# A teenager with ophthalmoparesis and dysphagia

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ABSTRACT

**The pharyngeal-cervical-brachial (PCB) variant is a rare presentation of Guillain–Barré syndrome (GBS), and there is a handful of case reports that overlap with the Miller–Fisher syndrome (MFS) variant of GBS. This overlap produces varied symptoms that may be confusing and challenging for physicians to diagnose timely and start appropriate treatment. In this article, we present a case report and review of the rare overlap of the PCB variant with the MFS variant of GBS.**

**KEYWORDS:** Miller–Fisher, pharyngocervical GBS, clinical neurology

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## Case presentation

An 18-year-old man, with no prior significant medical history, presented to neurology emergency with a 3-day history of acute onset, a progressive nasal twang in his voice, slurring of his speech and difficulty in swallowing, followed by bilateral ptosis and diplopia followed by an imbalance while walking. A week prior to this, the patient had a fever with a dry cough that lasted for 5 days, for which the patient took over-the-counter medications. There was no history of canned food consumption, loose bowels, exanthem, recent vaccination, or dog or snake bite. There was no family history of a similar illness.

His vital signs were normal. On neurological examination, the patient was conscious and alert, had bilateral ptosis, restricted extraocular movements with normal pupillary reaction to light, jaw weakness, bilateral lower motor neuron type of facial weakness, absent cough and gag reflex, and difficulty managing oral secretions and drooling. He had no limb weakness, wasting, fasciculations or sensory deficits. There was generalised hyporeflexia. Both plantar reflexes were flexor. On cerebellar examination, he had limb and gait ataxia. There were no signs of meningeal irritation.

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## Differential diagnosis

Ophthalmoplegia and ataxia can be localised to nuclear or infranuclear involvement of the cranial nerves three, four and six. Supranuclear lesions could be associated with gaze palsy rather than a squint. In this patient with bilateral extraocular movement restriction and ptosis, the lesion could be due to involvement of nucleus, fascicle or the third and sixth nerves with or without fourth nerve involvement. In a patient with frozen eyes with preserved pupillary light reflex, neuromuscular junction disorders (such as myasthenia and muscle involvement) are important considerations.[1]

Miller–Fisher syndrome (MFS) was considered since the patient had a triad of ophthalmoplegia, ataxia and hyporeflexia. Ataxia can be subtle and, in such patients, may come out only on physical examination.

However, the patient also had significant bulbar involvement. So other possibilities of MFS overlap with pharyngeal-cervical-brachial (PCB) variant of Guillain–Barré syndrome (GBS), *forme fruste* of Wernicke's encephalopathy, brainstem involvement due to demyelination, encephalitis or glioma, or other structural causes were also considered.

## Investigation

Nerve conduction studies and repetitive nerve stimulation (RNST) were normal. His ice pack test, neostigmine test and acetylcholine receptor antibody all were negative. Magnetic resonance imaging of the brain did not show any parenchymal lesion or brainstem pathology. A cerebrospinal fluid (CSF) examination was colourless with normal opening pressure 9 days after onset of illness; it was acellular with protein of 30 mg/dL (normal range 15–45) and glucose of 56 mg/dL (normal range 50–80), with corresponding blood sugar level of 98 mg/dL. Other infective work-up in CSF was negative. His serum ganglioside immunoglobulin (Ig) M and IgG panel were negative, as were the haematologic and biochemical work-up.

## Treatment

The patient was treated with high-dose methylprednisolone (1 g intravenously for 5 days) and five cycles of plasma exchange. In addition, symptomatic management was given: nasogastric feeding tube for dysphagia, eye patches to prevent diplopia, exposure keratitis and gait training. Following this, the patient started improving during his hospital stay. His ataxia significantly improved, and there was a partial improvement in the ptosis,

ophthalmoplegia and bulbar symptoms. The patient was discharged and, at follow-up after 1 week, the patient showed complete improvement in his ataxia and his bulbar symptoms were much better. At 1 month follow-up, the bulbar symptoms resolved, his jaw weakness and bulbar dysfunction recovered, and he started taking orally so the nasogastric tube was be removed.

