INTERNAL ☀ MEDICINE

□ CASE REPORT □

The Sequential Ultrasonographic, Electrophysiological and MRI Findings in a Patient with the Pharyngeal-cervical-brachial Variant of Guillain-Barré Syndrome from the Acute Phase to the Chronic Phase

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Abstract

Acute progressive weakness in bulbar, neck and limbs is included in several differential diagnoses, including the pharyngeal-cervical-brachial (PCB) variant of Guillain-Barré syndrome (GBS). Patients with the PCB variant of GBS are reported to have localized diagnostic cervical spinal nerve abnormalities that can be examined by nerve ultrasonography (NUS) and magnetic resonance neurography (MRN). We herein report the case of a 77-year-old man with the PCB variant of GBS. Although the nerve conduction study (NCS) findings were indirect indicators for an early diagnosis, the combination of NCS and NUS was a useful complementary measure that facilitated an early diagnosis. MRN did not show any apparent diagnostic abnormalities. After early treatment, the patient was discharged and returned home.

Key words: pharyngeal-cervical-brachial variant, cervical spinal nerve, nerve ultrasonography, electrophysiology, MR neurography

Introduction

Guillain-Barré syndrome (GBS) causes acute neuromuscular paralysis. The pharyngeal-cervical-brachial (PCB) variant of GBS is characterized by facial palsy, dysarthria, upper extremity muscle weakness, and areflexia of the upper limbs. The power of the lower limbs is usually preserved or only mildly affected, indicating that PCB represents a localized subtype of GBS. Since the PCB variant is quite rare and does not cause generalized limb weakness, which occurs in the acute inflammatory demyelinating polyradiculopathy type (the common form of GBS), the PCB variant is often misdiagnosed as brain stem stroke, myasthenia gravis, or botulism (1). The sites that are vulnerable to demyelination or axon injury in GBS include the spinal nerves (common entrapment sites for patients with entrapment neuropathy) and the motor nerve terminals, due to their relatively vulnerable blood brain barriers (2). Among these sites, we investigated the cervical spinal nerves in clinical practice using nerve ultrasonography (NUS), a nerve conduction study (NCS), and magnetic resonance neurography (MRN). Because localized injuries of the cranial nerves and the nerves of the cervical spine cause the main characteristic symptoms of the PCB variant of GBS, we thought that the examination of cervical spinal nerves could be useful for making an early diagnosis and in the planning of treatment (1, 3). NUS, NCS, and MRN were performed and the sequential cervical spinal nerve findings from the onset of symptoms to recovery were compared in a patient with the PCB variant of GBS.

Case Report

A 77-year-old man was referred to our hospital with a three-day history of progressive dysarthria, dysphagia, and bilateral upper limb weakness. He also noticed that his voice had slowly become nasal, and painless weakness of neck

Table.   **Sequential NCS Examinations.**

	Day 4	Day 9	Day 61	Day 100
Median nerve (recording site: APB)				
MCV (m/s, LLN is 49.5)	49/48	50/50	44/48	48/53
DML (ms, ULN is 4.6)	5.0/4.2	5.3/4.1	6.0/5.2	4.4/3.6
Distal CMAP amplitude (mV, LLN is 3.0)	5.1/6.3	3.8/7.4	4.8/5.5	4.8/7.0
F-latency (ms, ULN is 28.2)	28.9/28.3	30.4/29.1	32.4/30.3	28.5/26.7
Ulnar nerve (recording site: ADM)				
MCV (m/s, LLN is 49.9)	54/59	59/63	46/51	51/59
DML (ms, ULN is 3.8)	3.7/4.0	3.9/3.9	4.7/4.8	3.2/3.5
Distal CMAP amplitude (mV, LLN is 5.8)	6.0/4.0	5.1/3.0	7.6/4.8	6.5/5.6
Decrease of CMAP at the left cubital tunnel (%)	52	54	10	8
MCV between above and below elbow (m/s)	38	38	48	47
F-latency (ms, ULN is 29.7)	30.4/30.7	31.1/31.1	32.4/33.0	29.0/28.3
Tibial nerve (recording site: AH)				
MCV (m/s, LLN is 41.6)	43/48	43/39	43/NA	41/NA
DML (ms, ULN is 5.7)	4.2/5.1	4.4/4.6	5.3/NA	5.1/NA
Distal CMAP amplitude (mV, LLN is 4.3)	7.7/7.9	7.3/7.1	9.0/NA	8.6/NA
F-latency (ms, ULN is 51.7)	49.1/50.7	51.9/53.0	52.1/NA	49.8/NA

