DOI: 10.1002/jmv.27129

LETTER TO THE EDITOR

JOURNAL OF MEDICAL VIROLOGY WILEY

Diagnose SARS-CoV-2 associated Guillain–Barre syndrome upon appropriate criteria and after exclusion of differentials

To the Editor,

We read with interest the article by Akcay et al.[1] about a 6-year-old male who presented with sudden onset quadruparesis, including weakness of axial and respiratory muscles, this being attributed to acute motor axonal neuropathy upon dissociation cytoalbuminique and axonal neuropathy on nerve conduction studies (NCSs). As the patient was positive for SARS-CoV-2 a causal relation between Guillain–Barre syndrome (GBS) and the virus was suspected. The study is appealing but raises comments and concerns.

A first limitation of the study is that critical ill neuropathy/myopathy (CINP/CIMP) was not appropriately excluded. CINP/CIMP not only occurs in case of multiorgan failure and respiratory dysfunction, as indicated in the discussion, but also in association with mechanical ventilation, sepsis, artificial nutrition, or electrolyte imbalance. The patient had respiratory dysfunction as the presenting manifestation and required mechanical ventilation from hospital day 1 (hd1). As the initial NCSs were carried out not earlier than on hd14, it is conceivable that the patient had developed CINP during the interval between admission and first NCS. An argument for CINP is that the results of NCS can be also interpreted as axonal neuropathy, as has been done by the authors in the discussion. Improvement by hd50 on follow-up NCSs can be also found in CINP.

A second limitation of the study is that the anti-COVID-19 medication the patient received during hospitalization was not mentioned. Knowing the anti-COVID-19 medication is crucial, as several compounds are neurotoxic or myotoxic. Neurotoxic drugs frequently applied include daptomycin, linezolid, lopinavir, ritonavir, hydroxychloroquine, cisatracurium, clindamycin, tocilizumab, and glucocorticoids.[2] Neuropathy or myopathy in COVID-19 patients requiring intensive care unit treatment may also result from compression neuropathy, compartment syndrome, or from artificial nutrition, infection, electrolyte disorder, or sepsis (CINP, CIMP).[2] Myotoxic drugs include chloroquine (causes myopathy or myasthenia),[3] remdesivir/lopinavir (cause rhabdomyolysis),[4] azithromycin (causes myasthenia or myasthenic crisis),[5] tocilizumab (causes pyomyositis),[6] and steroids (cause myopathy).[7]

A third limitation is that no explanation was provided why the patient was initially treated with plasmapheresis (PLEX). GBS is usually treated with intravenous immunoglobulins (IVIGs) unless there are contraindications. As PLEX was obviously ineffective, the patient received steroids but not before hd18 IVIGs were applied. The patient required a second cycle of IVIGs before he started to improve.

A fourth limitation is that upon CSF investigations no inflammatory parameters, such as interleukin-6 (IL-6), IL-8, IL-1b, or tumor necrosis factor-alpha were determined in the CSF. From these inflammatory markers, it is well known that they are elevated in the CSF although the polymerase chain reaction is usually negative for SARS-CoV-2 in the CSF.[8]

We do not agree with the statement in the discussion that as of the end of January 2021 more than 60 patients with SARS-CoV-2 associated GBS have been reported.[1] As per the end of December 2020, already 220 patients with SARS-CoV-2 associated GBS had been identified.[9] The high frequency of SARS-CoV-2 associated GBS suggests that the prevalence of GBS has indeed increased with the pandemic.

As GBS may manifest as Bickerstaff encephalitis, it is crucial that GBS patients with respiratory insufficiency undergo MRI to rule out that a brainstem lesion was responsible for respiratory dysfunction.

Overall, diagnosing GBS requires the application of established diagnostic criteria, such as the Brighton criteria, and exclusion of various differentials, such as CINP. The neurotoxicity of the anti-COVID drugs should be considered as a cause of the increased prevalence of SARS-CoV-2 associated neuropathies.

AUTHOR CONTRIBUTION

Josef Finsterer: Concept, writing literature search, and discussion.

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