Case Report

COVID-19 – Associated Acute Transverse Myelitis in Children: A Case Report and Review of Literature

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ABSTRACT

Background: Several studies have reported neurological manifestations and complications related to specific coronavirus genotypes, including severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). In this study, we examined one of the rare clinical manifestations of Coronavirus disease 2019 (COVID-19), which was one of the first cases of acute transverse myelitis in children in the world.

Case presentation: This case report was dedicated to a little girl with COVID-19 admitted with weakness, lethargy, and constipation. Her magnetic resonance imaging (MRI) showed signal changes accompanied by edema. The patient did not show an optimal response to the methylprednisolone succinate and intravenous human immunoglobulins (IVIG) and experienced cardiorespiratory arrest. The patient was eventually discharged with partial recovery in limb power.

Conclusions: his study demonstrates the importance of rapid diagnosis and treatment of the sequelae of COVID-19 infections.

1. Introduction

At the end of 2019, a new and unknown disease emerged in Wuhan, China. In a few weeks, the global community was affected by pneumonia and acute respiratory distress syndrome caused by the novel coronavirus (1). Our knowledge about the disease caused by SARS-CoV-2, known as COVID-19, is rapidly changing and evolving (2). Although most published studies on SARS-Cov-2 are related to pulmonary and cardiovascular complications, the number of patients with extrapulmonary complications and neurological manifestations has increased and should not be neglected (3). Headache, dizziness, anosmia, taste disturbances, cerebrovascular accident, Guillain-Barre syndrome, acute encephalitis, and acute transverse myelitis are neurological involvement reported in the literature (4).

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Coronaviruses have spherical shapes with club-like projections on their surface, referred to as "spikes." The virus membrane contains four structural components, the spike (S), envelope (E), membrane (M), and nucleocapsid (N) protein. The S protein is the primary determinant for host tropism and pathogenicity. The coronavirus binds to the angiotensin-converting enzyme 2 (ACE2) via protein S and enters the target cell (5). Transverse myelitis refers to the focal inflammation and injury of the spinal cord following viral and bacterial infections. The exact pathophysiology of the disease is unknown and can have different etiologies (6). Here, we report a case of acute transverse myelitis in a child with COVID-19.

2. Case Presentation

The patient was a healthy 4-year-old girl (weight: 16 kg, height: 98 cm) with no history of diseases. She presented to a clinic in the east of Iran with symptoms of weakness, lethargy, constipation, severe pain in the back and right shoulder, and biting lips and tongue. Before her admission to the hospital, her family noticed her symptoms of weakness and lethargy and used hot water vapor as herbal medicine arbitrarily. Their treatment was unsuccessful and led to skin complications and burns. Then, the patient was brought to a hospital and hospitalized. During 5 days of hospitalization, she developed urinary and fecal incontinence. COVID-19 was diagnosed by positive results of both polymerase chain reaction (PCR) test and IgM and IgG antibodies. The values of anti-SARS-CoV-19 IgM and IgG were obtained at 1.5 and 1.3, respectively. For the PCR test, a nasopharyngeal swab specimen was taken. The patient had no previous history of hospitalization or contact with a person with COVID-19 disease. Examination of the limb power at admission showed that the power of her upper left, upper right, lower left, and lower right limbs were 3/5, 2/5, 0/5, and 0/5 respectively, indicating the reduction of power in all limbs.

Sensory examination of the right hand showed that it was numb. The left hand was also somewhat numb. On sensory examination, the patient was touched by hand to assess the sense of touch and examined with a tiny pinch to assess the pain sensation. The patient was fully conscious (Glasgow Coma Scale: 15) and could speak. Deep tendon reflexes were absent. The plantar reflex and the bilateral patellar reflex were unresponsive. The Achilles' reflex in both legs was absent. The biceps reflex of the upper limbs on both sides was also reduced. The physical examination of the eyes revealed bilateral sixth nerve palsy. Gag reflex was absent. There were movements similar to biting the tongue. High-resolution computed tomography (HRCT) of the lung looked normal. Valve and structural examination of the heart was performed twice with echocardiography. Only one mild tricuspid regurgitation was reported, which did not require special action. In the coronary artery examination, no pathological issue was seen, and it was normal. The ejection fraction was 65%. The patient's blood pressure, heart rate, and oxygen saturation were 130/80 mm Hg, 82 beats/min, and 95%, respectively. Table 1 presents the laboratory findings. During the first five days of hospitalization, methylprednisolone succinate was administered at 30 mg/kg/d. The patient was then sent to a pediatric referral hospital in northeast Iran to continue the treatment process and was hospitalized in the pediatric intensive care unit (PICU).

