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Acute Myelitis Secondary to COVID-19 in an Adolescent: Causality or Coincidence?

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Abstract: Coronavirus disease 2019 (COVID-19) first emerged in Wuhan, China in December 2019. Headache, dizziness, attenuated taste/smell, stroke, acute disseminated encephalomyelitis, encephalitis, Guillain-Barré syndrome, and myelitis are rare neurological symptoms and complications reported in adults. A 14-year-old girl presented with sudden-onset loss of strength in her right arm and leg. A nasopharyngeal swab was collected because the patient had a history of suspicious contact with a confirmed COVID-19 patient. SARS-CoV-2 nucleic acid testing of the patient's nasopharyngeal swab was positive. Her clinical presentation suggested transverse myelitis. On spinal MRI, a contrast-enhancing lesion causing expansion at the C2-C5 level was observed. On day 5 of pulse methylprednisolone treatment, the patient had 3/5 muscle strength in her right upper extremity and 5/5 muscle strength in her right lower extremity. This case emphasizes that during the pandemic, SARS-CoV-2 must be considered as the etiology in children presenting with neurological involvement if there is a history of contact.
Keywords: Acute Myelitis, COVID-19, Child.

1. Introduction

In December 2019, a large outbreak of pneumonia was reported in Wuhan, China (1). The disease, caused by the novel coronavirus SARS-CoV-2, was named Coronavirus disease 2019 (COVID-19) by the World Health Organization (WHO). On March 11, 2020, after the disease spread to dozens of countries, WHO declared COVID-19 a pandemic (2). The first case in Turkey was detected on March 10, 2020 (3).

COVID-19 is highly contagious and its clinical spectrum varies from asymptomatic infection to deadly pneumonia (2).

However, in series of suspected or confirmed COVID-19 pediatric patients, it has been reported that 13 to 27% of children positive for the virus had asymptomatic infection (4).

Coronaviruses damage the central nervous system (CNS) by directly infecting the CNS via the olfactory nerve, peripheral nervous system, and circulation or via the immune response they induce (5).

In such cases, COVID-19 patients exhibit neurological symptoms such as dizziness, headache, altered consciousness, ataxia, epilepsy, muscle involvement, loss of smell and taste, nausea, and vomiting (6,7).

Although cases of encephalopathy, viral encephalitis/meningitis, peripheral neuropathies, and Guillain-Barré syndrome have been reported in adult COVID-19 patients (6-9) there are few studies reporting the neurological involvement of COVID-19 in pediatric patients.

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In this report, we present the case of an adolescent who developed transverse myelitis presumably caused by SARS-CoV-2.

2. Material and Methods

2.1. Case

A 14-year-old girl presented to Atatürk University Faculty of Medicine on April 12, 2020 with sudden-onset loss of strength in her right arm and leg. Her vital signs were as follows: pulse: 82 beats/min, respiratory rate: 21 breaths/min, blood pressure: 115/83 mmHg, oxygen saturation: >97%, and body temperature: 36.9°C.

Other than right hemiplegia, the results of detailed physical and neurological examination were normal.

A nasopharyngeal swab was collected because the patient had a history of suspicious contact with a confirmed COVID-19 patient. SARS-CoV-2 nucleic acid testing of the patient's nasopharyngeal swab was positive. The patient was admitted to the isolation ward. Her clinical presentation suggested transverse myelitis. Cranial magnetic resonance imaging (MRI) was normal. On spinal MRI, a contrast-enhancing lesion causing expansion at the C2-C5 level was observed (shown in Fig 1, A-D). MR spectroscopy was normal. Routine hematological tests, biochemical tests, acute phase reactants, prothrombin time (PT), partial thromboplastin time (PTT), and international normalized ratio (INR) were normal. The patient's test results are presented in Table 1.

Lumbar puncture was performed. Cerebrospinal fluid (CSF) pressure was 170 mm/H_20, protein: 262 mg/dl, chlorine: 127 mmol/L, glucose: 81 mg/dL (simultaneous blood glucose: 105 mg/dL), and no cells were detected. COVID-19 PCR and COVID-IgM/IgG test of the CSF could not be performed.

