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Letter to Editor

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SARS-CoV-2 RNA in Cerebrospinal Fluid does not Necessarily Indicate Encephalitis

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We read with interest the article by Askin Turan et al. on a 71-year-old female with fever, fatigue, and confusion (1). The patient was diagnosed with SARS-CoV-2 associated encephalitis after imaging and documentation of SARS-CoV-2 RNA in the cerebrospinal fluid (CSF) (1). The patient benefited significantly from favipiravir (400 mg/d) and methylprednisolone (80 mg/d) (1). Subsequently, she developed symptomatic epilepsy during the course of the disease, so carbamazepine (400 mg/d) was added (1). The patient fully recovered within four weeks of hospitalization (1). The study is noteworthy but raises concerns that warrant further discussion.

The main limitation of the study is that the diagnosis of encephalitis remains unproven. The fact that the patient did not have pleocytosis and that the cerebral magnetic resonance imaging (MRI) was performed without contrast medium speaks against encephalitis. In addition, no cytotoxic oedema, which is usually observed in encephalitis by hyperintense diffusion-weighted imaging (DWI) and hypointensity on apparent diffusion coefficient (ADC) maps, was detected. Differential diagnoses not considered were ischemic stroke, vasculitis, venous sinus thrombosis (VST), acute disseminated encephalomyelitis (ADEM), and posterior reversible encephalopathy syndrome (PRES).

Another limitation of the study is that the patient was not systematically screened for immune encephalitis. Because encephalitis in SARS-CoV-2 infected patients is due to an immune response rather than an infectious agent (2), it is crucial that the index patient has been screened for antibodies associated with immune encephalitis. The presence of SARS-CoV-2 RNA in the CSF does not rule out immune encephalitis.

Another limitation of the study is that it remains unclear as to whether the patient actually had symptomatic epilepsy. According to the description of the electroencephalography (EEG), the patient had epileptiform discharges, but in the next sentence it is mentioned that the patient had no seizures (1). Surprisingly, the patient's restlessness was interpreted as seizures and anti-convulsive (ASD) treatment with carbamazepine (400 mg/d) was started. It should be clarified whether seizures were observed or not.

Another limitation of the study is that the CSF was only examined for SARS-CoV-2, herpes simplex virus (HSV), and Epstein-Barr virus (EBV) (1). However, many more viruses could have been responsible for the encephalitis. There were also no examinations of the CSF for fungi.

It should be explained why the patient was being treated with prednisolone (10 mg/d) at the time of admission (1). A history of hypothyroidism, arterial hypertension, and transnasal resection of a pituitary adenoma four months earlier does not convincingly explain the indication for prescribing prednisolone. Did the patient have hypocortisolism and cerebral oedema following pituitary surgery, or were steroids being administered for autoimmune hypothyroidism? Could steroid immunosuppression have facilitated SARS-CoV-2 infection?

In summary, this interesting study has several limitations that call into question the results and their interpretation. Clarifying these weaknesses would strengthen the conclusions and could improve the study. The presence of SARS-CoV-2 RNA in CSF does not necessarily indicate encephalitis.

AUTHORSHIP CONTRIBUTION

The author (JF) confirm responsibility for the following: study conception and design, data collection, analysis and interpretation of results, and manuscript preparation.

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