Case Report

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Multiple Cranial Neuropathies Without Limb Involvements: Guillain-Barre Syndrome Variant?

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Acute multiple cranial neuropathies are considered as variant of Guillain-Barre syndrome, which are immune-mediated diseases triggered by various cases. It is a rare disease which is related to infectious, inflammatory or systemic diseases. According to previous case reports, those affected can exhibit almost bilateral facial nerve palsy, then followed by bulbar dysfunctions (cranial nerves IX and X) accompanied by limb weakness and walking difficulties due to motor and/or sensory dysfunctions. Furthermore, reported cases of the acute multiple cranial neuropathies show electrophysiological abnormalities compatible with the typical Guillain-Barre syndromes (GBS). We recently experienced a patient with a benign infectious disease who subsequently developed symptoms of variant GBS. Here, we describe the case of a 48-year-old male patient who developed multiple symptoms of cranial neuropathy without limb weakness. His laboratory findings showed a positive result for anti-GQ1b IgG antibody. As compared with previously described variants of GBS, the patient exhibited widespread cranial neuropathy, which included neuropathies of cranial nerves III-XII, without limb involvement or ataxia.

Keywords Guillain-Barre syndrome, Cranial neuropathies, Bulbar palsy

INTRODUCTION

Numerous variants of Guillain-Barre syndrome (GBS) have been documented during the past decade [1,2]. These variants have similar symptoms and developmental, recovery, and treatment patterns. Cranial nerve (CN) palsies are common symptoms of GBS, but multiple cranial neuropathies as variant of GBS are rare and account for only 5% of patients [2]. Affected patients exhibit bilateral facial nerve palsy followed by bulbar dysfunctions (CN IX and X) with limb weakness and walking difficulties [1,2]. Because of its rarity, multiple cranial neuropathies as variant of GBS exhibiting normal motor and sensory limb functions have seldom been described in the literature [1-6].

We recently experienced an extremely rare case of multiple cranial neuropathies as variant of GBS with positivities for anti-GQ1b IgG antibody but without limb involvements. The patient was able to walk independently without any limb problems, but exhibited widespread

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cranial neuropathy, including neuropathies of CN III-XII. We hereby discuss the neurophysiologic abnormalities found in this case by the electrophysiological and cerebrospinal fluid (CSF) testing and magnetic resonance imaging, and also include a review of the literature.

CASE REPORT

A 48-year-old male patient was admitted for bilateral facial palsy, ptosis, diplopia, dysarthria, and dysphagia without limb weaknesses. His prodromal symptoms included watery diarrhea, fever, and myalgia for seven days. He had no remarkably neurological, medical, or family history and had worked in a piano making factory for 20 years. Following the acute treatment at the department of neurology, he was transferred to the department of physical and rehabilitation medicine. Specific CN tests were performed at the time of admission and periodically after his admission.

Regarding initial neurological symptoms, the patient reported an unpleasant sensation of the tongue with bilateral ptosis. At the same time, his speech became slurred and he experienced difficulty in swallowing and limitations of tongue movements with respect to lateralization and protrusion. He reported loosing bitter and sour taste sensations and was indicated as negative for gag reflex. At the time of admission, his eyes were in an internal strabismus state with complaints of diplopia in vertical gaze (Fig. 1). In addition, he had bilateral symmetrical facial palsy, marked impairments of mastication and deglutition, and together with aphonia and palatal palsy (which both continued until discharge), and weakened hearing. Sternocleidomastoid (SCM) and trapezius muscle strengths were compromised, but his gait was normal and tendon reflexes were well preserved (Table 1).

Comprehensively, he showed bilateral CN III, IV, V, VI, VII, VIII, IX, X, XI, and XII involvements, but no cerebellar signs, including ataxia, or other evidences were suggestive of autonomic or sphincter dysfunctions. He was alert without cognitive impairments. Manual muscle test grades of his upper and lower extremities were all normal. He showed no spasticity with respect to elbow, knee, or ankle joints (Modified Ashworth Scale grade zero). Sensation in limbs was intact.

