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# Presence of Severe Acute Respiratory Syndrome Coronavirus 2 in the Cerebrospinal Fluid of Guillain-Barré Syndrome Patients Requires Validation

***To the Editors:***

With interest, we read the article by Araújo et al[1] about a 17-year-old female who was diagnosed with Guillain-Barré syndrome (GBS), and subtype acute, demyelinating inflammatory polyneuropathy, 8 days after onset of a mild coronavirus disease 2019 infection. Surprisingly, cerebrospinal fluid (CSF) investigations were positive for RNA of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2).[1] The patient profited from IV immunoglobulins.[1] The study is appealing but raises concerns.

The main limitation is that the test upon which SARS-CoV-2 RNA was detected in the CSF was not specified. Although a control mock CSF tested negative for the virus, there is no mentioning if the applied test was validated for CSF testing. There is also no discussion about the possibility that the test was false positive. Sensitivity and specificity of the applied real-time polymerase chain reaction were not provided. No information about the test-retest reliability was provided. There were also no repeated CSF investigations for the virus during follow-up, why it remains unknown for how long the virus could be proven in the CSF.

A second limitation is that there was no discussion about the pathophysiologic implications of the test result. Because GBS is an immunologic and not an infectious disorder, it is rather unlikely that presence of the virus in the CSF had a direct pathophysiologic consequence. Anyhow, presence of SARS-CoV-2 is not uncommon. Particularly in patients experiencing meningitis or encephalitis, SARS-CoV-2 has been repeatedly found in the CSF.[2–4] In immune-mediated complications of SARS-CoV-2, however, SARS-CoV-2 is usually absent in the CSF. In a study of 220 patients with SARS-CoV-2–associated GBS, collected until the end of December 2020, CSF was investigated for the virus in 56 cases but was found in none of them.[5] Absence of the virus in the CSF was explained by the assumption that the virus never enters the CSF or that it enters the CSF but remains only for a short time before invading neurons or endothelial cells. An argument for the temporary presence of the virus in the CSF is that virus RNA has been found on autopsy studies in neurons and endothelial cells of the frontal lobe.[6]

There is also no discussion via which pathway the virus had entered the CSF. Speculations in the literature include retrograde migration of the virus along cranial or peripheral nerves, hematogenic spread, or intracellular transport in leukocytes via the blood–brain barrier.

Missing are the results of the cerebral magnetic resonance imaging with contrast medium. Because GBS can manifest as Bickerstaff encephalitis, it is crucial to know if there was immune encephalitis of the brainstem or not. In this respect, it should be mentioned if there was involvement of cranial nerves, the respiratory muscles or the bulbar muscles. Because GBS may be complicated by autonomic involvement, we should know if the patient ever developed autonomic dysfunction.

Although SARS-CoV-2–associated GBS is more prevalent in adults compared with children or adolescents, there is increasing evidence that also younger ages can be affected. In the study of 220 patients with SARS-CoV-2–associated GBS, 6 patients were below age 18 years.[5] A shortcoming of Table 1[1] is that no reference limits were provided.

Overall, the interesting study has limitations which challenge the results and their interpretation. There is a need to address these limitations to strengthen the conclusions.

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# Presence of SARS-CoV-2 in the CSF of Guillain-Barré Syndrome Patients Requires Validation

***To the Editors:***

We appreciate the interest in our article[1] and the opportunity to respond to the comments. In the published report, we present a pediatric case of COVID-19-associated GBS

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J.F. contributed to design, literature search, discussion, first draft, and critical comments.
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