Comment on: Neurological Manifestations Associated With SARS-CoV-2 in Children: A Case Series

Josef Finsterer 0

Neurology & Neurophysiology Center, Vienna, Austria.

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We read with interest the article by Venceslau et al. about four pediatric patients with severe neurological complications of a SARS-CoV-2 infection.¹ Three patients developed meningo-encephalitis, of whom two were positive for virus-RNA in the cerebrospinal fluid (CSF), and one patient Guillain-Barre syndrome (GBS).¹ Although one patient required transfer to the intensive care unit (ICU), the outcome was favourable without specific treatment in all of them.¹ The study is appealing but raises concerns that should be discussed.

We disagree with the statement in the abstract that in adults the majority of severe COVID cases results from respiratory complications.¹ There is ample evidence that adults can also experience severe neurological side effects from SARS-CoV-2 infections.^{2,3}

We disagree with the statement that presence of virus-RNA in the CSF indicates that the virus can cross the blood brain barrier (BBB).¹ Demonstration of SARS-CoV-2 in the CSF not necessarily demonstrates that the virus is capable to cross the BBB. As mentioned by the authors in the discussion, the virus can reach the brain also via trans-synaptic pathways.⁴

We disagree with the statement that the CSF in patient 4 was "indeterminate" as mentioned in Table 1^1 CSF investigations in patient 4 clearly demonstrate dissociation cyto-albuminique, suggesting GBS. We should know if patient 4 underwent nerve conduction studies (NCSs) to determine if neuropathy was of the demyelinating or the axonal type. Differentiating between these two subtypes of GBS is crucial as the outcome may vary considerably between the two.

Missing is the classification of progressive encephalopathy in patient $1.^1$ Wes should know if progressive encephalopathy was due to recurrent seizures, due to chronic meningitis, due to neuro-degeneration, or due to a hereditary disorder.

Since all four patients had a mild disease course of COVID-19, we should know why patient 3 was transferred to the ICU.¹ We should be informed if the family history was positive for cognitive decline in this patient and if her parents were consanguineous.

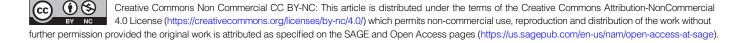
Missing is the anti-seizure drug (ASD) treatment in patient 1 and patient 3. We should be told if seizures resolved completely or if seizure frequency increased after the SARS-CoV-2 infection.

We should know why patient 1 was diagnosed with meningo-encephalitis.¹ Elevation of CSF leukocytes was only mild and there was no fever or neck stiffness. Was impaired consciousness a post-ictal phenomenon or were there any indications for a non-convulsive status epilepticus?

There is a discrepancy in the description of the clinical exam in patient 1. The patient was described with axial hypotonia but at the same time had perpendicular hypertonia.¹ This discrepancy should be solved.

Patient 1 had bilateral subdural hematoma (SDH) being attributed to suspected abuse head trauma.¹ Since the patient had long-term epilepsy, it is also conceivable that he experienced a fall from an unwitnessed, generalised tonicclonic seizure. Were there any indications that SDH resulted from uncontrolled seizure activity rather than child abuse? Upon which features did the authors suspect abuse? The outcome of seizures in patient 1 and 3 should be reported.

Overall, the interesting study has some limitations that call the results and their interpretation into question. Clarifying these weaknesses would strengthen the conclusions and could



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Author contribution

JF: design, literature search, discussion, first draft, critical comments, final approval.

ORCID iD

Josef Finsterer b https://orcid.org/0000-0003-2839-7305

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