Isolated hypercapneic respiratory failure as a presentation of GBS variant: A paraneoplastic association?

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Introduction

Guillain-Barré Syndrome (GBS) is an acute immune-mediated polyradiculoneuropathy, that classically presents with ascending weakness and generalized areflexia.[1] The Pharyngeal-Cervical-Brachial (PCB) variant is a rare GBS subtype characterised by oropharyngeal, neck and upper limb weakness with relatively preserved lower limb strength.[2] Isolated hypercapnic respiratory failure as the initial manifestation of PCB-GBS is exceedingly rare and may cause significant diagnostic delay.[3]

Although uncommon, paraneoplastic GBS has been associated with various malignancies, most commonly small cell lung cancer.[4–8] Association with thyroid neoplasm is extremely rare.[8] We report a unique case of PCB-variant GBS presenting as isolated respiratory failure as paraneoplastic manifestation of an underlying oncocytic follicular thyroid neoplasm. This case highlights the co-occurrence of extremely rare clinical presentations within the spectrum of GBS and emphasizes the importance of considering paraneoplastic triggers in atypical GBS.

Case Report

A 60-year-old male presented to the emergency department with a history of drowsiness for two days. He had recently returned to Mumbai, India from a 20-hour flight from Los Angeles, United States, where he had remained largely indoors due to the cold weather. For approximately a week prior to his return, he reported generalized weakness and somnolence. He had been self-medicating with melatonin tablets. On further questioning he recalled drooling of saliva and slurred speech over the preceding few days. There was no history of limb weakness, preceding fever, or history of travel during his stay in the United States.

On examination, he was drowsy but arousable to verbal stimuli. Vital signs revealed tachycardia (103/min, blood pressure 160/100 mmHg, respiratory rate 24/min and oxygen saturation of 61% on room air. Arterial blood gas analysis demonstrated severe hypercapnic respiratory failure (pCO_2 of 91.6 mmHg), prompting immediate initiation of non-invasive ventilation (NIV) (Table 1).

Magnetic resonance imaging (MRI) of the brain did not reveal any acute infarct or hemorrhage. Despite non-invasive ventilation, his respiratory status progressively worsened. Multiple attempts at laryngoscopy and endotracheal intubation failed. Ventilation with supraglottic airway was unsuccessful. An emergency tracheostomy had to be performed, he was shifted to an intensive care unit and invasive mechanical ventilation was initiated.

Table 1: Arterial blood gas (ABG) at arrival to the hospital and after initiation of mechanical ventilation

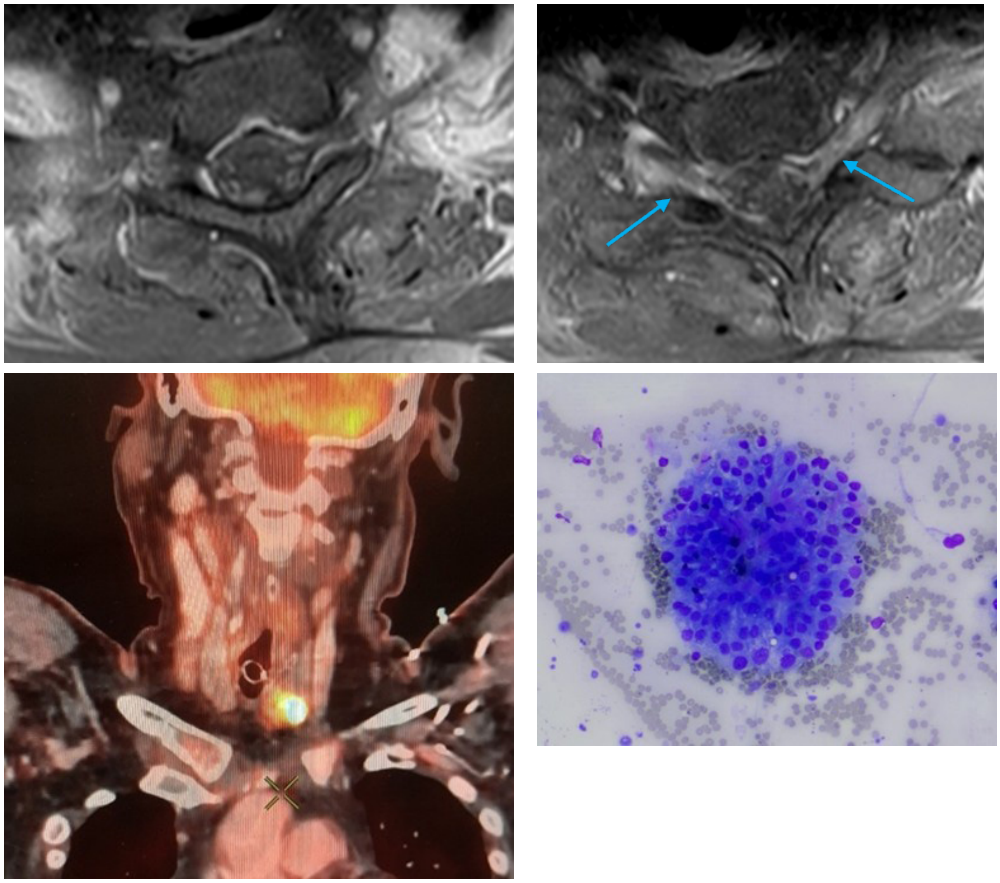
Arterial Blood gas	At arrival	After 3 hours of NIV	Post-tracheostomy and ventilation
pH	7.215	7.094	7.6
pCO2 (mmHg)	91.6	130	31.1
pO2 (mmHg)	87.5	87.8	131
HCO3 (mEq/L)	35.7	35	31.2

