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CASE REPORT

Guillain-Barré syndrome associated with COVID-19: a case report study

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Abstract

Acute respiratory distress syndrome (ARDS) caused by severe acute respiratory syndrome-coronavirus-2 (SARS-CoV-2) is spreading around the world. Patients with coronavirus disease 2019 (COVID-19) typically present fever, cough, and respiratory illnesses. It has been revealed that the comorbidities can turn it into severe types, and the managements meet unpredicted complications. Here, we report a case of coronavirus disease 2019 (COVID-19) coincidence with confirmed acute Guillain-Barré syndrome (GBS). Ten days after admission and therapeutic process, the patient developed autonomic dysfunction. Despite respiratory support and receiving intravenous immunoglobulin, the patient died due to cardiac arrest. Albeit it is yet scientifically doubtful, there are raising concerns toward a possible association between GBS and SARS-CoV-2 infection, demonstrating potential neurological symptoms of COVID-19.

Keywords Acute respiratory distress syndrome · COVID-19 · Guillain-Barré syndrome

Abbreviations

ARDS	Acute respiratory distress syndrome
CSF	Cerebrospinal fluid
COVID-19	Coronavirus disease 2019
GBS	Guillain-Barré syndrome
IVIG	Intravenous immunoglobulin
MERS	Middle East respiratory syndrome
RT-PCR	Real-time reverse transcription polymerase chain reaction
SARS	Severe acute respiratory syndrome
SARS-CoV-2	Severe acute respiratory syndrome-coronavirus-2
EMG	Electromyography
NCV	Nerve conduction velocity

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Background

The patients with coronavirus disease 2019 (COVID-19) have typical symptoms such as fever and respiratory illness (Halaji et al. 2020). However, there is little available information on the neurological aspects of COVID-19. It seems that the invasion to central nervous system (CNS) in severe acute respiratory syndrome-coronavirus-2 (SARS-CoV-2) could be similar to severe acute respiratory syndrome (SARS) and Middle East respiratory syndrome (MERS) viruses (Carod-Artal 2020; Kim et al. 2017).

Few studies concerning SARS and MERS have shown specific neurological appearances. These found that coronavirus could infect human neuronal cells (NT2) and induce systemic inflammatory response syndromes (Kim et al. 2017). Recently, some COVID-19-infected cases were also reported to have simultaneous stroke, cerebral venous sinus thrombosis, cerebral hemorrhage, subarachnoid hemorrhage, encephalitis, acute necrotizing hemorrhagic encephalopathy,

and acute Guillain-Barré syndrome (GBS) (Zhou et al. 2020).

GBS is an acute autoimmune polyradiculoneuropathy which can be triggered by a viral or bacterial infection with numerous clinical and pathological features. The main signs are ascending weakness started in lower limbs, extending to the upper limbs and face and complete loss of deep tendon reflexes (Willison et al. 2016).

In this heterogeneous disorder, while the white cell has a normal count, the concentration of proteins increases in the cerebrospinal fluid (CSF) (van der Meché et al. 2001). Encountering the antigenic agents, the immune system will be motivated, and the nerve roots and peripheral nerves are injured due to the similar structures of axons and myelin to the antigens of viral and microbial agents (Yuki and Hartung 2012).

Although there are several reports on the GBS manifestations associated with the COVID-19 (Rahimi 2020), more cases with other epidemiological and clinical aspects need to be carried out, and future investigations should be conducted to clear all dimensions of such disorder.

Here, we intend to report a case of acute GBS with COVID-19 coincidence. We have also reviewed literature for other coincidence of GBS and infection of COVID-19.

Case presentation

On April 5, 2020, a man aged 70 years presented an acute weakness in extremities, respiratory distress, and severe fatigue, progressing within a few days. His body temperature was 38.5 °C, oxygen saturation was 85% on room air, and respiratory rate was 20 breaths per min. Lung auscultation showed no abnormalities. Neurological examination disclosed symmetric weakness (Medical Research Council grade 4/5) and areflexia in both legs and feet. Three days after admission, his symptoms progressed. Muscle strength was grade 4/5 in both arms and hands and 3/5 in both legs and feet. Sensation to light touch and pinprick was decreased distally. Laboratory results on admission were clinically significant for lymphocytopenia.