Chest X-ray was normal. Venous blood IgM tests were negative for Chlamydia pneumoniae, Epstein–Barr virus (EBV) viral capsid antigen (VCA), Mycoplasma pneumoniae, cytomegalovirus (CMV), rubella, toxoplasma, herpes simplex virus 1 and 2, measles, mumps, parvovirus B19, varicella zoster virus.

Nasopharyngeal swab samples were also negative for influenza A virus, influenza A H1N1, influenza A H3N3, Bordetella pertussis, Bordetella parabronchi, Bordetella holmesii, influenza B virus, adenovirus, parainfluenza virus 1, 2, 3, and 4, rhinovirus, human metapneumonovirus (hMPV), and respiratory syncytial virus A and B. Acid-fast bacilli (AFB) staining of CSF was negative and tuberculosis PCR was also negative. Moreover, tests for Sm/RNP, SS-A, SS-B, dsDNA, ANA, pANCA, and cANCA were negative.

Table 1: Results of Routine Blood and Biochemical Tests.

Indicators (normal range)	**Results**	**Indicators (normal range)**	**Results**
White blood cell (4.5-13.5x10^3 μL)	5.36	Calcium (8.8-10.8 mg/dl)	8.5
Hemoglobin (12-16 g/dl)	14.3	Creatine kinase (50-240 U/L)	92
Platelet count (150-450x10^3 μL)	369	Ferritin (11-306 ng/ml)	20.6
Sedimentation (<20 mm/h)	11	Fibrinogen (220-440 mg/dL)	325
Procalcitonin (0.5-2 ng/mL)	0.02	Albumin (3.5-5.6 g/dL)	3.8
D-dimer (0-500 ng/mL)	356	Lactic dehydrogenase (0-248 U/L)	225
Alanine aminotransferase (5-45 U/L)	55	Glucose (60-100 mg/dL)	81
Aspartate aminotransferase (10-40 U/L)	36	Creatinine (0.5-1 mg/dL)	0.53
Troponin I (0-11.6 ng/L)	4.3	Uric acid (2.6-6 mg/dl)	3.6
C-Reactive Protein (0-5 mg/L)	5.07	Prothrombin time (12-16 s)	14.1
Phosphorus (2.9-5.4 mg/dL)	3.5	International normalized ratio INR (0.9-1.3)	1.04
B12 (180-505 pg/mL)	214	Folate (3.1-19.9 ng/ml)	13.3