CT pulmonary angiography showed a thrombus in the right lower lobar segmental artery, with no evidence of deep vein thrombosis. Two dimensional echocardiography revealed features suggestive of acute pulmonary embolism without right ventricular dysfunction. He was treated with subcutaneous enoxaparin 60 mg twice a day. Though his ventilatory parameters improved, multiple attempts to wean were unsuccessful with persistent hypercapnia. The small pulmonary embolism could not explain his respiratory compromise, prompting a neuromuscular consultation.

Neurological examination revealed mild facial weakness, neck flexor weakness and distal left upper extremity weakness (C8–T1 distribution) with generalized areflexia. Lower limb strength was preserved (Medical Research Council [MRC] grade 5/5) and sensory examination was normal. Notably, he had a remote history of electric injury to the right upper limb, that accounted for pre-existing weakness. Serum creatine phosphokinase was normal. Acetylcholine receptor and muscle-specific kinase antibodies were negative. Electrodiagnostic studies revealed reduced amplitude of the left ulnar motor response recorded at abductor digiti minimi with minimal chronic denervation in left C8–T1 muscles. No myopathic motor potentials were seen. 3 Hz repetitive nerve stimulation did not reveal a significant (>10%) decremental response.

Cerebrospinal fluid analysis was unremarkable (cell count 1/µL; protein 55 mg/dL; glucose 73 mg/dL). MRI Cervical spine with contrast demonstrated enhancement of bilateral C6–T1 nerve roots. (Figure 1A and 1B). Based on above, a clinical diagnosis of Pharyngeal-Cervical-Brachial (PCB) variant of Guillain-Barré Syndrome (PCB-GBS)

Figure 1: T1-Weighted post-contrast fat-sat axial sequence at C7-T1 level showing bilateral mild thickening and abnormal enhancement of dorsal and ventral nerve roots (Yellow Arrows) and (B) exiting nerve sheaths (Blue arrows)
(C) Whole body-FDG PET showing increased uptake in left lobe of thyroid (Green arrow)
(D) Left lobe thyroid nodule fine needle aspiration cytology: Smears stained by MGG showed loosely cohesive as well as singly scattered large cells with abundant granular cytoplasm. The cells had enlarged, round to oval nuclei with open chromatin and occasional inclusions.



was made. Serum anti-ganglioside antibody panel was negative.

He was initially treated with intravenous methylprednisolone 1g daily for 5 days by the intensive care team but without clinical improvement. This was followed by intravenous immunoglobulin (IVIG) 2 g/kg administered over 5 days, resulting in prompt recovery. Due to concurrent pulmonary embolism and no preceding illness, a paraneoplastic etiology was suspected. Whole-body PET CT identified an FDG-avid thyroid nodule (Figure 1C). Fine-needle aspiration cytology confirmed oncocytic follicular neoplasm (Bethesda Category IV) (Figure 1D). He underwent total thyroidectomy by day 28.

At 6 months follow up he is neurologically asymptomatic and free of malignancy.

