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Guillain-Barré Syndrome in a Child With COVID-19 Infection

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Drs Curtis, Bhumbra, Jordan, Friedman, Felker, Kim and Weber conceptualized and designed the study, drafted the initial manuscript, and reviewed and revised the manuscript. All authors approved the final manuscript as submitted and agree to be accountable for all aspects of the work.

Abbreviations:
Guillain-Barré Syndrome (GBS), Severe acute respiratory syndrome coronavirus 2 (SARS-CoV2), novel coronavirus disease 2019 (COVID-19), Acute Inflammatory Demyelinating Polyradiculoneuropathy (AIDP), pediatric intensive care unit (PICU), negative inspiratory force (NIF), intravenous immunoglobulin (IVIG)

Table of Contents Summary:
This is the first reported case of Guillain-Barré Syndrome in a child associated with infection with novel coronavirus disease 2019.
Abstract

Guillain-Barré Syndrome is characterized by a monophasic, ascending, and symmetrical paralysis with areflexia that progresses over days to weeks. It is typically a post-infectious autoimmune process that leads to destruction of myelin. Severe acute respiratory syndrome coronavirus 2 (SARS-CoV2), originated in Wuhan, China in late 2019 and rapidly spread around the world causing a pandemic of novel coronavirus disease 2019 (COVID-19). There have been scattered reports of adults with possible GBS and concurrent evidence of COVID-19, but no previous reports in children.

The patient is an 8-year-old male who presented to the emergency department with progressive, ascending weakness with areflexia. He was intubated for airway protection due to poor secretion control. MRI of the spine revealed abnormal enhancement of posterior nerve roots. A lumbar puncture demonstrated albuminocytologic dissociation with 1 nucleated cell/cumm and protein of 620 mg/dl. Electrodiagnostic findings were compatible with sensorimotor demyelinating polyneuropathy. The lumbar puncture, MRI and electrodiagnostics were all consistent with GBS. SARS-CoV2 nucleic acid amplification and SARS-CoV2 IgG antibody were positive. Treatment was initiated with intravenous immunoglobulin, he received a total of 2 g/kg. His neurological exam demonstrated improvement in the following days. He was extubated after 4 days of intubation.

This case illustrates the first reported case of a child with Guillain-Barré Syndrome in the setting of an acute COVID-19. This case shows the wide scope of presentations of COVID-19 and post-infectious processes. Clinicians should constantly have a high level of suspicion for COVID-19.

Introduction:

Guillain-Barré Syndrome (GBS) is the most common cause of severe, acute weakness in children, and Acute Inflammatory Demyelinating Polyradiculoneuropathy (AIDP) is the most common subtype in the western world.1 GBS is characterized by a monophasic, ascending, and symmetrical paralysis that progresses over days to weeks and is associated with areflexia. AIDP is typically a post-infectious autoimmune process believed to be caused by molecular mimicry to peripheral nerves leading to inflammation and destruction of myelin. Preceding infection can be identified in the majority of cases. The most common infectious triggers are minor respiratory illness, but gastrointestinal illnesses, other viral syndromes and immunizations have also been associated with GBS.2
Severe acute respiratory syndrome corona virus 2 (SARS-CoV-2), originated in Wuhan China in late 2019 and rapidly spread around the world causing a pandemic of novel coronavirus disease 2019 (COVID-19). The majority of pediatric disease is asymptomatic, but the common clinical presentations of COVID-19 are fever, malaise, and respiratory symptoms, which can range from mild cough to severe pneumonia, and occasional gastrointestinal symptoms. However, COVID-19 can present with a wide variety of other symptoms, including neurological symptoms in up to a third of adult patients. Ageusia and anosmia are some of the most common neurological presentations of those with COVID-19, however, others include encephalopathy, encephalitis, stroke, acute disseminated encephalomyelitis, as well as neuro-inflammatory auto-immune diseases.

There have been scattered reports of adults with possible GBS and concurrent evidence of COVID-19. There have not been any previously reported cases on GBS in children with evidence of COVID-19.