NCS examinations were performed at 4, 9, 61, and 100 days from onset of disease. Data of bilateral limbs are shown in the form of right/left. Bold and underlined values are above or below normative values. APB: abductor pollicis brevis, ADM: abductor digiti minimi, AH: abductor hallucis, MCV: motor nerve conduction velocity, m/s: meters per second, LLN: lower limit of normal, DML: distal motor latency, ULN: upper limit of normal, CMAP: compound motor action potential, ms: millisecond, mV: millivolt, NA: not applicable. When recording DML and distal CMAP amplitudes, stimulation sites were fixed as 80 millimeters with supramaximal stimulation. Calculations of MCV were based on data between wrist and elbow stimulations or data between ankle and popliteal fossa stimulations.

flexion and slight unsteadiness during walking had developed. He had not previously experienced such symptoms. He had experienced mild one-day diarrhea without fever 10 days before admission. A review of the other symptom was unremarkable. His medical history included hypertensive cerebellar hemorrhage (3 years previously), from which he had recovered fully without any symptoms and he was on no medications other than amlodipine and lansoprazole. Prior to his referral to our hospital, his doctor suspected a brain stem stroke and prescribed aspirin (100 mg/day) and (clopidogrel 75 mg/day). After repeated magnetic resonance imaging (MRI) examinations failed to detect any lesions, he was referred to our hospital with an acute exacerbation of his symptoms.

On physical examination, his blood pressure was 147/88 mmHg, and his heart rate was 86 beats per minute. He was alert and well oriented. He had normal S1 and S2 heart sounds and pulmonary sounds, and the other results of the physical examination were unremarkable. A neurological examination revealed moderate bulbar palsy involving the pharyngeal and palatal muscles, dysphonia (nasal quality), dysphagia (the reduced elevation of the larynx) and facial and tongue muscle weakness, reflecting injuries of cranial nerves VII, IX, X, and XII. His cervical flexion was decreased [manual muscle testing (MMT) 3] and his proximal muscle power was (MMT 3 to 4) bilaterally decreased in the upper extremities (proximal weaker than distal, right weaker than left, his right and left hand grip strengths were 8.2 kg and 2.5 kg, respectively). The patient's deep tendon reflexes were absent in the upper extremities and preserved in the lower extremities. No abnormal reflexes were observed. His sensory and cerebellar examination results were normal. He did not have gait ataxia.

