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Letter to the Editor

Neurologic Exam is Mandatory, Especially in Patients with Altered Mental Status and Callosal Lesions Due to SARS-CoV-2

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The article by Nagae *et al*. came to our attention because the 31-year-old male described in this article was suspected of suffering from SARS-CoV-2 encephalitis affecting the corpus callosum [1]. The patient was eventually diagnosed with mild encephalitis/encephalopathy with reversible callosal lesions (MERS) and fully recovered completely after three days of remdesivir [1]. The MRI lesions completely disappeared within six days [1]. The work is compelling, but some points should be discussed.

We disagree with the diagnosis SARS-CoV-2 related encephalitis. There are several arguments against such a diagnosis. First, COVID-19 was diagnosed based on the clinical presentation and antibodies to the SARS-CoV-2 spike protein. Diagnosis of SARS-CoV-2 base solely on neutralising antibodies is inadequate as these can persist for months [2] and therefore may not be associated with sore throat and fever three days before admission [1]. Second, SARS-CoV-2 was not detected in the cerebrospinal fluid (CSF) and therefore the lesion observed on MRI cannot be attributed to SARS-CoV-2 infection of the central nervous system (CNS). Since the symptoms disappeared with remdesivir, encephalitis caused by other viruses is also conceivable. Viral encephalitis can occur without pleocytosis, especially in the early stages of the disease. Therefore, it is recommended that CSF tests be repeated if symptoms persist. We should know the results of the CSF virus panel. Third, various differential diagnoses were not sufficiently excluded. Since the patient had an altered mental status upon admission, it is imperative to rule out non-convulsive status epilepticus (NCSE) by recording an electroencephalogram (EEG). Seizures may be associated with diffusion-weighted imaging hyperintensity. A second differential diagnosis that must be ruled out is immune encephalitis. In about half of cases, antibodies directed against various CNS components can be found in immune encephalitis. Therefore, we should know whether the antibodies in CSF associated with immune encephalitis were elevated or not. It is also mandatory to perform an MRI with contrast to possibly determine whether or not an enhancing lesion is present. Another differential diagnosis that must be ruled out is venous sinus thrombosis (VST). This is imperative as VST is a known complication of SARS-CoV-2 infections [3]. Another differential diagnoses not considered in the study is Machiafava bignami disease due to vitamin-B1 deficiency [4]. We should know whether the serum vitamin-B1 level was normal or decreased.

We disagree with the statement that "neurological tests could not be performed due to his drowsiness" [1]. One the contrary, a clinical neurological examination is easy to perform in patients with impaired alertness and is particularly important in these patients to determine whether there is clinical evidence of the cause of the impaired consciousness. Neurological exam in patients with impaired consciousness are performed in the same way as in alert patients, but without tests that require the patient's cooperation.

A limitation of the study is that CSF cytokines, chemokines and glial factors were not determined. These parameters have been repeatedly reported to be elevated in patients with CNS complications of SARS-CoV-2 infections [5]. It is also imperative to measure aquaporin-4, MOG, and NMO antibodies to rule out multiple sclerosis, MOG-related disorder, NMO-spectrum disorders.

Keywords: SARS-CoV-2, Corpus Callosum, Encephalitis, MERS, Impaired Consciousness

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