A Rare Axonal Variant of Guillain-Barré Syndrome as a Neurological Complication of COVID-19 Infection

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Abstract

Guillain–Barré syndrome (GBS) is a neurological disorder accompanied by several neurological signs and symptoms including progressive weakness and diminished or decreased reflexes. GBS was reported as one of the several neurological complications in MERS-CoV and SARS-CoV outbreaks. Several studies have reported GBS as a neurological complication in recent COVID-19 outbreak. We report on the case of a 55-years-old female who was hospitalized with dyspnea, dry cough, and myalgia. She developed Acute Motor & Sensory Axonal Neuropathy (AMSAN), a rare variant of GBS signs and symptoms including decreased muscle strength and pinprick sensation in both lower extremities during her hospitalization.

Keywords: Axonal neuropathy, COVID-19, Dyspnea, Guillain-Barre syndrome, Muscle strength


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Introduction

An outbreak of coronavirus infection (COVID-19) was first reported in Wuhan, Hubei, China on December 31, 2019 and eventually spread throughout the world.1 The clinical characteristics of COVID-19 infection are previously described.2,3 Guillain–Barré syndrome (GBS) is a neurological disorder accompanied by several neurological signs and symptoms including progressive weakness and diminished or decreased reflexes4,5 GBS was reported as one of the several neurological complications in MERS-CoV and SARS-CoV outbreaks in 2004 and 2017, respectively.6,7 The first and only COVID-19 infection presenting with GBS as initial manifestation was reported by Hua et al. They reported acute weakness in both lower extremities and fatigue followed by decreased sensation to light touch and pinprick distally in a 61-year-old female as the initial presentation of COVID-19.8 In an observational series in Italy, Toscano et al. reported an association between GBS and COVID-19 infection.9 Here, we report the case of a 55-year-old female who was hospitalized with dyspnea, dry cough, and myalgia. She developed GBS signs and symptoms including decreased muscle strength and pinprick sensation in both lower extremities during her hospitalization.

Case Report

A 55-year-old Iranian female was admitted to our general hospital after experiencing non-productive cough and myalgia for almost a week, followed by progressive dyspnea. She also complained of several episodes of fever and chills five days prior to admission. She had a past medical history that was significant for an unknown chronic lung disease and oxygen dependency. She denied any alcohol or drug abuse and there was no history of smoking cigarettes.

Upon admission, the patient’s oral temperature was 37.5°C, O₂ saturation was 56%, pulse rate was 126 beats per minute, and blood pressure was 140/80 mm Hg. At that time, she denied any nausea, vomiting, abdominal pain, weakness in hands or legs, or impaired sensation. Computed tomography (CT) of her lungs displayed bilateral diffuse ground glass opacities (Figure 1) which was consistent with COVID-19 infection.10 The PCR for COVID-19 confirmed our diagnosis. Hydroxychloroquine (HCQ; 200 mg twice a day) was initiated with other medicines including antiemetic, antipyretic, and O₂ therapy. The patient was initially admitted to the internal medicine ward but then transferred to the intensive care unit (ICU) after experiencing progression of dyspnea. Kaletra (lopinavir/ritonavir) was started for her in the ICU two days after her admission. She was intubated five days later due to respiratory deterioration. Subsequently, her respiratory status began to improve and she was taken off the mechanical ventilator and transferred to the ward receiving O₂ with mask (O₂ saturation: 92%) twelve days after intubation. She described decreased muscle strength in her lower limbs four days after her transfer to the ward (26 days after hospitalization) as shown in Figure 2. On physical examination, muscle force in both lower limbs...
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was 3 out of 5 using Medical Research Council (MRC) scale, pinprick sensation was decreased distally, and Deep Tendon Reflexes (DTRs) were absent. An electrodiagnostic test (EMG/NCV) was performed. The EMG/NCV findings were suggestive of Acute Motor & Sensory Axonal Neuropathy (AMSAN), a rare axonal variant of Guillain-Barré syndrome. Compound motor action potentials (CMAPs) and sensory nerve action potentials in the studied nerves were diminished or absent and no late response was seen, supporting the AMSAN variant of GBS (Tables 1 and 2). The cerebrospinal fluid (CSF) was also obtained and analyzed which was unremarkable with glucose: 78 mg/dL, protein: 48.4 mg/dL (normal value: under 50 mg/dL), and no white blood cells (WBCs). No bacteria were found in the CSF smear. We did not examine the CSF for detection of COVID-19. The Brighton Collaboration GBS Working Group criteria were used for GBS diagnosis. Given the diminished muscle strength in the patient’s lower extremities, her NCV study results and CSF analysis, we established a diagnosis of GBS (the AMSAN variant) based on Brighton criteria levels 2. Intravenous immunoglobulin was started for the patient but unfortunately, she passed away due to acute respiratory distress syndrome (ARDS) before the medication could start its effect.