Brain MRI, whole spinal cord MRI, and thoracic-abdominal-pelvic CT revealed no abnormalities. Laboratory analyses, including routine chemistry, the renal and liver profiles, thyroid function tests, CRP, ESR, and vitamin (including B1, B12) levels, as well as his levels of antinuclear antibody, angiotensin-converting enzyme (ACE), and acetylcholine receptor antibodies were within normal limits. The response to the tensilon test was negative. ECG showed bundle branch block characteristics. A decreased vital capacity (2.25 L, %VC was 71%) was seen on spirometry. Lumbar puncture at 6 days from the onset of symptoms showed an increased protein level of 57.4 mg/dl (normal <40 mg/dL), with normal cellularity in his cerebrospinal fluid (CSF). The results of conventional NCS at 4 days from the onset of symptoms showed the prolongation of distal motor latencies (DMLs) in the left ulnar nerve (5.0 ms) and right median nerve (4.0 ms), the prolongation of F-wave latencies in the bilateral median (28.9/28.3 ms) and ulnar nerves (30.4/30.7 ms), conduction block at the left cubital tunnel [motor conduction velocity (MCV) was 38 m/sec], and a suspected conduction block with bilateral decreases (48% in right, 50% in left) of the compound motor action potential (CMAP) between the Erb point and the axilla (Table and Fig. 1). The results of NUS at 5 days from the onset of symptoms showed the enlargement of bilateral 5th, 6th, and 7th cervical spinal nerves (3.8 mm and 3.1 mm in diameter at the right and left 5th cervical spinal nerves, 3.7 and 4.1
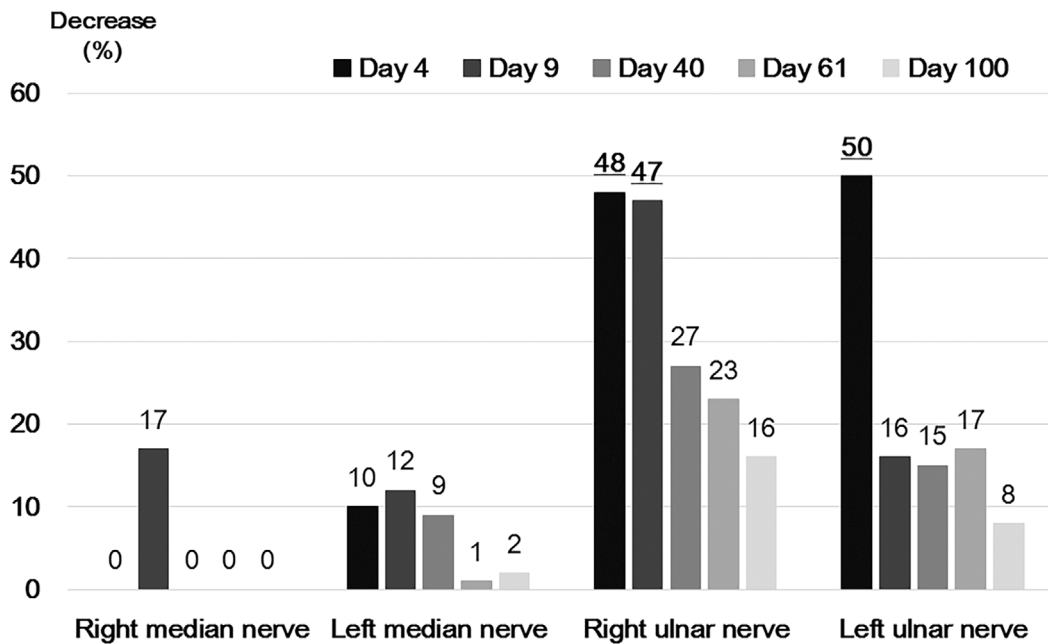
Figure 1. The percent decrease in the compound motor action potential (CMAP) between the Erb point and the stimulation of the axilla in the bilateral median nerves and ulnar nerves. Nerve conduction study (NCS) examinations were performed at 4, 9, 40, 61, and 100 days from the onset of disease. The bold and underlined values are interpreted as a conduction block (>50% decrease in CMAP) and conduction slowing, respectively.
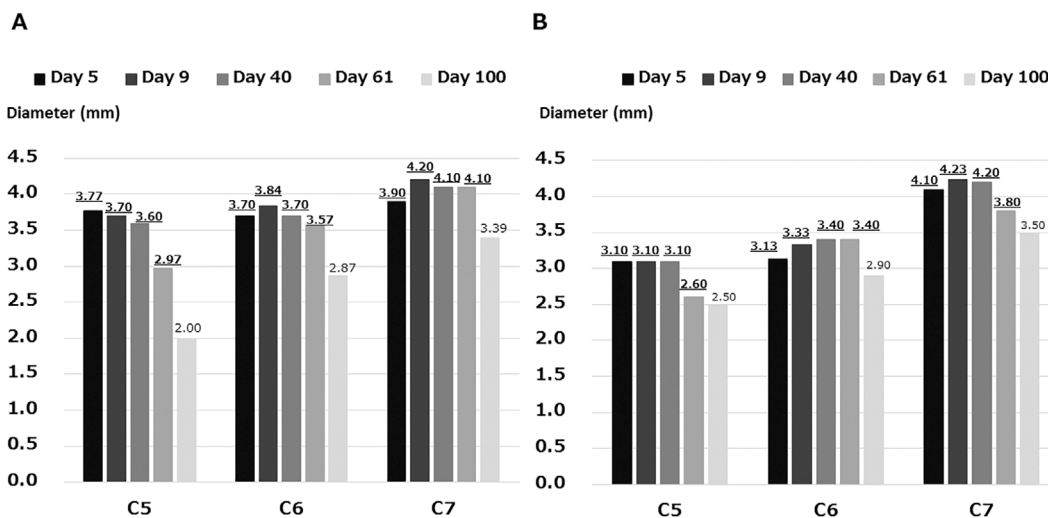

