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Workup of cerebral involvement in COVID-19 requires at least cerebral imaging, EEG, and cerebrospinal fluid studies

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Letter to the Editor

We read with interest the article by Chen et al. about five pediatric patients with severe neurological complications of acute SARS-CoV-2 infections [1]. It was concluded that a new mutation in the spike-protein of variant BA.2.3.7 could be responsible for sudden increase in neurological complications of COVID-19 [1]. The study is appealing but raises concerns.

The study design is unsuitable to draw conclusions about the incidence of neurological involvement in COVID-19 as expressed in the conclusions [1]. The investigated cohort included patients from only a single center, the period over which these patients were recruited was not mentioned, and the cohort was not compared with the total number of admissions during the same period.

A further limitation is that results of cerebral imaging were not provided. Because all five patients had cerebral involvement, it is crucial to know if there were indications for inflammation, demyelination, ischemia, bleeding, or thrombosis. Results of multimodal MRI, MR-angiography, and MR-venography should be provided.

Markedly elevated cell count in patient-2 suggests that there was bacterial encephalitis/meningitis. We should be informed whether neutrophils or lymphocytes were elevated and if cerebrospinal fluid (CSF) culture grew any bacterium.

We disagree with the statement that elevated inflammatory markers and negative PCR for SARS-CoV-2 in the CSF suggest a hyper-immune state rather than infection [1]. First, only three patients (patient-2, patient-3, patient-5) had undergone CSF investigations. Second, patient-2 had pleocytosis. Third, patient-3 had only mildly elevated procalcitonin, and patient-5 had only mildly elevated D-dimer and procalcitonin [1]. Fourth, patient-2 and patient-5 did not fulfil the diagnostic criteria for multisystem inflammatory syndrome in children (MIS-C) [2].

We disagree with the statement that blood tests showed prominent elevation of inflammatory markers in all patients [1]. Lactate-dehydrogenase (LDH) was elevated in only three patients, ferritin was elevated in only two patients, interleukin-6 was elevated in only two patients, and D-dimer was markedly elevated in only one [1].

Patient-1 had shock with multiorgan failure [1]. It should be reported if there was allergic, septic, neurogenic, or cardiogenic shock. Patient-1 also had elevated D-dimer. Was this due to the infection or due to thrombosis, such as venous sinus thrombosis? What was the cause of cerebral edema?

All five patients had seizures [1]. Missing are the EEGs and the anti-seizure drugs.

Overall, the interesting study has limitations that challenge the results and their interpretation. Clarifying these weaknesses would strengthen the conclusions and could upgrade the study.

Declarations

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Consent to participate: was obtained from the patient

Consent for publication: was obtained from the patient

Availability of data: all data are available from the corresponding author

Code availability: not applicable

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

References

1 Chen CS, Chang CN, Hu CF, Jian MJ, Chung HY, Chang CK, Perng CL, Hung KS, Chang FY, Wang CH, Chen SJ, Shang HS. Critical pediatric neurological illness associated with COVID-19 (Omicron BA.2.3.7 variant) infection in Taiwan: Immunological assessment and viral genome analysis in tertiary medical center. Int J Infect Dis. 2022 Sep 7:S1201-9712(22)00500-8. doi: 10.1016/j.ijid.2022.09.001.

2 Gaspar AD, Kuzma GSP, Amancio L, Floriani I, Bezerra VN, Bortolon GC, de Siqueira APV, Machado MP, Machado ACDS, Camargo CF, João PRD. Multisystem inflammatory syndrome in children: a case series. Rev Paul Pediatr. 2022 Apr 4;40:e2021046. doi: 10.1590/1984-0462/2022/40/2021046.