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CASE REPORT

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Polyneuritis cranialis combined with Horner's syndrome: a rare variant of Guillain Barré syndrome

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Abstract

Background Polyneuritis cranialis (PNC), a rare variant of Guillain-Barré syndrome (GBS), is usually characterized by ocular and pharyngeal weakness without obvious numbness or weakness of the limbs or ataxia. Horner's syndrome is extremely rare in patients with PNC. Here, we describe a case of GBS presenting with acute PNC and unilateral Horner syndrome.

Case presentation A 53-year-old male presented with headache, abducent paresis, peripheral-type facial palsy, bulbar type dysarthria, decreased gag reflex and tongue palsy. Neurological examination showed Cranial Nerve V, VI, VII, IX, X and XII were affected, and Horner's syndrome was observed. Cerebrospinal fluid analysis showed albuminocytologic dissociation. Sensorimotor conduction velocity and needle electromyography of limbs were normal. Magnetic resonance imaging of brain was normal. Finally, the patient was diagnosed as PNC combined with Horner's syndrome. The patient received plasma exchange and intravenous immunoglobulin, which relieved the symptoms rapidly.

Conclusion GBS presenting only as Horner syndrome and PNC is a challenge for etiological diagnosis. Clinicians need to know enough to distinguish GBS and its variants from other potential similar diseases.

Keywords Guillain-Barré syndrome, Polyneuritis cranialis, Horner's syndrome, Plasma exchange, Intravenous immunoglobulin

Background

Guillain-Barré syndrome (GBS) is an autoimmune disease with the main pathological characteristics of demyelination or axonal damage of peripheral nerves or nerve roots [1]. GBS has different kinds of variants with distinct clinical symptoms, of which diagnosis is very challenging. Cranial nerves may be involved in up to 50% of GBS patients [2]. However, GBS showing only polycranial neuritis is very rare. Polyneuritis cranialis (PNC) is an extremely rare variant of GBS that is usually characterized by ocular and pharyngeal weakness without obvious numbness or weakness of the limbs or ataxia [3].

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Autonomic dysfunction occurs in up to two thirds of GBS patients [4]. The common clinical manifestation of autonomic dysfunction includes cardiac arrhythmias, blood pressure fluctuations, and gastrointestinal motility dysregulation [5]. Horner's syndrome is a less common manifestation of autonomic nervous function. It is characterized by ipsilateral miosis, ptosis, anhidrosis, and enophthalmos due to disruption of the oculosympathetic pathway. It is very rare as presentation of GBS [6]. In addition, case of GBS presenting alone with Horner's syndrome and PNC have hardly been reported.

The present report describes a case of male patient with PNC and Horner's syndrome attributed to GBS, which is very rare. After a definite the diagnosis, treatment with plasma exchange (PE) and intravenous immunoglobulins (IVIg) relieved the symptoms rapidly.

Case presentation

A 53-year-old male patient presented to neurological department complaining of a paroxysmal moderate to severe drag-like headache around both eyes for 10 days. The pain occurred three to five times per day and lasted for several minutes, which cannot be relieved by conventional painkillers. 5 days later, he noticed drooping of his left eyelids. The following days he gradually developed right eyelid closure weakness, double vision, dysphagia and slurred speech. The above clinical symptoms did not fluctuate day and night. He denied any preceding history of flu-like symptoms or gastrointestinal infection. He had no history of diabetes and tumor.

Neurological examination showed normal mental status and dysarthria. Left ptosis was observed with enophthalmos and myosis but no anhidrosis. The left eyelid was about 2 mm lower than the right. Bilateral pupils were not equal, with 2 mm on the left and 3 mm on the right side in diameter. Bilateral pupils are sensitive to light. There were partial abducent paresis in right eye and right peripheral-type facial palsy. On protrusion the tongue was deviated to the right. Gag reflex was reduced. Other cranial nerves were unremarkable. Muscle tone and muscle strength of the upper and lower extremities were normal. Tendon reflexes had decreased in all extremities. Sensory examination was normal. There was no evidence of ataxia. Gait was normal. Bilateral Babinski signs were negative.

