



A wide spectrum of neurological manifestations in pediatric patients with the COVID-19 infection: a case series

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Abstract

Neurological symptoms in COVID-19 patients can also be found in the pediatric population, but they are usually described as mild symptoms. Herein, we described a case series of four pediatric patients with severe and highly heterogeneous central and peripheral nervous system manifestations. The objective was to report neurological manifestations of COVID-19 in children and adolescents. The design is case series. The participants are four children and adolescents with confirmed COVID-19. The main outcome and measures are as follows: Clinical data were gathered from electronic medical records, and data of all neurologic symptoms were checked by a trained neurologist. We reported four pediatric patients with COVID-19 and different neurologic symptoms. **Case 1** was a 16-year-old girl with a sensory and motor polyradiculopathy with RT-qPCR for COVID-19 and dengue both detected in CSF that improved after appropriate treatment. **Case 2** was a 15-year-old boy with Guillain–Barre syndrome and had good response after using human immunoglobulin. **Case 3** was a 5-year-old girl with acute intracranial hypertension that improved after going through lumbar puncture and using acetazolamide. **Case 4** was a 2-month-old male infant with focal epileptic seizures that recovered after antiepileptic treatment. We highlight the need to consider different neurologic manifestations as part of the COVID-19 clinical spectrum.

Keywords COVID-19 · Epilepsy · Seizure · Polyradiculoneuropathy · Idiopathic intracranial hypertension · Guillain-barré syndrome · SARS-CoV-2 Infection

There are no prior publications or submissions with any overlapping information, including studies and patients.

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Introduction

COVID-19 in the pediatric population it is commonly described as a disease with mild symptoms (She et al. 2020; Dong et al. 2020). In children, fever and cough are the most common clinical manifestations, which sometimes is combined with fatigue, myalgia, nasal congestion, runny nose, sneezing, sore throat, vomiting and abdominal pain (She et al. 2020).

The most common neurological manifestations in adults infected by COVID-19 infection in adults are dizziness, headache, anosmia, stroke, ataxia, and epilepsy (Abdel-Mannan et al. 2020; Mao et al. 2019). Neurological symptoms could also be found in the pediatric population, such as headache, muscle weakness, and encephalopathy (She et al. 2020; Dong et al. 2020; Abdel-Mannan et al. 2020). Herein, we described a case series of four pediatric patients with COVID-19, from a pediatric hospital at Fortaleza,



Fig. 1 Neuroimaging findings in patients with COVID-19. **A, B, C** Images of the patient 1. **A** Axial T1-weighted contrast-enhanced brain MR image demonstrates bilateral contrast enhancement in the cranial nerves VII/VIII complex, inside the internal auditory canal (arrows). **B, C** T1-weighted contrast-enhanced MR images of the thoracic

spine, in sagittal (**B**) and axial (**C**) slices, show contrast enhancement in the anterior roots of the medullary cone (arrows). **D** Image of the patient 2. Sagittal T1-weighted contrast-enhanced MR image of the thoracic spine shows thickening and contrast enhancement on the anterior surface of the medullary cone (arrow)

Ceará state, Brazil, with highly heterogeneous neurological manifestations.

Cases descriptions

Case 1

A 16-year-old girl with diarrhea presented, after 5 days, paresthesia and progressive difficulty to walk. Neurological examination showed acute and progressive paraparesis, with hypoesthesia below Th6 level. No sphincter dysfunction was reported. Brain, cervical, thoracic, and lumbar MRI showed contrast enhancement in the anterior roots of the medullary cone, as well as in the bilateral cranial

nerves VII/VIII complex (Fig. 1). Cerebrospinal fluid (CSF) analysis showed pleocytosis with predominance of lymphocytes (Table 1). Real-time qPCRs for SARS-CoV-2 (RT-qPCR-COVID) and dengue virus, both in CSF, were positive. COVID-19 serological rapid test IgM/IgG (COVID-RT) was also positive. Serial electroneuromyography (EMG) assessment showed normal nerve conduction studies (NCS) associated with absence of H reflex, widespread fibrillations, and positive waves (including in paraspinal muscles) associated with acute neurogenic motor recruitment, compatible with polyradiculopathy. The patient was treated at day 9 with acyclovir, for 14 days, followed by intravenous human immunoglobulin 0.4 g/kg/day, for 5 days. At day 17, we used methylprednisolone 1 g for 5 days. She presented with progressive

Table 1 Laboratorial findings of the four patients

Laboratory tests	Case 1	Case 2	Case 3	Case 4
CSF				
Cells count, number/mm ^c	18 (S-16/L-59) ^a	10 (S-0/L-85/M-15) ^a	0.33 (S-25/L-50/M-25) ^a	5.33 (S-1/L-45/M-54) ^a
Protein, mg/dL	28.5	94	11.4	46.9
Glucose, mg/dL	61	79	74	48
Opening pressure ^b , cmH ₂ O	–	–	70	–
RT-qPCR-COVID	Positive	Negative	Negative	–
RT-qPCR-dengue	Positive	–	–	–
Serological rapid test IgM/IgG	Positive	Positive	Positive	Positive
Nasopharyngeal swabs RT-qPCR-COVID	–	–	–	Positive

