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Short communication

Non-demyelinating, reversible conduction failure in a case of pharyngeal–cervical–brachial weakness overlapped by Fisher syndrome

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ABSTRACT

Pathophysiologically, Guillain–Barré syndrome is divided into demyelinating and axonal subtypes. Recent studies have shown that serial nerve conduction studies (NCSs) are required to differentiate a demyelination–remyelination pathophysiology from one with axonal nodal reversible conduction failure. Cases with an overlap of pharyngeal–cervical–brachial weakness and Fisher syndrome (PCB/FS) are uncommon; the NCS findings of such cases have not been well described and the evolution of the NCS findings has not been previously studied. We describe the clinical features and serial NCS findings of a patient with PCB/FS. The evolution of abnormalities in NCS reflected a clinical pattern of weakness that progressed from the top of the body and descended toward the legs, and terminated before reaching the legs. The amplitudes of motor and sensory potentials were decreased, as is consistent with acute motor-sensory axonal neuropathy. However, the amplitudes recovered without the appearance of dispersed potentials seen in remyelination, implicating the pathophysiology of nodal reversible conduction failure. Together with the electrophysiological evidence of the pathophysiology of nodal reversible conduction failure in previously reported PCB patients and FS patients, our case suggests that PCB, FS and PCB/FS fall in a continuous spectrum with axonal GBS subtypes.

1. Introduction

Patients with Guillain–Barré syndrome (GBS) typically present with symmetrical weakness of both upper and lower limbs, along with generalized areflexia. Ropper [1] first reported 3 patients who developed prominent weakness in the pharyngeal–cervical–brachial regions without sensory disturbance. Their illnesses ended without affecting the power of their legs. He called this condition pharyngeal–cervical–brachial weakness (PCB) and considered this an abortive form of GBS that did not progress to cause generalized weakness. He further described another patient who had ophthalmoplegia, ataxia and generalized areflexia, in addition to PCB, and suggested that it was a case of PCB overlapped by Fisher syndrome (PCB/FS) [2]. Because the clinical features of PCB and PCB/FS are similar to those of myasthenia gravis and botulism, nerve conduction studies (NCSs) are useful in differential diagnosis.

Pathophysiologically, GBS is divided into demyelinating and axonal subtypes [3,4]. Conduction block seen in NCS has classically been deemed a feature of demyelination. However, recent studies suggest that conduction block or slowing can also be due to conduction failure from immune-mediated disruptions at the nodes of Ranvier without internodal demyelination [5–7]. The conduction block or slowing resolves promptly with the reversal of conduction failure at the nodes without development of excessive temporal dispersion characteristic of remyelination [8,9]. Thus, serial NCSs are required to differentiate between a demyelination and remyelination pathophysiology from one with axonal, reversible conduction failure [8,9]. NCS findings in PCB/FS have not been well described and the evolution of abnormalities has not been previously studied. Here, we report the clinical features and serial NCS findings in a PCB/FS patient whose NCS results implicate a pathophysiology of axonal reversible conduction failure.

2. Case report

One week after recovering from a mild diarrheal illness, a 61-year-old lady was admitted. She reported a 1-day history of non-vertiginous dizziness and finger paresthesia that was maximal at the fingertips bilaterally. Initial examination revealed mild gait ataxia but no other neurological abnormality. In particular, Romberg test and tendon reflexes were normal. A CT brain showed no relevant abnormality.

Examination on the next day showed dysarthria, dysphagia, external ophthalmoplegia and arm weakness. Deep tendon reflexes had become absent globally. The patient's power of shoulder abduction, elbow flexion and extension were Grade 2 under the Medical Research Council's (MRC) scale for testing muscle strength, while her power of wrist movements were MRC grade 4 bilaterally; her lower limb power was full. The progression of her symptoms led to the need for intubation and treatment with intravenous immunoglobulin (0.4 g/kg/day for 5 days). She remained alert, with no evidence of ptosis and

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did not complain of dry mouth. A cerebrospinal fluid (CSF) study conducted on Day 2 showed 3 white cells/μL and a protein level of 0.4 g/L. Anti-acetylcholine receptor antibodies were positive at 0.65 nmol/L (normal, less than 0.4 nmol/L) in serum obtained on Day 2, but the serum antibodies were negative on Day 13. Repetitive nerve stimulation studies and NCS on Day 2 showed no significant abnormality (Table 1). Anti-*Campylobacter jejuni* antibodies were not tested.

On Day 6, her proximal upper limb power had improved to MRC grade 4 and she became independent of ventilatory support. Her pupils remained reactive, but despite improvement of her ophthalmoplegia, she developed right partial ptosis. By Day 16, this, along with her bulbar symptoms, had improved markedly, and she was discharged home with almost complete resolution of her limb weakness. At her follow-up outpatient visit on Day 52, examination showed no neurological deficits. Serum obtained from the patient on Day 2 contained high titers of IgG antibodies against GT1a and GQ1b, but not with GM1, GM1b, GD1a, GalNAc-GD1a and GD1b.

A second NCS done on Day 7 showed marked decreases in amplitudes of the bilateral ulnar and median nerve compound motor action potentials (CMAPs) and lesser decreases in peroneal and tibial CMAPs and sural sensory nerve action potentials (SNAPs) (Table 1). Bilateral ulnar and median SNAPs could not be obtained. A NCS conducted on Day 15 showed some improvement in the amplitudes of the bilateral ulnar and median CMAPs, while SNAPs of these nerves remained absent; mild further decreases in the amplitudes of the peroneal and tibial CMAPs and radial SNAPs were seen. A subsequent NCS done on Day 52 showed recovery in the amplitudes of the ulnar and median CMAPs and SNAPs, while the peroneal and tibial CMAPs and radial SNAPs remained depressed. A NCS on Day 122 showed recovery of amplitudes in all nerves. The upper limb nerves showed more marked amplitude decreases, with most reaching a trough on Day 7. Amplitudes of lower limb nerves showed lesser decreases, reaching troughs later at Day 15 or Day 52. F-latencies, conduction velocities and distal latencies, except for median nerve latencies, did not show much change. Median nerve latencies were longer on Day 122, suggesting the presence of subclinical median neuropathy at the carpal tunnels.