Case:

The patient was a previously healthy, Hispanic 8-year-old male who presented to an emergency department with progressive weakness. He had suffered a fall onto his buttocks one week prior to presentation, after which he had lower back pain but was able to ambulate. Over the next couple days, he began to experience bilateral lower extremity weakness that progressed to paralysis and the inability to walk. He was evaluated at a local emergency department where lumbar spine and right ankle x-rays were as normal; he was discharged home. Over the next few days, his weakness worsened as he began to develop upper extremity weakness and dyspnea. He again presented to a local emergency department where head and cervical spine CTs were negative. The patient was transferred to a tertiary care children’s hospital for further evaluation.
The patient denied any recent illnesses within the past 2 months; including fever, upper respiratory infection, cough, shortness of breath, rash, diarrhea or emesis. The patient did not have urinary or fecal incontinence, but he had not passed a bowel movement in 3 days and reported difficulty voiding. He had lower back pain and bilateral foot paresthesia. Other family members denied any recent respiratory or febrile illness. The father was an essential employee and worked outside the home daily. The patient had only left home once for a visit to a local grocery store 3 weeks prior to presentation, during which he wore a mask.

At the time of admission to the pediatric floor, the patient was afebrile with blood pressure 139/97 mmHg, heart rate of 135 beats per minute, respiratory rate of 35 breaths per minute, and oxygen saturation of 95% on room air. He appeared anxious but was alert and oriented. He was dyspneic, only able to speak 2-3 words at a time. Cranial nerves were intact except for intermittent left esotropia and dysconjugate gaze concerning for possible left sixth nerve palsy. Overall muscle strength was diminished with 3/5 in the upper extremities and 2/5 in the lower extremities. He had bilateral pronator drift. Deep tendon reflexes were absent in upper and lower extremities bilaterally. Sensation was intact to light touch, but proprioception of the distal lower extremities was abnormal. Baseline negative inspiratory force (NIF) was -60 mmHg.

The patient rapidly developed increased secretions with poor clearance and cough. He was transferred to PICU due to difficulty clearing secretions and worsening NIF of -40. He was intubated for airway protection and further work up.

An MRI of the spine was done and revealed abnormal enhancement of the posterior nerve roots from the T11 level through the cauda equina. (Figure 1) A lumbar puncture was also performed. The cerebrospinal
fluid demonstrated albuminocytologic dissociation with 1 nucleated cell/cumm, 3 RBCs/cumm, and protein of 620 mg/dl. Gram stain, culture and a rapid meningitis-encephalitis multiplex panel (BioFire Diagnostics) were negative.

Electrodiagnostic testing performed 12 days after symptom onset demonstrated prolonged distal latencies and low amplitude responses in the upper and lower extremities, with the tibial and median nerve responses in the demyelinating range, decreased conduction velocities in the peroneal and median nerves, and significant temporal dispersion but overall normal conduction velocity in the tibial nerve. The sural sensory nerve conduction was absent. Needle examination revealed absent activation of the anterior tibialis muscle but no abnormal resting activity and some activation of the vastus lateralis muscle with normal motor unit potentials (Table 1). These findings were compatible with a sensorimotor demyelinating polyneuropathy.

A diagnosis of GBS, AIDP form, was established. Patient underwent infectious evaluation for a trigger of the GBS. Respiratory viral PCR panel (BioFire FilmArray Respiratory Panel 2) of tracheal aspirates and respiratory viral culture were negative. Blood, urine, and stool cultures were negative.

The patient’s SARS-CoV-2 nucleic acid amplification was positive on two separate samples on hospital days 1 and 5. SARS-CoV2 IgG antibody was detected in his serum. Further work up related to COVID-19 showed CRP 8.3 mg/dL, ESR 51mm/hr, IL-6 23.6 pg/mL (normal ≤6.3 pg/mL) and D-Dimer 527 ng/mL. Workup was also notable for leukocytosis (14,200/cumm), with neutrophilia (11,400/cumm). Electrolytes, hepatic function panel, fibrinogen and ferritin were normal. Patient did not meet Centers for Disease Control and Prevention criteria for
multisystem inflammatory syndrome in children. The patient’s CSF was tested by real-time polymerase chain reaction targeting the SARS-CoV-2 E and RdRp genes and was found to be negative.

Treatment was initiated with intravenous immunoglobulin (IVIG) on day two of hospitalization. He was given a total of 2 g/kg of IVIG over 48 hours. His exam demonstrated improvement over the next several days following IVIG with 4+/5 upper extremity strength and 3/5 lower extremities bilaterally. The patient was extubated on hospital day five and transferred to the floor the following day on room air. Intensive physical, occupational, and speech therapy were initiated.

