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Development of COVID-19 associated Guillain-Barre syndrome in a child: A case report

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Abstract

Background: At the end of 2019, a new virus appeared, the SARS-CoV-2 virus which led to a pandemic. Firstly, the virus was detected in Wuhan, China and spread rapidly across the world, triggering a new coronavirus disease pandemic which was named Coronavirus Disease 2019 (COVID-19). Coronaviruses mainly affect the respiratory system. However, a literature review shows that coronaviruses can affect the nervous system.

Case Presentation: We describe the case of a fifteen-year-old boy, who presented with post-inflammatory Guillain-Barre syndrome (GBS) related to COVID-19 infection. The patient developed Acute Sensory-Motor Axonal Neuropathy (ASMAN), a variant of GBS, with a high titer of positive antibodies SARS-CoV-2, thirteen days after a febrile infection with anosmia, hypogeusia, diarrhea, weakness, and fatigue. He responded perfectly to the administration of immunoglobulin.

Conclusion: Several reports suggest that GBS could be a neurological complication of COVID-19. More studies about neurological complications arising during or after COVID-19 infection are required.

Keywords

Guillain-Barre syndrome; COVID19; SARS-CoV-2; demyelination.

Abbreviations

SARS-CoV: Systemic acute coronavirus respiratory syndrome; MERS-CoV: Middle east respiratory syndrome; GBS: Guillain–barré syndrome; CSF: Cerebrospinal fluid; CNS: Central nervous system.

Introduction

In December 2019, several patients from Wuhan, China, presented with severe and unexplained respiratory infections. Eventually it turned out that the cause of these cases of pneumonia, which spread all over the world, leading to a pandemic, was a new virusthat belongs to the coronavirus family and causes symptoms similar to those of systemic acute coronavirus respiratory syndrome (SARS-CoV) and Middle East respiratory syndrome (MERS-CoV). The virus was named SARS-CoV-2 while the disease was named Coronavirus Disease 2019 (COVID-19) [1,2].

Several studies associated COVID-19 with a range of neurological symptoms [3,12]. Regarding children, 16% of them have reported mild neurological symptoms, such as headache, fatigue, loss of smell or taste [22], 1% have had specific neurological involvement, such as encephalopathy, meningitis and/or seizures. Very rarely, Guillain-Barré syndrome, cranial nerve palsy, or intracranial haemorrhage have been reported [15]. However, it is still unclear if the neurological effects caused by SARS-CoV-2 are due to direct injury from the virus or due to complications such as multiple organ dysfunction, systemic inflammation or a generalized immune response. It has been established that some coronaviruses like 229E, OC43 and SARS-CoV have been shown to be neurotropic and neuroinvasive, leading to central and peripheral nervous system diseases [23]. The same seems to be true of the SARS-CoV-2 virus [8,24].

Guillain–Barré Syndrome (GBS) is a rare but serious autoimmune condition that affects the peripheral nervous system through inflammatory demyelination of peripheral nerves. It mainly occurs in remission of an infectious disease but can be combined with autoimmune and other diseases. The main clinical characteristicsare subacute onset of paresthiseas and muscle weakness of the lower extremities, absent tendon reflexes, with or without cranial nerve involvement, ascending course and symmetrical distribution [4].

The etiology of the syndrome is thought to be the result of an immunization procedure as antibodies against gangliosides have been detected in patients' serum [11]. About the SARS-CoV-2 virus, there is insufficient information on how affects the peripheral nervous system. It has not been shown so far that there is a direct invasion of the SARS-CoV-2 virus into the motor neurons and peripheral nerves resulting in the development of inflammation and/or degeneration [10].

Cases of patients who developed Guillain-Barré syndrome (GBS) both during and after the onset of SARS-CoV-2 infection, mainly in adults, have recently begun to appear in the literature [5]. In children, however, only three cases of Guillain-Barré syndrome have been reported so far [16-18]. In all three cases, intravenous immunoglobulin was administered with a satisfactory response. The most probable cause appears to be post-infectious immune system dysregulation caused by SARS-CoV-2. Herein, we describe a pediatric patient with an ASMAN variant of GBS after infection with theSARS-CoV-2 virus.

