# COVID-19-associated acute motor axonal neuropathy, a variant of Guillain-Barré Syndrome: Expanding the neurological manifestations of SARS-CoV-2

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**COVID-19-associated acute motor axonal neuropathy, a variant of Guillain-Barré Syndrome: Expanding the neurological manifestations of SARS-CoV-2**

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**Highlights**

Guillain-Barré Syndrome and other autoimmune neurological diseases may be an important complication of COVID-19 infection

**Abstract**

*BACKGROUND:* COVID-19 pandemic changed the way we live and while continuing to do so; it has had an extremely significant impact on the healthcare community. While predominantly involving cardiorespiratory systems, a diverse range of neurological manifestations of COVID-19 infection have also emerged. Few cases of Guillain-Barré Syndrome (GBS) associated with COVID-19 have been reported recently.

*CASE PRESENTATION:* We present a case of acute motor axonal neuropathy (AMAN), a variant of GBS, preceded by COVID-19 infection with initial presentation as gastroenteritis. Expanding on the case, we explore the affinity of the Spike protein on SARS-CoV-2 to angiotensin-converting enzyme 2 receptors (ACE-2) and sialic acid-containing gangliosides and glycoproteins, which may play a role in increasing transmissibility and development of neuro-autoimmunity.

*CONCLUSION:* Any case of acute monophasic paralysis illness in the current scenario must alert the frontline physician to take into consideration the possibility of preceding COVID-19 infection. As more data emerges on neurological manifestations of COVID-19 infection, it will further clarify regarding the incidence of GBS and other autoimmune neurological diseases secondary to SARS-CoV-2.

**Keywords:** COVID-19; SARS-CoV-2; Guillain-Barré Syndrome; GBS;

**Background:**

The worldwide spread of COVID-19 has brought a multitude of physicians including neurologists and neurologist-in-training to the frontline. We continue to understand this multisystemic disease with a particular interest in neurological manifestations due to autoimmune response. We report a case of GBS that was preceded by COVID-19 gastroenteritis. A limited number of cases have been reported in the literature and this case is a further addition. To our best knowledge, all COVID-19 related GBS reported so far were preceded by a respiratory infection. We present the first case of GBS related to COVID-19 gastroenteritis.

**Case presentation**

A 25-year-old man, with no significant past medical history, presented with a two-day history of upper and lower limb weakness. He also complained of fever and diarrhea for five days prior to to presentation. Diarrhea was acute in onset, non-bloody, watery, and occurred 3-5 times a day before resolving spontaneously. He denied nausea, vomiting, or abdominal pain. Weakness in bilateral upper and lower extremities started gradually over a period of two days and worsened to the extent that the patient was unable to stand or walk on his own. Weakness first started in the left upper extremity, which was the weakest of all four extremities upon presentation. He also complained of pain in the lower part of the neck which started along with the weakness in upper extremities. Patient reported no history of visual disturbances, facial weakness, difficulty in swallowing, shortness of breath, loss of sensations or paresthesia. He also denied anosmia, cough, sore throat or any flu-like symptoms. On examination, the patient was afebrile, blood pressure of 127/90mmHg, heart rate of 93 beats per min, and respiratory rate of 18 breaths per min, with oxygen saturation of 100% on room air. Both pupils were equal, round, and reactive to light and accommodation. Examination of cranial nerves and facial muscles was normal. Further examination revealed proximal strength in right upper extremity of 3/5, left upper extremity 1/5, right lower extremity 2/5, and left lower extremity 3/5; with distal strength of 4/5 in all extremities. Reflexes were absent in both upper and lower extremities with plantars down going bilaterally. The remaining systemic examination including respiratory system exam was unremarkable. *Lab investigations can be found in Table 1 and CSF analysis from lumbar puncture can be found in table 2.*

Table 1 – Laboratory investigations upon admission.

| Investigation | Result | Reference |
|---|---|---|
| WBC | 14.3 x10^3/µL | 4 - 10 x10^3/µL |
| RBC | 6.8 x10^6/µL | 4.5 - 5.5 x10^6/µL |
| Hemoglobin | 15.1 gm/dL | 13.0 - 17.0 gm/dL |
| Platelets | 352 x10^3/µL | 150 – 400 x10^3/µL |
| Lymphocytes | 2.8 x10^3/µL | 1.0 – 3.0 x10^3/µL |
| CRP | < 5.0 mg/L | 0- 5.0 mg/L |
| Vitamin B12 | 455.0 pmol/L | 145 - 596 pmol/L |
| COVID-19 PCR Nasopharyngeal swab | **Positive** | |
| *Camplyobacter Jejuni* Antigen stool | Negative | |
| HIV antigen/ antibody test | Negative | |
| Stool culture | No growth for pathogenic organism | |
| Stool for ova and parasite | Negative | |