The CSF testing (day 4) showed normal cell counts (5×10^6/L, normal: 0–8×10^6/L) and increased protein level (402 mg/dL, normal: 8–43 mg/dL). Due to ICU admission, intubation, and connection of the patient to the ventilator, it was not possible to perform electromyography (EMG) and nerve conduction velocity (NCV) for this patient.

He was diagnosed with Guillain-Barré syndrome and subsequently received intravenous immunoglobulin. On day 6 (Jan 28), the patient developed dry cough and a fever of 38.2 °C. Chest CT showed ground-glass opacities in both lungs. Oropharyngeal swabs were positive for SARS-CoV-2 on real-time reverse transcription polymerase chain reaction (RT-PCR) assay.

From initial days of hospitalization, the patient was transferred to the ICU due to the worsening of his respiratory symptoms and was given respiratory support and received supportive care and antiviral drugs of arbidol, lopinavir, and ritonavir. Ten days after admission, the patient developed autonomic dysfunction, which was one of the complications of GBS. Despite respiratory support and receiving intravenous immunoglobulin (IVIG), the patient died due to cardiac arrest.

Discussion

The most common infections associated with the development of GBS are Campylobacteriosis and viral infections such as Cytomegalovirus, Epstein-Barr virus, human immunodeficiency virus, and most recently Zika virus (Galan et al. 2020; Kim et al. 2017). The proposed mechanism is an autoimmune reaction where antibodies against pathogen surface glycoproteins are developed that also correspond to similar protein structures of peripheral nerve components (molecular mimicry) (Galan et al. 2020). In our patient, we believe the respiratory illness due to COVID-19 has triggered this neurological process.

We are not aware of GBS association with this infection. Moreover, the recent report of GBS possibly associated with COVID-19 raises concern for this virus to be a possible trigger. It has been demonstrated that other coronaviruses are involved in neurologic disease. In a retrospective study of the MERS-CoV outbreak, one patient was diagnosed with Bickerstaff's encephalitis with overlapping GBS during his treatment course (Neri and Pichi 2020). Neuromuscular involvement was also reported by Tsai et al., in patients infected with the SARS-CoV (Padroni et al. 2020). The first case of GBS associated with SARS-Cov-2 infection was reported in a patient who had returned from Wuhan in January 2020 (Zhao et al. 2020). Zhao et al. reported an old woman infected by COVID-19 with acute GBS. Initially, she presented acute weakness in both legs and severe fatigue, progressing without fever, cough, chest pain, or abnormalities in the lungs. She showed disclosed symmetric weakness and areflexia in both legs and feet and her symptoms progressed in next days. She also showed sensation to light touch and delayed distal motor latencies. A weak after admission she presented dry cough, fever, and ground-glass opacities in both lungs. Her oropharyngeal swabs RT-PCR tests were also positive. After receiving supportive care and antiviral drugs, she regained her health respiratory and neurologically. Her laboratory consequences had already revealed lymphopenia and thrombocytopenia on admission time.

Hence, there was suggestion of infection, at least based on blood tests on presentation. They concluded that there is a possible association between GBS and SARS-CoV-2 infection which showed the requirement of considering potential neurological symptoms of COVID-19 infection. The authors suggested a "para-infectious" profile pattern of GBS in their patient instead of the usual encountered post-infectious neurological deficit seen in GBS. The authors suggested a possible association between the GBS and COVID-19 pending more epidemiological data (Zhao et al. 2020).

Virani et al. also a 54-year-old male case of GBS with typical symptoms of numbness and progressive weakness of his lower extremities and an areflexic motor strength deficit with confirmed COVID-19 infection (Virani et al. 2020).

Toscano et al., in another report in Italy, introduced five patients with GBS after infection by COVID-19. Their symptoms included common COVID-19 symptoms, lower-limb weakness, and paresthesia (in four patients) and facial diplegia followed by ataxia in one patient (Toscano et al. 2020).

Sedaghat et al. described an old man infected with common COVID-19 and GBS symptoms which represented acute progressive symmetric ascending quadriparesis. It seems that COVID-19 stimulates inflammatory cells and produces various inflammatory cytokines, and as a result, it creates immune-mediated processes such as GBS as an immune-mediated disorder. Thus, one of neurological complications of COVID-19 infection is GBS which could treat with IVIG or plasmapheresis stimulatingly with antiviral drugs (Sedaghat and Karimi 2020; Sheikhshahrokh et al. 2020).

