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Commentary

SARS-CoV-2 related Guillain-Barre syndrome has many clinical facets and requires comprehensive work-up

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We read with interest the article by Pimentel *et al*. on a systematic review about Guillain Barre syndrome (GBS) in association with a SARS-CoV-2 infection [1]. It was concluded that patients with SARS-CoV-2 associated GBS frequently require admission to the intensive care unit (ICU), that the occurrence of GBS is related to the severity of COVID-19, and that the outcome is favourable despite the severity of GBS [1]. The study is excellent but has limitations that raise concerns and should be discussed.

A limitation of the study is that not all subtypes of SARS-CoV-2 related GBS were addressed. A subtype of GBS not addressed in the review is brainstem Bickerstaff encephalitis (BBE). BBE is clinically characterised by brainstem encephalitis in addition to polyradiculitis. Particularly in GBS patients with cranial nerve lesions, including ophthalmoparesis, it is crucial to carry out cerebral MRI with contrast medium to rule out BBE. In a review about the neurological complications of SARS-CoV-2 infections, five patients with BBE were reported [2]. Another patient with SARS-CoV-2 associated BBE has been reported by Llorente-Ayuso *et al* [3].

Another GBS subtype not addressed in the review is polyneuritis cranialis. GBS can manifest not only with affection of a single cranial nerve but multiple cranial nerves simultaneously [4]. Particularly Miller-Fisher syndrome (MFS) is commonly associated with polyneuritis cranialis [5].

Another limitation is that diagnostic work up for GBS should not only include cerebral MRI to rule out BBE, but also MRI of the cervical or spinal nerve roots. Several cases of SARS-CoV-2 associated GBS have been reported showing thickening or enhancement of the spinal or cranial nerve roots [6]. Particularly in case of cranial nerve affection, MRI should be applied as nerve conduction studies are applicable for only few cranial nerves.

Autonomic dysfunction in GBS is more widespread than reported in the review. In addition to hypotension, hypertension, orthostasis, arrhythmias, bladder dysfunction, bowel dysfunction, gastroparesis, sweating, dry mouth, and erectile dysfunction [1], patients may develop sleep disorder, oversensitivity to light, loss of appetite, temperature dysregulation, dizziness, hypoglycaemia, bloating, nausea, vomiting, dysphagia, heartburn, and hypohidrosis.

Not only the 7th, 9th, or 10th cranial nerve can be affected in SARS-CoV-2 related GBS but also the 3rd 4th 5th 6th, and 12th cranial nerve [7, 8]. There are even patients in whom the accessory nerve was affected from the SARS-CoV-2 infection [9].

Another limitation is that inflammatory parameters of the CSF were not included in the evaluation. It is well known that cytokines, chemokines, 14-3-3, and glial factors can be elevated in the CSF of GBS patients [10].

A further limitation of the study is that only articles listed in PubMed were included [1]. However, the number of patients with SARS-CoV-2 related GBS is much higher if data from other platforms would have been considered.

Overall, the interesting study has limitations that put the results and their interpretation into perspective. Clarifying these limitations would strengthen the conclusions and could improve the study. SARS-CoV-2 related Guillain-Barre syndrome has many clinical facets and requires comprehensive work-up.

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