Table 2 – Cerebrospinal fluid analysis from lumbar puncture

| investigation | Result | Reference |
|---|---|---|
| CSF WBC | 11 /µL ( 80% lymphocytes) | 0- 5 /µL |

| investigation | Result | Reference |
|---|---|---|
| CSF RBC | 221 /μL | 0- 2 /μL |
| CSF Protein | 1.50 gm/L | 0.15- 0.45 gm/L |
| CSF Glucose | 3.38 mmol/L | 2.22- 3.89 mmol/L |

MRI spine of the lumbar and sacral region showed L4-L5 mild disc desiccation, with mildly reduced T2 signal intensity and mild diffuse posterior disc bulge with slight thecal indentation, and an otherwise normal examination. MRI head was also essentially unremarkable. Nerve conduction studies performed six weeks after the onset of illness revealed reduced compound muscle action potential (CMAP) amplitude with reduced conduction velocity from the right median and ulnar nerve. F wave was absent in all the upper limb nerves. Lower limb motor conduction study showed reduced CMAP amplitude of the right tibial nerve with normal conduction velocity. F-waves were normal for all the lower limb nerves. The sensory nerve conduction study showed normal conduction parameters of all nerves tested. H-reflex study of the left tibial nerve was also normal. Overall, the nerve conduction study was compatible with non-length-dependent axonal motor neuropathy, confirming the diagnosis of acute motor axonal neuropathy (AMAN) variant of GBS. *The parameters of nerve conduction studies can be found in table 3.*

Table 3 – Parameters of the nerve conduction study.

| Nerve | Latency | Amplitude (M-mV/S-uV) | Conduction velocity (m/s) | F-M lat |
|---|---|---|---|---|
| Median Motor Right Wrist- APB Elbow- wrist | 4.67 9.60 | 1.1 0.72 | 42.6 | Absent |
| Ulnar Motor Right Wrist- ADM Bl. Elbow- wrist Ab. Elbow- Bl/ elbow | 3.33 8.18 10.5 | 0.71 0.29 0.36 | 45.4 43.1 | Absent |
| Tibial Motor left Ankle- Abd hal PF-Ankle | 5.20 13.4 | 4.4 2.5 | 45.1 | 44.5 |
| Tibial Motor Right Ankle- Abd hal PF-Ankle | 4.04 13.3 | 2.9 2.7 | 40.7 | 45.2 |
| Peroneal Motor left Ankle – EDB Bl. Fib. Head- ankle Ab.Fib head- Bl fib. head | 4.84 12.7 14.6 | 3.9 3.3 3.2 | 40.7 42.1 | 53.0 |

**Outcome and Follow up**

Upon confirmation of COVID-19 upper respiratory tract infection (URTI), the patient was treated with a 5-day course of azithromycin and hydroxychloroquine. He received a five-day course of intravenous immunoglobulin two weeks after the initial presentation. COVID-19 PCR from the nasopharyngeal swab was negative after four weeks from the day of admission. The patient showed mild improvement in power in bilateral upper and lower extremities at six weeks. As of now, he is admitted in a dedicated rehabilitation facility for intensive physiotherapy and is gradually recovering strength in all extremities.

**Discussion & Conclusion:**

The eponym Guillain-Barré Syndrome (GBS) is a group heterogenous conditions which take into account acute immune-mediated polyneuropathies. The disease is mostly characterized by acute monophasic paralyzing illness which is preceded by an infection. Although *Campylobacter jejuni* is one of the most common preceding infections, it can also be caused by Human Immunodeficiency Virus (HIV), cytomegalovirus, Epstein-Barr virus, Zika virus, influenza virus, enteroviruses, herpes simplex virus, *Mycoplasma pneumoniae* , and *Haemophilus influenzae,* etc [1]. We report the first case of COVID-19-associated GBS in the State of Qatar, preceded by a diarrheal illness caused by SARS-CoV-2. A pooled analysis revealed that in patients with COVID-19, an overall onset of diarrheal illness is up to 10.4% [2]. Our patient had a diarrheal illness followed by onset of weakness in upper and lower extremities bilaterally, which was confirmed as AMAN variant of GBS. Other common etiologies of GBS were ruled out. Cyto-albuminological dissociation in CSF and results of nerve conduction studies confirmed the diagnosis of GBS.

