Parainfectious Guillain Barre Syndrome in a Patient Diagnosed with COVID-19

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Case Report

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Abstract

An accumulating evidence suggesting the neurotropic characteristics of the SARS-CoV-2. Although the pathogenesis is unclear, the relationship between COVID-19 and Guillain Barre Syndrome(GBS) has been previously reported. We present a 66-year-old male with para- infectious COVID-19-related GBS admitted with a 2-day bilateral weakness in distal lower limbs. His neurological findings occurred on the third day of the diagnosis of COVID-19. A cerebrospinal fluid examination revealed albumin-cytological dissociation.

To the best of our knowledge, this is the first para-infectious GBS case related to the SARS-CoV-2 reported from Turkey. Clinicians should be aware of this kind of complication to manage patients.

Background

SARS-CoV-2 causes a wide range of clinical symptoms since it uses angiotensin-converting enzyme-2 (ACE2), which presents in various organs and systems. The evaluation of neurological manifestations of 214 patients with COVID-19 revealed that dizziness, headache, taste disturbance, and hyposmia were the main findings of central and peripheral nervous system involvement[1]. The COVID-19 related Guillain Barre Syndrome(GBS) cases have rarely been reported[2]. This is a new defined issue of which clinicians should be aware to manage cases properly.

Case Presentation

A 66-year-old male patient was admitted to another hospital with the complaint of diarrhea and tested for SARS-CoV-2 PCR since he had a high-risk contact history with his wife who had a diagnosis of laboratory-confirmed COVID-19. Oropharyngeal swab sample tested for SARS-CoV-2 PCR resulted positive. He was treated with favipiravir as an outpatient. On the fifth-day of treatment, he was admitted to the emergency department(ED) with a 2-day acute symmetric weakness in distal lower limbs. He had no respiratory symptoms.

On initial physical examination, muscle strength was found as 2/5 on lower extremities and 4/5 and 5/5 on the upper right and left extremity, respectively. Deep tendon reflexes of the lower limbs were absent. The blood oxygen saturation level was 97%. The laboratory analysis revealed white blood count $12.3 \times 10^9/L$ (neutrophil count $10.69 \times 10^9/L$ and lymphocyte count $0.51 \times 10^9/L$), C-reactive protein 0.0187 g/L, procalcitonin $<0.03 \mu g/L$, D-Dimer 1.96 mg/L, and fibrinogen 5.72 g/L. Brain Magnetic Resonance Imaging was normal and there was no diffusion restriction. Chest Computed Tomography showed typical early findings of COVID pneumonia that included bilateral ground-glass opacities. Oxygen support was not needed on the follow-up. Lumber puncture was performed with the suspicion and clinical diagnosis of GBS. CSF analysis revealed albumin-cytological dissociation: protein 2335.13 mg/L(normal range: 150-400), albumin 1393 mg/L (normal range: 100-300), no white blood cell. SARS-CoV-2 PCR resulted in negative.

Since he had high levels of D-dimer, anticoagulant therapy with low molecular weight heparin was given to decrease the risk of venous thromboembolism. Intravenous immunoglobulin (IVIG) 0.4 g/kg per day (35 g/day) treatment was planned for five days. On the third day of hospitalization, the patient's muscle weakness progressed and the strength of lower extremities was 2/5 and the upper extremities were 3/5. Bilateral hypoesthesia was also determined in the lower extremities. Plasmapheresis therapy was suggested due to the clinical progression on IVIG treatment and it was given seven times every other day. The patient was admitted to the Intensive Care Unit (ICU) to implement plasmapheresis on the third day of admission. He developed dysphagia and facial paralysis on the eighth day of symptoms onset for COVID-19. He was intubated due to the respiratory muscle involvement on the 11th day of admission. Although he was given plasmapheresis and IVIG therapies, neurological findings worsened progressively and he became quadriplegic. He was followed as ventilatory-dependent for 40 days in the ICU. He had secondary infections (ventilator-associated pneumonia and candidemia) on the ICU follow-up, and died on the 48th day of ICU admission despite he had been given 14-days of meropenem plus colistin and 17-days of echinocandin therapy. The timeline for the progress of findings of GBS and implementations of therapies are summarized in Fig.1.

