

Guillain-Barré Syndrome after COVID-19 accompanied by Dysautonomia

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Abstract

The COVID-19 pandemic that emerged in Wuhan, Hubei Province, China in December 2019 is ongoing. COVID-19 may also cause neurological symptoms with central or peripheral nervous system or skeletal muscle involvement. Guillain-Barré syndrome (GBS) is an autoimmune disorder of the peripheral nervous system that is usually triggered by bacterial or viral infections. Autonomic nerve involvement can be seen in GBS. Case reports suggest that GBS is linked to COVID-19 infection. Here, we present a case of GBS occurring after COVID-19, accompanied by dysautonomia.

Keywords: COVID-19; Dysautonomia; Guillain-Barré Syndrome; SARS-COV-2

INTRODUCTION

In December 2019, a new coronavirus, called severe acute respiratory coronavirus 2 (SARS-COV-2), was detected. The disease caused by this virus was named coronavirus disease 19 (COVID-19). At the time of writing, the epidemic continues worldwide (1). The symptoms of this new coronavirus infection are very similar to those of SARS-COV (2). Both enter the cell through fusion with the angiotensin converting enzyme 2 (ACE2) receptor (3). Most seriously affected patients have an underlying disease, such as diabetes, hypertension, or cardiac disease (4). After an average incubation period of 5.2 days, the most common symptoms are fever, fatigue, and general respiratory distress (hacking cough, shortness of breath, chest pain, and pneumonia) (5). Neurological symptoms include central nervous system (CNS; headache, dizziness, impaired consciousness, acute brain disease, seizures, and ataxia), peripheral nervous system (PNS; anosmia, visual impairment, nerve pain), and skeletal muscle involvement (6).

Guillain-Barré syndrome (GBS) is an autoimmune disorder of the PNS (2). GBS shows progressive, ascending, symmetrical limb weakness, with a reduction or loss of deep tendon reflexes. Sometimes cranial nerve involvement accompanies these findings (7). Autonomic nerve involvement can be seen (8). Symptoms of dysautonomia include excessive blood pressure fluctuations, tachycardia or bradycardia, ileus, and

urinary retention (8). While protein concentrations in the cerebrospinal fluid (CSF) increase, the white cell count is normal (albuminocytological dissociation) (9). Symptoms peak within 4 weeks (2). GBS is usually triggered by bacterial or viral infections. The immune system is activated in response to the antigen and nerve roots and peripheral nerves are damaged due to the structural similarity of this antigen to axon and myelin (10).

This study presents a case of GBS occurring after COVID-19 accompanied by dysautonomia and reviews the literature on GBS associated with COVID-19 infection.

CASE REPORT

A 65-year-old man presented with the inability to walk. A COVID PCR test performed 1 month earlier because of diarrhoea and fatigue was positive. The patient was isolated at home and his mild complaints resolved within 10 days without medication. Marked numbness in the lower extremity had started 20 days earlier. The patient was referred to us from a neurology outpatient clinic with a diagnosis of acute polyneuropathy. He had been a smoker, but quit 15 years ago. His father has a history of ischemic stroke. On neurological examination, there was 4/5 muscle strength in the arms and 2/5 in the legs. There were no sensory defects in the arms, but position and superficial sensory defects in the legs. The deep tendon reflexes were reduced in the arms and absent in the legs. No pathological reflexes were detected. A complete

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blood count, blood sugar, kidney and liver function tests, Vitamin B12, folate and Vitamin D were within normal limits. Cranial and spinal magnetic resonance imaging was normal. PCR was negative for COVID-19 and other viral and bacterial agents in the CSF. CSF protein was 55.1 mg/dL; no cells were observed on direct examination. Electroneuromyography showed signs of motor-sensory polyneuropathy with axonal degeneration accompanied by marked demyelination of motor nerves (Table 1). With a diagnosis of Guillain-Barré syndrome, 0.4 g/kg/day intravenous immunoglobulin (IVIg) was started.

The patient developed bradycardia (40–45 /min) on the second hospital day and a theophylline infusion was started, considering autonomic involvement. Due to a low-grade fever, high C-reactive protein, and burning on urination, an infectious diseases consultation was requested. Ceftriaxone was initiated upon the growth of *Escherichia coli* in urine cultures. The patient's muscle strength approached normal after 10 days of IVIg and he was mobilized without support. On discharge, the patient's pulse was 60–65 /min.