^aCell differential in percentage: L lymphocytes, M monocytes, S segmented

^bAssessment with patient lying in lateral position

^cWhite cells (WBC) count for millimeter

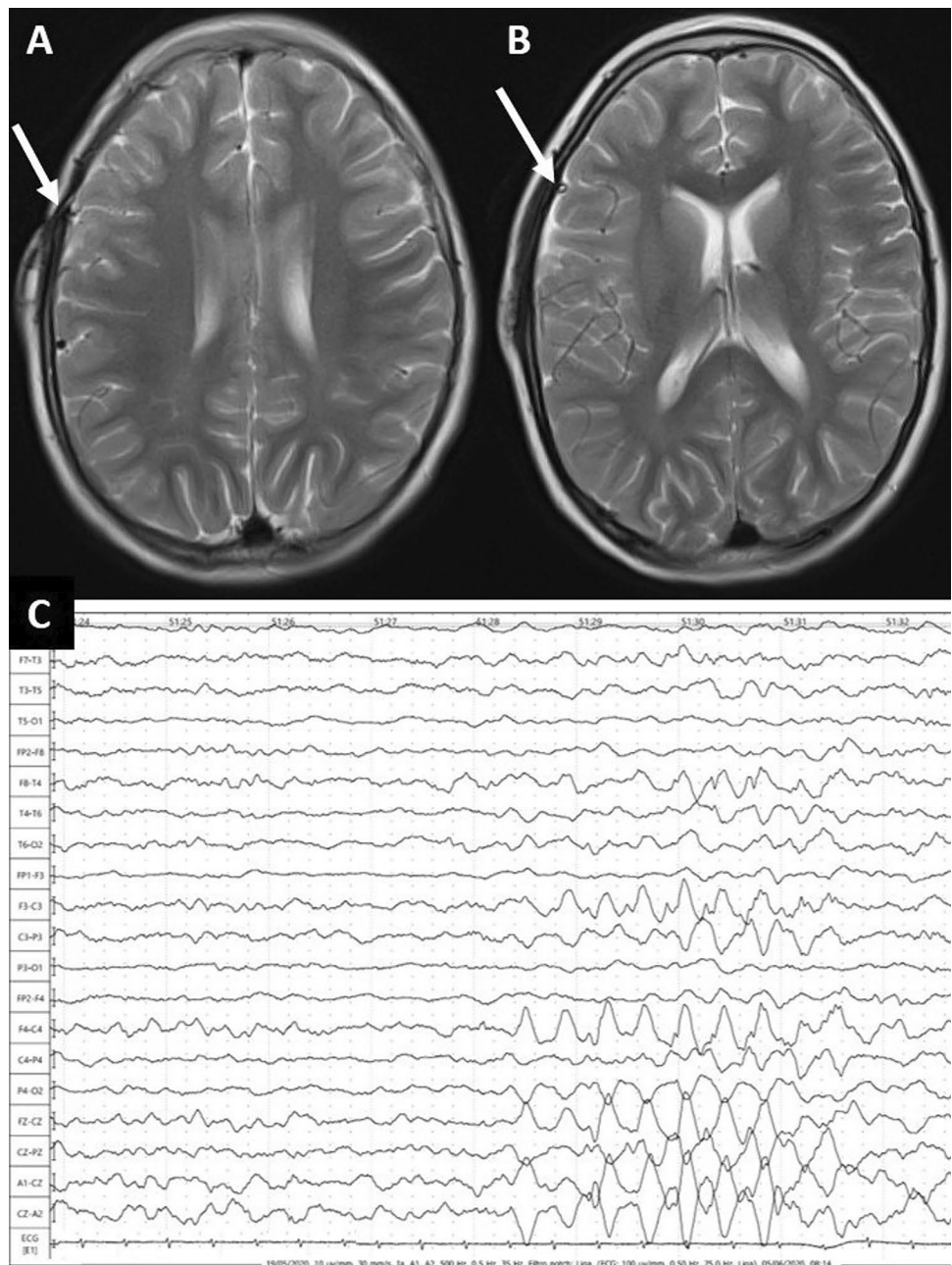
improvement and after 21 days was discharged from the hospital walking without help.

Case 2

A 15-year-old boy presented, initially, rhinorrhea and dry cough. The disease evolved after 15 days with pain, paresthesia, and weakness in the lower limbs followed by the upper limb's involvement, without respiratory impairment. No bladder or bowel dysfunctions were reported. Neurological examination showed absence of deep tendon reflexes, quadriparesis, and reduction of superficial and deep

sensitivity at the four limbs. COVID-RT was positive. CSF analysis showed mild pleocytosis with increased protein (Table 1). Brain MRI was normal, but thoracic and lumbosacral MRI showed enhancement of the nerve roots, mainly at ventral roots (Fig. 1). Electrophysiological examination showed demyelination features in peripheral nerves with prolonged distal motor latencies, non-uniform decrease of motor nerve conduction velocities, and prolonged F wave latencies with no active denervation in needle EMG. The patient received 0.4 g/kg/day of intravenous human immunoglobulin for 5 days with a significant improvement, restoring the ability to walk independently after 2 weeks.