Laboratory studies, including complete blood cell count, biochemical test (liver, renal, electrolyte and glucose), cancer biomarkers(cytokeratin 19 fragment, gastrin-releasing peptide precursor, CA19-9, CEA, and AFP), indicators of autoimmune diseases (ESR, serum complement levels, immunoglobulins, ASO, rheumatoid factor, M protein, lupus anticoagulant, anti-neutrophil cytoplasmic antibodies (ANCA), anti-nuclear antibody spectrum, anti-cardiolipin antibodies), and thyroid function were normal. Neostigmine test, fatigue test and repetitive nerve stimulation were performed to rule out myasthenia gravis (MG). A lumbar puncture was performed with an opening pressure of 15 cm H_2O. Results from the cerebrospinal fluid (CSF) analysis indicated albuminocytological dissociation, with a protein of 1.49 g/L and a nucleated cell number of 3.0×10^6/L. Tests of CSF cultures and viral encephalitis nucleic acid by PCR-fluorescent probe were all negative, including herpes simplex virus (HSV)-1, HSV-2, varicella zoster virus (VZV), Epstein-Barr virus (EBV), cytomegalovirus (CMV), and human herpesvirus 6 (HHV-6). Moreover, serum ganglioside antibodies IgG and IgM, including sulfatides, GM 1, GM 2, GM 3, GM 4, GD 1a, GD 1b, GD 2, GD 3, GT 1a, GT 1b, and GQ 1b, were all negative. Lesions in skull base and cavernous sinus were excluded due to normal head MRI. Serology, MRI imaging of the head and the ultrasonography of the head and neck vessels showed no evidence of vasculitis. Thyroid ultrasound, cervical lymph node ultrasound, and chest CT scan were performed to rule out space occupying lesions of lung and neck.

Electrophysiological nerve conduction studies (NCS) demonstrated prolonged distal motor latency and decreased amplitudes of compound motor action potentials in right facial nerve, NCS of left facial nerve and Needle electromyography of bilateral orbicular muscles were normal. NCS and Needle electromyography of upper and lower limbs were normal. (Fig. 1)

The patient was diagnosed as cranial variant of GBS. Five rounds of PE treatment were initiated for the patient on December 8th, 2021. His symptoms are better than before, but he has not fully recovered. IVIg was started at 0.4 g/kg daily on December 24th, 2021 for five consecutive days. His headache, eyelid drooping, diplopia, swallowing and slurred speech gradually improved after one month. The patient returned to our hospital over three months later for a follow-up consultation. His headache had gradually disappeared, his slurred speech and facial paralysis had significantly improved, and his Horner's syndrome had fully recovered. Reexamination of the electromyography showed that the conduction of the right facial nerve had returned to normal (Fig. 2). After three years of follow-up, the patient did not experience any recurrence of facial paralysis or other symptoms, which is consistent with the improvement seen after treatment.

Discussion

The patient had paroxysmal drag-like headache around both eyes at onset, which cannot be relieved by conventional painkillers such as ibuprofen. First branch of bilateral cranial nerve (CN) V was affected based on pattern and region of headache. On examination, the patient had abducent paresis, peripheral-type facial palsy, bulbar type

