LETTER TO THE EDITOR

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If SARS-CoV-2 is blamed for causing meningoencephalitis, the virus must be detected in the CSF

Josef Finsterer[1], Fulvio A Scorza[2]

[1] *Neurology and Neurophysiology Center, Vienna, Austria*
[2] *Disciplina de Neurociência. Universidade Federal de São Paulo/Escola Paulista de Medicina (UNIFESP/EPM). São Paulo, Brazil*

DEAR EDITOR,

We have read with interest the article by Watroba and Bryda on a new-born male with SARS-CoV-2 associated meningo-encephalitis, post-inflammatory hydrocephalus and seizures [1]. Neuro-COVID in this patient was treated with a polypragmatic approach, including phenobarbital, acetazolamide, fluconazole, acyclovir, cefotaxime, and vancomycin [1]. The study is appealing but has limitations that raise concerns and should be discussed.

A limitation of the study is that the infectious nature of meningo-encephalitis was not confirmed as the RT-PCR for SARS-CoV-2 was negative in the cerebrospinal fluid (CSF) [1]. We would like to know why the patient was diagnosed with meningo-encephalitis due to SARS-CoV-2 without evidence of a causative agent in the CSF. The CSF was tested only for cytomegaly and SARS-CoV-2 viruses, but no other viruses. We would like to know whether the authors diagnosed infectious or immune meningo-encephalitis.

A second limitation of the study is that the CSF was not investigated for specific antibodies associated with immune encephalitis, such as antibodies against Hu, Yo, Ma1/2, CRMP5, Tr, Ri, recoverin, GAD65, amphiphysin, NMDAR, AMPAR, LGI1, CASPR2, GABAa-R, GABAb-R, mGluR1, GlyR, VGCC, and mGluR5. Suspecting immune encephalitis requires measuring these antibodies [2].

A third limitation of the study is that the patient did not undergo cerebral magnetic resonance imaging (MRI) with contrast medium earlier than 71 days after admission. To confirm the diagnosis meningo-encephalitis, documentation of enhancing lesions can be helpful in the acute stage of the disease. Carrying out an early cerebral MRI is also mandatory to rule-out differential diagnoses.

A fourth limitation is that there is no mention of the time point after admission that the electroencephalography (EEG) was recorded. Because the patient had seizures, it is mandatory to record an EEG as early as possible to eventually modify the antiepileptic treatment. An EEG is also mandatory to rule out differential diagnoses.

A fifth limitation of the study is that multi-inflammatory syndrome in childhood (MIS-C) as one of the differential diagnoses in a child with COVID-19 was not entirely ruled out [3]. According to the WHO diagnostic criteria for MIS-C, the following six criteria must be met: 1) age <20y, 2) fever >2 days, 3) clinical signs of multisystem involvement, 4) elevated inflammatory markers, 5) no other obvious microbial cause of inflammation, and 6) confirmed SARS-CoV-2 infection [4]. The index patient fulfilled all criteria.

It is unclear why the patient received antifungal, antiviral, and antibiotic medication without evidence of a fungal, viral, or bacterial infection. More likely than an infectious state, the index patient has experienced an immune response to the SARS-CoV-2 virus, which could benefit from corticosteroids or IVIG rather than antimicrobials.

Overall, the interesting study has limitations that call into question the results and their interpretation. Clarifying these weaknesses would strengthen the conclusions and could improve the study. When blaming SARS-COV-2 as causative for meningo-encephalitis, the virus needs to be documented in the CSF.

Corresponding author: Josef Finsterer, MD, PhD, Postfach 20, 1180 Vienna, Austria
Tel. +43-1-5861075, Fax. +43-1-5861075

E-mail: fifigs1@yahoo.de

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