Case Report

A 15-year-old boy developed fever of up to 40°C, anosmia, hypogeusia, weakness, fatigue and diarrhea, lasting for four days. He received treatment with azithromycin and dexamethasone by a private

physician. After thirteen days later and while the patient had recovered and returned to his daily activities, he complained of weakness, photophobia, nausea and numbness, so he was transported to the emergency department of local hospital. The main finding from the neurological examination was that the tendon reflexes were not released in the lower extremities, therefore GBS was suspected. Lumbar puncture was performed. The analysis of Cerebrospinal Fluid (CSF) showed normal cell count, normal glucose level and high protein level (238 mg/dL [normal range, 15–45 mg/dL]), which confirmed the presence of albuminocytic dissociation. So, with these findings, it was decided to initiate intravenous immunoglobulin infusions at a dose of 0,4 gr/kg/day for 5 days. However, the patient deteriorated, showing signs of bilaterally facial nerve palsy and severe muscle weakness, so he was transported to the pediatric intensive care unit of University Hospital. During the neurological examination there was a good level of awareness and communication. The examination of muscle strength showed weakness in the four limbs according to the Medical Research Council (MRC) scale as follow; 4+/5 in proximal and distal of the upper extremities, 1/5 in proximal and 2/5 in distal of the lower extremities. Deep tendon reflexes remained absent in the lower extremities. There was a reduction in the vibration and fine touch sensation distal to the ankle joints and also bifacial nerve palsy (House–Brackmann Grade: 4). He had no spine sensory level. Meningeal irritation signs and upper motor neuron disorder signs were negative. A nasopharyngeal swab testing for SARS-CoV-2 with real-time polymerase chain reaction assay (RT-PCR) was performed which was negative. Magnetic resonance imaging of the brain parenchyma was normal. Post Gadolinium magnetic resonance imaging of the spinal cord revealed surface thickening and contrast enhancement on the conus medullaris and the nevre roots of the cauda equina (Figure 1a,1b). The aforementioned findings were compatible with the diagnosis of GBS. A neurophysiological study was also performed. The electromyography showed absent F waves in the tibial nerve and axon reflex in the peroneal nerve (table 3). The study of sensory conductivity was normal (table 2) and the study of motor conduction in the upper extremities did not reveal any pathological findings (table 1). These findings were also consistent with GBS.

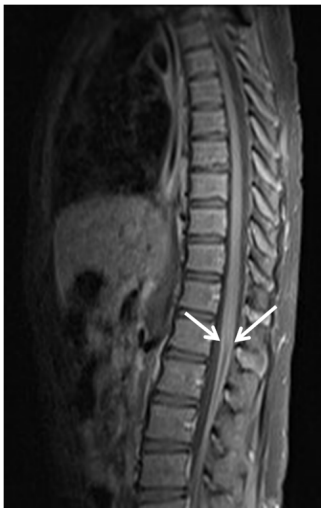

Figure 1a: Sagittal T1 Post GD Fat SAT at the midline shows surface thickening and contrast enhancement on the conus medullaris and the nerve roots of the cauda equina (thick white arrows).

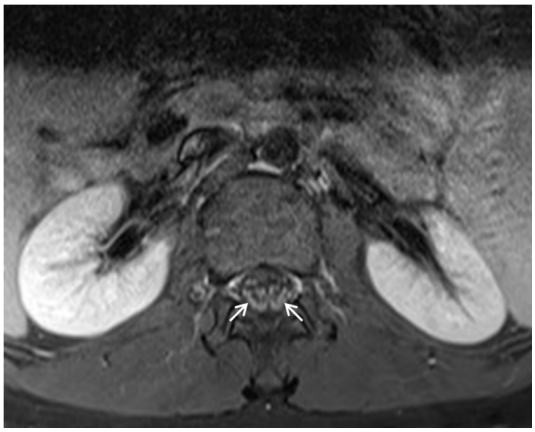

Figure 1b: Axial T1 Post GD Fat SAT at the level of L2 vertebrae, shows characteristic bilateral enhancement of quada equine nerve roots (short white arrows).