Based on the neurological examination, the patient developed urinary and fecal incontinence, which was exacerbated compared to the first day of hospitalization. Although the results of the neurological and sensory examination on the first day of hospitalization were not available, the patient had a sensory disturbance up to the neck. In spinal primary Magnetic Resonance Imaging (MRI) with contrast (Figure 1), signal changes accompanied by edema were observed in the thoracic and lumbar spinal cord. The patient had plate atelectasis on her left lung base, according to the second HRCT. Lumbar puncture was unsuccessful, so no cerebrospinal fluid (CSF) sample was taken from the patient. The patient was treated with methylprednisolone succinate for another 5 days, accompanied by 5 doses of intravenous human immunoglobulin (IVIG). IVIG was administered at a dose of 400 mg/kg/d, and in total, for 5 days, the received dose was 2 g/kg. Administration of methylprednisolone succinate and IVIG did not lead to a favorable response from the patient, and the force of her limbs did not improve either.

Because of severe edema and inflammation in the spinal cord, it was impossible to obtain cerebrospinal fluid from the lower lumbar region. It was recommended to take a sample from the cervical spinal cord, but it did not happen. The patient underwent plasmapheresis, which was stopped due to hemodynamic disorders after two sessions. Because of hemodynamic disorders and arrest, the patient was transferred to PICU again. The patient regained hemodynamic stability in PICU. She was discharged with stable vital signs, and three-fifths of limb power (all 4 limbs) improved compared to her previous condition. Also, there was a relative improvement in her impaired sense of touch and pain. In the follow-up performed one month after discharge, the force of the limbs was about three-fifths in the right hand and legs and four-fifths in the left hand, which significantly changed compared to the time of admission.

