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Acute cerebellitis in SARS-CoV-2 infection: A case report

SARS-CoV-2 enfeksiyonunda akut serebellit: Bir olgu sunumu

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ABSTRACT

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), first identified in Wuhan, China, in December 2019, has emerged as a major global public health threat. The literature on the severe neurological manifestations of coronavirus disease 2019 (COVID-19) has expanded substantially, with numerous studies and reviews documenting a wide spectrum of neurologic involvement. Nevertheless, COVID-19-associated cerebellitis in infants without accompanying systemic symptoms has not been previously described. Herein, we reported the case of a 12-month-old patient who presented with acute ataxia and was diagnosed with COVID-19-associated acute cerebellitis based on characteristic magnetic resonance imaging findings. The patient demonstrated notable clinical improvement following a five-day course of intravenous immunoglobulin. This case highlights the potential of SARS-CoV-2 to mimic diverse neurologic presentations, even in the absence of systemic manifestations, and underscores the importance of maintaining a high index of suspicion for COVID-19 in infants presenting with acute cerebellar dysfunction.

Keywords: Cerebellitis, COVID-19, immunotherapy, intravenous immunoglobulin.

ÖZ

Aralık 2019'da Çin'in Wuhan kentinde ilk kez tanımlanan şiddetli akut solunum sendromu koronavirüsü 2 (SARS-CoV-2), önemli bir küresel halk sağlığı tehdidi olarak ortaya çıkmıştır. Koronavirüs hastalığı 2019 (COVID-19)'un ciddi nörolojik belirtileriyle ilgili literatür önemli ölçüde genişlemiş olup, nörolojik tutulumun geniş bir yelpazesini belgeleyen çok sayıda çalışma ve derleme bulunmaktadır. Bununla birlikte, ek sistemik semptomlar olmaksızın infantil dönemde görülen COVID-19 ile ilişkili serebellit daha önce tanımlanmamıştır. Bu raporda, akut ataksi ile başvuran ve karakteristik manyetik rezonans görüntüleme bulgularına dayanarak COVID-19 ile ilişkili akut serebellit tanısı alan 12 aylık bir hasta sunuldu. Hasta, beş günlük intravenöz immünoglobulin tedavisinin ardından belirgin klinik iyileşme gösterdi. Bu olgu, SARS-CoV-2'nin sistemik bulgular olmaksızın bile çeşitli nörolojik prezentasyonları taklit edebileceğini göstermekte ve akut serebellar disfonksiyon ile başvuran infantlarda COVID-19 için yüksek düzeyde klinik şüphe gerekliliğini vurgulamaktadır.

Anahtar Sözcükler: Serebellit, COVID-19, immünoterapi, intravenöz immünoglobulin.

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Although coronavirus disease 2019 (COVID-19) is generally asymptomatic or follows a mild to moderate course in children, severe cases have also been reported.[1-3] Emerging evidence indicates that COVID-19 can present with a range of neurological manifestations. During the pandemic, both central and peripheral nervous system involvement has been documented in adults and children infected with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). In pediatric patients, reported neurologic findings include headache, anosmia, encephalitis, seizures, acute disseminated encephalomyelitis, acute necrotizing hemorrhagic encephalopathy, cerebellar ataxia, myositis, and Guillain-Barré syndrome.[4-8] However, only a limited number of studies have described an association between COVID-19 and acute cerebellitis in children. Herein, we reported an infant with acute cerebellitis who tested positive for COVID-19 on nasopharyngeal reverse transcription polymerase chain reaction.

CASE REPORT

A previously healthy 12-month-old female patient presented with a six-day history of ataxia and head titubation, as well as vomiting and sleeplessness for the preceding two days. The patient was admitted directly to the hospital. There was no known history of COVID-19 exposure or recent infection. Upon admission, the patient tested positive for COVID-19 on a nasopharyngeal reverse transcription polymerase chain reaction (RT-PCR) test, despite having no respiratory symptoms. Neurological examination revealed truncal ataxia, head titubation, and increased deep tendon reflexes in the bilateral lower extremities, while reflexes in the upper extremities were normoactive. No signs of meningeal irritation were observed. Vomiting and sleeplessness were also noted based on clinical history.