Table 1: Motor Conduction Studies

Nerve	Latency	Amplitude	Duration	CV
	ms	mV	ms	m/s
Right Median Motor				
Wrist – APB	3.56	8.8	4.3	
Right Peroneal Motor				
Ankle – EDB	4.13	2.4	7.0	
Bl. fib. head-Ankle	10.5	2.4	6.8	51.0
Right Tibial Motor				
Med. mal - Abd hal	6.93	5.3	3.7	
Right Ulnar Motor				
Wrist – ADM	2.69	7.1	5.9	
Bl. Elbow-ADM	6.40	6.5	6.0	
Bl. Elbow-Wrist	6.40	6.5	6.0	68.7

Table 2: Sensory Conduction Studies.

Nerve	Distal Latency	Amplitude	CV
	ms	uV	m/s
Right CTS Sensory			
Wrist L UI - 5th Fig	0.98	25.7	91.8
Wrist R - 3rd Fig	1.38	36.8	72.5
Right Sural Sensory			
Ankle-Lat.Malleolus	1.90	43.1	63.2

Table 3: F Wave Studies.

Nevre	F wave latency (min)	F wave latency(max)	%F
	ms	ms	%
Right Median F Response			
Wrist - APB	24.4	29.3	100
Right Peroneal F Response			
Ankle - EDB	44.3	46.6	97.0
Right Tibial F Response			
Ankle - Abd hal	21.5	29.0	100
Right Ulnar F Response			
Wrist – ADM	22.9	31.0	100

The virological test for HAV, HBV, HCV, Cytomegalovirus, Epstein–Barr Virus, Coxsackievirus, Echovirus, H1N1 virus, Campylobacter jejuni, Mycoplasma pneumoniae was negative, except from low anti-EBV VCA-IgG and anti-CMV IgG titers and high titer of IgG antibodies against SARS-CoV-2.

During his hospitalization, the patient showed gradual improvement of the weakness and mobility in the lower limbs, while the facial palsy showed significant improvement. He followed a daily physiotherapy program and he was treated also with a complex of vitamins (B1, B6, B12). Before discharge from the hospital, a new electrophysiological study was performed on the patient. Compared to the previous study, the F-waves disorders were improved, while the electromyographic control was negative for denervation. The findings showed that there is a reversible conduction disturbance. After twenty-two days of hospitalization, the patient was discharged in order tocontinue his recovery in a rehabilitation center.

Discussion

We report a pediatric patient who developed GBS. The most important finding in this case is that clinical features, electrophysiological findings, as well as the presence of a high titer of IgG antibodies against SARS-CoV-2, was consistent with the chronological profile of antibody onset [6], supported the diagnosis of meta-COVID-19 GBS.

Generally, the studies conducted so far worldwide in both adults and children show that this virus affects these two populations differently. Some of these differences are the milder clinical course and the fewer complications that children experience. In rare cases hospitalization is required and concerns those children with underlying diseases resulting in a particularly serious clinical picture [7,12]. In terms of complications from the nervous system, it is believed that the continued development of a child's nervous system makes children more susceptible to the various infectious and post-infectious mechanisms associated with COVID-19, leading to neurological damage [12]. There is a hypothesis that the virus initially infects the olfactory nerves and then invades the central nervous system (CNS) via cribriform plate [19]. An acute and intense inflammatory response is then activated [20]. The para- and post-infectious inflammatory responses could possibly manifest as neurological symptoms [20]. Regarding the development of GBS in children infected with the SARS-CoV-2 virus, it is thought to be mediated by post-infectious autoimmune responses [21]. Laboratory studies have shown that the SARS-CoV-2 spike protein binds to glycoproteins and sialic acid-containing ganglia on cell surfaces. Molecular mimicry between SARS-CoV-2 and ganglia in peripheral nerves may contribute to autoimmunity [13]. In addition, the reaction between T cells with the coronavirus and myelin basal protein may also contribute to demyelination [14]. In the literature, there are mainly published cases of adults with GBS after SARS-CoV-2 infection andmuch fewerpediatric cases.

Conclusion

More studies about neurological complications arising during or after COVID 19 infection are required. Our case report supports data that have already been published on the occurrence of the GBS after SARS-CoV-2 infection [5,8,9]. However, the relationship between SARS-CoV-2 and GBS, which is only described in individual case reports and in small series of cases, needs to be confirmed in larger observational studies for both adults and children.

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