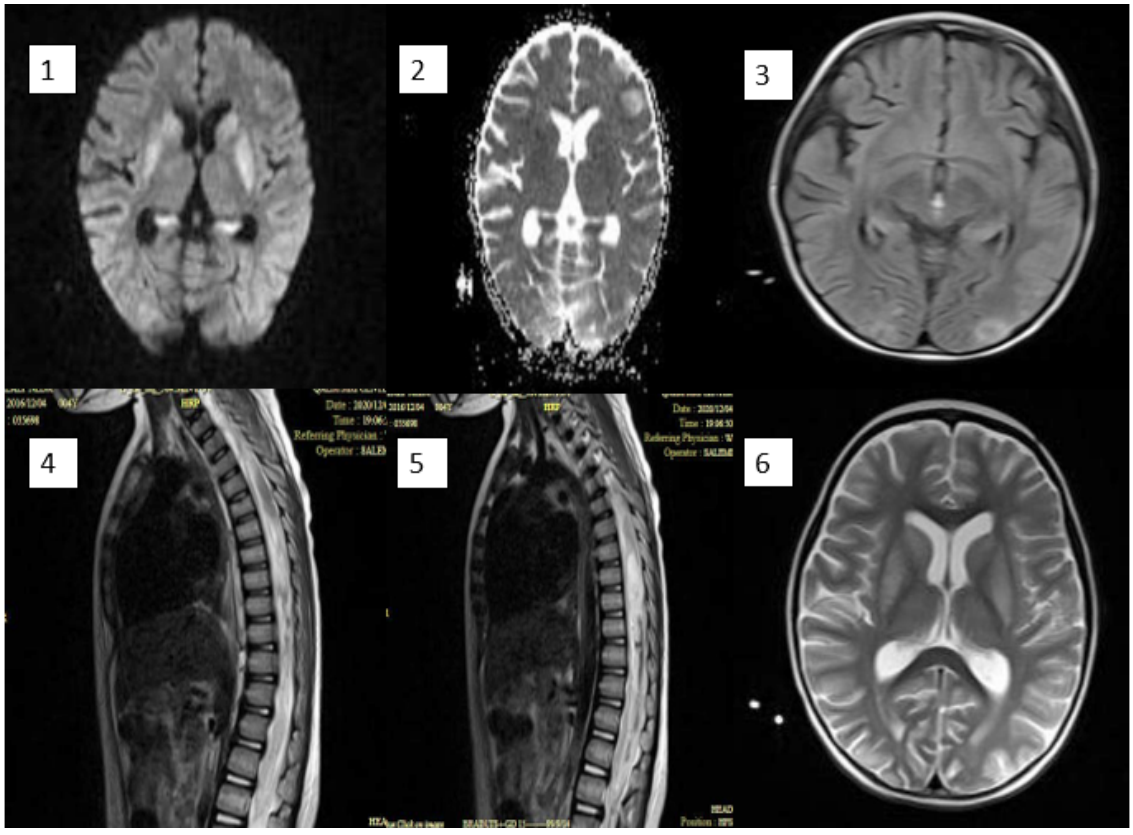

Figure 1. Magnetic Resonance Imaging (MRI) of cervical spine

1: DWI; signal increase in basal ganglia can be seen in the diffusion-weighted sequence, while in the same cut in the ADC map, hyposignal shows restriction in bilateral basal ganglia, 2: ADC map, 3: Axial flair; signal increase in the left Parieto-occipital, 4: T2, 5: injection of enhancement lepto-meningeal, 6: T2; signal increase in the bilateral basal ganglia.

3. Discussion and Review of Literature

Diagnostic criteria of acute transverse myelitis

The extensive spinal cord involvement (multiple pigments) and signal change in MRI with sensory and motor dysfunction raised the possibility of acute transverse myelitis. According to the confirmation of the patient's infection with COVID-19, the diagnosis of acute transverse myelitis due to COVID-19 was strongly proposed. The diagnostic criteria of acute transverse myelitis (that our patient had most of the criteria) are as follows (7):

- Sensory, motor, or autonomic dysfunction attributable to the spinal cord
- Bilateral signs and or symptoms
- Clearly defined sensory level
- No evidence of compressive cord lesion
- Inflammation is defined by cerebrospinal fluid pleocytosis or elevated IgG index, or gadolinium enhancement
- Progression to nadir between 4 and 21 days

From the beginning of the pandemic, SARS-CoV-2 has shown several neurological symptoms or complications in mild and severe cases (8). The case presented here fulfills the criteria of transverse myelitis. Although transverse myelitis has been known as a preliminary sign of neurologic conditions and is associated with some immune system disorders, more than half of cases remain idiopathic. Hence, there is no definite information about the pathophysiology of the disease. Reviewing the history of specific coronavirus genotypes, including the 2002-2004 outbreak of severe acute respiratory syndrome caused by coronavirus (SARS-CoV-1), showed neurotropic properties of the disease (6).

The pathogenesis of this kind of manifestation has not been fully elucidated. Based on evidence from the previous extensive SARS-CoV structural analyses, the COVID-19 virus uses angiotensin-converting enzyme 2

Table 1. Results of laboratory tests

Blood Sugar	**110 mg/dL**	
Urea	35 mg/dL	
Creatinine	0.4 mg/dL	
White blood cells	11.9×103/mL	PMN 76% Lym 16%
Hemoglobin	10.9 g/dL	
Platelets	260×103/µL	
Aspartate aminotransferase	27 IV/L	
Alanine aminotransferase	12 IV/L	
Na	129 meq/L	
K	3.8 meq/L	
Mg	2 mg/dL	
Ca	7.3 mg/dL	
Albumin	2.7 g/dL	
Total protein	4	
Alkaline phosphatase	156 IV/L	
Lactate dehydrogenase (LDH)	1222 IV/L	
Creatine phosphokinase (Cpk)	53 IV/L	
C-Reactive protein (CRP)	74 mg/dL	
Erythrocyte sedimentation rate (ESR)	37 mm/h	
Creatine phosphokinase-MB (CKMB)	35 ng/mL	
Pro Bnp	14.1 pg/mL	
Troponin I (Tpi)	+ ng/mL	
Ferritin	135 ng/mL	
Fibrinogen	484 mg/dL	
D-dimer	12000 ng/mL	
Prothrombin time (PT)	13 s	
International normalized ratio (INR)	1.58	
Partial thromboplastin time (PTT)	35 s	

(ACE2) as a receptor to interact with host cells (9). Given the similarities in the structure and mode of infection of most coronavirus infections (CoVs), it is hypothesized that the infectious mechanisms previously found for other CoVs may also apply to SARS-CoV-2. Neurotropism is a common feature of CoVs, and most βCoVs go beyond respiratory infections and can invade the central nervous system and cause neurological disease (10).