### Discussion

SARS-CoV-2, SARS-CoV and MERS-CoV are enveloped RNA viruses from the *Alphacoronavirus* and *Betacoronavirus* families. Several studies during previous outbreaks showed that these viruses have neurotrophic and neuroinvasive features. Arbour et al and Zumla et al in two separate studies in 2000 and 2015 reported that coronaviruses RNA can be found in the CNS of infected patients. Another study showed that MERS-CoV can infect human neural cells (NT2) *in vitro*. To date, there are few published data available regarding the neurological complications during treatment of infections caused by these viruses. In a retrospective study in 2017, Kim et al evaluated 23 MERS patients admitted to a single hospital in

### Table 1. Motor Nerve Conduction Study

<table>
<thead>
<tr>
<th>Nerve and Site</th>
<th>Latency (ms)</th>
<th>Amplitude (mV)</th>
<th>Latency Difference (ms)</th>
<th>Distance (mm)</th>
<th>Conduction Velocity (m/s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Left tibial</td>
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<tr>
<td>Wrist</td>
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<td>2.1</td>
<td>3.6</td>
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<tr>
<td>Elbow</td>
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<td>4.1</td>
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Ms, millisecond; mV, millivolt; mm, millimeter; m/s, meter/second.

CMAPs of tibial and peroneal nerves were absent. There is reduced amplitude of median motor nerve. Peroneal & Tibial F-waves and Tibial H-reflexes were absent on both sides (not shown above).

### Table 2. Sensory Nerve Conduction Study

<table>
<thead>
<tr>
<th>Nerve and site</th>
<th>Onset Latency (ms)</th>
<th>Peak Latency (mV)</th>
<th>Amplitude (mV)</th>
<th>Distance (mm)</th>
<th>Latency Difference (mm)</th>
<th>Conduction Velocity (m/s)</th>
</tr>
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<tbody>
<tr>
<td>Right sural</td>
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<td>Lower leg</td>
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The above examination shows no response in sural nerve.
Korea for neurological complications during treatment. They reported Bickerstaff’s encephalitis overlapping with GBS, alongside the drugs’ side effects and ICU-acquired weakness in four patients. The authors concluded that understanding and evaluating neurological findings during treatment of these acute respiratory diseases is important because they may have been underdiagnosed or neglected. Interestingly, we only found one study reporting GBS as the initial manifestation of COVID-19. In contrast, our patient showed neurological signs and symptoms including symmetrical decrease in muscle strength in her lower limbs and weakness in both lower extremities approximately three weeks after her initial COVID-19 manifestations (Figure 2). Our findings are more consistent with the report by Kim et al that showed MERS neurological complications appear to be non-concomitant with respiratory symptoms. In the same study, neurological symptoms were delayed by 2-3 weeks. Our patient received Ribavirin and Kaletra (lopinavir/ritonavir) to treat COVID-19. Ribavirin is not associated with peripheral neuropathy. Kaletra can be a possible causative drug but the risk of peripheral neuropathy in patients receiving Kaletra is still unclear. Another possible cause for our patient’s neurological complications is critical illness neuropathy. However, given the short intubation time (11 days) and the fact that our patient’s symptoms started three days after ICU discharge, this would be a poor possibility.

CSF analysis in patients with GBS shows high protein levels and normal WBC. Protein levels increase by the end of the second week of initiation of GBS signs and symptoms in 90% of patients. However, the protein levels may be normal in the early stage similar to what we observed in our patient and Tocano et al reported in their study. Our patient showed progressive respiratory deterioration and ARDS which led to her death seven days after the initial GBS symptoms. Whether the patient’s ARDS and death was a fatal complication of COVID-19 infection or a result of her unknown chronic lung disease or GBS progression, is a topic that needs further investigation.

While we were preparing this study, several other studies around the world also reported similar findings in patients following COVID-19 infection. Our study reports AMSAN, a rare variant of GBS in a patient following COVID-19 infection.

In conclusion, our study and other similar studies suggest that care providers should be aware of newly developed neurological symptoms and/or signs in COVID-19 patients, especially those hospitalized. More studies could be helpful to increase our knowledge about neurological manifestations of COVID-19 and guide our investment in more effective therapies.

Authors’ Contribution
MAA and MK: study design, data collection, manuscript preparation and literature search. HM: Study design, data interpretation and manuscript preparation.

Conflict of Interest Disclosures
All authors declared no conflict of interest.

Ethical Statement
This case report is reviewed and evaluated at national committee for ethics in biomedical research and it is registered at: http://ethics.research.ac.ir, with the ethical code of 1399.013.

References
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