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Reply

We thank Finsterer and colleagues for their useful comment and the update regarding the reported new cases of Guillain-Barré syndrome (GBS) in the context of SARS-Cov-2 infection. As shown by the authors and others,[1] the number of cases of GBS associated with coronavirus disease 2019 (COVID-19) is rapidly increased since our search (May 17, 2020), but we are pleased to note that the clinical presentation and course is similar to that we had reported based on the first 18 published cases. We fully agree with Finsterer et al. that the correlation between SARS-Cov-2 infection and GBS, a condition that in recent years has been linked to other emergent infections, such as Zika virus, is still only speculative, and, as we also stated in our review, a coincidental association remains possible. We however do not agree with the authors regarding their arguments against a causal relation between SARS-CoV-2 infection and GBS. Presence of the bacterial or viral agent in the CSF is neither necessary nor common in GBS. For instance in a series of 244 tested cases of GBS associated with ZIKA virus only 10 cases had positive ZIKV polymerase chain reaction (PCR) in the CSF.[2] Also the fact that in a minority of patients (6%) GBS started before clinical manifestations of COVID-19 is still compatible with a causal association, considering the incubation period of COVID-19 can last up to 24 days[3] while the incubation period of GBS is reported to be typically between 10 and 14 days.[4] The authors also state that a further argument against a causal relation between SARS-CoV-2 and GBS is that the overall prevalence of GBS did not increase since the outbreak of the pandemic. However, a proof for this speculation was not provided. An Italian multicenter case-control study is investigating the nature of the association between COVID-19 and GBS (causal or coincidental) and we look forward to know the results.

Finally, we agree with the authors that there is growing evidence that COVID-19 cause inflammation and thus cranial nerve involvement might be caused by dysimmune mechanisms, as in GBS. However, considering the frequency of anosmia and hypogeusia (up to 50% of infected patients) and the short incubation period of these symptoms (about 7 days) we believe that the hypothesis of a direct trans-neuronal dissemination related to viral neurotropism seems more likely. This is also supported by the fact that the clinical presentation of Miller-fisher syndrome (MFS) in the context of SARS-CoV-2 infection seems to resemble that of classic MFS, and that in some of these patients the cranial neuropathies and the ataxia improved after intravenous immunoglobulins whereas anosmia and ageusia did not.[8,9]

Overall, our understanding of the neurologic symptoms and complications of COVID-19 is still at the very beginning and further translational and epidemiological studies are needed to share more light on this interesting topic. An increasing number of GBS cases in association with SARS-Cov-2 infection have been reported since March 2020, and the clinical presentation and course emerging from their analysis seem similar to that of classic GBS. Whether this association is causal or coincidental is still speculative.

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