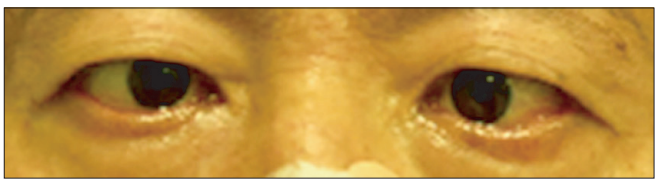

Fig. 1. He showed bilateral ptosis and internal strabismus.

Table 1. Cranial nerve evaluation in our case

Number	Cranial nerve	Physical finding
I	Olfactory nerve	Intact
II	Optic nerve	Intact
III	Oculomotor nerve	Bilateral ptosis/mydriasis/superior extraocular muscle palsy
IV	Trochlear nerve	Bilateral inferolateral extraocular muscle palsy (diplopia)
V	Trigeminal nerve	Bilateral masseter weakness Facial numbness (V1, V2, V3)
VI	Abducens nerve	Severe both lateral rectus palsy (internal strabismus)
VII	Facial nerve	Both symmetrical facial palsy (peripheral type) Taste sensory change (anterior two-thirds of the tongue)
VIII	Auditory nerve	Bilateral hearing difficulty
IX	Glossopharyngeal nerve	Dysphagia & dysarthria Taste sensory change (posterior one-third of the tongue)
X	Vagus nerve	Failure of soft palate elevation Voice change (hoarseness), gag reflex (-/-)
XI	Accessory nerve	Bilateral shoulders shrugging weakness (trapezius) Bilateral head rotation abnormality (sternocleidomastoid)
XII	Hypoglossal nerve	Bilateral tongue movement weakness (protrusion, lateralization, retraction, elevation)

Brain magnetic resonance images obtained at admission were normal. Nerve conduction studies (NCS), including motor, sensory, and F-wave examination, were performed on all limbs, and needle electromyography, repetitive nerve stimulation (RNS), and blink reflex testing were performed on hospital days of 3, 17, and 59. NCS and RNS findings were normal for all limbs. However, blink reflexes and facial nerve conduction velocity (NCV) were not evoked bilaterally, and at his last facial NCV study conducted 6 weeks after presentation, his left side findings had improved to normal and right side findings remained abnormal. Needle electromyography studies showed acute denervation (positive with fibrillation in the resting state, reduced recruitment, and polyphasic motor unit potentials during the volition state) of bilateral facial (frontalis, orbicularis oculi, orbicularis oris, nasalis) and laryngeal muscles (cricothyroid, thyroarytenoid), masseter, hyoglossus, and SCM muscles. Six weeks after onset, the motor evoked potentials (MEP), brainstem auditory evoked potentials (BAEP), somatosensory evoked potentials (SEP), and NCV and EMG follow-up studies were performed, and the NCV were normal and needle EMG findings remained abnormal. Transcranial magnetic stimulation (TMS) evoked MEPs recorded from the first dorsal interosseous and tibialis anterior muscles using surface gel electrode were normal. For this TMS study, the active electrode was placed over muscle bellies, while the reference electrode was placed over the distal interphalangeal joint of the index finger or the medial malleolus in upper and lower extremities. The motor cortex area was stimulated. BAEP study was performed by using a click sound for stimulation at 90 dB. Interpeak latencies and amplitudes were recorded. Results revealed shallow waves on right sides. SEP studies using the trigeminal nerve stimulation revealed delayed latencies on both sides, and SEP studies using the median nerve stimulation showed normal values with no statistical difference on both sides.

CSF analysis performed at admission showed elevated IgG (12.04 mg/dL) but a normal albumin level. Serum anti-ganglioside Ab analysis revealed positivity for anti-GQ1b IgG Ab (140 titer units) and negativity for anti-GM1 Ab. All other laboratory findings were normal.

Three days after the onset, intravenous immunoglobulin (IVIg) was started at 2 g/kg for five consecutive days. During the 11 weeks of inpatient period, many cranial neuropathies recovered slowly. In particular, his hearing difficulty and SCM weaknesses were completely normalized, but on the other hand, the mild diplopia, dysphonia, and dysphagia persisted at discharge. Videofluoroscopic studies were performed at 4 and 9 weeks after presentation and showed liquid aspiration during swallowing at 4 weeks but no aspiration or penetration at 9 weeks (functional dysphagia scale 71 → 53). Despite the mild improvements being observed, an extended transit time of oral phase due to a tongue propelling weakness, and the pharyngeal phase due to reduced pharyngeal peristalsis, the cricopharyngeal function remained (Fig. 2).