As the pandemic continues to spread, there has been significant interest in neurological manifestations of COVID-19 which includes GBS in particular. The first documented case of GBS associated with COVID-19 was reported in China [3], which followed with reports of six cases in Italy [4,5]. Two cases reported in Spain showed Miller Fisher syndrome (MFS) and polyneuritis cranialis after COVID-19 infection [6]. Similar cases, although limited in number, have been reported in other parts of the world [7,8,9,10]. It is worthwhile to note that most cases of GBS had preceding COVID-19 symptoms, which were predominantly flu-like symptoms or related to the respiratory system. This case is the first in the literature to describe diarrheal illness secondary to COVID-19 leading to GBS.

We, as a scientific community, continue to understand more and more about the pathogenesis of SARS-CoV-2, the seventh identified coronavirus with high infectivity rate in humans. This virus utilizes angiotensin-converting enzyme 2 (ACE2) and serine protease TMPRSS2 receptor for Spike (S) viral protein priming [2]. Apart from being expressed in the lungs, ACE2 and TMPRSS2 are also found in small intestinal epithelial cells. ACE2 is also expressed in liver, colon and upper esophagus [2]. This renders SARS-CoV-2 capable of causing gastrointestinal symptoms at a rate higher than other coronaviruses. The proposed mechanism for GBS includes an antecedent infection that evokes an immune response which leads to cross-reactivity with components of peripheral nerves due to molecular mimicry (sharing the same cross-reactive epitope) [11]. GD1b ganglioside antibody was reported positive in the MFS case report and has recently spiked great interest (in contrast to the typical GQ1b antibody associated with GBS) [6]. It has also been demonstrated that the S protein binds to sialic acid-containing gangliosides and glycoproteins on various cell surfaces which further increases transmissibility [12]. The exact molecular mechanism of GBS induced by COVID remains unknown but this opens door to screening for anti-ganglioside antibodies to establish a causal relationship between COVID-19 and neuro-autoimmunity.

To conclude, physicians and neurologists must be aware of the potential atypical presentations and neurological complications of COVID-19 including GBS. As recent data has confirmed, SARS-CoV-2 may not only trigger GBS but may also cause other autoimmune neurological diseases [13]. A high index of suspicion must be maintained for patients with gastrointestinal symptoms or even possibly asymptomatic patients with new-onset GBS in the COVID-19 era.

**Abbreviations**

GBS: Guillain-Barré Syndrome

AMAN: Acute motor axonal neuropathy

ACE-2: Angiotensin-converting enzyme 2 receptors

CMAP: Compound muscle action potential

HIV: Human Immunodeficiency Virus

MFS: Miller Fisher syndrome

**Declarations :**

**Ethics approval and consent to participate**

Medical research committee at Hamad Medical Corporation approved the case study for publication. ( MRC-04-20-475)

**Consent for publication**

Written informed consent was obtained from the patient for publication of this case report. A copy of the written consent is available for review by the Editor-in-Chief of this journal.

**Availability of data and materials**

Data and materials regarding the case report are available to the Editor-in-Chief and can be requested from the corresponding author.

**Competing interests**

The authors have no conflict of interest relevant to this case.

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**Author contributions**

The first authors (RS and SS) contributed equally to the writing and preparation of this article. RS and SS have written the initial draft of the manuscript and performed the literature review. The draft was revised and updated by RS and SS with supervision from GAA & NS. RS, PI, AA, GAA and NS were part of the medical treating team. All the authors critically reviewed the initial and the final draft of the manuscript and approved it for submission.

**Appendix 1**

| Name | Location | Contribution |
|---|---|---|
| Rohit Sharma | Hamad Medical Corporation, Doha, Qatar | Writing the initial draft of the manuscript, Medical ma |
| Sundus Sardar | Hamad Medical Corporation, Doha, Qatar | Writing the initial draft of the manuscript, Revising th |
| Phool Iqbal | Hamad Medical Corporation, Doha, Qatar | Medical management of the case, Revising the manuscr |
| Ayisha Ameen | Hamad Medical Corporation, Doha, Qatar | Medical management of the case, Revising the manuscr |
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| Abdel-Naser Elzouki | Hamad Medical Corporation, Doha, Qatar | Conceptualization and supervision, Revising the manus |

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