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SARS-CoV-2 in CSF

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Abstract: Infectious encephalitis due to SARS-CoV-2 is rare, why such cases need to be extensively examined to learn more about the behaviour of the virus in the CNS. To confirm the diagnosis it is mandatory that cerebral computed tomography (CCT) and cerebral magnetic resonance imaging (MRI) are carried out without contrast medium. Application of contrast medium eventually allows to localise the infected cerebral lesion and to study the progression of the lesion. If patients with encephalitis present with headache and elevated D-dimer it is mandatory to rule out venous sinus thrombosis (VST). VST is a common complication of SARS-CoV-2 infections and often manifests with seizures in addition to behavioural changes and headache. VST can be most easily excluded by magnetic resonance venography (MRV) with contrast medium or with computed tomography venography. If patients with encephalitis present with behavioural changes, confusion, drowsiness, and disorientation, it is also mandatory to rule out non-convulsive status epilepticus.

Keywords: Infection, SARS-CoV-2, encephalitis, cerebrospinal fluid, brain.

LETTER TO THE EDITOR

With interest we read the article by Darvishnia, *et al*., on a 77 year-old male diagnosed with SARS-CoV-2 encephalitis and treated with corticosteroids, remdesivir, acyclovir, interferon-beta, and tocilizumab [Darvishnia, D. *et al*., 2022]. In the meantime the patient had to be mechanically ventilated because of respiratory insufficiency [Darvishnia, D. *et al*., 2022]. The patient made an incomplete recovery and was discharged on hospital day 29 with headache and dizziness [Darvishnia, D. *et al*., 2022]. The study is excellent but has limitations that are cause of concerns and should be discussed.

A limitation of the study is that cerebral computed tomography (CCT) and cerebral magnetic resonance imaging (MRI) were carried out without contrast medium. Because encephalitis was suspected, it is mandatory to apply contrast medium to eventually localise the infected cerebral lesion and to study the progression of the lesion.

Another limitation is that no electroencephalogram (EEG) was recorded to rule out non-convulsive epileptic state. Because the patient presented with behavioural changes, confusion, drowsiness, and disorientation, starting five days after onset of the infection, it is mandatory to rule out non-convulsive status epilepticus.

Because the patient presented with headache and had markedly elevated D-dimer it would have been mandatory to rule out venous sinus thrombosis (VST). VST is a common complication of SARS-CoV-2 infections and often manifests with seizures in addition to behavioural changes and headache [LoBue, S. A. *et al*., 2022]. The VST is most easily excluded with a magnetic resonance venography (MRV) with contrast medium or with computed tomography venography.

Because central nervous system (CNS) involvement in COVID-19 is characterised by intrathecal immunoglobulin synthesis, elevation of cytokines, chemokines, neopterin, 14-3-3, neurofilament (NFL) light chains, and glial factors [Chaumont, H. *et al*., 2023] in the cerebrospinal fluid (CSF), we should know if these parameters were also abnormal in the index patient.

It would be interesting to know if the CSF was tested also for viruses other than SARS-CoV-2, if the patient had undergone a second lumbar puncture to assess when SARS-CoV-2 was no longer detectable in the CSF, and after which time the patient completely recovered after discharge.

There is a discrepancy between the statement that the neurological exam was normal and the statement that the patient presented with drowsiness and disorientation to time and place [Darvishnia, D. *et al*., 2022]. If there is confusion the neurological exam cannot be classified as normal.

A limitation of the study is that no reference limits for blood and CSF tests were provided.

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

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status of the study. Infectious encephalitis due to SARS-CoV-2 is rare, why such cases need to be extensively examined to learn more about the behaviour of the virus in the CNS.

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