



Neurological complications of COVID-19 in pediatric patients require comprehensive evaluation

Josef Finsterer¹

Received: 2 September 2021 / Revised: 2 September 2021 / Accepted: 28 February 2022 / Published online: 11 March 2022
© Journal of NeuroVirology, Inc. 2022

Letter to the Editor

With interest we read the article by Krueger et al. about four pediatric patients with symptomatic COVID-19 who experienced severe neurological complications from the viral infection (Krueger et al. 2021). A 16-year-old female experienced polyradiculitis (patient-1), a 15-year-old male developed Guillain–Barre syndrome (GBS) subtype acute, inflammatory, demyelinating neuropathy (AIDP) (patient-2), a 5-year-old female developed acute intracranial hypertension (patient-3), and a 2-year-old male experienced focal seizures during the infection (patient-4) (Krueger et al. 2021). The study is appealing but raises some concerns and comments.

We do not agree with the notion that COVID-19 in pediatric patients usually takes a mild course (Krueger et al. 2021). There are several reports about paediatric patients with severe COVID-19 or its complications (O’Loughlin et al. 2021; Grewal et al. 2021).

Cranial MRI of patient-1 showed contrast enhancement of cranial nerves VII and VIII bilaterally but clinical neurological exam did not detect any abnormalities of these nerves (Krueger et al. 2021). How do the authors explain this discrepancy? We should be told if there was hearing impairment, vertigo, or facial palsy bilaterally.

A limitation is that Table 1 does contain reference limits (Krueger et al. 2021). Applying our own reference limits, patient-1 had only mild pleocytosis, which does not exclude GBS, particularly in the light that patient-1 also had dengue. Thus, it is conceivable that the patient had GBS triggered by dengue and not by SARS-CoV-2.

Concerning patient-3, it is not certain that SARS-CoV-2 was responsible for intracranial hypertension. The patient had a history of a hypertensive arachnoid cyst requiring

cerebro-spinal fluid (CSF) derivation via a ventriculo-peritoneal shunt (Krueger et al. 2021). It is conceivable that the shunt function was impaired due to an altered composition of the CSF resulting in increased intracranial pressure. It is also conceivable that the patient had experienced venous sinus thrombosis (VST), a frequent complication of SARS-CoV-2 infections (Abdulgayoom et al. 2021). We should be informed about the results of magnetic resonance venography (MRV) and the D-dimer levels.

Concerning patient-4, we should be told if “cerebral MRI” also included MRV and if the D-dimer was elevated. VST is frequently complicated by seizures (Uluduz et al. 2020). We should also know if the family history was positive for epilepsy and if patient-4 had seizures already prior to the SARS-CoV-2 infection. A causal relation between COVID-19 and epilepsy in this patient remains unproven.

It should be emphasised that SARS-CoV-2 RNA was found in the CSF of patient-1 (Krueger et al. 2021). This finding is remarkable as only in two other patients (one adult, one pediatric patient) SARS-CoV-2 was detected in the CSF so far (Khan et al. 2021; Araújo et al. 2021). Virus RNA is usually absent in the CSF of patients with SARS-CoV-2-associated GBS (Finsterer and Scorza 2021) but in infectious polyradiculitis presence of SARS-CoV-2 in the CSF may support the speculation that an intrathecal virus infection was truly responsible for the clinical presentation.

Overall, the elegant study has several limitations which challenge the results and their interpretation. SARS-CoV-2-infected patients with severe neurological complications need to be thoroughly investigated to explain the clinical presentation and to apply appropriate treatment. Before establishing a causal relation between COVID-19 and neurological compromise, a thorough work-up and exclusion of differentials is compulsory.

✉ Josef Finsterer
ffigs1@yahoo.de

¹ Neurology and Neurophysiology Center, Postfach 20,
1180 Vienna, Austria

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

Declarations

Conflict of interest The author declares no competing interests.

References

- Abdulgayoom M, Abdelmahmuod E, Elfaki A, Halabiya MA (2021) Cerebral venous sinus thrombosis as an unexpected complication of COVID-19 pneumonia. *Cureus* 13(7):e16498. <https://doi.org/10.7759/cureus.16498>
- Araújo NM, Ferreira LC, Dantas DP, Silva DS, Dos Santos CA, Cipolotti R, Martins-Filho PR (2021) First report of SARS-CoV-2 detection in cerebrospinal fluid in a child with Guillain-Barré syndrome. *Pediatr Infect Dis J* 40(7):e274–e276. <https://doi.org/10.1097/INF.0000000000003146>
- Finsterer J, Scorza FA (2021) Guillain-Barre syndrome in 220 patients with COVID-19. *Egypt J Neurol Psychiatr Neurosurg* 57(1):55. <https://doi.org/10.1186/s41983-021-00310-7>
- Grewal MK, Gregory MJ, Jain A, Mohammad D, Cashen K, Ang JY, Thomas RL, Valentini RP (2021) Acute kidney injury in pediatric acute SARS-CoV-2 infection and multisystem inflammatory syndrome in children (MIS-C): is there a difference? *Front Pediatr* 9(9):692256. <https://doi.org/10.3389/fped.2021.692256>
- Khan F, Sharma P, Pandey S, Sharma D, Vijayarman V, Kumar N, Shukla S, Dandu H, Jain A, Garg RK, Malhotra HS (2021) COVID-19-associated Guillain-Barre syndrome: postinfectious alone or neuroinvasive too? *J Med Virol* 93(10):6045–6049. <https://doi.org/10.1002/jmv.27159>
- Krueger MB, Montenegro RC, de Araújo Coimbra PP, de Queiroz LL, Fiorenza RM, da Silva Fernandes CJ, Pessoa MSL, Rodrigues CL, da Cruz CG, de Araújo VV, de Carvalho Araújo FM, Braga-Neto P, Sobreira-Neto MA (2021) A wide spectrum of neurological manifestations in pediatrics patients with the COVID-19 infection: a case series. *J Neurovirol* 26:1–5. <https://doi.org/10.1007/s13365-021-01004-9>
- O’Loughlin L, Alvarez Toledo N, Budrie L, Waechter R, Rayner J (2021) A systematic review of severe neurological manifestations in pediatric patients with coexisting SARS-CoV-2 infection. *Neurol Int* 13(3):410–427. <https://doi.org/10.3390/neurolint13030041>
- Uluduz D, Midi I, Duman T, Yayla V, Karahan AY, Afsar N, Goksu EO, Mengulluoglu N, Aytac E, Sungur MA, Yesilot N, Ince B, Yalin OO, Oruc S, Senol MG, Yilmaz A, Gokce M, Demirci S, Kusbeci OY, Uzuner G, Caglayan HZB, Acikgoz M, Kurucu H, Ozdag F, Baybas S, Ekmekci H, Cabala M, Yaman M, Yürekli VA, Tekeli H, Genc H, Utku U, Sahin S, Tokuc FEU, Uzuner N, Bektas H, Kablan Y, Goksel BK, Milanlioglu A, Orken DN, Aluclu U, Colakoglu S, Tufekci A, Bakar M, Nazliel B, Tascilar N, Goksan B, Kozak HH, Demir S, Mısırlı CH, Kucukoglu H, Cinar N, Domac FM, Ozturk S, Gunes T (2020) Epileptic seizures in cerebral venous sinus thrombosis: subgroup analysis of VENOST study. *Seizure* 78:113–117. <https://doi.org/10.1016/j.seizure.2020.02.017>

Publisher's Note Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.