Table 1
Findings on serial nerve conduction studies.

	Day 2	Day 7	Day 15	Day 52	Day 122
Motor conduction studies					
Right median					
DML (ms)	4.3	4.3	4.2	4.1	4.9
CMAP (mV)	5.6	**3.5**	6.3	6.8	7.5
CV (m/s)	57	51	51	54	48
Right ulnar					
DML (ms)	2.4	2.3	2.3	2.1	2.5
CMAP (mV)	7.1	**3**	**5.5**	8.5	8.6
CV (m/s)	64	55	56	55	50
Right tibial					
DML (ms)	3.7	3.6	3.2	3.8	4.0
CMAP (mV)	11.1	**8.6**	**7.1**	**7.6**	10.2
CV (m/s)	45	42	40	51	40
Right peroneal					
DML (ms)	3.9	3.0	3.6	4.0	3.4
CMAP (mV)	5.5	4	3	3	3.7
CV (m/s)	46	45	44	41	42
Sensory conduction studies					
Right median					
Peak latency (ms)	3.5			3.9	4.1
SNAP (μV)	**2.4**	**0**	**0**	**3.9**	**5.9**
CV (m/s)	41			47	36
Right ulnar					
Peak latency (ms)	2.4		2.3	2.7	2.8
SNAP (μV)	6.0	**0**	**3.4**	**3.1**	8.0
CV (m/s)	66		47	50	43
Right radial					
Peak latency (ms)	1.8	1.5	3.2	1.8	1.8
SNAP (μV)	45.3	35.5	**8.8**	21.2	47.8
CV (m/s)	54	64	50	69	56
Right sural					
Peak latency (ms)	2.4	1.8	2.1	2.9	2.5
SNAP (μV)	21.5	6.8	**5**	**1.6**	10.0
CV (m/s)	40	48	41	63	38

DML = distal motor latency; CMAP = compound muscle action potential; CV = conduction velocity; SNAP = sensory nerve action potential. The abnormal values have been underlined and significant changes in values highlighted in bold.

3. Discussion

Our patient's clinical presentation is consistent with PCB/FS, although other differentials were also considered. The acute onset of symptoms initially led us to consider brainstem vascular ischemia or hemorrhage, but the presence of generalized areflexia, symmetrical bilateral weakness and ophthalmoplegia, together with bulbar weakness and preserved consciousness, was inconsistent with these diagnoses. Myasthenia gravis was also considered, but the sudden occurrence of onset, absence of fatigability and areflexia did not favor this diagnosis. Thus, the initial low-titre positive result of anti-acetylcholine receptor antibodies on Day 2 was false positive. Although areflexia can be seen in botulism, the patient did not have dry mouth and a history of suspicious food consumption, and her gastrointestinal symptoms had subsided 1 week prior to presentation.

A literature search found few reported cases of PCB/FS [2,13–15]. Our patient had preceding diarrhea, but in other reported cases, upper respiratory tract infections were more common as antecedent illnesses [6]. Our patient also presented with numbness and ataxia rather than diplopia, which was the most common initial symptom in previous reports [2,13]. One case was unusual in having optic neuritis as the initial presentation [13]. External ophthalmoplegia was seen in all patients with internal ophthalmoplegia in a few [2,13–15]. Most of the patients had generalized areflexia. One patient had preserved reflexes in the lower limbs [13], and the median days, from onset to nadir, in this patient were close to 7 days [13–15]. Our patient developed blepharoptosis on Day 6 of her illness when limb and bulbar weakness had started to improve. Such occurrence has not been reported previously, whereas delayed development or worsening of facial palsy when other neurologic symptoms were lessening has been seen in patients with FS [12].

Our diagnosis of PCB/FS is supported by the presence of IgG anti-GT1a and -GQ1b antibodies [13,15]. In 100 patients who manifested progressive weakness of the pharynx, neck and upper limbs within 4 weeks of the initial onset, IgG anti-GT1a antibodies were found in 51% of these patients, while IgG anti-GQ1b antibodies were found in 39% [13]. Among these 100 patients, there were 13 cases of pure PCB, 8 cases where PCB weakness was present with preserved tendon reflexes, 48 cases of GBS overlap where leg weakness was also present, 26 cases of PCB/FS, and 5 cases of Bickerstaff brainstem encephalitis overlap where there was impaired consciousness. The study concluded that these conditions form a continuous spectrum of GBS presentations. In the 26 PCB/FS patients, anti-GT1a and -GQ1b antibodies were present in 73% and 81% of them, respectively.

It is interesting to note, in the NCS, a bilateral symmetry in nerve involvement, and a pattern where the upper limb nerves were affected more and earlier than the lower limb nerves, reaching troughs in amplitudes and recovering before the lower limb nerves (Table 1, Fig. 1). These changes lagged behind the clinical features, and the abnormalities in lower limb nerves were subclinical. The evolution of NCS abnormalities fits a descending weakness pattern that was 'aborted' before clinical weakness reached the legs. Ropper [2] had observed the bilateral but regional pattern of weakness in PCB, with "symmetry about the coronal plane" instead of a random distribution in the peripheral nervous system. Although GBS classically has an ascending weakness pattern, some cases present with PCB weakness before descending toward the legs [16]. The explanations for these are still unknown.