SARS-CoV-2 Infection- or Vaccination-Related Neurological Disease Requires Careful Investigation

We read with interest the article by George *et al*.[1] about a retrospective study of the neurological manifestations of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection and neurological side effects of SARS-CoV-2 vaccinations encountered in two neurological centers in Kerala. Among 1270 coronavirus disease 2019 (COVID-19) admissions, 42 patients (3.3%) developed neurological abnormalities, 35 patients during a SARS-CoV-2 infection and 7 patients after a SARS-CoV-2 vaccination.[1] The study is appealing but raises concerns that need to be discussed.

In Table 5, patient 33 is described with "cranial nerve-II palsy."[1] We should be told what cranial nerve palsy of the optic nerve means, particularly if the authors mean optic neuritis. Optic neuritis has been previously reported as a complication of SARS-CoV-2 vaccinations.[2] Optic neuritis has been also reported in patients experiencing acute, disseminating encephalomyelitis (ADEM),[3] neuromyelitis optica spectrum

disorder,[4] myelin oligodendrocyte glycoprotein (MOG) antibody-associated disorder,[5] or multiple sclerosis,[6] after a SARS-CoV-2 vaccination. We should know if MOG-antibodies or aquaporin antibodies were elevated in this particular patient.

Among the six patients with peripheral nerve involvement in COVID-19, three (patient 40, patient 41, patient 42) had foot drops and an axonal lesion on nerve conduction studies (NCSs).[1] Patient 40 and patient 42 had severe COVID-19 and patient 41 had moderate COVID-19. The cause of the peroneal nerve lesion is not provided. We should be told if peroneal nerve lesions were due to polyradiculitis, neurotoxic drugs, or pressure palsies due to bedding in the intensive care unit (ICU) or if these patients had previous neuropathy, which became symptomatic during the infection.

Seven of the 42 patients developed the neurological disease after a SARS-CoV-2 vaccination requiring hospitalization. Patient 11 developed "ischemic seizures," patient 22 developed non-enhancing, periventricular hyperintensities, patient 23 transverse myelitis, patient 24 isolated optic neuritis, patient 25 encephalitis, patient 31 a seizure, and patient 39 facial diplegia.[1] We should be told what is meant by "ischemic seizures" in patient 11. Did the patient experience a stroke and was the stroke caused by the vaccination? Unclear remains the cause of non-enhancing periventricular hyperintensities in patient 22.[1]

The caption of Table 5 suggests that the four presented patients had infectious diseases in addition to COVID-19.[1] However, only patient 33 had mucormycosis in addition to COVID-19.[1] The other three patients had obviously SARS-CoV-2 associated meningitis (patient 34) or encephalitis (patient 35, patient 36).[1] Surprisingly, the cerebro-spinal fluid (CSF) was not investigated for SARS-CoV-2 in any of these four patients. We should be told how meningitis or encephalitis was diagnosed without confirming the virus in the CSF. Furthermore, patient 33 was diagnosed with venous sinus thrombosis (VST).[1] We should know if multiple cranial nerve lesions in these patients were due to mycosis or the VST.

We do not agree with the statement in the discussion that facial diplegia has not been previously reported after vaccination with the Astra Zeneca vaccine (AZV).[1] Polyradiculitis with facial diplegia has been reported in a 59 years old female 13 days after the first dose of the AZV.[7] Polyradiculitis with facial diplegia has been also reported in a 59 years old male developing 10 days after receiving the AZV.[8]

Overall, the interesting study has some limitations and inconsistencies that call the results and their interpretation into question. Clarifying these weaknesses would strengthen the conclusions and could add value to the study.

Ethics approval

Was in accordance with ethical guidelines. The study was approved by the institutional review board

Availability of data

All data are available from the corresponding author.

Author contribution

JF: design, literature search, discussion, first draft, critical comments, final approval, DM, FS, CS, AF: literature search, discussion, critical comments, final approval.

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Conflicts of interest

There are no conflicts of interest.

Daniel Matovu, Fulvio A. Scorza[1], Carla A. Scorza[1], Ana C. Fiorini[2], Josef Finsterer[3]

Departamento de Neurologia e Neurocirurgia, [1]Disciplina de Neurociência Escola Paulista de Medicina, Universidade Federal de São Paulo, Brazil, [2]Departamento de Fonoaudiologia, Programa de Estudos Pós-Graduado em Fonoaudiologia, Pontifícia Universidade Católica de São Paulo (PUC-SP), Escola Paulista de Medicina/Universidade Federal de São Paulo (EPM/UNIFESP), São Paulo, Brazil, [3]Neurology and Neurophysiology Center, Vienna, Austria

Address for correspondence: Prof. Josef Finsterer, Postfach 20, 1180 Vienna, Austria.
E-mail: fifigs1@ahoo.de

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