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Letter to the Editor

The characterization of GBS caused by the Omicron variant of SARS-CoV-2 requires appropriate study designs

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Letter to the Editor

We were interested to read the article by Gui *et al*. on a retrospective case-control study investigating the characteristics of Guillain-Barre syndrome (GBS) and its subtypes following infection with the Omicron variant of the SARS-CoV-2 virus (SC2I) [1]. The median latency period between the previous infection and the onset of neurological symptoms was 10 days, 38 patients had classic sensorimotor neuropathy of the lower limbs, 17 patients also had cranial neuropathies, and 21 patients had predominantly acute motor-sensory axonal neuropathy or acute motor axonal neuropathy [1]. It was concluded that GBS during the Omicron onset was characterized by sensorimotor axonal neuropathy [1]. The study is noteworthy, but several points should be discussed.

The first point is the retrospective design of the study [1]. Retrospective designs have several disadvantages [2]. They allow only limited control over the sampling of the population and only limited control over the type and quality of predictor variables. In addition, the relevant predictors may not have been recorded in the medical record, and it may be difficult or impossible to detect confounding variables and causality. Furthermore, it may be inevitable that some information is missing, as the data are based on the review of medical records that were not originally intended for the collection of data for research purposes. Selection and recall errors also affect the results [2].

The second point is that the total number of patients included in the study was small (n=41) and that nerve conduction studies (NCPs) were only performed in 32 patients. Therefore, it is questionable whether the conclusions drawn are reliable.

Thirdly, it is not reported whether all included patients were really tested for the presence of the Omicron strain or whether infection with the Omicron strain was only assumed because it was the most prevalent strain at the time of the study.

The fourth point is that SC2I was confirmed not only by PCR but also by antigen tests. Since antigen tests have lower sensitivity and specificity than PCR tests [3], patients diagnosed solely by antigen testing should be excluded from the analysis.

The fourth point is that SC2I can manifest not only in the peripheral nervous system (PNS) with smell and taste disorders, GBS and muscle weakness [1], but also with single or multiple involvement of other cranial nerves [4], Parsonage-Turner syndrome, plexopathy or plexitis [5] and with post-synaptic transmission disorders [6].

The fifth point is that it was not reported how an infectious or immunologic disease of the central nervous system (CNS) was excluded in the five patients with pleocytosis [1]. We should know whether the cerebrospinal fluid (CSF) was examined for viruses, bacteria, fungi or protozoa. Was the brainstem affected in these five patients so that the criteria for Bickerstaff encephalitis of the brainstem (BBE) were met? Was an MRI of the brain performed to rule out encephalitis, meningitis and vasculitis? Were antibodies associated with autoimmune encephalitis (AIE) determined in serum or CSF and were they positive?

The sixth point is that it was not convincingly confirmed that the SC2I and not another infectious agent causing gastrointestinal infection was indeed the trigger of GBS in the three patients with previous gastrointestinal infection. The most common cause of GBS worldwide is still Campylobacter jejuni [7]. Have infections with these pathogens been thoroughly ruled out?

The seventh point is that it was not stated how many of the included patients had respiratory muscle involvement and required invasive or non-invasive ventilatory support. This is crucial as outcomes can differ significantly between patients with and without respiratory muscle involvement.

The eighth point is that it is not understandable why GBS was treated with glucocorticoids in 25 patients. Steroids are known to be barely effective in GBS [8], which is why GBS patients should rather receive immunoglobulins or plasmapheresis. Steroids can even make GBS worse [8].

We should also know how GBS was diagnosed in the two patients with "equivocal" electrophysiologic results and how it was ruled out that the control subjects did not have subclinical SC2I in the three months before the onset of GBS.

Before drawing conclusions such as those from the index study, several limitations should be addressed as they may affect the interpretation of the results. Large, homogeneous groups and studies with a prospective design are needed to characterize GBS caused by the Omicron variant of SARS-CoV-2.

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