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LETTER TO THE EDITOR

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Consider differentials before diagnosing SARS-CoV-2 associated Guillain–Barre syndrome

To the Editor

With interest, we read the article by Manganotti et al.[1] about five patients with coronavirus disease 2019 (COVID-19) who developed Guillain–Barre syndrome (GBS) 14–33 days after onset of the viral infection.[1] Three patients required mechanical ventilation. Among the four patients with mild facial nerve involvement, one was diagnosed with polyneuritis cranialis (PNC).[1] Three patients had a dissociation-cyto-albuminique.[1] Four patients profited from intravenous immunoglobulins (IVIG) and one from steroids.[1] It was concluded that COVID-19 can be complicated by neurological disease, which favorably responds to IVIGs.[1] The study is appealing but raises the following comments and concerns.

The main shortcoming of the study is the diagnosis "GBS." The Brighton criteria for diagnosing GBS were not applied.[2] Subtypes of GBS diagnosed in the five included patients were not specified.[1] The most frequent subtype in the Western world is acute, demyelinating polyneuropathy and in Asia acute motor and axonal neuropathy. Rare subtypes of GBS include acute motor and sensory, axonal neuropathy, Miller–Fisher syndrome, PNC, the pharyngeal, cervical, and brachial variant, and Bickerstaff encephalitis.[3] In addition to PNC in patient-3, the subtypes of GBS in the remaining four patients should be specified.[1]

Furthermore, differentials of GBS were not sufficiently considered. One of the differentials of GBS is critical ill neuropathy. Prolonged F-wave latency, increased F-wave dispersion, conduction block, and reduced F-wave amplitude can be also found with critical ill neuropathy. Accordingly, critical ill neuropathy needs to be excluded before attributing the electrophysiological abnormalities to GBS. With regard to critical ill neuropathy, we should know for how long the five patients were treated in the intensive care unit and all drugs the patients received during hospitalization should be reported.

Since four of the five patients received neurotoxic drugs, such as daptomycin, linezolide, lopinavir, ritonavir, hydro-chloroquine, cis-atracurium, clindamycin, tocilizumab, or glucocorticoids,[4] it is conceivable that the anti-COVID-19 medication contributed to the development of neuropathy.

We do not agree with the notion that overproduction of the cytokines interleukin-6 and interleukin-8 necessarily leads to severe COVID-19.[1] There is no linear correlation between cytokine levels and severity of COVID-19. TNF-alpha and interleukin 1-beta levels in patients with COVID-19 maybe even similar to those in healthy controls.[5] However, upregulated interleukin-6[6] and interleukin-8[7] suggest a poor prognosis.[6]

Overall, this interesting study has several limitations which challenge the conclusions. Diagnostic criteria of GBS should be met and differentials, particularly critical ill neuropathy, should be appropriately excluded. The neurotoxic effect of the anti-COVID-19 medication applied should be considered. Whether cytokine levels truly predict severity and outcome of COVID-19 patients requires further studies.

CONFLICT OF INTERESTS

All the authors declare that there are no conflict of interests.

ETHICS STATEMENT

The study was in accordance if ethical guidelines. The study was approved by the institutional review boardopenResearch.

AUTHOR CONTRIBUTIONS

Josef Finsterer: design, literature search, discussion, first draft, critical comments, final approval. **Fulvio A. Scorza**: literature search, first draft, discussion, critical comments, final approval Informed consent: was obtained.

DATA AVAILABILITY STATEMENT

Data sharing is not applicable to this article as no new data were created or analyzed in this study.

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