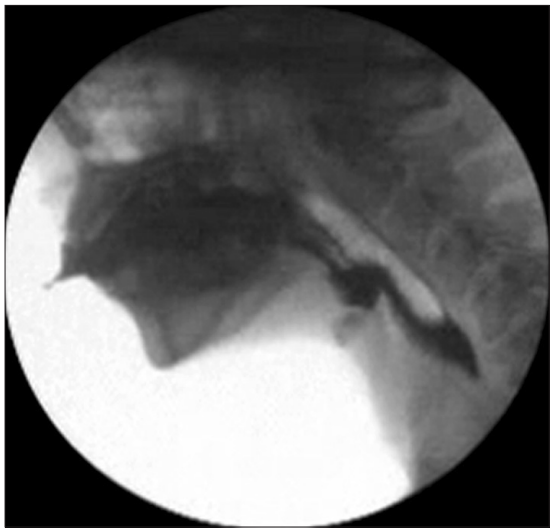

Fig. 2. The videofluoroscopic swallowing study on lateral view showed remnant of material in valleculae space and pyriform sinus.

A dysarthria test performed in a speech therapy room at 5 weeks after presentation showed poor tongue movements in all directions (protrusion, retraction, lateralization, and elevation), and these persisted at discharge. Voice and speech patterns were low-pitched with short phrase phonations and hypernasal resonances.

DISCUSSION

Multiple cranial neuropathies can occur as variant of GBS. This variant, which has been referred to as polyneuritis cranialis in the literature, accounts for 3%–5% of the variant cases [2]. The majority of multiple cranial neuropathies as variant of GBS patients are presented with facial or orbital pains and primarily exhibit involvements

of motor cranial nerves with limb involvements, that is, the involvements are limited to lower CNs. In particular, the CN VII or CN IX and CN X dysfunctions were found to be common CN abnormalities in previous studies [1-6]. Furthermore, previous studies have reported distinct upper or lower limb numbness and weakness in addition to limited cranial neuropathy [1,2].

The differential diagnosis of acute multiple cranial neuropathies without limb weaknesses after a preceding infection includes the Miller Fisher syndrome, pharyngeal-cervical-brachial weakness type variant GBS, Bickerstaff brainstem encephalitis, and acute ophthalmoplegia. For our patient, the adequate investigations allowed us to rule out these diseases. In particular, some symptoms of our case resembled those of atypical Miller Fischer syndrome, which presented acute ophthalmoplegia without ataxia or areflexia or without both, however, our findings showed more widespread cranial neuropathy [7,8].

Acute multiple cranial neuropathies without limb weakness are rare GBS variants. In our case, cranial neuropathies were widespread and included CN III-XII, which differentiates our case from others with more limited CN impairments. Like the other more common cases of acute multiple cranial neuropathies, our patient exhibited distinct abnormalities in CN VII, IX, X, and V [2]. And the recoveries of these CN impairments were remarkably delayed.

Laboratory findings at admission indicated the presence of anti-GQ1b IgG antibody but the absence of anti-GM1 IgG antibody. The GQ1b ganglioside is enriched in the paranodal regions of the extra-medullary portion of the human oculomotor, trochlear, and abducens nerves [4]. The anti-GQ1b antibodies bind at neuromuscular junctions where they cause a massive release of acetylcholine from nerve terminals which block the neuromuscular transmission and eventually, induce the breakdown of motor nerve terminals [8]. In addition, anti-GQ1b antibody cross-reacts with GT1a, GD3, GD1b, which are similar molecular structures to GQ1b [9]. The GT1a is specifically distributed in the lower CNs and is associated with bulbar palsy, and thus, cross-reactions between anti-GQ1b and GT1a can cause bulbar palsy. In addition, anti-GT1a antibody cross-reacts with GQ1b [9], and although anti-GT1a antibody does not cross-react with other gangliosides, it is more specific for bulbar palsy. Thus, it appears that these cross-reactions between anti-ganglioside antibodies could explain the symptoms observed in our case.