Table 1. Sensorymotor nerve conduction studies in the patient with GBS

Motor Nerve Conduction Studies (MNCS)				
Nerve	Latency (ms)	Amplitude (mV)	CV (m/s)	F wave (ms)
Medianus (L)				
Wrist-APB	6.5	3.95		
Below elbow-Wrist	16.5	3.92	27.0	59
Ulnaris (L)				
Wrist-ADM	6.21	3.9		
Below elbow-Wrist	14.2	3.4	33.6	54
Peroneus (L)				
Ankle-EDB	-	-		
Below knee-Ankle	-	-	-	-
Tibialis (L)				
Ankle-AH	-	-		
Pop.fossa-Ankle	-	-	-	-
Sensory Nerve Conduction Studies (SNCS)				
Nerve	Latency (ms)	Amplitude (µV)	CV (m/s)	
Medianus (L)				
Dig. II-Wrist	-	-	-	
Ulnaris (L)				
Dig. V-Wrist	-	-	-	
Suralis (L)				
Mid.Lowerleg-Lat mal.	-	-	-	

CV: Conduction velocity, L:left, APB: Abductor pollicis brevis, ADM: Abductor digiti minimi, EDB: Extensor digitorum brevis, AH: Abductor hallucis, Pop. fossa: Popliteal fossa, Dig II: Digtorum II, Dig. V: Digtorum V Mid: Middle, Lat Mal: Lateral malleolus

DISCUSSION

Here, we report a case of GBS concomitant by dysautonomia after SARS-CoV-2 infection. The most frequently reported first symptoms of COVID-19 are fever, cough, and difficulty breathing (11), although there are many neurological findings, including polyneuropathy, myopathy, stroke, and GBS, as reported in other beta coronavirus infections(12). Since the beginning of the COVID-19 pandemic, there have been reports of a link between GBS and COVID-19 infection (13).

In classical GBS, neurological findings occur 1–4 weeks after an infection, as reported in many COVID-19-related GBS cases (2). However, a few GBS cases occurring

at the time of diagnosis have been reported (14). In addition, some patients who were diagnosed with GBS did not show symptoms of COVID-19, but were found to be PCR-positive for SARS-CoV-2 (15). It is important to consider asymptomatic COVID-19 in terms of respiratory symptoms in patients diagnosed with GBS. In our case, GBS was diagnosed on the 10th day after COVID-19 was diagnosed, which is consistent with the typical interval.

Most cases of GBS after COVID-19 have been reported in older men, as seen with non-COVID-19 causes (2). A single case of GBS due to COVID-19 in a child has been reported (16). Our patient was an older male, consistent with current reports.

Muscle weakness is the most common neurological symptom of GBS (16). Acute flaccid quadriplegia has been detected in most cases of GBS caused by COVID-19 (2), as in our patient. Demyelinating polyneuropathy is observed more frequently in GBS due to COVID-19 compared to axonal variants (2). Demyelinating polyneuropathy was also in the foreground in our case. There are also reports of GBS due to COVID-19 with facial diplegia (17).

In GBS, the CSF protein levels are high, while the cell count is normal (9). The CSF examination is similar in GBS cases due to COVID-19 (2), as in our case.

Some GBS cases associated with COVID-19 require intensive care (18), so an accurate, timely diagnosis of GBS due to COVID-19 is required (2).

Coronaviruses are neurotropic and neuroinvasive (11). The ACE2 receptor is present in the cell membranes of multiple human organs, such as the lungs, kidneys, liver, nervous system and skeletal muscle (6). It is thought that coronaviruses cause GBS via an inflammatory mechanism involving the ACE2 receptors in neuronal tissues or by creating an immune response (14). Increased levels of interleukin-6 (IL-6) that stimulates the inflammatory cascade and damages tissues can be detected in immune reaction related with SARS-CoV-2. These immunological processes are probably responsible for most neurological symptoms (1). It is uncertain if COVID-19 induces the production of antibodies against specific gangliosides as in general occurs in some GBS forms (1).

An analysis of COVID-19 patients in Wuhan, China, showed that those with CNS symptoms had lower lymphocyte and platelet counts and higher blood urea nitrogen levels than those with PNS findings or without neurological symptoms (6). Our patient's findings did not support this.

Dysautonomia refers to autonomic dysfunction, including blood pressure fluctuations, tachycardia or bradycardia, vasomotor dysfunction, and gastrointestinal motility disorder (19). Given that these patients are generally stable at admission, early monitoring for respiratory or cardiovascular collapse is important. The mortality in these patients can reach 7%, and an early diagnosis and appropriate treatment are important (19). The literature suggests that GBS is associated with dystonia in up to two-thirds of patients (20). We found only one case report of dysautonomia among GBS cases due to COVID-19 (15). The answer to the question of whether the incidence of dystonia in GBS due to COVID-19 is lower than in GBS with other causes will emerge with future case reports.

CONCLUSION

There seems to be a relationship between COVID-19 and GBS. It is important that research on the relationship between COVID-19 and the nervous system not be limited to the pandemic period and that necessary measures can be taken if we encounter a new type of this virus in the future. IVIG or plasmapheresis therapy should be initiated in conjunction with antiviral therapy. Dysautonomia has

been reported only in one COVID-19-related GBS case so far and its frequency and progress should be monitored compared to other GBS cases.

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