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Case report

Guillain-Barré Syndrome associated with SARS-CoV-2 infection

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ABSTRACT

We present a case of Guillain- Barré Syndrome (GBS) in a patient with confirmed COVID-19 infection. GBS in commonly encountered after an antecedent trigger, most commonly an infection. To date, only one case of GBS associated with this infection has been described. Clinicians should consider this entity since it may warrant appropriate isolation precautions especially in a patient who may not present primarily with typical constitutional and respiratory symptoms associated with COVID-19.

Introduction

First reported in December 2019 as a cluster of pneumonia cases in Wuhan (China), the novel coronavirus (SARS-CoV-2) has been under intense research and investigation. The first known case in the United States was documented in January 2020 in Seattle, Washington [1]. While the most common symptoms of COVID-19 are fever, cough, and shortness of breath, we present a case in which a SARS-CoV-2 positive patient developed progressive, ascending weakness consistent with Guillain-Barré syndrome (GBS). GBS is a demyelinating disease in which symmetric progressive weakness typically begins distally and moves proximally [2]. In severe cases it can involve respiratory muscles and warrant use of mechanical ventilation [2]. While the world is still grasping at all the complications associated with the initial presentation of COVID-19, we must also realize that a serious neurological sequela may be associated with this viral infection.

Case

A 54-year-old male presented to an outside hospital with complaints of numbness and weakness of his lower extremities of 2-day duration. The weakness progressed to the point that he could not get out of bed and this prompted his family to seek immediate medical attention. In the emergency room, patient also reported having fever, as high as 102 F, and a non-productive cough of 10-day duration that did not improve with a short course of oral amoxicillin and steroids that his primary care physician had prescribed. He subsequently developed diarrhea, was diagnosed with *Clostridium difficile* colitis 2 days ago, and started on treatment that resulted in improvement of symptoms. Vital signs on presentation were remarkable for respiratory rate of 24 breaths per minute with oxygen saturation of 92 % on room air, but otherwise stable. Physical exam was most notable for absent lower extremity deep tendon reflexes along with decreased lower extremity strength compared to upper extremities. Complete blood count showed a white blood cell count of 8.6×10^3 cells/mL, hemoglobin of 15.4 g/dL and platelet count of 211×10^3 cells/mL with an otherwise normal differential. Procalcitonin was noted to be 0.15 ng/mL and a complete metabolic panel was within normal limits. Given the existing epidemiological scenario and symptoms of fever and cough, COVID-19 infection was suspected. Appropriate isolation precautions were implemented, and a respiratory viral panel testing (nasopharyngeal PCR) was sent. Rhinovirus was detected in the specimen; SARS-CoV-2 test was awaited. While still undergoing initial work-up, the patient reported new onset urinary retention prompting magnetic resonance imaging (MRI) of thoracic and lumbar spine that did not reveal any abnormal spinal pathology. This imaging, however, did reveal incidental findings of bilateral basilar opacities in the lungs. Over his short course at the outside hospital patient complained of difficulty breathing and weakness was noted to ascend up to his nipples. He was electively placed on mechanical ventilator support for concerns of impending respiratory failure and transferred to our facility.

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On arrival to our hospital, he was evaluated by the neurology team and noted to have 2/5 strength in his lower extremities with 3/5 in his upper extremities. There was absence of deep tendon reflexes. Given his clinical history of ascending paralysis with supporting physical exam findings, history of recent infection, negative MRI results, and respiratory failure without obvious parenchymal pathology to explain the same, a diagnosis of GBS was made. Patient was immediately started on 400 mg/kg of intravenous immune globulin (IVIG) therapy for a planned 5-day course. Upon arrival, SARS-CoV-2 testing was repeated for purposes of expedited results. Both tests, at our facility and the outside hospital, resulted positive and patient was started on hydroxychloroquine 400 mg for the first two doses with subsequent 200 mg dose twice a day for an additional eight doses. Given the classic clinical picture of GBS in absence of other identifiable etiology for his neurologic disease and strict infection control measures, additional supportive testing with EMG and lumbar puncture (LP) was not pursued. Furthermore, given that a normal CSF protein (lack of albuminocytological dissociation) is found in one-third to one-half of patients within the first week of symptom onset [2], an LP would not have refuted the diagnosis. His clinical course showed improvement in his respiratory status with liberation from mechanical ventilation on day 4 of IVIG therapy. Neurologically, his upper extremity weakness resolved after completion of the course of IVIG. Lower extremity weakness persisted, however. He was transitioned out of the intensive care unit with eventual discharge to rehabilitation facility where is currently getting physical therapy.