The complete blood count showed lymphopenia, with a lymphocyte count of $0.27\times10^3/\mu L$ (normal range: $1\text{-}3.5\times10^3/\mu L$). C-reactive protein level, erythrocyte sedimentation rate, creatine kinase, liver function tests, electrolytes, serum vitamin B12, fibrinogen, and ferritin levels were all within normal limits. The nasopharyngeal SARS-CoV-2 RT-PCR test was positive. Cerebrospinal fluid (CSF) analysis revealed a protein level of 86 mg/dL (normal range: 15-45 mg/dL) and a glucose level of 65 mg/dL (normal range: 40-70 mg/dL), with a corresponding serum glucose level of 112 mg/dL. The CSF demonstrated mild pleocytosis (five nucleated cells), with 92% lymphocytic predominance. Cerebrospinal fluid RT-PCR for SARS-CoV-2 was negative. The CSF meningitis PCR panel, which detects pathogens such as *Cryptococcus neoformans/gattii, Streptococcus pneumoniae*, *Streptococcus agalactiae*, *Neisseria meningitidis, Listeria monocytogenes, Haemophilus influenzae, Escherichia coli* K1, herpes simplex viruses 1, 2, and 6, cytomegalovirus, human parechovirus, and enterovirus, showed no evidence of infection. Cerebrospinal fluid culture, Lyme disease panel, and cryptococcal antigen testing were all negative. West Nile virus immunoglobulin (Ig) M and IgG, varicella-zoster PCR, and VDRL PCR were all negative.

Serum and CSF paraneoplastic and autoimmune panels were negative for anti-gamma-aminobutyric acid (GABA) B receptor, anti-AMPA receptor, anti-Yo, anti-Hu, anti-Ri, anti-glutamic acid decarboxylase, anti-NMDA (N-methyl-D-aspartate) receptor, anti-CASPR2 (contactin-associated protein 2), and LGI1 (leucine-rich glioma-inactivated protein 1) antibodies. Background electroencephalograhic activity was within normal limits.

Contrast-enhanced magnetic resonance imaging (MRI) revealed cortical hyperintensity in the cerebellar folia on axial T2-weighted images. Diffusion-weighted imaging/apparent diffusion coefficient sequences showed restricted diffusion consistent with cytotoxic edema in the same region. Magnetic resonance imaging angiography was normal. These findings were indicative of cerebellitis (Figure 1). A chest radiograph was obtained due to the COVID-19 diagnosis, but no abnormalities were detected.

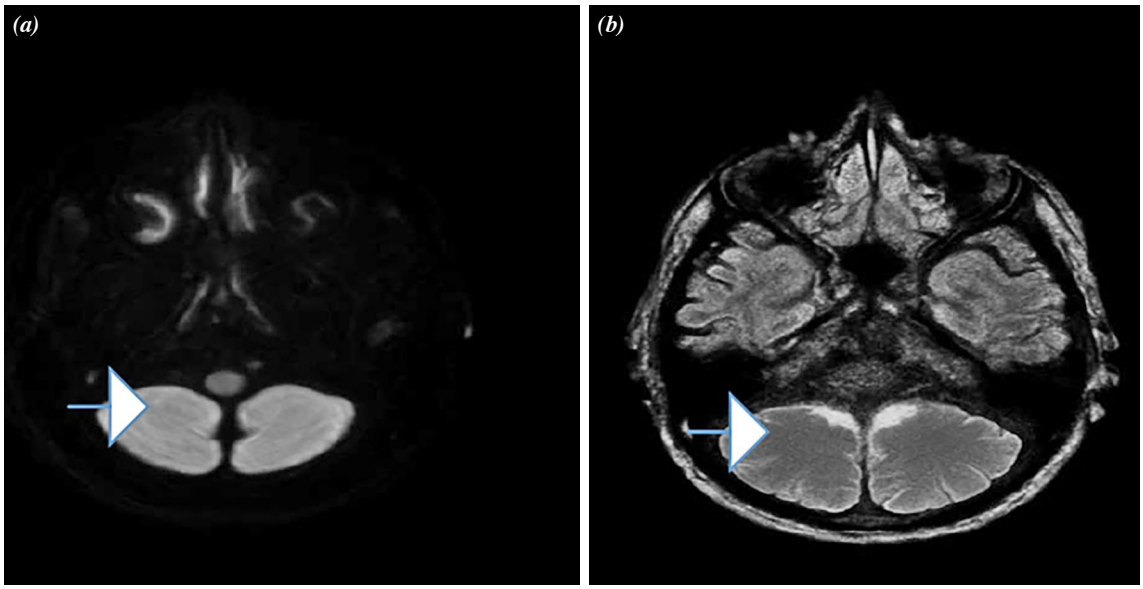

Figure 1. ***(a)*** *Diffusion-weighted cranial magnetic resonance imaging with tetra brightness in the cerebellar parenchyma, and* ***(b)*** *its equivalent axial T2-weighted images.*