Figure 2. The cervical spinal nerve diameters measured by nerve ultrasonography (NUS). A is for the right side, while B is for the left. NUS examinations were performed at 5, 9, 40, 61, and 100 days from the onset of disease. C5 stands for the 5th cervical spinal nerve; the other nerves are similarly labeled. The bold and underlined values are higher than the mean values in healthy Japanese adults.

mm at the 6th, and 3.9 and 4.1 mm at the 7th) (Fig. 2). The mean diameter values for healthy Japanese adults were previously reported and used as reference (4). NUS was performed with a high-frequency 14-MHz probe real-time broadband linear array scanner (Aplio 500 TUS-A 500, Toshiba Medical Systems, Otawara, Japan) by trained examiners. NUS examinations of the peripheral nerves did not reveal carpal tunnel syndrome of the bilateral wrists or cubital tunnel syndrome of the left elbow. MRN of the neck at 5

days from the onset of symptoms showed no diagnostic findings (Fig. 1). MRN was performed with a 1.5-T MRI scanner (MAGNETOM Aera Version syngo MR D13, SIEMENS, Berlin and Munich, Germany). A presumptive diagnosis of the PCB variant of GBS was made, and he received the first 5-day course of intravenous immunoglobulin (IVIg) (2 g/kg in 5 days) at 6 days from the onset of symptoms. His neurological symptoms showed gradual recovery after a phase of severe neurological impairment at 13-16 days from
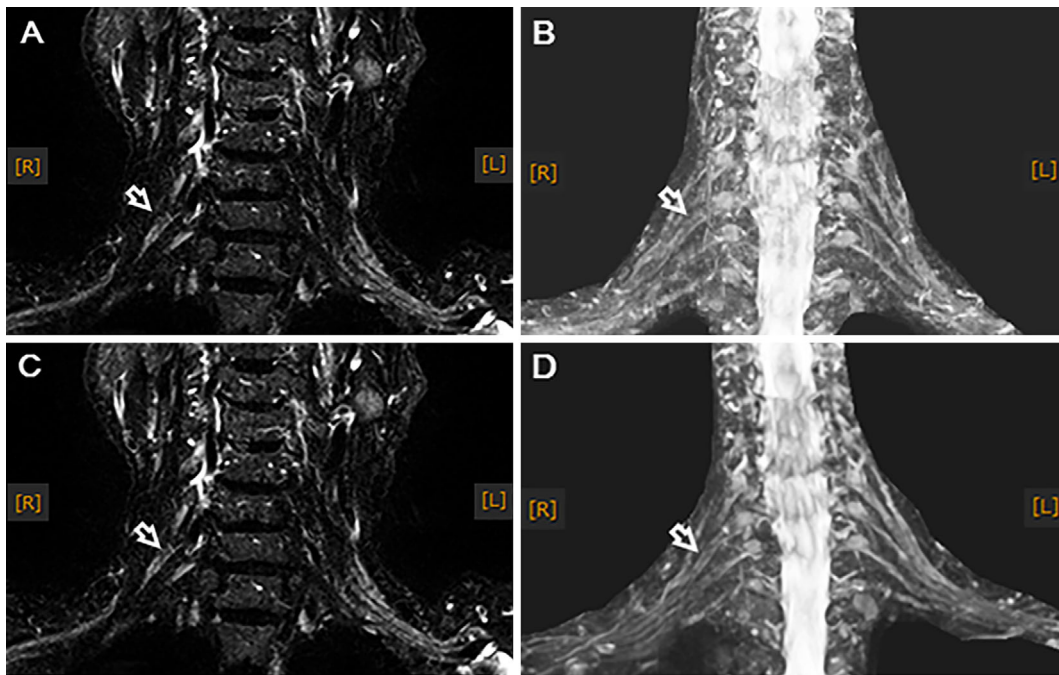
Figure 3. The MR neurography images at 5 days (A, B) and 60 days from the onset of disease (C, D). The coronal short-tau inversion recovery (STIR) source image shows the almost symmetrical mild hyperintensity of each cervical nerve in the acute phase (A), and no significant change in comparison to the chronic phase (C). The post-processed STIR images with maximum intensity projection (MIP) reconstruction in the acute (B) phase and those in the chronic phase (D) are also shown. Right, the 6th spinal nerve seemed to be mildly enlarged, but not changed from the acute phase to the chronic phase (arrow).

