Case series

Neurological manifestations in pediatric patients with COVID-19: A case series

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ABSTRACT

In this case series of two male and one female patient with an age range of 2-12 years, only one patient had a history of neurological disorder and underwent ventriculoperitoneal shunt for a medulloblastoma, which describes coronavirus disease-associated neurological manifestations in pediatric patients, among which seizures and sensory disturbances are noticeable. In order to describe the various clinical and neurological manifestations that appeared earlier or developed over the course of illness, a series of cases of pediatric patients with coronavirus disease was documented.

Keywords: COVID-19; SARS-CoV-2; neurological manifestations; pediatric patients; antibiotics.

INTRODUCTION

The causative agent of coronavirus disease (COVID-19) is severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) (1). Due to the increased number of COVID-19 cases, neurological manifestations have been reported more frequently. Neurological manifestations such as headache, seizures, impaired consciousness, anosmia, and paresthesia (2, 3), which are common in the advanced stages of the disease, are observed in pediatric patients with COVID-19 (4). A total of four pediatric patients have reported new-onset neurologic COVID-19-associated symptoms, diagnosed with multisystem inflammatory syndrome (5).

Data on the clinical characteristics and prognostic factors of pediatric patients with neurological manifestations due to SARS-CoV-2 infection are limited. Herein, we present three clinical cases of pediatric patients diagnosed with COVID-19 and treated at our hospital, along with a description of the clinical and neurological manifestations that appeared earlier or developed over the course of illness.

Case 1

A one-year-old boy presented with fever and cough, eight days earlier. On admission, he presented with severe cough, flaccid paralysis, and circumoral cyanosis, without fever or diarrhea. Both SARS-CoV-2 IgG/IgM rapid test and reverse-transcription polymerase chain reaction (RT-PCR) for the infant and his mother were positive; he was hospitalized for five days, as he presented with respiratory symptoms. He was readmitted three days after discharge, with episodes of involuntary movement-associated cyanosis, but without fever, vomiting, or cough. Transfontanelle ultrasonography was normal. He fully recovered after treatment, without seizures or cyanosis.

Case 2

A nine-year-old boy who had undergone seeding of ventriculoperitoneal shunt for a medulloblastoma had a two-day history of fever, irritability, and decreased consciousness. He was admitted to the intensive care unit due to suspected ventriculoperitoneal shunt malfunction. Multi-slice spiral computed tomography of the brain (without hydrocephalus) and cerebrospinal fluid analysis were performed; the results for both were negative. His mother's SARS-CoV-2 IgG/IgM rapid test was positive, while the patient tested negative, but RT-PCR results were positive for both. He was treated with ceftriaxone and amikacin. On day 4, the regimen was changed to meropenem, and vancomycin combined with dexamethasone and acyclovir for 6 days, due to no symptom improvement. A cerebrospinal fluid analysis was performed on the same day, showing a white blood cell count of ≤8,000/μl; therefore, viral encephalitis secondary to COVID-19 was suspected. The patient showed complete remission and was discharged after 12 days of treatment.

Case 3

A 12-year-old girl had a 2-week history of thigh pain that further radiated down her legs and into the feet, along with paresthesia and difficulty walking for a week. She did not present with fever or respiratory symptoms and denied contact with patients who tested positive for SARS-CoV-2.

Table 1: Clinical characteristics of pediatric patients with COVID-19

Characteristics	**Case 1**	**Case 2**	**Case 3**
Age	1-year-old	9-year-old	12-year-old
Gender	Male	Male	Female
Early clinical manifestations	Fever, Involuntary movements and circumoral cyanosis	Fever, irritability and decreased consciousness	Decreased muscle strength and tendon reflexes
Co-existing disease	No	Medulloblastoma	No
Respiratory symptoms	Yes	No	No
Treatment			
Azithromycin	Yes	Yes	Yes
Antibiotic therapy	Yes	Yes	Yes
Immunoglobulins	No	No	Yes
Methylprednisolone	No	No	No
Mechanical ventilation	No	No	No
Hospital stay(days)	5/4	12	8

Table 2. Data from laboratory tests in pediatric patients with COVID-19

Variable	**Case 1**	**Case 2**	**Case 3**
Hemoglobin (g/dl)	12.9	13.2	13.5
Hematocrit (%)	38.9	41.3	39.7
White-cell count (per µl)	9000	6789	7990
Lymphocytes (per µl)	1350	1245	1096
Neutrophils (per µl)	4690	5348	6330
Thrombocytes (per µl)	306,000	250,000	323,000
Sodium (mmol/liter)	136	140	139
Urea nitrogen (mg/dl)	6	8	6
Creatinine (mg/dl)	0.82	0.77	1.1
Glucose (mg/dl)	109	103	112
ALT (U/liter)	20	22	16
AST (U/liter)	23	18	20
Creatine kinase	56	68	91
LDH (U/liter)	122	135	178
Lactic acid (mmol/liter)	1.6	1.2	0.9
ESR (mm/hr)	12	8	6
CRP (mg/liter)	0.8	0.7	0.9
Ferritin (µg/liter)	312	269	247
D-dimer (ng/ml)	411	346	423

ALT = Alanine aminotransferase, AST = Aspartate Aminotransferase,
LDH = Lactate dehydrogenase, ESR = erythrocyte sedimentation rate, CRP = C-reactive protein

Clinical examination revealed decreased muscle strength and diffused reduction of deep tendon reflexes, with no respiratory signs or symptoms, while Guillain Barré syndrome was suspected. The patient's SARS-CoV-2 IgG/IgM rapid test result was positive and RT-PCR result was negative. She was treated with immunoglobulin (2g/kg) for 6 days. She was discharged on day 8, after experiencing less pain and improved muscle strength. Clinical characteristics and data from laboratory tests are shown in Table 1 and 2 respectively.

DISCUSSION

In this case series of two male and one female patients with an age range of 2-12 years, only one patient had a history of neurological disorder and underwent ventriculoperitoneal shunt for a medulloblastoma. Clinical manifestations included sensory disturbances (Case 2), involuntary movements (Case 1), muscle weakness, and hyporeflexia (Case 3).

In case 1, the patient experiencing seizures remained febrile over the course of the disease; the respiratory symptoms and seizures could be due to a coinfection (6). Recognition of coinfections is important for guidance on clinical evaluation and management of children with COVID-19.

In cases 2 and 3, no respiratory symptoms were present; however, in case 1, the patient did experience respiratory symptoms. It is noteworthy that none of the three pediatric patients experienced severe respiratory complications, unlike adults (7, 8). Likewise, none of the three cases presented with multisystemic inflammatory syndrome, which has been reported as one of the most severe complications in this age group, thereby suggesting that SARS-CoV-2 would exclusively affect the nervous system. Cases

with meningitis and Guillain-Barré syndrome are usually associated with critically ill adult patients (9); this does not occur in the pediatric population, as described in this report, where neurological manifestations occur without other systemic compromises.

Most pediatric patients tested positive due to household contacts (10). In this study, patients in cases 1 and 2 were positive due to household contact, which was confirmed by a rapid test. Information on SARS-CoV-2 penetration into the central and peripheral nervous systems remains unknown; one theory comprises the hematogenous spread of the virus from the systemic to the cerebral circulation, while another comprises dissemination through the cribriform plate into the olfactory bulb (11). Angiotensin-converting enzyme 2 receptors in endothelial cells (brain vasculature) act as entry points for SARS-CoV-2 (12). This report describes COVID-19-associated neurological manifestations in pediatric patients, among which seizures and sensory disturbances are noticeable.

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CONFLICT OF INTEREST

The authors declare no conflicts of interest.

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