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Letter to the Editor

Diagnosing pediatric para-infectious brain damage requires comprehensive work-up

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We eagerly read the article by Gombolay *et al*. about a retrospective cohort study of 883 pediatric patients referred for a first seizure and an infection with coronavirus, influenza, parainfluenza, adenovirus, or mycoplasma [1]. The study is appealing but raises concerns.

It was found that meningo-encephalitis was rare but the limitations mention that CSF studies including viral testing had not been carried out in many patients. If only few patients had CSF investigations, meningo-encephalitis will be out of necessity diagnosed only rarely. No valid conclusions about the frequency of meningo-encephalitis can be drawn if patients were not appropriately investigated for meningo-encephalitis. We should know if all those diagnosed with encephalitis had CSF studies indicative of encephalitis.

A stroke mechanism not considered in SARS-CoV-2 positive stroke patients is hypercoagulability and thrombocytopenia leading to venous sinus thrombosis (VST) [2]. Because VST is frequently complicated by ischemic stroke, it is crucial that VST is ruled out as the cause of ischemic stroke. Did all patients with ischemic stroke undergo multimodal MRI including magnetic resonance venography? How often was stroke due to angiopathy, embolism, coagulopathy, hemodynamic impairment, or hypercellularity?

We disagree with the notion that only children with neuropsychiatric symptoms have elevated CSF cytokines [1]. Elevated CSF cytokines have been also reported in all SARS-CoV-2 related central nervous system (CNS) diseases and in GBS [3].

A limitation of the study that the current medication was not abstracted from the medical records. Knowing the current medication is crucial as it may cause neurological side effects, which may be misinterpreted as infection-related.

Several important issues were not mentioned in the manuscript. In how many patients was epilepsy (≥2 unprovoked seizures with a delay of >24h) newly diagnosed? How many of the patients with epilepsy had genetic epilepsy, structural epilepsy, or unclassified epilepsy? How many patients had a positive family history for epilepsy? How many patients required treatment with anti-seizure drugs? How many patients had seizures during follow-up?

Not only parainfluenza infection may be complicated by endothelial damage, but also SARS-CoV-2 infections. There is increasing evidence that SARS-CoV-2 infections can be complicated by endothelialitis, thus resulting in endothelial damage and consecutive thrombosis.

We should know how “encephalopathy” and “hypoxic encephalopathy” were defined. How was encephalopathy delineated from hypoxic encephalopathy? Did all patients with hypoxic encephalopathy undergo MRI? Did MRI reveal a typical hypoxic cerebral damage manifesting as T2-hyperintensities of the cortex, thalamus, or the basal ganglia [4]?

Declarations

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Consent for publication: Was obtained from the patient.

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Code availability: Not applicable.

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

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