Fig. 2 Brain MRI and electroencephalography of patients with COVID-19. **A, B** Patient 3 T2-weighted brain MR images in axial sections show changes related to previous surgical procedure, without other significant findings. **A** Signs of discontinuity of the skullcap (arrow). **B** Derivation catheter (arrow). **C** Electroencephalogram of the patient 4 showing brief ictal-appearing rhythmic discharges (BIRDs) at bilateral posterior regions



Case 3

A 5-year-old girl, with previous hypertensive arachnoid cyst treated with ventriculoperitoneal derivation, was asymptomatic since surgery. She was admitted with intense headache, fever, vomiting, and horizontal diplopia. Neurological examination confirmed the horizontal diplopia, with no other findings. Brain MRI and digital angiograph were normal (Fig. 2). CSF showed an open pressure of 70 cmH₂O (normal < 25cmH₂O) and normal analysis (Table 1). COVID-RT was positive. The symptoms improved after CSF withdrawal and the use of acetazolamide, with gradual reduction after 1 month.

Case 4

A 2-month-old male infant, with a term deliver without any problem, presented dry cough, fever, and diarrhea. After 15 days, these symptoms were followed by dyspnea and hypoxemia, needing mechanical ventilation. His mother was diagnosed with COVID-19, and the COVID-RT of the patient was also positive. After 3 days of the admission, he presented with the deviation of the eyes and automatic masticatory movements. Brain MRI, angiography MRI, and CSF analysis were normal (Table 1). Electroencephalography with synchronized video showed acute transients and brief ictal-appearing rhythmic discharges (BIRDs) at posterior regions (bilateral temporo-occipital region) (Fig. 2). He was treated with intravenous phenobarbital with an improvement of the epileptic events and was discharged after 25 days without any apparent neurologic deficits. After 3 months, the patient was reevaluated, without new epileptic seizures and with normal neurological examination.

Discussion

Herein, we described four pediatric patient cases with different neurological manifestations associated with COVID-19, involving both the central and peripheral nervous systems, and their responses to different treatments.

The first report of Guillain-Barré Syndrome (GBS) associated with COVID-19 occurred with a 61-year-old woman in the end of January 2020 (Zhao et al. 2020). From that date up to now, other cases were described, but neither of them in pediatric patient (Badat et al. 2018; Li et al. 2020). Possible mechanism for this coexistence is a molecular mimicry between the new coronavirus and the peripheral nerve, creating an immune-mediated process (Finsterer et al. 2020). The virus was found in CSF of patient 1 together with dengue virus, an endemic condition in our region. This coinfection could exacerbate the

immune response, but we should also consider direct virus lesion. As documented in the previous papers, the onset of the neuropathy symptoms of patient 1 and 2 overlapped with the period of the infection (Li et al. 2020; Toscano et al. 2020). This pattern is distinct from the classic postinfectious profile, reported in GBS.

A recent case of idiopathic intracranial hypertension (IHH) was described in a 35-year-old woman with COVID-19, and, as patient 3, she also had an acute increase of intracranial hypertension (Noro et al. 2020). Possibly, the pathological process of the disease interfered with cerebrospinal liquid dynamic, but the mechanism is not clear. Recently, a large population-based case–control study demonstrated an association between infectious and inflammatory disorders with the IHH (Sundholm et al. 2020).

The epileptic seizure is a common symptom in COVID-19 patients, and recently, a study using electroencephalography in COVID-19 critically ill patients documented seizure in 63.6% of them (Galanopoulou et al. 2020). This study reported epileptiform activity more often in the frontal region, but patient 4 presented the epileptiform activity at the brain's posterior regions. The reason for the seizures in our patient is probably related to hypoxia and its consequences. However, we could not preclude the virus invasion and the immune attack to the central nervous system (Zhao et al. 2020).

A causal relationship between the virus and the different neurologic disorders in children should be confirmed with a larger population and a longitudinal study. Although these manifestations are rare in this population, the cases reported here reinforce the need to evaluate them in COVID-19 pediatric patients.

Author contribution All the authors made significant contributions to this study. Mariana Krueger (MK), Manoel Sobreira (MS), Pedro Braga-Neto (PB), Pablo Picasso Coimbra (PP) conceived the idea of the study; MK, MS, PB were involved in planning and work management; MK, MS, PP, Raquel Montenegro (RM), Luanna Lemos (LL), Regiane Fiorenza (RF), Carla Fernandes (CF), Mariana Pessoa (MP), Cleonísio Rodrigues (CR), Camila Cruz (CC), Verlene Veridiano (VV), Fernanda Araújo (FA) carried out patient assessments and follow-up and data analysis; MK, PB, MS, MP, CR, PP prepared the manuscript and wrote the first draft; MK, PB, MS, CR, and PP discussed and critically reviewed to the final manuscript.

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Declarations

Ethics approval This study was approved at Ethical Approval of Studies, and all the patients agreed to the Informed Consent Form.

Competing interests The authors declare no competing interests.

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