The patient was transferred to the inpatient rehabilitation unit three weeks after completion of IVIG with a projected stay of at least eight weeks. At the time of publication, six weeks following IVIG, he continues to demonstrate slow improvement. He has regained bilateral dorsiflexion and plantarflexion, the ability to sit independently, and is working on ambulating in parallel bars with two-person assistance. He was serial tested SARS-CoV-2 for clearance and had 2 negative tests on hospital days 27 and 31.

Discussion

This case illustrates the first reported case of a child with GBS in the setting of an acute SARS-CoV-2 infection to our knowledge. GBS in a child has been reported associated with other forms of coronavirus. The patient presented with classic symptoms of GBS with back pain followed by symmetric ascending weakness with loss of reflexes. The workup subsequently was consistent with GBS, AIDP form. The CSF had elevated protein without pleocytosis, there was enhancement of the posterior nerve roots in the cauda equina on MRI, and electrophysiological findings (EMG) demonstrated a demyelinating process.
The association between COVID-19 and GBS has been described previously in case reports of adults with a wide spectrum of GBS variants, including demyelinating, axonal, and Miller-Fisher in connection with COVID-19. Parainfectious GBS, as in our patient, and typical post-infectious presentations have been seen. SARS-CoV-2 and other coronaviruses, SARS and MERS specifically, have been shown to have neurotropic nature and lead to diseases of the central and peripheral nervous system. The lack of SARS-CoV-2 in the CSF is consistent with other reports. The exact nature and mechanisms of these phenomena have yet to be determined.

This case illustrates the ever widening scope of presentations of COVID-19 and associated complications. Clinicians need to constantly have a high level of suspicion for COVID-19 in all patients admitted to the hospital, especially in patients with unexplained symptoms. Children with an unexplained neurological process should be tested for SARS-CoV-2. Repeat PCR testing or antibody testing may also be required due imperfect sensitivity of the SARS-CoV-2 PCR testing. If COVID-19 is not diagnosed, there may be a missed opportunity for anti-viral treatment, and there will be increased risk of exposure and infection for hospital staff.

More study of the spectrum of neurological disease due to COVID-19 is needed. There is an ongoing, observational study of the neurological complications related to SARS-CoV-2 infection being done through the Neurocritical Care Society.

Acknowledgments:

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References:


Table 1. Nerve conduction studies and EMG examination

<table>
<thead>
<tr>
<th></th>
<th>Distal latency (ms)</th>
<th>Amplitude</th>
<th>Conduction velocity (m/sec)</th>
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<tr>
<td><strong>Motor nerve conduction</strong></td>
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<tr>
<td><strong>Left median nerve</strong></td>
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<td></td>
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<tr>
<td>Wrist</td>
<td>8.7 (n &lt; 4.4)</td>
<td>2.0 mV</td>
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<tr>
<td>Elbow</td>
<td>14.0</td>
<td>1.4 mV (n &gt; 4)</td>
<td>37.7 (n &gt; 49)</td>
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<td><strong>Left peroneal nerve</strong></td>
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<td></td>
<td></td>
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<tr>
<td>Ankle</td>
<td>7.6 (n &lt; 6.5)</td>
<td>1.0 mV</td>
<td></td>
</tr>
<tr>
<td>Knee</td>
<td>15.3</td>
<td>0.6 mV (n &gt; 2)</td>
<td>38.9 (n &gt; 44)</td>
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<tr>
<td><strong>Left tibial nerve</strong></td>
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<tr>
<td>Ankle</td>
<td>8.6 (n &lt; 5.8)</td>
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<tr>
<td>Knee</td>
<td>16.5</td>
<td>0.5 mV (n &gt; 4)</td>
<td>43.0 (n &gt;41)</td>
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<td><strong>Sensory nerve conduction</strong></td>
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<td><strong>Left sural nerve</strong></td>
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<tr>
<td>Calf</td>
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<thead>
<tr>
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<tr>
<td><strong>Left vastus lateralis</strong></td>
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Figure 1-MRI Images of Lumbar and Sacral Spine

Sagittal T1-weighted MRI of the spine pre-contrast (A) and post-contrast (B) demonstrating enhancement of the posterior nerve roots involving the distal cord and cauda equina.
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