Our patient also responded to immune modulation therapy, although multiple issues, such as, facial, oculomotor, and bulbar palsy had remained. EMG and EP studies were used to evaluate neurophysiologic changes in CN involvement, and the facial and laryngeal muscles produced the most severe findings of denervation at initial and final follow-up studies.

In summary, in most cases, the occurrence of multiple cranial neuropathies is a clinical indication of a Guillain-Barre regional variant. In previous cases, at onset, the CN involvement was almost limited to CN VII, IX, and X impairments, such as facial palsy, dysphagia, and dysarthria [2-4]. These patients almost showed similar clinical features, including motor or sensory impairments, and were positive for anti-GQ1b antibodies. The limited CN involvements in previously reported cases could be due to the location of GQ1b ganglioside enrichment [2-4,8].

However, our case showed more widespread cranial neuropathy that involved CN III-XII without limb involvement. This case is extremely rare. Although GQ1b ganglioside is also presented in oculomotor, trochlear, and abducens nerves [10], the widespread CN involvement in our case suggested that other factors except the anti-ganglioside antibodies were responsible for our patient's symptoms.

Our patient also exhibited a normal gait with normal limb motor and sensory functions. Nevertheless, the clinical recovery was delayed and more sequelae remained than for typical cases of polyneuritis cranialis variant GBS. In previous cases, immunoglobulin therapy appeared to be effective and should be the preferred treatment for patients with multiple CN impairments at the onset of GBS. However, our case was an exception which showed incomplete recovery after IVIg therapy.

Neurological features of other typical polyneuritis cranialis cases were confined to muscles innervated by V, VII, IX, and X CNs [2]. Furthermore, the CNs, including V, VII, IX, and X, innervated muscles of specific embryological origin, that is, branchial muscles [3]. However, symptoms attributed to CN III-XII involvements in our case cannot be explained based on the considerations of embryonic origins.

We suspected that widespread multiple cranial neuropathies of variant GBS without limb involvements re-

sult from neurophysiologic mechanisms that differ from those of other polyneuritis cranialis as Guillain-Barre variants.

CONFLICT OF INTEREST

No potential conflict of interest relevant to this article was reported.

REFERENCES

1. Lyu RK, Chen ST. Acute multiple cranial neuropathy: a variant of Guillaine-Barre syndrome? Muscle Nerve 2004;30:433-6.
2. Wang Q, Xiang Y, Yu K, Li C, Wang J, Xiao L. Multiple cranial neuropathy variant of Guillaine-Barre syndrome: a case series. Muscle Nerve 2011;44:252-7.
3. Polo A, Manganotti P, Zanette G, De Grandis D. Polyneuritis cranialis: clinical and electrophysiological findings. J Neurol Neurosurg Psychiatry 1992;55:398-400.
4. Edvardsson B, Persson S. Polyneuritis cranialis presenting with anti-GQ1b IgG antibody. J Neurol Sci 2009;281:125-6.
5. Ropper AH. Unusual clinical variants and signs in Guillain-Barre syndrome. Arch Neurol 1986;43:1150-2.
6. Yuki N, Odaka M, Hirata K. Acute ophthalmoparesis (without ataxia) associated with anti-GQ1b IgG antibody: clinical features. Ophthalmology 2001;108:196-200.
7. Lo YL. Clinical and immunological spectrum of the Miller Fisher syndrome. Muscle Nerve 2007;36:615-27.
8. Rigamonti A, Lauria G, Longoni M, Stanzani L, Agostoni E. Acute isolated ophthalmoplegia with anti-GQ1b antibodies. Neurol Sci 2011;32:681-2.
9. Kim JK. Anti-ganglioside antibodies and Guillain-Barre syndrome. Korean J Neuromuscul Disord 2010;2:14-20.
10. Chiba A, Kusunoki S, Obata H, Mechinami R, Kanazawa I. Ganglioside composition of the human cranial nerves, with special reference to pathophysiology of Miller Fisher syndrome. Brain Res 1997;745:32-6.