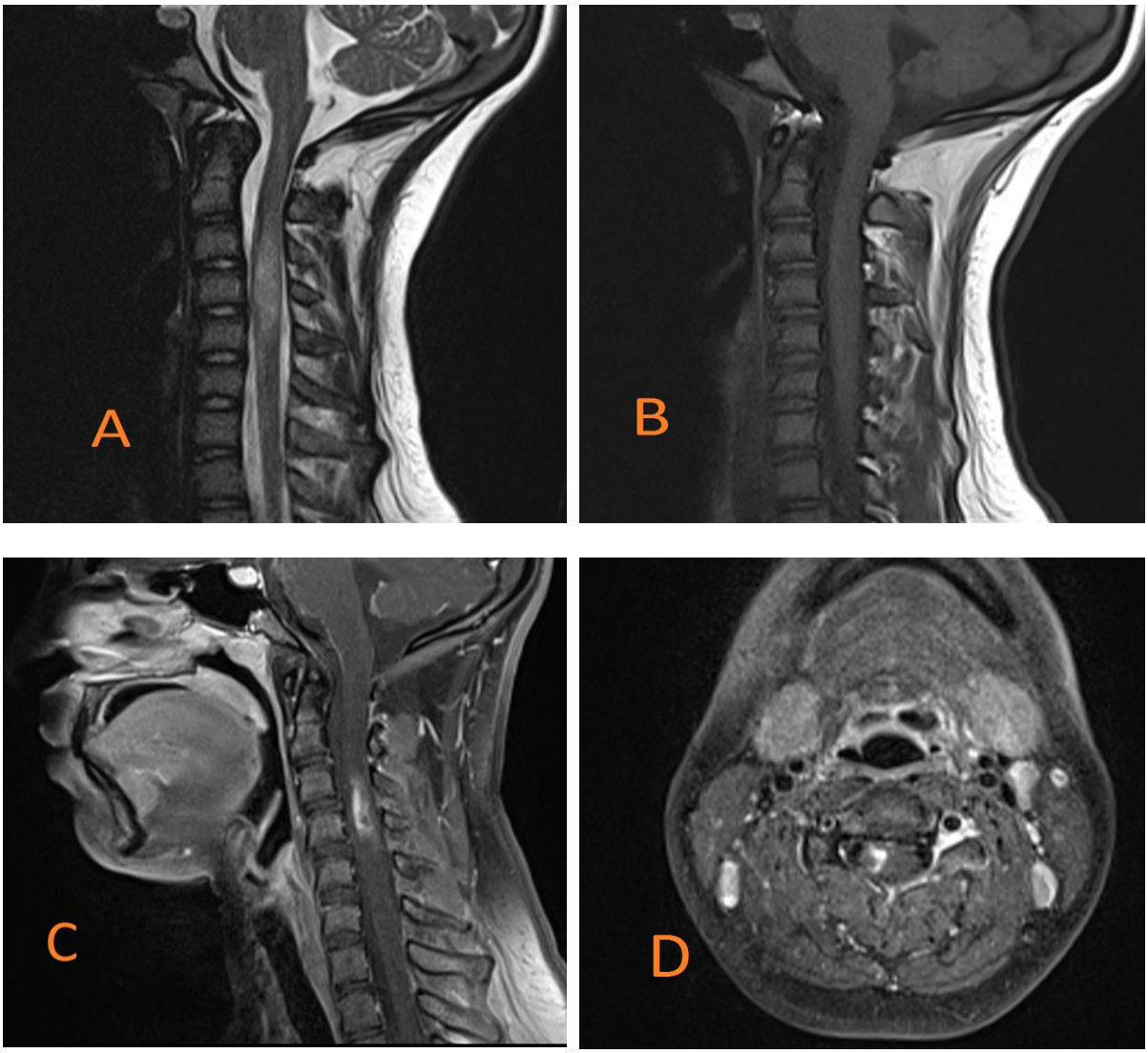

Figure 1: Images of the lesion causing expansion in the medulla spinalis at the C2-C5 level: **A)** Sagittal T2-weighted image showing hyperintense lesion, **B)** Sagittal T1-weighted image showing heterogeneous, iso-hypointense lesion causing medulla spinalis expansion, **C)** Sagittal and **D)** Axial T1-weighted fat-suppressed contrast-enhanced images showing marked irregular contrast enhancement surrounding the lesions.

Transverse myelitis associated with SARS-CoV-2 infection was suspected. Intravenous immunoglobulin (IVIg) was administered at 400 mg/kg/day for 5 days. Fentanyl and gabapentin were initiated for neuropathic pain in the patient's right arm and leg. The patient showed no clinical response to IVIg therapy. Pulse methylprednisolone therapy was given at 30 mg/kg/day for 7 days. On day 5 of steroid treatment, the patient had 3/5 muscle strength in her right upper extremity and 5/5 muscle strength in her right lower extremity.

She exhibited right foot drop, but started to walk unsupported. CSF culture was negative. Serum anti-NMO IgG and CSF oligoclonal band were negative. Serum COVID-19 IgM/IgG test was negative. The patient was recommended home isolation and physical therapy upon discharge 16 days after hospital admission.

3. Discussion

In this report, we present the first pediatric patient with acute transverse myelitis associated with COVID-19. The patient underwent SARS-CoV-2 nucleic acid test due to her history of contact with a confirmed COVID-19 patient and was found to be positive. Moreover, tests for other potential etiologies of acute myelitis were negative. Acute myelitis in this case was either caused by SARS-CoV-2 or occurred coincidentally. However, we believe that the former is more likely.