Galan et al., in another case report study, presented a case of GBS associated with COVID-19. Their patient displayed symmetrical and global weakness in the four limbs with progressive intensity and inability to ambulate, as well as alteration in the sensitivity of the four limbs at the distal level accompanied by symptoms of respiratory infection. In this case, the possibility of SARS-CoV-2 infection was considered the cause of GBS (Galan et al. 2020).

In other report by Otmani et al., an old woman with mild respiratory symptoms linked to a COVID-19 rapidly presented bilateral weakness and tingling sensation in all four extremities resulting in a total functional disability. This was a case of SARS-Cov-2 induced GBS (El Otmani et al. 2020).

The other old man was reported with history of cough, dyspnea, diarrhea, and fever. A week later from recovering, he referred for fast progressive lower-limb weakness, apyretic, generalized areflexia, severe flaccid paraparesis—mainly affecting proximal muscles—and a decreased proprioceptive length-dependent sensitivity involving the four limbs. These symptoms and neurological tests strongly resembled GBS which could indicate possible post-SARS-CoV-2 disorder (Arnaud et al. 2020).

The other post-SARS-CoV-2 GBS was reported with neurological symptoms such as progressive proximally pronounced paraparesis, areflexia, and sensory loss without preceding fever or respiratory symptoms (Scheidl et al. 2020).

Meshref et al. described an 18-year-old female case with confirmed positive COVID-19 and also acute quadriparesis of both upper and lower limbs with equal grade of proximal weakness and difficulty in swallowing for two days. The patient's condition improved with the treatment course including improvement in weakness, difficulty swallowing, and nasal tone of speech (Meshref et al. 2021).

Zito reported a 57-year-old male patient with a variant of GBS with developing acute motor-sensory axonal neuropathy after SARS-CoV-2 infection (Zito et al. 2020).

Kamel also described a 72-year-old male case in Kuwait with acute progressive and ascending lower-limb weakness emerging 3 weeks after testing positive SARS-CoV-2 (Kamel et al. 2021).

Our case adds to this recently reported case. Moreover, the presentation in our patient also suggests the "para-infectious" profile rather than the generally encountered relatively longer time period between the triggering event and development of GBS.

Considering the temporal association, we speculate that SARS-CoV-2 infection might have been responsible for the development of GBS in our reported patient. Furthermore, the onset of GBS symptoms in this patient overlapped with the period of SARS-CoV-2 infection. Hence, GBS associated with SARS-CoV-2 might follow the pattern of a para-infectious profile, instead of the classic postinfectious profile, as reported in GBS associated with Zika virus (Zhao et al. 2020).

Although many new insights into the pathogenesis and immunity of COVID-19 have been provided, the main molecular mechanisms mediating COVID-19 nerve damage are still unclear (Allahyari et al. 2021; Hosseini et al. 2021). One hypothesis described that coronavirus may invade the neuroephithelium of the olfactory nerve. It may also travel via retrograde axonal transport from trigeminal and vagal endings (Zuberbuhler et al. 2021). As an immune-mediated disease, molecular mimicry could play a role in GBS. This mechanism may trigger by inflammatory cytokines produced by COVID-19. Scientists also assumed that COVID-19 could directly attack on the nerves through angiotensin-converting enzyme 2 (ACE2) receptors and causes peripheral neuropathy similar to other viruses (Kamel et al. 2021).

Overall, this single case report only suggests a possible association between GBS and SARS-CoV-2 infection, and more information on the cases with similar epidemiological data is needed to support such causal relationship. This

case also suggests the need to consider potential neurological symptoms of SARS-CoV-2 infection.

Conclusion and expert opinion

Bacterial and viral infections are known as the trigger of GBS. Therefore, we suggest that clinicians should be aware that the acute GBS may be a neurological complication of COVID-19 infection. So, patients with GBS symptoms should be screened for COVID-19 during this pandemic. Besides, the farther we go from the peak of COVID-19, the more we have to wait for its neurological effects, because the peak of neurological complications may occur with a delay compared to the peak of the disease outbreak.

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Declarations

Consent for publication Written consent for publication of this case report and clinical details or any accompanying images was obtained from the patient.

Conflict of interest The authors declare no competing interests.

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