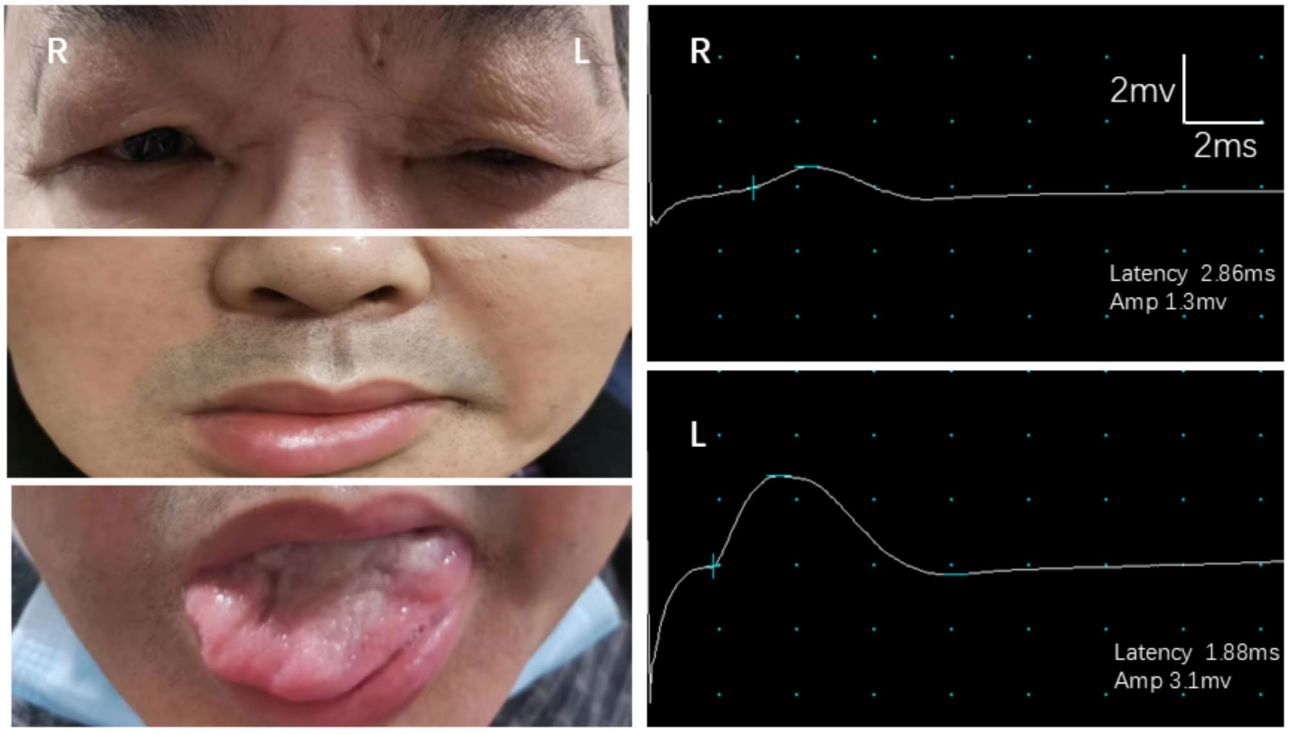

Fig. 1 The patient presented with Horner syndrome on the left and peripheral facial paralysis on the right. Electromyography (EMG) showed prolonged latency (2.86ms) and decreased amplitude (1.3mv) in the right facial nerve. Left facial nerve conduction is normal.

