Guillain-Barré Syndrome in a Child With Multisystem Inflammatory Syndrome Related to COVID-19

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Abstract: Guillain-Barré syndrome has been associated with acute severe acute respiratory syndrome coronavirus 2 infection in children. Here, we report a 4-year-old boy who developed Guillain-Barré syndrome in the course of multisystem inflammatory syndrome related to COVID-19.

Key Words: Guillain-Barré syndrome, multisystem inflammatory syndrome, child, COVID-19

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COVID-19 infection is more likely to be asymptomatic or has a mild to moderate disease course in children. Most reported symptoms in a systematic review were fever, cough, sore throat, rhinorrhea, nose obstruction and gastrointestinal manifestations.

A novel syndrome in children and adolescents termed multisystem inflammatory syndrome in children (MIS-C) related to COVID-19 was reported. This condition similar to Kawasaki disease is characterized by persistent fever, multiorgan involvement (≥2), elevation of inflammatory markers, linked to severe acute respiratory syndrome (SARS) coronavirus 2 (CoV-2) (positive real-time polymerase chain reaction or serology) and the exclusion of other infections. Both acute COVID-19 infection and MIS-C syndrome in children can lead to several neurologic disorders [headache, meningoencephalitis, ischemic stroke, intracerebral hemorrhage, seizure, Guillain-Barre syndrome (GBS) and acute disseminated encephalomyelitis]. Most of these neurologic manifestations occurred in the course of MIS-C syndrome.

GBS has not been reported as neurologic complication of MIS-C.

In this paper, authors report the case of a 4-year-old boy admitted to pediatric department for GBS associated with MIS-C post-COVID-19 infection. Parental informed consent was taken to publish the case.

CASE PRESENTATION

A previously healthy 4-year-old boy was admitted for prolonged fever evolving in the past 2 weeks and inability to walk. He presented diarrhea and progressive, ascending weakness for the last 3 days.

The initial clinical examination was as follows: body temperature: 38.2 Celsius, pulse rate: 81 BPM; blood pressure: 100/65 mm Hg. Respiratory status was stable with a respiratory rate at 24 breaths/min and pulse oximetry of 99% at ambient air. Pediatric Glasgow coma scale 15/15, there was no sign of neurologic focalization nor swallowing disorder. Deep tendon reflexes were absent in lower extremities bilaterally with inability to walk. He had arthritis of the right elbow.

Blood test revealed microcytic hypochromic anemia (8.5g/dL), normal white blood cell count (6000 cells per microliter), C reactive protein 200mg/L (normal value: <5mg/L), blood sedimentation rate 44mm, D-Dimers 360 μg/L (normal value: <500), sodium 139 mmol/L, potassium 4.6 mmol/L, urea 3.9 mmol/L, creatinine 27 μmol/L, alanine amino transferase 139 UI/L (normal range: 8–31) and aspartate amino transferase 196 UI/L (normal range: 17–43).

SARS-CoV-2 real-time reverse transcription polymerase chain reaction on nasopharyngeal swab was negative, while SARS-CoV-2 antibody testing was positive. Echocardiography, performed to rule out signs of MIS-C, showed correct ventricular systolic function and left ventricular concentric hypertrophy, dilated left main coronary artery with aneurysm of 5 mm. The right coronary artery was not dilated.

These clinical and echocardiography findings with positive SARS-CoV-2 antibody testing, fulfilled the criteria of MIS-C syndrome related to COVID-19. Electroneuromyography showed acute inflammatory demyelinating polyradiculoneuropathy compatible with GBS.

Lumbar puncture was not performed. The diagnosis of GBS associated with MIS-C post-COVID-19 was established; and the patient was treated with intravenous immunoglobulin 2 kg/g with methylprednisolone intravenous (2mg/kg/d for 3 days switched by oral corticosteroids). The patient improved gradually and was discharged on day 10 with prednisolone 2 mg/kg/d to be tapered after three weeks, and aspirin 5mg/kg/d. After 1-month follow-up, he remained symptom-free and he had normal neurologic examination. Echocardiography performed after 15 days showed left ventricular hypertrophy and dilation of the left coronary artery (4 mm).

DISCUSSION

We describe a case of GBS in a pediatric patient with MIS-C related to SARS-CoV-2 infection. The diagnosis of GBS was established on the association of progressive, relatively symmetrical weakness with absent myotatic reflexes and electroneuromyography showed acute inflammatory demyelinating polyradiculoneuropathy. Furthermore, our patient met all WHO’s criteria of MIS-C: he presented fever lasting for more than 3 days, diarrhea and cardiac aneurysm associated with elevated inflammatory markers and the presence of antibodies against SARS-CoV-2. Arthritis of the right elbow may be part of MIS-C.

SARS-CoV-2 could be responsible for many neurologic manifestations, which can be divided into 3 different scenarios, related to the presumed pathophysiologic mechanism: neurologic involvement during acute COVID-19; neurologic involvement that arises after the recovery from COVID-19 and neurologic involvement during MIS-C.

Two mechanisms were suggested to explain how SARS-CoV-2 may induce neurologic damage such as GBS: direct viral infection of nervous system through angiotensin-converting enzyme 2 receptors and inflammatory injury mediated by cytokines.
release\(^6,7\); this para-infectious process is attested by the detection of SARS-CoV-2 virus in the cerebrospinal fluid of at least 2 published cases of COVID-19 associated with GBS.\(^8,9\) GBS and other neurological manifestations can be part of MIS-C indirect mechanism: the cytokine storm, characterized by high levels of tumor necrosis factor \(\alpha\), interleukin (IL)-1\(\beta\), IL-6, IL-12 and interferon \(\gamma\). The integrity of the blood-brain barrier may be disrupted by cytokine-driven injury without nervous system direct invasion by the virus.\(^10\)

In our case, the immune mediated phenomenon in MIS-C associated GBS seems plausible.

Nepal et al\(^10\) in a meta-analysis published in 2021 proclaimed that overall neurological manifestations in MIS-C patients was 27.1%. The main symptoms in MIS-C patients were headaches (27%), meningism/meningitis (17.1%) and encephalopathy (7.6%).

Other neurological complications in the course of MIS-C were reported such as acute cerebellitis,\(^11\) acute disseminated encephalomyelitis,\(^4\) seizure,\(^12\) pseudotumor cerebri,\(^13\) cerebral edema,\(^14\) stroke\(^15\) and ocular myasthenia.\(^16\)

Although COVID-19-associated GBS has been observed in children, the association of MIS-C and GBS has not, to the best of our knowledge, been reported before.

**CONCLUSIONS:**

Several neurological complications were observed in the course of MIS-C. Our case highlights that neurologic complications may be possibly due to an immunological reaction, to the virus.

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