 after admission showed improved CMAP in all nerves with absent sensory nerve action potential (SNAP) (Tables 1, 2). F waves were normal. When the patient was reassessed in the outpatient department on day 40, she had proximal upper limb strength of MRC grade 4/5, and she could walk without assistance. NCS performed on day 120 showed further improvement in the CMAP amplitudes in the median, ulnar, and tibial motor nerve conduction studies compared with the findings on the third NCS; in addition, the previously absent ulnar, median, and sural SNAP became recordable (Tables 1, 2).

3. Discussion

GBS is an acute, immune-mediated polyneuropathy, and according to the underlying nerve pathology, GBS is divided into demyelinating and axonal subtypes. Serial nerve conduction studies performed in some acute motor axonal neuropathy (AMAN) patients show nerve conduction blocks, which promptly resolved without development of temporal dispersion of CMAP; this feature is termed reversible conduction failure (RCF) [4]. Further, RCF has been reported in acute motor and sensorial axonal neuropathy (AMSAN), MFS, PCB, and GBS/MFS patients [5–9]. The electrodiagnostic study in our patient initially suggested that an axonal process was significantly affecting the sensory fibres, without demyelinating features. The second study revealed decreased CMAP in the upper limbs and absent SNAP, which is consistent with an AMSAN. Subsequently, the CMAP amplitudes markedly increased without temporal dispersion, which is consistent with RCF, and the SNAP subsequently became recordable.

The presence of IgG anti-GQ1b antibodies is a supporting finding for the diagnosis of PCB/MFS in our patient. In a large retrospective analysis of 100 patients with PCB, 73% of the 26 patients with PCB/MFS were positive for anti-GQ1b IgG antibodies [10]. Our patient also had high titers of IgG antibodies against GD1a, and GD1b. RCF may be induced by anti-ganglioside antibodies, which causes a transitory and limited complement mediated attack on the axolemma of the nodes of Ranvier, leading to nodal ionic imbalance [11,12]. In a previous study, the excitability properties of motor axons in patients with multifocal motor neuropathy (MMN) with distal conduction blocks were examined, and the findings suggested a reduction in resting paranodal and internodal K^+ conductance related to membrane hyperpolarisation [13]. Acute and chronic neuropathies, including AMAN, AMSAN, acute sensory

Table 2
Findings of serial sensorial nerve conduction studies

	Day 1	Day 10	Day 19	Day 120
Right median				
Peak latency (ms)				3.1
SNAP amp (μV)	**–**	**–**	**–**	**8.7**
CV (m/s)				50
Left median				
Peak latency (ms)				3.5
SNAP amp (μV)	–	**–**	**–**	**6.9**
CV (m/s)				44
Right ulnar				
Peak latency (ms)				3.0
SNAP amp (μV)	–	**–**	–	**5.9**
CV (m/s)				50
Left ulnar				
Peak latency (ms)				3.2
SNAP amp (μV)	–	**–**	–	**7.9**
CV (m/s)				40
Right suralis				
Peak latency (ms)				3.2
SNAP amp (μV)	–	–	–	**3.7**
CV (m/s)				45.8
Left suralis				
Peak latency (ms)				3.2
SNAP amp (μV)	–	–	–	**2.2**
CV (m/s)				55.8
Right peroneal superficialis				
Peak latency (ms)				
SNAP amp (μV)	**–**	**–**	**–**	**–**
CV (m/s)				
Left peroneal superficialis				
Peak latency (ms)				
SNAP amp (μV)	–	–	–	–
CV (m/s)				

The abnormal values have been highlighted in bold.
Amp = amplitude, CMAP = compound muscle action potential, CV = conduction velocity, DML = distal motor latency, SNAP = sensory nerve action potential, – = absent response.

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ataxic neuropathy, PCB, MFS, and MMN associated with anti-ganglioside antibodies against GM1, GD1a, GD1b, GT1a, and GQ1b, characterised by an immune mediated attack that begins and remains confined to the nodal region resulting in a pathophysiologic continuum from transitory nerve conduction failure to axonal degeneration have been categorised as nodo-paranodopathy by Uncini et al [2,3]. Three patterns have been electrophysiologically described in acute nodo-paranodopathies: (1) conduction block or reduced distal CMAP amplitude, which promptly resolves without the development of excessive temporal dispersion, as occurred in our patient; (2) conduction block followed by low amplitude CMAP from all nerve stimulation sites without persistent features of demyelination; and (3) low amplitude CMAP on early recordings, which do not improve during follow-up [3].

We conclude that serial NCS are required for differentiating RCF from demyelinating and axonal degenerating subtypes of GBS in PBC/MFS overlap patients in the continuous spectrum of newly categorised nodo-paranodopathies.

Conflicts of Interest/Disclosures

The authors declare that they have no financial or other conflicts of interest in relation to this research and its publication.

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