the onset of symptoms. However, we thought that his bulbar palsy would remain and that the patient would require nasogastric tube feeding, and a second 5-day course of IVIg (2 g/kg in 5 days) was started at 33 days from the onset of symptoms. Follow-up sequential NCS during the administration showed a deterioration followed by the recovery of CMAP, MCV, and F-wave latency in each nerve (Table and Fig. 1). Follow-up sequential NUS showed the ultrasonographic enlargement of all of the cervical spinal nerves, which tended to be maintained until 2 months after the onset of the disease. The abnormalities then gradually recovered in the chronic phase (Fig. 2). Follow-up MRN showed no apparent change (Fig. 3). Follow-up NCS, NUS, and MRN were performed in the same settings as the first examinations. IgG antibodies against GD1a (+, positive) and GT1a (++, strong positive) were detected at 28 days after the onset of symptoms. The serum antibody levels were measured by an enzyme-linked immunosorbent assay. After he achieved a favorable recovery from all of his symptoms through multidisciplinary therapy, including rehabilitation in our hospital, he was discharged. He returned home at 63 days from the onset of symptoms with only a mild nasal voice and mild weakness of neck flexion. He did not require any outpatient rehabilitation, and he is now completely independent in his activities of daily living.

Discussion

This patient presented with classical clinical features that were consistent with the PCB variant of GBS, namely albuminocytological dissociation in the CSF, electrophysiological evidence of neuropathy, the presence of anti-GT1a antibodies, and a favorable recovery within a few months after IVIg therapy. Although the PCB variant of GBS was assumed to have pathological changes that were localized to the cranial nerves and the cervical spinal nerves, a few cases have been reported that involved sequential morphological changes of the cervical spinal nerves (1). The cervical spinal nerves were evaluated by serial NUS, NCS, and MRN examinations from the acute to the chronic phase in the present case.

Autopsy studies of GBS have shown that the process of Wallerian-like degeneration was in a more advanced stage in the spinal nerves than in the peripheral nerves (3, 5). Some pathological findings in acute GBS patients support the hypothesis that inflammatory edema, which might be predominant in the spinal nerves in the acute phase, would imply an increase of endoneurial fluid pressure, constricting the transperineurial microcirculation and potentially producing an ischemic injury (3, 6). Appropriate evaluations of the spinal nerves would be diagnostically important in acute GBS. The absence, reduced variety, and prolonged latency of F-waves with relatively preserved CMAP and DML in peripheral