Discussion

While it was determined to have originated in the China's Hubei province, at the writing of this paper, the SARS-CoV-2 has infected over 1.7 million individuals worldwide with over 100,000 deaths directly attributed to COVID-19 [3]. The virus belongs to the betacoronavirus subgroup of the Coronaviridae family and is comprised of an enveloped single stranded Ribonucleic acid (RNA) genome [4]. Genetic analysis found it to be similar to SARS-CoV and MERS-CoV in its sequence, but different enough to be considered a novel virus [4]. Most immediate causes of death involve acute respiratory distress syndrome (ARDS) and its sequelae along with overwhelming shock from a surge of cytokines [5]. Post viral complications of the infection have not been fully explored at this point.

GBS is an acute areflexic paralytic state that most commonly presents with progressive symmetric weakness, as in our patient. These symptoms generally develop 3 days to 6 weeks following an upper respiratory infection or diarrheal type illness [6]. While the most common infection associated with the development of GBS is campylobacteriosis, viral infections such as cytomegalovirus, Epstein-Barr virus, human immunodeficiency virus and most recently Zika virus have also been associated [6,7]. The mechanism proposed is an autoimmune reaction where antibodies to surface glycoproteins are developed on the offending pathogen that also correspond to similar protein structures of peripheral nerve components (molecular mimicry) leading to neurologic involvement [6]. In our patient, the respiratory illness was COVID-19 which we believe to have triggered this neurological process. He was also diagnosed with *Clostridium difficile* infection 2 days prior to presentation. We are not aware of GBS associated with this infection with this much commonly encountered infection in clinical practice to date. Moreover, the recent report of GBS possibly associated with COVID-19, alluded to below, raises concern for this virus to be a possible trigger.

Previous research has implicated other coronaviruses in neurologic disease. Looking at murine models with infections with the coronavirus, Houtman and Fleming proposed use of an immune compromised mouse model with infection by a coronavirus variant to model human multiple sclerosis, another known demyelinating disease [8,9]. Evidence has shown spike glycoprotein involvement with murine infection of the neurologic system with support from the hemagglutination proteins, making betacoronavirus a more likely strain of coronavirus to infect neurologic cell lines [10]. In a retrospective study of the MERS-CoV outbreak, one patient was diagnosed with Bickerstaff's encephalitis with overlapping GBS during his treatment course [11]. Neuromuscular involvement was also reported by Tsai et al. in patients infected with the SARS-CoV [12].

To date, there has been one reported case of GBS associated with SARS-Cov-2 infection in a patient who had returned from Wuhan in January 2020 [13]. That person presented with the classic features of GBS but developed fever and respiratory symptoms subsequently. Her laboratory work up had already revealed lymphopenia and thrombocytopenia on admission though. Hence, there was suggestion of infection, at least based on blood tests on presentation. The authors suggested a 'parainfectious' profile pattern of GBS in their patient instead of the usually encountered post-infectious neurological deficit seen in GBS. The authors suggested a possible association between the GBS and COIVD-19 pending more epidemiological data. Our case adds to this recently reported case. Moreover, the presentation in our patient too suggests the 'parainfectious' profile rather than the generally encountered relatively longer time period between the triggering event and development of GBS.

Conclusion

Clinicians should be cognizant of the neurological presentation of GBS that is likely associated with SARS-CoV-2 infection. While bacterial and viral infections are known to trigger GBS, awareness of such presentation is important because the typical respiratory and constructional symptoms may not be present on admission such as the case reported by Zhao et al. Also, while the presenting clinical features may primarily be neurological, a thorough review of systems should be obtained to ensure no features of COVID-19 infection are overlooked. This has infection prevention implications since appropriate precautions could be taken when encountering similar patients during the current pandemic.

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Consent

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 on request.

Author contribution

All authors were equally involved in data gathering and manuscript writing.

Declaration of Competing Interest

Tariq Cheema, MD is on the speaker's bureau for Boehringer Ingelheim and Glaxo smith Kline.

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