Discussion

Neurological manifestations were reported in 36.4% of COVID-19 patients[1]. GBS is a typical postinfectious disease that generally occurs within four weeks of disease onset[3]. However, parainfectious GBS related to SARS CoV-2 was reported previously[4]. Neuro-invasion or autoimmune response of the virus via ACE2 receptors in neuronal tissues is thought to play a role in the etiology[4].

GBS mainly progresses with limb weakness and areflexia development[3]. This is how it developed in our case, as well. He had rapid progressive neurological findings resulting in quadriplegia, facial paralysis, and dysphagia. Cranial neuropathies including facial paralysis consist of a rare form of GBS[5]. The diagnostic criteria for GBS can be evaluated with the Brighton Criteria[6], and our patients presented all the defined criteria. The neurological findings and CSF examination were consistent with GBS. CSF examination revealed no pleocytosis but increased protein levels, and albumin-cytological dissociation was identified[5]. In addition, the test for SARS CoV-2 PCR in CSF was negative. Published reports of GBS in the literature have indicated negative results in all tested 32 patients with COVID-related GBS[5].

Electromyography (EMG) is the main tool to determine the subtype of GBS. EMG was performed after his admission to ICU and prolonged distal latencies, conduction block, slowing of conduction velocities, and low action potentials were identified. F waves were absent as were all sensory nerves, except the sural nerve, which has been typically reported in patients with GBS. The needle EMG revealed evidence of abnormal insertional activity in the form of positive waves and fibrillation potentials in the muscles of both upper and lower extremities. Overall, electrical abnormalities were consistent with the demyelinating form of GBS with secondary sensory-motor axonal degeneration.

The review of published 37 COVID-19 cases with GBS revealed that the mean-time between COVID-19 symptoms onset and GBS symptoms onset was 11 ± 6.5 days[2]. Another review of 51 COVID-19-related GBS cases reported that 70.5% of the patients were post-infectious whilst 24.5% were para-infectious [5]. Respiratory failure via GBS and the requirement of mechanical ventilation were reported as 17%-30%[7]. Besides, para-infectious COVID-19-related GBS cases were found riskier for ventilator requirement[5]. In the present case, GBS symptoms developed on the third-day of symptom onset of COVID-19.

Although IVIG treatment was given on the second day of admission, limb weakness progressed and bilateral facial paralysis developed. Hence, plasmapheresis was started. Although the recommended treatment regimens were implemented, rapid progression to quadriplegia developed. He needed intubation via respiratory muscle involvement and needed ICU follow-up, similar to 20%-30% of non-COVID GBS patients[6].

The severity of clinical progress is highly variable in patients with GBS, ranging from mild weakness of muscles to serious weakness resulting in quadriplegia and the need for ventilator support[3]. IVIG and plasmapheresis were accepted as efficient treatment modalities[3,8]. Either of them should be implemented as soon as possible after disease onset to prevent the occurrence of permanent nerve damage[3,9,10]. IVIG(0.4 g/kg per day) or plasma exchange for five days constitute effective treatment alternatives. However, a combination of them was not reported as more beneficial compared to the use alone[3]. There is a clear need for more effective treatment agents since many of the patients have developed progressive weakness despite using IVIG or plasmapheresis[3].

GBS is a life-threatening disease with the mortality rate of 3%-7%[3]. The development of respiratory insufficiency via respiratory muscle involvement constitutes one of the most probable causes of death in patients with GBS[3].

Since there is a risk of mortality due to respiratory muscle involvement in GBS, the rapid diagnosis and early treatment is critical in all patients, especially in patients with COVID-19, which may be characterized by extensive lung involvement. Moreover, since para-infectious COVID-19-related GBS has poorer outcomes, the probability of this syndrome should be kept in mind in patients with neurological findings of COVID-19 to manage cases properly without delay.

Conclusions

SARS CoV-2 is a newly defined cause of GBS. Clinicians should be aware of the risks, signs, and symptoms of COVID-19-related GBS since there is an ongoing pandemic with a huge number of individuals affected by SARS-CoV-2 increasing day by day.

Declarations

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Authors Contributions:

Concept, design: AB, HB, HB

Data collection/ processing, literature search and writing: AB, CB

Critical review: All authors

Consent: The patient consented to participate and publish his clinical data.

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Figures

Figure 1

Timeline of the clinical progress of the patient diagnosed with COVID-19 related parainfectious GBS ICU; Intensive Care Unit, LP; Lomber Punction, MV; Mechanical Ventilation