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Case Report

Acute cerebellar ataxia during acute COVID-19: A case series and review of the literature

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ABSTRACT

Acute coronavirus disease 2019 (COVID-19)-associated cerebellar ataxia without multisystem inflammatory syndrome in children (MIS-C) or encephalopathy in children has been rarely reported. We reviewed medical records of hospitalized children who had developed cerebellar ataxia during the acute phase of COVID-19 infection, without MIS-C or encephalopathy, in our center. We also conducted a literature review and summarized the clinical characteristics, treatment, and outcomes. We found three cases in our center and additional three cases in the literature. All patients were male and five were preschool children. The cerebellar symptoms started between day 2 and day 10 during the acute phase of the COVID-19 infection. Two cases were complicated by mutism. One patient received therapy for acute cerebellar ataxia with corticosteroids, and others did not receive any specific therapy for acute cerebellar ataxia. The symptoms improved completely in all patients, with the recovery interval ranging from one week to two months. Further studies are warranted to elucidate the pathogenesis of acute cerebellar ataxia during acute COVID-19 in children.

1. Introduction

Coronavirus disease 2019 (COVID-19), caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV2) is not just a respiratory infection, but a systemic disease affecting almost every organ, including the central and peripheral nervous systems [1]. The neuromuscular symptoms have been well described in adults [1]. Systematic reviews, mainly in adults, have shown that neurological symptoms were observed in more than 90% of hospitalized patients in the acute phase of COVID-19 [1]. Major symptoms include dizziness, headache, myopathy, dysgeusia, and dyssomnia, whereas cerebellar ataxia rarely occurs [1]. There are even fewer reports of pediatric patients with COVID-19-associated cerebellar ataxia, and most of them had multisystem inflammatory syndrome in children (MIS-C) or encephalopathy [2,3]. Cerebellar ataxia in pediatric patients without MIS-C has rarely been reported.

We described three cases of children with acute COVID-19-associated cerebellar ataxia, without MIS-C or encephalopathy, and performed a review of the literature.

2. Case report

A 20-month-old boy presented to the emergency department with recurrent febrile clonic convulsions within 24 hours and loss of consciousness. He was born after an uneventful pregnancy, and his developmental milestones were normal; he started walking independently at 12 months old and using two-word sentences at 18 months old. He and his 3-year-old brother had a history of febrile seizures. Two hours after the convulsions, he woke up and could follow his mother with his eyes but did not speak any words. He had a high temperature of 40.1 °C and a Glasgow coma scale score of 11/15 (E4, V1, M6) without other symptoms, such as cough, vomiting, or headache. Physical examination revealed normal pupil reaction to light and muscle tone, without myoclonus, involuntary movements, or meningeal signs. Commercial

Abbreviations: COVID-19, Coronavirus disease 2019; MIS-C, multisystem inflammatory syndrome in children; SARS-CoV2, severe acute respiratory syndrome coronavirus 2.

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Table 1
Characteristics of six cases of acute cerebellar ataxia associated with acute COVID-19.

	Age	Sex	Past history	Neurological symptoms	Symptoms related to ataxia	Latency	Brain imaging	Ancillary testing	Treatment	Outcome
Case 1	1y 8 m	Male	Febrile seizure	Acute ataxia Mutism Febrile seizure	Gait disorder Dysmetria Intention tremor	Day 2	CT: Unremarkable MRI: Unremarkable	Hyponatremia High lactate level CSF: Unremarkable	Observation	Improved in a week
Case 2	1y 4 m	Male	Febrile seizure	Acute ataxia Febrile seizure	Gait disorder	Day 5	No imaging		Observation	Improved in a week
Case 3	1y 8 m	Male	None	Acute ataxia Mutism Febrile seizure	Gait disorder	Day 2	CT: Unremarkable	Hyponatremia RSV coinfection CSF: Unremarkable EEG: Unremarkable	Antibiotics	Improved in a week
Tomar LR, 2021 [4]	13y	Male	None	Acute ataxia Dysarthria	Nystagmus Gait disorder Dysmetria	Day 10	MRI: Unremarkable	CSF: Unremarkable	Steroid pulse therapy[a]	Improved in 20 days
O'Neill KA, 2021 [5]	5y	Male	Type 1 Diabetes mellitus	Acute ataxia Dysarthria	Truncal ataxia Dysmetria Double vision	Day 8	MRI: Unremarkable	Hyponatremia Hyperglycemia CSF: Unremarkable	Observation	Improved in 2 months
Sanchez MAE, 2021 [6]	2y	Male	None	Acute ataxia	Unknown	Unknown	Unknown	CSF: Proteins 89, Cells 6	Observation	Improved

MRI, magnetic resonance imaging; CT, computed tomography; CSF, cerebrospinal fluid; EEG, electroencephalogram; RSV, respiratory syncytial virus.
[a] Steroid pulse therapy was intravenous methylprednisolone 500 mg once daily for 5 days.

multiplex respiratory PCR assay by FilmArray (BioFire Diagnostics, Salt Lake City, UT) using a nasopharyngeal sample was positive for SARS-CoV-2 but negative for all the other twenty pathogens. The laboratory data indicated mild hyponatremia (132 mEq/L) and normal range of white blood cell count (6.35×10^9/L), serum C-reactive protein (0.01 mg/dL), and transaminases. A lumbar puncture revealed no pleocytosis (white blood cells <1/μL), total protein content of 13.9 mg/dL, and glucose of 67 mg/dL when serum glucose was 94 mg/dL; CSF analysis was normal. Cultures of the cerebrospinal fluid, blood, and urine were all negative. The brain computed tomography (CT) showed no brain edema, hemorrhage, or space-occupying lesions. The chest radiograph showed no signs of cardiomegaly or pulmonary infiltrates.