After all examinations, the patient was diagnosed with acute cerebellitis. To initiate treatment, ceftriaxone, vancomycin, and acyclovir were administered. The patient received intravenous Ig for five consecutive days at a dose of 400 mg/kg. However, antibiotics were discontinued after CSF Gram stain, culture, and herpes simplex virus panel results returned negative on the fifth day.

By the third day following initiation of intravenous Ig therapy, the patient demonstrated emerging signs of cerebellar dysfunction, characterized by ataxic gait, titubation, and impaired coordination of voluntary movements. Lymphopenia resolved by the sixth day of treatment. The patient's condition gradually improved over time, and she was discharged on the 10th day. At the one-month follow-up, the patient remained symptom-free and at her cognitive baseline. A repeat diffusion-weighted brain MRI demonstrated complete resolution of the pathological signal changes in the cerebellar hemispheres. Written informed consent for publication was obtained from the parents of the patient.

DISCUSSION

In this report, we presented a case of a previously healthy child who was diagnosed with acute cerebellitis and COVID-19. The child's condition improved following treatment with intravenous immunoglobulin. Acute cerebellitis in children has been associated with various pathogens, including varicella-zoster virus, herpes simplex virus, Epstein-Barr virus, rotavirus, echovirus, coxsackievirus, mumps, measles, and rubella. In our patient, SARS-CoV-2 was considered a likely etiologic agent, supported by a positive nasopharyngeal RT-PCR test, while no alternative infectious causes were identified. The negative CSF culture and the elevated CSF protein level were also supportive of a COVID-19-related inflammatory process. Cerebellar ataxia associated with infection can be classified into two categories: acute cerebellitis and parainfectious or postinfectious/vaccinal cerebellar ataxia. Differentiation between these entities is based on the onset and timing of ataxia, the patient's mental status, and MRI findings.[9,10] Diagnosis of cerebellitis typically involves brain MRI and lumbar puncture to exclude alternative etiologies.[11]

Acute cerebellitis may present with a wide range of severity, from mild and self-limiting forms to rapidly progressive and severe disease. Truncal ataxia and head titubation are key clinical findings that support the diagnosis of acute cerebellitis. Although rare, this condition carries significant risk. The associated inflammation can lead to increased intracranial pressure, which may become life-threatening due to brainstem compression and the potential for subsequent herniation.[12,13] In our patient, moderate acute cerebellar inflammation was observed.

Coronavirus disease 2019 has been linked to various neurological disorders, including acute disseminated encephalomyelitis, stroke, Guillain-Barré syndrome, and encephalopathy, although acute cerebellitis associated with COVID-19 has only been reported a few times.[14] A study by Sharma et al.[13] described two children with cerebellitis related to acute COVID-19 infection, both of whom recovered rapidly and showed significant clinical improvement. Physicians should be aware that neurological symptoms in COVID-19 may reflect an abnormal immune response, and further research is needed to clarify these mechanisms.[15,16] We diagnosed our patient with COVID-19-related cerebellitis based on a positive COVID-19 PCR test, a negative CSF PCR test for SARS-CoV-2, clinical signs of cerebellar dysfunction, and MRI findings consistent with cerebellar involvement without an alternative explanation. Our case is compatible with the existing literature in this regard. Despite being diagnosed with moderate COVID-19 cerebellitis, the patient received prompt and appropriate treatment and achieved a favorable clinical outcome.

In conclusion, pediatricians should recognize that COVID-19 can present with neurological manifestations that mimic other conditions. In this case, the patient exhibited signs of acute viral cerebellitis upon hospital admission, despite the absence of typical systemic symptoms of COVID-19. This report is particularly noteworthy as it involves the youngest documented patient with COVID-19-associated acute cerebellitis, underscoring the need for heightened clinical vigilance for SARS-CoV-2 infection in infants presenting with severe neurological symptoms.

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