

The Diagnosis of SARS-CoV-2 Associated Encephalitis Requires the Detection of the Virus in Brain and Exclusion of All Differentials

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LETTER TO THE EDITOR

We read with interest the article by AlHendawi, *et al.*, who reported a 2-year-old male diagnosed with SARS-CoV-2 related encephalitis and myelitis based on the clinical presentation, imaging findings, and the treatment response [AlHendawi, T. *et al.*, 2022]. The patient manifested clinically with fever, three tonic-clonic seizures, postictal impaired consciousness, and mild cough [AlHendawi, T. *et al.*, 2022]. He benefited from midazolam for seizures, ceftriaxone, vancomycin, acyclovir, intravenous immunoglobulins, methylprednisolone, and plasmapheresis [AlHendawi, T. *et al.*, 2022]. The study is excellent but has limitations that should be discussed.

There is a discrepancy between the statement that the index patient was “previously healthy” and the statement that he had a “history of febrile seizures one year ago” [AlHendawi, T. *et al.*, 2022]. This should be clarified. We should also know which diagnostic procedures the index patient underwent after the febrile seizures at the age of 1, particularly if cerebrospinal fluid (CSF) examinations were performed and whether cerebral MRI with contrast medium was done. It is also important to know whether the electroencephalography (EEG) showed epileptiform discharges and whether or not anti-seizure drugs (ASDs) were given.

We disagree with the diagnosis SARS-CoV-2 related encephalitis [AlHendawi, T. *et al.*, 2022]. Arguments against SARS-CoV-2 related encephalitis are that cerebrospinal fluid (CSF) examination was not indicative of encephalitis and that the PCR for SARS-CoV-2 in the CSF was negative. A limitation in this regard is that CSF studies were not repeated for CSF abnormalities developing during the disease course. There is no mention at which time-point the index patient was tested positive for SARS-CoV-2 and if this was via a nasal swab test or blood examination.

There is also discrepancy between the statement that “head computed tomography (CT) was normal” and the statement that cerebral MRI showed microbleeds [AlHendawi, T. *et al.*, 2022]. Assuming that microbleeds were already present on admission, they should have been visible already on the cerebral CT on admission. How many days were between the cerebral CT and the MRI? Why were the white matter changes reported on MRI but not visible on cerebral CT?

A differential diagnosis not ruled out was vasculitis. No MRI angiography with contrast medium or digital subtraction angiography was done. No black blood sequences were driven.

Other limitations of the study are that the long-term outcome was not reported and that no MRI images were presented.

Overall, the interesting study has limitations that call the results and their interpretation into question. Addressing these issues would strengthen the conclusions and could improve the status of the study. For diagnosing SARS-CoV-2 related encephalitis it is mandatory to document the virus within the cerebrum or CSF and to thoroughly rule out all differential diagnoses.

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Ethical Compliance Statement: The authors confirm that the approval of an institutional review board or patient consent was not required for this work. We confirm that we have read the Journal’s position on issues involved in ethical publication and affirm that this work is consistent with those guidelines. This article is based on previously conducted studies and does not contain any new studies with human participants or animals performed by any of the authors.

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