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Post Covid Guillain–Barré Syndrome and pulmonary embolism: A rare combination

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ABSTRACT

We hereby report a case with rare combination of Guillain-Barré Syndrome (GBS), Deep Vein Thrombosis (DVT) and Pulmonary embolism (PE) during post-covid period.

A 67-year-old male presented with acute breathlessness and calf pain for seven days. He suffered from COVID-19 four weeks prior. He recovered fully then but was not on prophylactic anticoagulants.

His lower limb venous doppler confirmed DVT. CT Pulmonary Angiography (CTPA) confirmed PE. His neurological examination revealed bilateral diminished ankle jerks and Babinski flexion reflex, though he had no neurological complaints. Nerve conduction studies revealed acute motor sensory axonal neuropathy (AMSAN) variant of GBS.

He was treated with enoxaparin followed by rivaroxaban for thromboembolism and with intravenous immunoglobulins for GBS, to which he responded well. Early diagnosis of GBS saved him from further morbidity. Post Covid GBS has been rarely reported from India. Concurrence of GBS with DVT and PE is further rare.

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KEYWORDS

Guillain-Barré Syndrome (GBS), Pulmonary Embolism (PE), Computed Tomography Pulmonary Angiography (CTPA), Deep Vein Thrombosis (DVT)

BACKGROUND

As the treatment protocols are getting standardized for Covid, the focus is now shifting to various post covid complications.

Several central and peripheral neurological manifestations associated with severe COVID-19 have been reported. Guillain-Barré Syndrome (GBS) which is a known but rare complication of viral infections has also been reported with covid. There is paucity of published data from India on post-covid GBS till date as per the Medline search. The relationship between COVID-19 and GBS undoubtedly deserves further attention.

COVID-19 is associated with a high incidence of vascular thromboembolic events (VaTEs) in hospitalized patients.[1] However, there is limited data on the occurrence of VaTEs during post-covid period, following hospital discharge. It remains uncertain whether the severity of COVID-19 is an independent risk factor for these events.[2]

Pulmonary embolism (PE) accounts for majority of thromboembolic events in COVID-19.

CASE PRESENTATION

A 67-year-old non-smoker male, known diabetic for five years with current uncontrolled status; presented to us with complaints of acute onset breathlessness and right lower limb pain for seven days.He had history of RT-PCR confirmed COVID-19, four weeks prior. He was hospitalized then for observation and was given supportive treatment as he had mild symptoms. He was not given any antiviral medicines and did not require oxygen support. He was discharged without preventive anticoagulants as per the treatment norms then.

On clinical examination, he was afebrile with pulse rate of 80 beats per minute, respiratory rate of 28 breaths per min, Blood Pressure of 130/90 mmHg but had oxygen saturation of 89% on room air and 97% on oxygen support at the rate of 4L/min via nasal prongs. His respiratory examination revealed crepitations in bilateral infra scapular areas. He had right lower limb swelling which was more prominent in the calf region along with tenderness. This prompted us to a diagnosis of Deep Vein Thrombosis (DVT) with pulmonary embolism (PE).

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Routine neurological examination revealed bilateral diminished ankle jerks along with bilateral Babinski flexion reflex which made us suspicious of early Guillain–Barré Syndrome. He however had no significant neurological complaints then. There was no signs of cranial nerve involvement or meningeal irritation or bladder/ bowel involvement.

INVESTIGATIONS

Investigations were ordered to confirm the clinical diagnosis and rule out other differentials. Bilateral lower limbs venous and arterial doppler revealed thrombi in both right & left intramuscular veins and in proximal portion of right posterior tibial vein. CT Pulmonary Angiography (CTPA) showed multiple hypodense filling defects in subsegmental branches of right upper lobe. These findings were confirmative of pulmonary embolism. Multiple areas of ground glass opacities with patchy consolidation and interlobular septal thickening in both lungs suggested post-covid fibrosis. 2D Echo confirmed normal LV function without any raised pulmonary pressure or wall motion abnormalities.

Nerve conduction studies (Figure 1) were ordered to evaluate the neurological signs. There was reduced CMAP amplitude in both right and left median nerves, ulnar nerves, tibial nerves and in right peroneal nerve. Left peroneal nerve showed absent CMAP amplitude. The SNAP amplitude was reduced in bilateral median nerves and ulnar nerves and was absent in both sural nerves. These findings were suggestive of Axonal sensory-motor polyneuropathy involving lower limbs more than upper limbs. Cerebrospinal fluid (CSF) examination showed albumin-cytological dissociation that was consistent with GBS. Based on these clinical and electrophysiological findings, the diagnosis of AMSAN Variant of GBS was made.

DIFFERENTIAL DIAGNOSIS

The patient presented with acute onset breathlessness in post-covid period. Important post-covid complications such as pneumothorax and secondary bacterial/ fungal/ mycobacterial infection needed consideration. These were ruled out with appropriate sputum examination.

Patients who were bedridden with prolonged hospital stay due to severe covid often show skeletomuscular dysfunction during post-covid period. We therefore have a protocol of thorough neurological examination in all post-covid patients. Hence our patient’s GBS could be diagnosed very early though he had almost no symptoms.