Discussion

This case illustrates an unusual presentation of the pharyngeal-cervical-brachial variant (PCB) of Guillain-Barré syndrome, initially manifesting as isolated hypercapnic respiratory failure. Respiratory compromise in neuromuscular disorders typically occurs in the context of generalized weakness, isolated respiratory failure as the presenting feature is uncommon.

There are several reports of type II respiratory failure as the initial presentation of undiagnosed myasthenia gravis.[9–11] However, in our patient, myasthenia gravis seemed less likely as he had no history of prior symptoms suggestive of myasthenia gravis, no demonstrable eyelid fatigability, negative antibody profile and a normal repetitive nerve stimulation study. Similarly adult-onset Pompe disease and inflammatory myopathies can present with prominent respiratory failure but were excluded based on normal serum creatine kinase levels and electromyography[12]. Rarely, amyotrophic lateral sclerosis (ALS) can present with isolated respiratory failure; however, this was inconsistent with the clinical presentation in our patient.[13,14]

Guillain-Barré Syndrome (GBS) is classically characterized by acute onset of ascending limb weakness and generalized areflexia; yet respiratory failure as the

predominant initial manifestation is rare.[3] The clinical diagnosis of GBS can be particularly challenging in such cases due to the paucity of limb weakness, normal nerve conduction study with no albumin-cytological dissociation on cerebrospinal fluid analysis. Clinical clues for GBS in our patient were presence of bulbar features (drooling of saliva, slurred speech, dysphagia), facial weakness, neck weakness and generalized areflexia. Electrophysiological testing was essentially unremarkable except for chronic C8,T1 motor axon loss which was presumed to be due to old electrical current injury. CSF analysis was unremarkable. MRI cervical spine with contrast showed enhancement of several cervical nerve roots.

Selective involvement of oropharyngeal and neck muscles, generalized areflexia and cervical nerve root enhancement was suggestive of a pharyngo-cervico-brachial variant of GBS. The PCB variant of GBS is characterized predominantly by axonal involvement rather than demyelination.[2,15] It represents a focal form of acute motor axonal neuropathy (AMAN) and is often associated with anti-GT1a IgG antibodies in 51%.[2] Recent evidence suggests that anti-GT1a antibodies frequently cross-react with GQ1b. This immunological overlap supports the concept of PCB-GBS and Fisher syndrome existing along a continuous clinical and serological spectrum.[2] The ganglioside panel that was tested in our patient did not include anti-GT1a antibody. He was initially treated with intravenous methylprednisolone 1000 mg for 3 days by the treating physician as MRI spine showed some subtle STIR hyperintensity in the cervical spine and the diagnosis of GBS was not considered initially by the Intensive care team. However, a careful Neuromuscular evaluation was consistent with the diagnosis of PCB variant of GBS. Plasmapheresis was advised however the family opted for IVIG. IVIG 2g/kg over 5 days was started to which he responded quite well and was off the ventilator by the 5th day of IVIG.

The absence of antecedent infection and concurrent pulmonary embolism raised the suspicion for an underlying malignancy. Although GBS is classically post-infectious, paraneoplastic GBS has also been described albeit rarely. Isolated reports of GBS with lung cancer, squamous cell carcinoma and renal cell carcinoma suggest a possible paraneoplastic immune-mediated mechanism.[6,16,17] Only one prior case of GBS associated with papillary thyroid carcinoma has been reported[8]. In our patient, a thyroid malignancy was found. However a causative link between GBS and cancer could not be established. We cannot establish if this co-occurrence is by chance or a paraneoplastic syndrome. Serum paraneoplastic panel was suggested however was deferred by the treating physician.

This case underscores several important points. First, PCB-GBS should be considered in patients with otherwise unexplained hypercapnic respiratory failure, even in the absence of generalized weakness. Second, electrophysiological studies may be non-diagnostic in early or atypical cases, and supportive findings such as CSF protein elevation and nerve root enhancement on MRI may be useful. Finally, the concurrent occurrence of pulmonary embolism and absence of infection prompted malignancy screening, highlighting the need for a multidisciplinary, systematic approach in atypical GBS presentations.

Conclusion

This case emphasizes the importance of considering neuromuscular causes, particularly PCB variant of Guillain-Barré Syndrome, in patients presenting with unexplained hypercapnic respiratory failure. The unusual co-occurrence of PCB-GBS with pulmonary embolism prompted evaluation for an underlying thyroid malignancy. A comprehensive evaluation and a multisystemic diagnostic approach are essential for timely diagnosis and management.

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