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Letter to the editor

SUDEP as Endpoint of SARS-CoV-2 Associated Encephalitis with Status Epilepticus

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With interest we read the article by Farias et al. on a 31 year-old, previously healthy male with SARS-CoV-2 related meningo-encephalitis who died suddenly and unexpectedly during a status epilepticus on the intensive care unit (ICU) [1]. Because the patient was co-infected with influenza-A, it was suspected that meningo-encephalitis was due to infection with both viruses [1]. No autopsy was performed. The study is excellent, but has limitations that are cause of concerns and should be discussed.

The main limitation of the study is that the patient did not undergo autopsy. To clarify whether SARS-CoV-2 or influenza-A was truly present inside neurons and glial cells, it is critical to have the results of histological, immune-histological, and electron microscopy examinations of the brain. Autopsy is also critical to assess whether the lung was affected or not since no CT of the lungs had been done intra vitam.

Another limitation of the study is that no cerebral MRI with contrast medium had been done intra vitam to document the extension and localisation of encephalitis. It would have been also interesting to know whether the patient had developed cerebral edema or brainstem herniation with progression of encephalitis.

Another limitation is that RT-PCR for SARS-CoV-2 and influenza-A in the CSF was not repeated and the initial test results were not confirmed by using a different kit to rule out a false positive result on the first test.

It is speculative to assume that the patient had both, SARS-CoV-2 encephalitis and influenza-A encephalitis. Since presence of the influenza-A virus was not documented in the CSF, it is rather unlikely that the patient also had influenza-A encephalitis.

A cause of death not discussed in the report is sudden unexpected death in epilepsy (SUDEP). SUDEP has been repeatedly reported as a complication of witnessed and unwitnessed seizures [2]. Because the patient died suddenly and unexpectedly during a status epilepticus on the ICU, it cannot be ruled out that SUDEP was responsible. SUDEP is assumed due to neurogenic pulmonary edema, autonomic dysreflexia, or acute cardiac disease, such as Takotsubo syndrome (TTS), acute heart failure, or ventricular arrhythmias. Therefore, we should know whether the ECG shortly before or during resuscitation on the ICU was abnormal or not and whether a bedside

echocardiography was done during CPR. We disagree with the statement that the patient had only neurological symptoms [1]. Figure 1 clearly shows that the patient also had coughing, fever, and running nose, which are all non-neurological.

Meningo-encephalitis, myelitis, and ADEM are neither neurological symptoms nor neurological syndromes, as stated in the introduction [1]. All of them are simply central nervous system (CNS) diseases.

At the beginning of 2022 anti-SARS-CoV-2 vaccinations were already available. We therefore should know if the patient was vaccinated and had a breakthrough SARS-CoV-2 infection or if she was unvaccinated.

There is no mention of the anti-seizure drugs the patient received for the initial tonic clonic seizure and for status epilepticus.

There is also no mention of the reference limits of the blood and CSF values reported.

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. Before claiming that encephalitis was due to SARS-CoV-2 and influenza-A, repeated documentation of the presence of both viruses is warranted. This can be achieved by autopsy, or repeated CSF investigations, both of which were not carried out in the index patient.

Keywords: SUDEP, SARS-CoV-2, encephalitis, epilepsy, sudden death

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