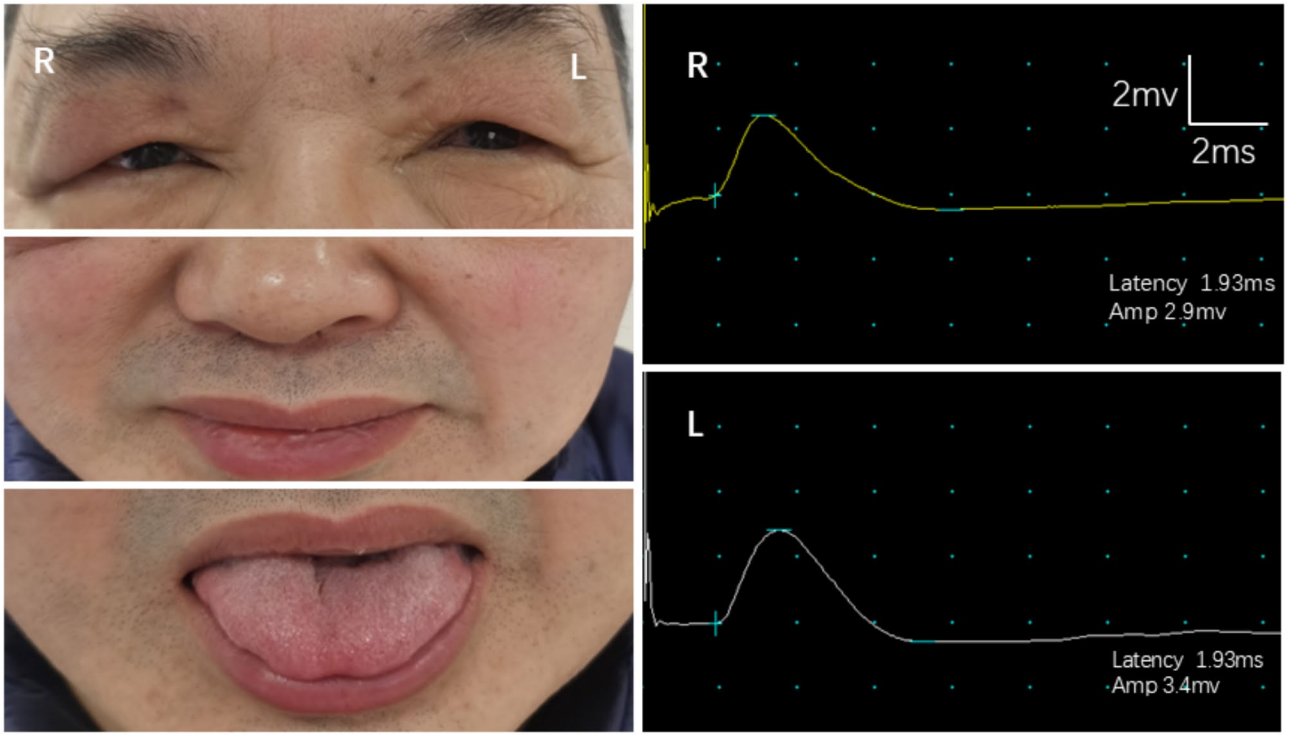

Fig. 2 After treatment, the patient's left-sided Horner syndrome and right-sided peripheral facial paralysis showed significant improvement. Electromyography revealed normal bilateral facial nerve conduction.

dysarthria, decreased gag reflex and tongue palsy, suggestive of CN VI VII, IX, X and XII affected. Vascular, infectious and neoplastic lesions in central nervous system can be ruled out due to normal brain MRI and CSF culture and PCR. Systemic diseases such as connective tissue disease and endocrinopathy can also be excluded in accordance with normal chest CT scan and serological tests. Multiple cranial neuropathy with no limb weakness and ataxia, hyporeflexia, albuminocytological dissociation, and abnormal NCV studies in this case suggest GBS variant called PNC. Myasthenia gravis (MG) is considered to be one of the differential diagnoses. Moreover, GBS and MG can occur simultaneously in the same patient [7]. Absence of diurnal fluctuation of clinical features and negative repetitive nerve stimulation, fatigue and neostigmine tests excluded MG in our case. The patient's clinical features did not support diagnosis of botulism as an etiology.

PNC has been defined in patients who exhibit multiple cranial neuropathies and GBS clinical features simultaneously and do not fulfil diagnostic criteria for Miller Fisher Syndrome (MFS) or other GBS subtypes with prominent CN involvement [8]. Classical MFS is characterized by ophthalmoplegia, areflexia, and ataxia. Anti-GQ1b IgG antibody is usually related to MFS and GBS with ophthalmoplegia, however, up to 15% of patients are negative [9]. In our case, the patient had bulbar weakness but no ataxia and anti-GQ1b antibody, thus excluded MFS variants. Up to 85% PNC patients displayed ocular weakness, facial weakness or trigeminal sensory disturbance and bulbar weakness [10], as in this case. Facial weakness was often asymmetric. Based on the clinical features of 15 historical cases of PNC attributed to GBS, a new diagnostic criterion for PNC (oculomotor-pharyngeal subtype of GBS) was proposed [10]. Required features for PNC include: unilateral or bilateral oculomotor and oropharyngeal weakness, absence of ataxia and disturbed consciousness and prominent limb weakness, monophasic illness pattern and interval between onset and nadir of cranial nerve involvement between 12 h and 28 days and subsequent clinical plateau and absence of identified alternative diagnosis [10]. Features strongly supportive of the diagnosis include: antecedent infectious symptoms, hyporeflexia, cerebrospinal fluid albumin cytological dissociation, neurophysiological evidence of neuropathy, presence of anti-GQ1b or anti-GT1a IgG antibodies. The patient's course and pattern of multiple cranial nerve involvement was consistent with the required and supportive feature of the PNC diagnostic criteria mentioned above except for presence of anti-ganglioside antibodies. As we know, anti-ganglioside antibodies are usually negative in patients with demyelinating neuropathy [10]. We ultimately diagnosed the patient as PNC, which is a separate subtype at the interface between MFS and GBS.

