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Case Report

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PARA-INFECTIOUS GUILLAIN BARRE SYNDROME IN A PATIENT DIAGNOSED WITH COVID-19

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Abstract

Accumulating evidence suggests 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 described previously. In this report, a 66-year-old male with para-infectious COVID-19-related GBS admitted with bilateral weakness in distal lower limbs was presented. Five days ago, since he had a risky contact with the COVID-19 patient, the SARS-CoV-2 PCR test was performed and resulted in positive. Favipiravir treatment was given as outpatient therapy. On the fifth day of antiviral treatment, he had applied to Emergency Department with two days of muscle weakness of lower extremities consistent with GBS; hence lumbar punction was performed. The cerebrospinal fluid examination revealed albumin-cytological dissociation. Despite the administration of immunoglobulin infusions, neurological findings worsened, dysphagia, and facial paralysis occurred. Although he was stable for COVID, he was followed up in the intensive care unit for plasmapheresis and then intubated for the respiratory involvement of GBS. Early diagnosis and treatment are critical in GBS related to COVID-19. Since para-infectious COVID-19-related GBS has poor outcomes, clinicians should be aware of this kind of complication to manage patients as it's supposed to be.

Keywords: COVID-19, para-infectious GBS, SARS CoV-2, Guillain Barre Syndrome.

Introduction

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.[1] The COVID-19 related Guillain-Barre Syndrome(GBS) cases have rarely been reported.[2] Parainfectious GBS is a newly defined rare form of COVID-19 related GBS and has poorer outcomes. Clinicians should be aware of this syndrome to define and manage cases properly.

Case Report

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. The oropharyngeal swab sample tested for SARS-CoV-2 PCR was positive. On the fifth day of favipiravir 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 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%. Brain magnetic resonance imaging was normal, and there was no diffusion restriction. Chest Computed-Tomography showed typical early findings of COVID pneumonia. Oxygen support was not needed on the follow-up. A lumbar puncture was performed with the suspicion and clinical diagnosis of GBS. Cerebrospinal fluid(CSF) analysis revealed albumin-cytological dissociation: protein 2335.13 mg/L (normal range: 150-400), albumin 1393mg/L (normal range: 100-300), no white blood cell. SARS-CoV-2 PCR was negative.

Intravenous immunoglobulin(IVIG) 0.4g/kg per day (35 g/day) treatment was planned for five days. On the third day of hospitalization, the patient's muscle weakness progressed. Bilateral hypoesthesia was also determined in the lower extremities. Plasmapheresis therapy was suggested due to the clinical progression of IVIG treatment, and it was given seven times every other day. The patient was admitted to the Intensive Care Unit(ICU) to implement plasmapheresis. He developed dysphagia and facial paralysis on the eighth day of symptoms onset for COVID-19. He was intubated due to respiratory muscle involvement on the 11thday of admission. Although he was given plasmapheresis and IVIG therapies, neurological findings worsened progressively, and he became quadriplegic. He had secondary infections (ventilator-associated pneumonia and candidemia) on the ICU follow-up and died on the 48thday of ICU admission, although he had been given effective antimicrobial therapy. The timeline for the progress of findings of GBS and implementations of therapies are summarized in Figure 1. Informed consent was obtained from the patient for publication at the time of diagnosis.

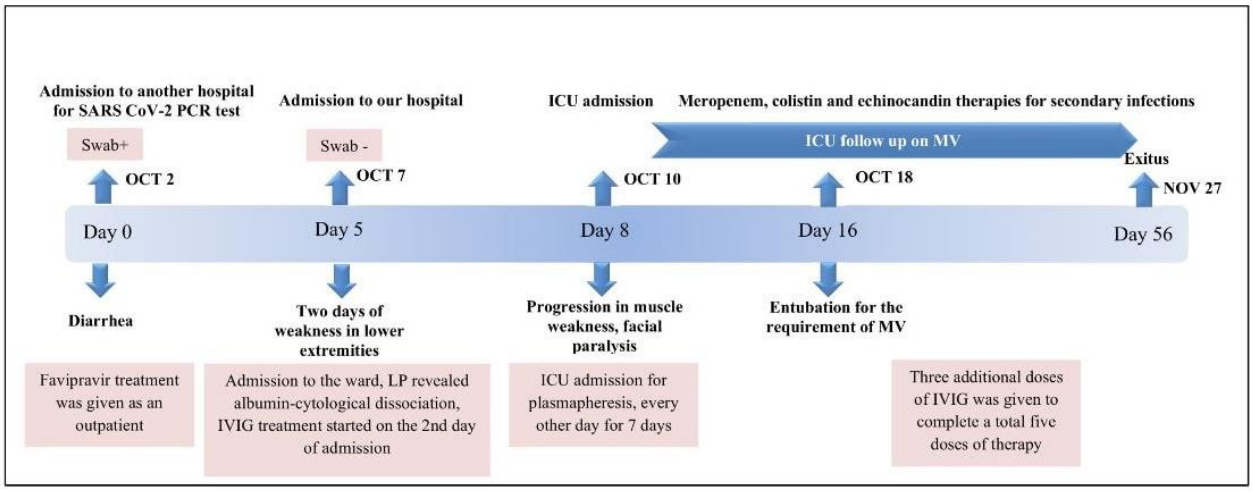

Figure 1. Timeline of the clinical progress of the patient diagnosed with COVID-19 related parainfectious GBS (ICU: Intensive Care Unit, LP: Lumbar Puncture, MV: Mechanical Ventilation)

Discussion

Neurological manifestations were reported in 36.4% of COVID-19 patients.[1] GBS is a typical post-infectious disease that generally occurs within four weeks of disease onset.[3] However, para-infectious 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, and our patients had all the defined criteria.[6] CSF examination revealed no pleocytosis, but increased protein levels and albumin-cytological dissociation were identified consistent with GBS.[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] Nerve conduction studies are the main tool to determine the subtype of GBS. Electromyography(EMG) was performed after his admission to ICU, and prolonged distal latencies, conductions 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. 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 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 the 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 a 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] Early diagnosis and treatment are critical in GBS related to COVID-19. Moreover, since parainfectious COVID-19-related GBS has poor 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. Comprehensive studies are needed to find out the different patterns of COVID-19 related GBS.

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Conflict of Interest: None to declare

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