SARS-CoV-2 enters the human body by binding to ACE2 receptors on cells (10). ACE2 receptors have also been detected on the surfaces of spinal cord neurons (11). Although molecular mimicry is implicated in the pathogenesis of acute myelitis, there may be a relationship between acute myelitis and spinal cord ACE2 receptors. Furthermore, as the liver, bile

ducts, and proximal renal tubules are sites with high ACE2 receptor density like the lungs, COVID-19 can manifest with multiorgan failure in addition to respiratory system signs and symptoms (10).

Many factors play a role in the etiology of postinfectious acute myelitis. The probable pathogenesis of acute myelitis induced by infectious or parainfectious diseases can be explained by the molecular mimicry theory. According to this theory, antigenic structures in the cell walls of pathogenetic microorganisms show antigenic similarity to the surface structures of host neurons. As a result, immune activation against these microorganismic antigens causes cross-reactivity with the antigenic structures on the neuronal surface. This reaction leads to neuronal damage. However, it is not clear why the activated immune system is unable to recognize the host's own cells and tissues (12). Molecular mimic can induce the formation of antibodies that cross-react with self-antigens, leading to immune complex formation and complement-mediated or cell-mediated damage in self tissue (13,14). These autoantibodies may function as an agonist to cellular receptors, altering cellular signaling, metabolism or activity (14). Inflammatory changes were detected in the tissue samples of all patients with a diagnosis of transverse myelitis. These pathologic abnormalities included focal infiltration by monocytes and lymphocytes into segments of the spinal cord and perivascular spaces. Superantigens are peptides capable of stimulating lymphocytes more effectively than conventional antigens. Transverse myelitis may be the fulminant activation of lymphocytes by microbial superantigens. Stimulation of large numbers of lymphocytes can trigger autoimmune disease. Additionally, patients with a diagnosis of transverse myelitis have significantly higher levels of interleukin -6 and nitric oxide in the spinal fluid (15). M. pneumoniae, EBV, CMV, rhinoviruses, and measles are the microorganisms most commonly reported in the etiology (10-12,16).

COVID-19 typically leads to pneumonia characterized by cough, fever, and respiratory distress (1). Neurological involvement in COVID-19 patients is usually reported in adult case studies and manifests with headache, dizziness, and hypogeusia, stroke, coma, and muscle injury (5,6).

Microbiological diagnosis of viral encephalitis is made based on virus isolation, specific IgM positivity, and PCR analysis of the CSF. However, since SARS-CoV-2 titers are very low in the CSF of COVID-19 patients, virus isolation is difficult (17). If we had been able to demonstrate the presence of SARS-CoV-2 in CSF using PCR or specific IgM assay, we could say with more confidence that this case was associated with COVID-19. However, we were unable to perform these tests. Yeh et al. reported a 15-year-old boy with acute disseminated encephalomyelitis in whom human coronavirus (hCoV) was detected in both CSF and nasopharyngeal samples by PCR (18).

Kang Zhao et al. recently reported an adult patient with acute myelitis associated with COVID-19. In their case, acute myelitis was observed together with the typical clinical signs of COVID-19 such as fever, cough, and respiratory distress (10). Moriguchi et al. reported a case of viral encephalitis caused by SARS-CoV-2 in a 24-year-old man. In this case, presence of SARS-CoV-2 in CSF was confirmed via genome sequencing, thus demonstrating that COVID-19 can cause nervous system damage (7). Similarly, among adult COVID-19 patients there are reported cases of Miller Fisher syndrome, polyneuritis cranialis (ageusia, bilateral abducens palsy, areflexia), Guillain-Barré syndrome, encephalopathy, encephalitis, anosmia, acute cerebrovascular disease and stroke (8-10,19).

4. Conclusions

In this report we present the first case of a pediatric patient developing transverse myelitis following SARS-CoV-2 infection and asymptomatic COVID-19. Especially during the pandemic, SARS-CoV-2 should be considered as the etiology in children presenting with neurological involvement if they have a history of risky contact.