nerve studies have been recognized as a pattern of an indirect electrophysiological indicator of dysfunction in the spinal nerves of patients with GBS (3, 7). As a direct electrophysiological indicator, a cervical nerve root stimulation study using needle electrodes is considered to be an invasive procedure and is not well-suited for patients with acute diseases such as GBS. Examinations with Erb point stimulation in conventional NCS are generally considered as a substitute for the direct measurement of the cervical spinal nerves in clinical practice. In the present patient, sequential findings of severely reduced CMAP amplitude (considered to be a conduction block) between the Erb point and the axilla suggested an axonal pathology with evidence of reversible axonal conduction failure and rapid recovery in the absence of temporal dispersion on follow-up studies (Fig. 1) (8). In fact, the PCB variant of GBS was thought to represent a form of acute motor axonal neuropathy (1). However, a first-time NCS examination to confirm the decrease of the CMAP amplitude between the Erb point and the axilla (such as conduction slowing or blocking) would be difficult because the results of Erb point stimulation might occasionally be susceptible to patient factors, the competence of the examiners, and the timing of the examination in relation to the disease stage.

With regard to NUS, the ultrasonographic enlargement of the spinal nerves in the very early stage of GBS has been reported to be more prominent than that in the peripheral nerves and has been recognized as a good early diagnostic indicator (6, 9, 10). The regression of abnormalities within 6 months was reported to be associated with a clinical recovery over time (11). Similar correlations between the ultrasonography findings and the clinical course were observed in the present patient through the acute to chronic phases of his disease. Furthermore, numerous sequential NUS data of the cervical spinal nerve roots in the acute phase of GBS are available. On the first examination at 5 days from the onset of the PCB variant of GBS, the ultrasonographic enlargement of the right 5th and 6th cervical spinal nerves was greater than that of the left 5th and 6th cervical spinal nerves. These findings corresponded with the fact that the proximal weakness in the bilateral upper limbs was greater on the right side than on the left. After muscle weakness peaked at 13-16 days from the onset of disease, the gradual regression of the ultrasonographic enlargement of the the bilateral cervical spinal nerves was observed from 40 to 61 days after the onset of disease (Fig. 2). Inflammatory edema in the cervical spinal nerves might be one of the reasons why the ultrasonographic enlargement lasted until 40 days from the onset of disease (5, 6). We hypothesized that the incomplete secondary degeneration of the affected nerves contributed to the early electrophysiological recovery (Table and Fig. 1), the regression of the ultrasonographic enlargement (Fig. 2), and the present patient's satisfactory clinical recovery from weakness. Although the sequential NUS findings of the nerve roots were useful for achieving an early diagnosis and determining the clinical course in this patient,

we need to be mindful that ultrasonographic enlargement in acute GBS is not usually as prominent as that observed in demyelination-dominant diseases such as chronic inflammatory demyelinating polyneuropathy and Charcot-Marie-Tooth disease.

NUS of the peripheral nerves has been reported to be useful in the diagnosis of electrophysiological abnormalities at common entrapment sites. The common entrapment sites are susceptible to entrapment neuropathies, and are also common target lesions of acute GBS because of their vulnerable blood-nerve barriers (2). In the present patient, the NUS examination of the peripheral nerves at 5 days after the onset of disease did not reveal any diagnostic findings of entrapment neuropathies at the left cubital tunnel or the right carpal tunnel, where abnormal NCS findings were found at 4 days from the onset of disease. This contributed to the early diagnosis of the PCB variant of GBS. The electrophysiological abnormalities had almost disappeared in the chronic phase (Table).

With regard to MRN, the cervical spinal nerves in the chronic phase showed no apparent changes in comparison to the acute phase. Possible reasons for the lack of apparent changes on MRN might be as follows: this patient with the PCB variant of GBS seemed to have a full recovery from the acute axonal injuries without strong degeneration or demyelination that could induce nerve swelling. Although the detectability of moderately or severely enlarged nerves by MRN has already been established in chronic demyelinating neuropathies, the detectability of mildly enlarged nerves by MRN seems to not have been fully established in acute GBS. As for the MRI findings in GBS, the future development of neuro-imaging techniques is expected and is currently in progress.

The cervical spinal nerves were observed from the acute to the chronic phase of the PCB variant of GBS using NCS, NUS, and MRN. A combination of NCS and NUS as complementary measures might be useful for facilitating an early diagnosis determining the clinical course.

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