He was administered a 22.5 mg/kg/dose of fosphenytoin sodium hydrate to prevent the recurrence of seizures and was admitted to our hospital to monitor neurological manifestations. On the second day of hospitalization, he became afebrile, and could eat a meal. However, he became unstable and required support to maintain his sitting position. He could neither stand up nor speak, and also had dysmetria on both upper extremities. During a video chat with his mother on the third day, he cried but did not speak any meaningful words when his name was called. Although his muscle tone and deep tendon reflexes were normal, his Glasgow Coma Scale score was still 11/15 (E4, V1, M6). Brain magnetic resonance imaging (MRI) showed no significant findings. We diagnosed acute cerebellar ataxia and mutism. His neurological symptoms gradually recovered, and he could maintain a stable sitting position on the fifth day, start standing on the sixth day, and could walk independently and speak meaningful words on the seventh day. On the tenth day, he was able to run around, and talk without dysmetria.

We conducted a systematic search for pediatric patients with acute cerebellar ataxia associated with COVID-19. We searched in MEDLINE and the Cochrane Library using the following terms: ["COVID-19" OR "coronavirus" OR "SARS-CoV-2"] and ["ataxia"] with filter of "children" (birth to 18 years old), excluding cases that are associated with encephalopathy or MIS-C. We also reviewed medical records of patients with COVID-19 who were admitted to the National Center for Child Health and Development, a tertiary care children's hospital in Tokyo, from July 1, 2020 to August 31, 2022. Patients were excluded if they had encephalopathy or MIS-C. We excluded children if we could not obtain written and oral informed consent from their parents.

Table 1 summarizes the clinical characteristics of children presenting with COVID-19-associated cerebellar ataxia who did not have encephalopathy or MIS-C. We found a total of seven patients (four admitted to our hospital and three from the previous reports) [4–6]; however, parents of one patient did not consent to medical research participation. We, therefore, included six patients in this report. All patients were male, and five (83%) were younger than 6 years old (preschool children). One patient had an underlying disease (type I diabetes mellitus) [5]. Four patients did not receive COVID-19 vaccines and vaccination status of two patients was unknown. The symptoms were limb or truncal ataxia (100%), dysmetria (50%), dysarthria (33%), and mutism (33%). Three patients presented with ataxia after febrile seizures. The cerebellar symptoms began between day 2 and day 10 during the acute phase of COVID-19 infection. Four patients underwent brain imaging (two MRI and three CT scans) without significant findings. One patient was treated with corticosteroids, and the others did not receive any specific therapies. Signs and symptoms of cerebellar ataxia improved completely in all patients, and the interval to recovery ranged from one week to two months.

3. Discussion

This study shows the clinical characteristics of six children with cerebellar ataxia in the acute phase of COVID-19. The majority of them were preschool boys who recovered within two months without specific treatment. None had underlying diseases predisposing them to cerebellar ataxia. As far as we know, this may be the first case series of cerebellar ataxia associated with COVID-19 in children.

A retrospective study of acute cerebellar ataxia in 120 children before the emergence of COVID-19 showed that the most common etiology was infection (59%), 85% of the patients were one to six years old, and the majority of them (91%) recovered within 30 days [7]. Acute cerebellar ataxia is also known to be slightly more common in boys than girls [8]. The results of our study were generally consistent with these previous reports.

In this study, two of six patients developed mutism. This symptom improved parallel to the recovery from cerebellar ataxia suggesting that mutism was one of the manifestations of cerebellar ataxia. Mutism is known as a rare manifestation of acute cerebellar ataxia, cerebellitis, and status post posterior fossa surgery [9]. Interestingly, adults with COVID-19-associated ataxia rarely present with mutism. One report described ataxia associated with COVID-19 that occurred in 0.3% of adult patients [1], with major concurrent neurological findings, including cognitive changes (45.5%), myoclonus (36.4%), and the Miller-Fisher variant of Guillain-Barré Syndrome (21.2%), whereas mutism has rarely been reported [10]. Mutism may be a relatively characteristic manifestation of acute COVID-19-associated cerebellar ataxia in children, implying that pathogenesis in children is different from that in adults. Further accumulation of similar cases is required.

This study has several limitations. First, the results of brain MRI examination were obtained in only three of six patients, and encephalopathy, such as MERS (mild encephalitis/encephalopathy with a reversible splenial lesion), might not have been completely excluded in some patients. However, clinical encephalopathy was not evident in our case series. Second, we cannot fully rule out the possibility that the symptoms of acute ataxia resulted from febrile seizures in some cases. However, as mental status and neurological symptoms other than cerebellar ataxia improved promptly, we believe that acute ataxia was unlikely to be directly related to febrile seizures.

In conclusion, we systematically reviewed COVID-19-associated cerebellar ataxia in six children. The majority of them were preschool boys who improved without any specific therapeutic intervention; two cases were complicated with mutism. Further studies are required to elucidate the pathogenesis and risk factors associated with acute cerebellar ataxia during acute COVID-19.

Conflicts of interest disclosures

The authors declare no conflicts of interest associated with this manuscript.

Authorship statement

HT and RO wrote the first draft of the manuscript. HI and IH modified and reviewed the manuscript. CO supervised and revised the manuscript. All authors approved the final manuscript.

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