According to Valiuddin et al., COVID-19 can result in an inflammatory cascade and affects the multiple organ systems, while the classic COVID-19 symptoms are absent following inflammatory complications of the spinal cord, which affect the myelin (11). There is no specific treatment for transverse myelitis. Conventional treatments are performed only to prevent or minimize permanent neurological defects. These treatments include corticosteroids and other medications that suppress the immune system, such as plasmapheresis in the absence of a satisfactory response to initial treatment. Relative recovery of the disease lasts three months to two years after the initial diagnosis. The muscle power may not be fully restored, but physiotherapy improves the results (12).

The first case of acute myelitis caused by SARS-CoV-2 was a case of Guillain-Barre syndrome and was reported from a center in Wuhan, China (13). According to Toscanto et al., the PCR assay of cerebral spinal fluid (CSF) had a negative result for many cases of Guillain–Barré syndrome due to SARS-CoV-2 (14). Based on a systematic review regarding Guillain–Barré syndrome associated with SARS-CoV-2 infection, the time interval between the onset of infectious disease and the first neurological symptoms and a negative PCR test result for SARS-CoV-2 in half of the patients suggests a post-infectious unsafe underlying pathological mechanism rather than the direct effect of the virus (15).

Until recently, the number of studies regarding pediatric neurological symptoms of COVID-19 was minimal. As in the case presented in our study, in New Mexico, a 3-year-old girl with progressive extremity weakness and decreased sensation was hospitalized while her PCR was positive for SARS-CoV-2 (16). Gag reflex was absent in both studies. Contrary to our study where the patient had been symptomatic at home, the 3-year-old patient had no symptoms before the onset of weakness.

Another case of acute transverse myelitis in children was an 11-year-old girl referred to the treatment center with symptoms, including lower limbs paresis, urinary and fecal retention, epigastric pain, and fever. The PCR test was positive (6). According to a case series, 4 children with COVID-19 and multisystem inflammatory syndrome who were admitted to ICU had neurological symptoms, including headache, muscle weakness, and decreased reflexes, while they had no underlying condition of neurological disorders or prior symptoms (17). Frank et al. reported a 15-year-old male patient with positive PCR of COVID-19 who was presented with frontal headache and retro-orbital pain along with fever, weakness, and pain in the limbs. They believed that a direct relationship might not be present between the severity of COVID-19 in children and the incidence of neurological manifestations (18).

Ethical Considerations

Compliance with ethical guidelines

Ethical considerations and the confidentiality of patient information were considered.

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Authors' contributions

The authors participated equally in the preparation of the article.

Conflicts of interest

The authors declared no conflict of interest.

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References

1. Karbuz A, Akkoc G, Demirdag TB, Ciftdogan DY, Ozer A, Cakir D, et al. Epidemiological, clinical, and laboratory features of children with COVID-19 in Turkey. Frontiers in Pediatrics. 2021; 9:631547. [DOI:10.3389/fped.2021.631547] [PMID] [PMCID]

2. Christy A. COVID-19: A review for the pediatric neurologist. Journal of Child Neurology. 2020; 35(13):934-9. [DOI:10.1177/0883073820939387] [PMID]

3. Padda I, Khehra N, Jaferi U, Parmar MS. The neurological complexities and prognosis of COVID-19. SN Comprehen-

sive Clinical Medicine. 2020; 2(11):2025-36. [DOI:10.1007/s42399-020-00527-2] [PMID] [PMCID]

4. Chakraborty U, Chandra A, Ray AK, Biswas P. COVID-19-associated acute transverse myelitis: A rare entity. BMJ Case Reports CP. 2020; 13(8):e238668. [DOI:10.1136/bcr-2020-238668] [PMID] [PMCID]