TREATMENT

The patient required high flow oxygen on hospital admission. After confirmation of the diagnosis, he was treated with Enoxaparin followed by Rivaroxaban for DVT and PE. He was also given intravenous immunoglobulins for GBS. He responded well to the treatment. His GBS did not progress to disabling neurological symptoms and the neurological signs gradually reverted back to normal. His oxygen requirements gradually reduced. He was discharged on Rivaroxaban.

OUTCOME AND FOLLOW-UP

On subsequent follow up after 1 month, he showed good clinical improvement and was able to do his daily activities. His repeat bilateral lower limbs venous and arterial doppler done after four weeks showed complete resolution of the thrombi.

DISCUSSION

SARS-Cov-2 virus not only affects the lung but also affects other organs systems, particularly cardiovascular, musculoskeletal and the nervous systems.

COVID-19 may affect the nervous system possibly by four pathways:

(a) Direct viral invasion causing injury to nervous tissue.[3]

(b) Injury resulting from hyperimmune response, as a part of cytokine storm.

(c) Post infective demyelination.[4]

(d) Indirect viral injury due to systemic sickness.

SARS-CoV-2 can enter the brain through the olfactory tract in the early stages of infection. After SARS-CoV-2 infects nasal cells, it reaches the entire brain and cerebrospinal fluid through the olfactory nerve and olfactory bulb within seven days and cause inflammation and demyelinating response.[5,6] Minimization of lysosomal activity leads to protein aggregation in neurons and thus cause neurodegenerative disease.

Cytokines can cross the blood-brain barrier and cause acute necrotizing encephalopathy.[7]In some cases, peripheral nerve damage is thought to be driven by the production of autoreactive antibodies (anti-ganglioside antibodies).[8]

Polyradiculitis, polyradiculoneuritis or Guillain-Barré Syndrome (GBS) is a disabling neurological illness with ascending motor palsy often leading to ventilatory failure that may require mechanical ventilation.

GBS has various subtypes that include acute inflammatory demyelinating neuropathy (AIDP) (classic type), acute motor axonal neuropathy (AMAN), acute motor sensory axonal neuropathy (AMSAN), Miller-Fischer syndrome (MFS), polyneuritis cranialis (PNC), the pharyngeal, cervical, brachial (PCB) variant, and Bickerstaff encephalitis (BFE).[9]

SARS-CoV-2 associated GBS (SC2-GBS) is most likely secondary to an immune response to SARS-CoV-2 since the virus has not been found in CSF of any SC2-GBS patient reported till date. SC2-GBS occurs at any age. SC2-GBS does not differ from non-SC2-GBS regarding clinical presentation and treatment, but outcome of SC2-GBS is worse compared to non-SC2-GBS patients. As there are no studies available about the optimal treatment of SC2-GBS subtypes, these cases are treated in the same way as non-SC2-GBS subtypes. Early diagnosis of SC2-GBS is very important because early appropriate treatment ensures better outcome.[10]

Various studies have demonstrated a prothrombogenic effect of SARS-CoV-2 infection that may lead to pulmonary thromboembolism sometimes despite conventional thromboprophylaxis.[11]There is limited data available on prevalence of VaTEs in patients with mild or moderate Covid as the studies are more focused on critically ill patients. VaTEs incidence is significantly higher in patients requiring critical care compared with ward-level care.[12] There are few studies which show a higher proportion of PE among VaTEs in COVID-19 patients in comparison with non-COVID-19 patients and more segmental/sub-segmental PE compared to main/lobar arteries. Thromboembolic events during covid convalescence are uncommon and there are very few case reports.

LEARNING POINTS

- GBS is a rare sequela following COVID-19.
- Thorough clinical examination can pick up early GBS. Early treatment ensures complete and quick recovery.
- Prophylactic antiplatelet /anticoagulant medication should be considered even for mild cases of COVID-19.

Patient consent for publication: Obtained

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FIGURE CAPTIONS

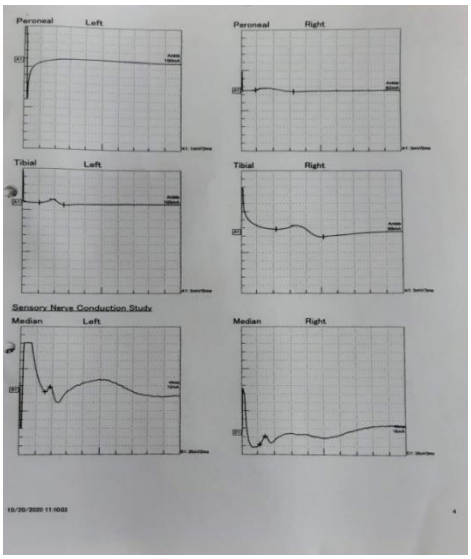

Figure 1: Nerve conduction study of the patient shows absent SNAP amplitude in left peroneal nerve and reduced CMAP amplitude in right tibial nerve. It also shows reduced SNAP amplitude in bilateral median nerves. This supports a diagnosis of both sensory and motor involvement.

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