It is challenging for clinicians to diagnose the acute ptosis. Several lesions such as oculomotor complex, oculosympathetic pathway and neuromuscular junction can lead to acute ptosis [11]. Considering that Muller muscle innervated by oculosympathetic nerve only causes eyelid elevation for 1–2 mm, obvious ptosis cannot be attributed to sympathetic dysfunction [12]. In a study, all recruited 5 GBS patients with mild bilateral ptosis showed ocular sympathetic dysfunction, which has been demonstrated to be early and characteristic feature of GBS [13]. In our case the left mild ptosis and miosis occurring in this case was attributed to sympathetic dysfunction rather than oculomotor dysfunction, which is called Horner's syndrome. The possibility of cervical sympathetic nerve compression was ruled out by thyroid ultrasound, cervical lymph node ultrasound, and chest CT scan. There is limitation that whether pre or postganglionic sympathetic nerve was affected has not been determined by medication such as cocaine and hydroxy amphetamine drops. Considering anhidrosis did not exist in the patient, it is speculated that post-ganglionic sympathetic nerve was involved. This is because the external carotid plexus innervating the facial sweat glands can be spared when only the sympathetic fibers in the internal carotid plexus is affected [14].

In treatment, IVIg and PE are considered effective treatments for GBS [15]. The improvement of clinical symptoms in the patient with IVIg and PE further confirms PNC and Horner' syndrome were associated with GBS and immune-mediated. GBS is conventionally managed with either intravenous immunoglobulin (IVIG) or plasma exchange, as combination therapy is not typically recommended [16]. However, in this specific case, the patient initially received plasma exchange, which yielded only partial improvement in facial palsy. Considering the patient's strong motivation for recovery and the suboptimal response to plasma exchange, we opted to administer intravenous immunoglobulin as a secondary therapeutic intervention to optimize clinical outcomes. This case illustrates that combined therapeutic approaches may enhance prognostic outcomes in selected patients by addressing the complex immune dysregulation through multiple mechanisms of action.

Conclusions

This is the first report of GBS presenting only with acute polyneuritis cranial and unilateral Horner syndrome. This case suggested that when a patient present with PNC, GBS should be considered as a cause after excluding other etiologies such as ischemia, infectious, or neoplastic lesions of the skull base or brainstem. We also need to pay more attention to incidence of Horner' syndrome in GBS. Multicenter studies are needed further

to better understand pathogenesis and diagnosis of this variant of GBS.

Abbreviations

PNC	Polyneuritis cranialis
GBS	Guillain-Barré syndrome
CA19-9	Cancer antigen 19 – 9
CEA	Carcinoembryonic antigen
AFP	Alpha-fetoprotein
ASO	Anti-streptolysin O
ANCA	Anti-neutrophil cytoplasmic antibodies
PE	Plasma exchange
IVIg	Intravenous immunoglobulins
CSF	Cerebrospinal fluid
HSV	Simplex virus
VZV	Varicella zoster virus
EBV	Epstein-barr virus
CMV	Cytomegalovirus
HHV-6	Human herpesvirus 6
NCS	Nerve conduction studies
DML	Distal motor latency
CMAP	Compound motor action potentials
CN	Cranial nerve
MG	Myasthenia gravis
MFS	Miller fisher syndrome

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Author contributions
Xiangtao Nie and Wei He made the diagnosis and is responsible for the case management, writin the first draft, editing the manuscript and approval of the final version of the manuscript. Lei Hao and Xiuming Guo contributed in writing and editing the manuscript and approval of the final manuscript. Wenjing Qi, Yongbo Ma and Geke Zhu contributed in completing the information related to the case. All authors read and approved the final manuscript.

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Data availability
No datasets were generated or analysed during the current study.

Declarations

Ethics approval and consent to participate
We confirm that we have read the journal's position on issues involved in ethical publication and affirm that this report is consistent with those guidelines. As this is a case report describing clinical observations, ethics approval was waived.

Consent for publication
Written informed consent was obtained from the patient for publication of this case report and accompanying images.

Competing interests
The authors declare no competing interests.

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