## Discussion

The first case of GBS was described in 1916, which illustrated acute onset areflexic flaccid paralysis with albuminocytological dissociation.[2] It is the leading cause of acute flaccid paralysis worldwide after the elimination of poliomyelitis, with an incidence of 1–2 cases per 1,00,000 population per year.[3,4] There is ample evidence of autoimmune pathology triggered by preceding infection leading to polyradiculoneuropathy. Acute inflammatory demyelinating polyradiculoneuropathy (AIDP) is the most common form of GBS, seen in 80%–85% of GBS patients.[2,3] AIDP is the classic form of GBS with a straightforward diagnosis; however, other variants of GBS, like PCB, can be missed if not well thought out.[5] Overlap of PCB with MFS is also a rare entity. It is a diagnostic challenge and symptoms are confusing with other disease entities, which may delay treatment or, worse, wrong treatment, which may produce disability or mortality in patients.[5]

Occurrence of the MFS variant is seen in 5%–10% of cases of GBS, and the PCB variant is seen in 3% of cases of GBS, with some cases showing overlap of symptoms between these two variants.[4,5]

MFS manifests as acute onset ophthalmoplegia, ataxia and areflexia. Clinical features of the PCB variant of GBS include acute weakness of the oropharyngeal, neck and shoulder muscles with swallowing dysfunction.[4,5] Patients with the PCB variant may also have facial weakness, and leg power and reflexes are usually preserved.[5] Our patient had overlapping clinical features between the MFS and PCB variants of GBS. The PCB variant may present in a pure form, GBS overlap, PCB with preserved muscle stretch reflexes, MFS overlap and Bickerstaff syndrome overlap.[6] In the case series of 100 patients with PCB, 26 patients showed overlap with MFS.[6] Table 1 shows the comparison of clinical features of our patient with the study by Nagashima *et al*.[6]

Symptoms of PCB and MFS overlap syndrome may be confused with symptoms of botulism, myasthenia gravis, diphtheria, Wernicke's encephalopathy, brainstem stroke and neuro-Behcet's, so careful history and examination are required to rule these out.

Pathophysiologically, PCB is considered the limited form of GBS due to target-specific antibodies involving particular structures only.[5] However, antiganglioside antibody testing may be helpful in clinical practice to identify patients with atypical symptoms of variants of GBS. In a retrospective case study, 70 cases out of 100 showed positive antiganglioside IgG antibody, out of which, 51 cases were positive for anti-GT1a, 39 cases were positive for anti-GQ1b and 27 cases were positive for GM1, GM1b and GD1a.[6] Of those PCB patients with MFS overlap, 81% were positive for GT1a and 73% were positive for anti-GQ1b. However, our patient was negative for ganglioside antibodies.[6]

Electrophysiological characterisation of PCB is axonal conduction failure that mimics acute motor axonal neuropathy (AMAN) or acute motor and sensory axonal neuropathy (AMSAN) variants of GBS.[5,7] However, our patient did not have any limb weakness, and his nerve conduction test was normal.

**Table 1. Comparison of clinical features of our patient with the study by Nagashima *et al*[6]**

| | Nagashima *et al*, PCB cases, n=100 | Nagashima *et al*, PCB with MFS, n=26 | Our case, n=1 |
|---|---|---|---|
| **Median age, years** | 43 | 53 | 18 |
| **Male:female** | 56:44 | 13:13 | 1:0 |
| **Preceding infection, n** | | | |
| Upper respiratory tract infection | 71 | 18 | 1 |
| Diarrhoea | 30 | 6 | 0 |
| **Arm weakness** | 29 | 1 | 0 |
| **Dysphagia** | 17 | 1 | 1 |
| **Diplopia** | 17 | 7 | 1 |
| **Nasal voice** | 7 | 3 | 1 |
| **Ophthalmoplegia** | 55 | 26 | 1 |
| **Facial palsy** | 64 | 16 | 1 |
| **Hyporeflexia/ areflexia** | 91 | 26 | 1 |
| **Ataxia** | 43 | 26 | 1 |
| **Cerebrospinal fluid albuminocytological dissociation** | 42 | 12 | 0 |

MFS = Miller–Fisher syndrome; PCB = pharyngeal-cervical-brachial.

Treatment for PCB is like standard treatment for GBS syndrome, including plasmapheresis or intravenous immunoglobulin and supportive care. Recovery is typically seen 2–3 weeks after initiation of treatment. Our patient showed improvement within 1 week of plasmapheresis initiation and showed near-complete recovery in follow-up after 1 month.

## Conclusion

In patients presenting with acute onset cranial neuropathy, the PCB variant of GBS should be considered in differentials. One should be aware of overlapping variants and features of PCB for correct diagnosis and timely treatment to avoid complications. In patients presenting as a *forme fruste* of MFS, recognising this entity is essential to differentiate from myasthenia gravis and, thus, avoid long-term immunosuppressive therapy.

## Key points

- Acute onset of ophthalmoparesis and ataxia has a wide range of differentials.
- Atypical features and overlap syndromes may lead to diagnostic difficulty.
- Overlap of PCB and MFS is rare and demands a high degree of suspicion.
- Overlap syndromes can be confused with other conditions like botulism, myasthenia gravis, brainstem stroke, Wernicke's encephalopathy etc, which may delay diagnosis and correct treatment. ■

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