Conflict of interest statement

The authors declare that they have no conflict of interest.

References

1. Zhu N, Zhang D, Wang W, et al. A novel coronavirus from patients with pneumonia in China, 2019. *N Engl J Med* **2020**; 382: 727-733.
2. Park SE. Epidemiology, virology, and clinical features of severe acute respiratory syndrome - coronavirus-2 (SARS-CoV-2; Coronavirus Disease-19). *Clin Exp Pediatr* 2020; 63: 119-124.
3. Mehmet Şahin. Impact of weather on COVID-19 pandemic in Turkey. *Sci Total Environ* **2020**; 728: 138810.
4. Bialek S, Gierke R, Hughes M, et al. Coronavirus Disease 2019 in Children United States, February 12–April 2, 2020. *MMWR Morb Mortal Wkly Rep* **2020**; 69: 422-426.
5. YeshunWu, Xiaolin Xu, Zijun Chen, et al. Nervous system involvement after infection with COVID-19 and other coronaviruses. *Brain Behav Immun* **2020**.
6. Werner C, Scullen T, Mathkour M, et al. Neurological Impact of Coronavirus Disease (COVID-19): Practical Considerations for the Neuroscience Community. *World Neurosurg* **2020**; 139: 344-354.
7. Moriguchi T, Harii N, Goto J, et al. A first case of meningitis/encephalitis associated with SARS-Coronavirus-2. *Int J Infect Dis* **2020**; 94: 55-58
8. Consuelo Gutiérrez-Ortiz, Antonio Méndez, Sara Rodrigo-Rey, et al. Miller Fisher Syndrome and polyneuritis cranialis in COVID-19. *Neurology* **2020.**

9. Zhao H, Shen D, Zhou H, et al. Guillain-Barré syndrome associated with SARS-CoV-2 infection: causality or coincidence? *Lancet Neurol* **2020**; S1474-4422(20)30109-5.

10. Zhao K, Huang J, Dai D, Feng Y, et al. Acute myelitis after SARS-CoV-2 infection: a case report. *Med Rxiv* **2020**.

11. Y. Ogata, W. Nemoto, R. Yamagata. Anti-Hypersensitive Effect of Angiotensin (1-7) on Streptozotocin-Induced Diabetic Neuropathic Pain in Mice. *Eur J Pain* **2019**; 23: 739-749.

12. Varina L. Wolf, Pamela J. Lupo, Timothy E. Lotze. Pediatric Acute Transverse Myelitis Overview and Differential Diagnosis. *J Child Neurol* **2012**; 27: 1426-1436.

13. Levin M.C, Lee S.M, Kalume F, et al. Autoimmunity due to molecular mimicry as a cause of neurological disease. *Nat Med* **2002**; 8(5): 509-513

14. DeGiorgio LA, Konstantinov KN, Lee SC, et al. A subset of lupus anti-DNA antibodies cross-reacts with the NR2 glutamate receptor in systemic lupus erythematosus. *Nat Med* **2001**; 7(11): 1189-1193.

15. Krishnan C, Kaplin AI, Deshpande DM, et al. Transverse myelitis: pathogenesis, diagnosis and treatment. *Front Biosci* **2004**; 9: 1483-1499

16. T.W. West, C. Hess, B.A. Cree. Acute Transverse Myelitis: Demyelinating, Inflammatory, and Infectious Myelopathies. *Semin Neurol* **2012**; 32: 97-113

17. Ye M, Ren Y, Lv T. Encephalitis as a clinical manifestation of COVID-19. *Brain Behav Immun* **2020**; S0889-1591(20): 30465-7.

18. Yeh EA, Collins A, Cohen ME, et al. Detection of coronavirus in the central nervous system of a child with acute disseminated encephalomyelitis. *Pediatrics* **2004**; 113(1 Pt 1): 73-76.

19. Ellul M, Benjamin L, Singh B, Lant S, Michael BD, Easton A, et al. Neurological Associations of COVID-19. *Lancet Neurol* **2020**, S1474-4422(20)30221-0.

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