5. Felsenstein S, Herbert JA, McNamara PS, Hedrich CM. COVID-19: Immunology and treatment options. Clinical Immunology. 2020; 215:108448. [DOI:10.1016/j.clim.2020.108448] [PMID] [PMCID]

6. Nejad Biglari H, Sinaei R, Pezeshki S, Khajeh Hasani F. Acute transverse myelitis of childhood due to novel coronavirus disease 2019: The first pediatric case report and review of literature. Iranian Journal of Child Neurology. 2021; 15(1):107-12. [DOI:10.22037/ijcn.v15i1.31579] [PMID] [PMCID]

7. Robert M, Kliegman, Geme JS. Nelson Textbook of Pediatrics, 2-Volume Set, 21st Edition. 2020. https://www.us.elsevierhealth.com/nelson-textbook-of-pedias-.html

8. Zachariadis A, Tulbu A, Strambo D, Dumoulin A, Di Virgilio G. Transverse myelitis related to COVID-19 infection. Journal of Neurology. 2020; 267(12):3459-61. [DOI:10.1007/s00415-020-09997-9] [PMID] [PMCID]

9. AlKetbi R, AlNuaimi D, AlMulla M, AlTalai N, Samir M, Kumar N, et al. Acute myelitis as a neurological complication of Covid-19: A case report and MRI findings. Radiology Case Reports. 2020; 15(9):1591-5. [DOI:10.1016/j.radcr.2020.06.001] [PMID] [PMCID]

10. Li YC, Bai WZ, Hirano N, Hayashida T, Hashikawa T. Coronavirus infection of rat dorsal root ganglia: Ultrastructural characterization of viral replication, transfer, and the early response of satellite cells. Virus Research. 2012; 163(2):628-35. [DOI:10.1016/j.virusres.2011.12.021] [PMID] [PMCID]

11. Valiuddin H, Skwirsk B, Paz-Arabo P. Acute transverse myelitis associated with SARS-CoV-2: A case-report. Brain, Behavior, & Immunity - Health. 2020; 5:100091. [DOI:10.1016/j.bbih.2020.100091] [PMID] [PMCID]

12. Bohmwald K, Gálvez NMS, Ríos M, Kalergis AM. Neurologic alterations due to respiratory virus infections. Frontiers in Cellular Neuroscience. 2018; 12:386. [DOI:10.3389/fncel.2018.00386] [PMID] [PMCID]

13. Zhao K, Huang J, Dai D, Feng Y, Liu L, Nie Sh. Acute myelitis after SARS-CoV-2 infection: A case report. medRxiv. 2020; April. [DOI:10.1101/2020.03.16.20035105]

14. Toscano G, Palmerini F, Ravaglia S, Ruiz L, Invernizzi P, Cuzzoni MG, et al. Guillain-Barré syndrome associated with SARS-CoV-2. The New England Journal of Medicine. 2020; 382(26):2574-6. [DOI:10.1056/NEJMc2009191] [PMID] [PMCID]

15. De Sanctis P, Doneddu PE, Viganò L, Selmi C, Nobile-Orazio E. Guillain-Barré syndrome associated with SARS-CoV-2 infection. A systematic review. European Journal of Neurology. 2020; 27(11):2361-70. [DOI:10.1111/ene.14462] [PMID] [PMCID]

16. Kaur H, Mason JA, Bajracharya M, McGee J, Gunderson MD, Hart BL, et al. Transverse myelitis in a child with COVID-19. Pediatric Neurology. 2020; 112:5-6. [DOI:10.1016/j.pediatrneurol.2020.07.017] [PMID] [PMCID]

17. Abdel-Mannan O, Eyre M, Löbel U, Bamford A, Eltze Ch, Hameed B, et al. Neurologic and radiographic findings associated with COVID-19 infection in children. JAMA Neurology. 2020; 77(11):1440-5. [DOI:10.1001/jamaneurol.2020.2687] [PMID] [PMCID]

18. Frank CHM, Almeida TVR, Marques EA, de Sousa Monteiro Q, Feitoza PVS, Borba MGS, et al. Guillain-Barré syndrome associated with SARS-CoV-2 infection in a pediatric patient. Journal of Tropical Pediatrics. 2021; 67(3):fmaa044. [DOI:10.1093/tropej/fmaa044] [PMID] [PMCID]