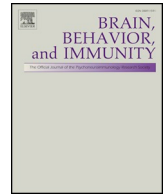




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## Letter to the Editor

## Is COVID-19-related Guillain-Barré syndrome different?



We read with interest the report of Guillain-Barré syndrome secondary to SARS-Cov-19 infection (Coen et al. 2020). Recently, there have been multiple reports of Guillain-Barré syndrome (GBS) associated with the COVID-19 infection (Sedaghat et al., 2020, Toscano et al., 2020, Zhao 2020). Most COVID-19-related GBS presented with acute onset of areflexic quadriparesis. However, there are some important differences to highlight (table 1). (Garg et al., 2018). Most patients with COVID-19-related GBS were elderly. Preceding symptoms like ageusia and hyposmia were unique for COVID-19 infection. Patients with COVID-19-related GBS had a severe disease with respiratory failure due to lobar pneumonia and interstitial pneumonitis. They showed ground-glass appearance of lungs on chest computerized tomography. Increased severity of disease is also evident from the electrophysiology study. Where demyelinating neuropathy is more common with typical GBS and GBS related to dengue and Zika virus, majority of COVID-19-related GBS patients had axonal motor (AMAN) and axonal motor-sensory polyneuropathy (AMSAN). A few of these patients showed enhancement of caudal nerve roots on Gadolinium-enhanced MRI of spine. Most COVID-19 patients received hydroxychloroquine, azithromycin, lopinavir and ritonavir in addition to intravenous immunoglobulin (IVIG). However, more than half of patients showed poor outcome in the form of long ICU stay, residual paresis and dysphagia.

Is COVID-19-related GBS has a different pathogenesis? The polyneuropathy in GBS is believed to be due to cross-immunity against epitopes of peripheral nerve components that it shares with the epitopes on the cell surface of bacteria that produces an antecedent infection.

This mechanism of “molecular mimicry” is best understood with the *Campylobacter jejuni* -related GBS. *C. jejuni* expresses various gangliosides antigen on its outer core. Antecedent infection with *C. jejuni* results in antibody formation against specific gangliosides present on axonal membrane (GM1, GD1a, GalNac-GD1a, GD1b and GQ1b). Presence of these anti-ganglioside antibodies is strongly associated with AMAN, AMSAN and Miller-Fischer variants of GBS (Ogawara et al., 2000).

The cross-immunity between viral antigens and peripheral nerve glycolipids have not been well-documented. Positive GD1a antibody was reported in a few patients with dengue virus-related GBS (Simon et al., 2016). Anti-ganglioside antibody was not found in patients with COVID-19 and Zika virus-related GBS (Cao-Lormeau et al., 2016). This has led to speculation that the neuropathy in viral infections-related GBS could be due to other autoantibodies that are not detected as yet or the viruses produced nerve damage due to other neurotoxic effects. However, there is paucity of evidence of direct infection of peripheral nerves by viruses from the pathological studies. Good response to immunotherapy in viral infection-related GBS is also against the direct neurotoxic effects of viruses. COVID-19 patients with AIDP responded better as compared to those with axonal variants of GBS; a difference also seen in patients with dengue and Zika virus-related GBS. Recently, a good clinical response in pneumonia has been seen in COVID-19 patients with plasma therapy. Does plasma therapy produce good recovery in COVID-19-related GBS is yet to be seen.

Table 1

Differences in the presentation of Typical GBS, Dengue, Zika virus and COVID SARS related GBS.

Feature	Typical GBS	Dengue-related GBS	Zika virus-related GBS	COVID SARS related GBS
Geographical distribution	Global	Latin America, India	Latin America, Europe, East Asia, North America	China, Iran, Europe, USA
Age	All age groups	All age groups	Middle age to elderly	Usually elderly
Sex	Males 1.5 times more affected	Males:Females Equal	More males	More males
Preceding illness	Respiratory or gastrointestinal	Fever, rash, myalgia, headache	Fever, headache, rash, arthralgia, diarrhea, conjunctivitis	Fever, cough, dyspnea, ageusia, hyposmia
Mean time to GBS	< 6 weeks	1–30 days	0–10 days	5–14 days
Initial symptoms	Paresthesia, pain followed by weakness of limbs	Ascending weakness, paresthesia, facial weakness	Limb pains, paresthesia, lower limb weakness, facial weakness	Paresthesia, lower limb weakness, facial weakness
	Less common		More common	

(continued on next page)

Table 1 (continued)

Feature	Typical GBS	Dengue-related GBS	Zika virus-related GBS	COVID SARS related GBS
Dysphagia	Areflexic quadreparesis	Less common	Areflexic quadri/paraparesis	Less common
Signs	Common	Areflexic quadri/paraparesis	Common (> 50%)	Areflexic quadri/paraparesis
Facial diplegia	Common	Common	Common (up to 30%)	Common
Dysautonomia	Common	Less common	Common (up to 70%)	Less common
AtaxiaRespiratory failure	Less common	Less common	Less common	Less common
Other cranial nerves involved	25%	Less common	3rd cranial nerve	Common
Leukopenia	Ocular nerves	Glossopharyngeal nerve	-	-
Thrombocytopenia	Uncommon	Common	-	Common
Nerve conduction	Uncommon	Common	AIDP > AMAN, AMSAN	-
CT chest	AIDP	AIDP, AMSAN	-	AMSAN, AMAN, AIDP
MRI Brain/spine	-	-	-	Pneumonia, interstitial pneumonitis
Treatment	-	-	IVIG, Plasmapheresis	Enhancement of caudal nerve roots
Outcome	IVIG, Plasmapheresis	IVIG, Plasmapheresis	Good, half may require ICU care	IVIG, Lopinavir, ritonavir, HCQ, Azithromycin,
	Good, persistent disability in 20%–30%	Good		Poor, residual weakness, dysphagia, long ICU stay

AIDP – Acute inflammatory demyelinating polyneuropathy, AMAN – Acute motor axonal neuropathy, AMSAN – Acute motor sensory axonal neuropathy.

## Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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## Appendix A. Supplementary data

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