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Guillain Barre Syndrome and COVID – 19 Pandemic, Cause or Effect

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Patient: Male, 52-year-old Male

Final Diagnoses: Guillain – Barre Syndrome, COVID -19, SARS-CoV-2, Hypoxic Respiratory Failure

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Objective: Unusual clinical course

Background

At the time of writing this article, an estimated 6.36 million people worldwide have lost their lives to the COVID-19 pandemic1. Compared to other common respiratory viruses like rhinovirus or common coronaviruses, the maladaptive immune response to COVID-19 gives rise to an inordinate number of complications including hypoxic respiratory failure and adult respiratory distress syndrome (ARDS)2. Additionally, COVID-19 has been shown to cause a severe autoimmune inflammatory response affecting the peripheral nerves, thus causing a form of Guillain-Barre Syndrome (GBS)3,4. This excessive and misdirected immune response targets the peripheral nerves causing destruction and potentiates other neurological comorbidities, increasing weakness, and causing progressive difficulty in movement and ventilation. Maintaining a high index of suspicion for GBS in COVID-19 patients can allow prompt recognition of the early signs of neurological involvement, such as acute paralyses and diminished or absent deep tendon reflexes (DTRs), allowing early treatment and preventing further morbidity and mortality.

We present a case of a 62-year-old male with history SARS-CoV-2 infection treated in the ICU. This patient was admitted with respiratory distress, intubated using a low-tidal-volume, high-peep ventilator strategy, and treated with dexamethasone, remdesivir, and antibiotics. Despite improvement of both the A-a gradient and hypoxemia, this patient failed multiple spontaneous breathing trials (SBTs), initially failing to be weaned from the ventilator. Neurological exam revealed absence of deep tendon reflexes, (DTR) which led to lumbar puncture and subsequent diagnosis of GBS. Patient underwent plasmapheresis, eventually leading to successful liberation from the ventilator.

Case

This patient is a 52-year-old male with history of COPD, hypertension, and diabetes, who presented to the emergency room with dyspnea, cough, and shortness of breath. Upon arrival he was found to be hypoxic and was immediately started on 2 liters of oxygen. His vitals included a pulse of 120 bpm, blood pressure 122/72, respiratory rate of 15, and O2 saturation of 80% on room air. Physical exam was initially significant for BMI of 38 kg/m2, tachypnea, and hypotension. Rapid PCR for COVID-19 was positive, and CXR showed bilateral ground glass changes. Lab results showed C-reactive protein to be

169 mg/L and WBC 16,500 cells/mm3. The patient was admitted to the COVID ICU and treated with remdesivir, dexamethasone, and meropenem. He was intubated and mechanically ventilated, starting with a PEEP of 10 cmH2O and 100% FiO2. The PEEP was titrated to 15 cmH2O, and the patient was proned. The patient required mechanical ventilation for one week and, with aggressive therapy, was weaned to FiO2 of 35%. The patient failed two SBTs despite awakening and following commands. Additionally, physical exam showed newly absent DTRs in all extremities, and the patient reported feeling weak when sitting up vertically, as though in a chair, while still being ventilated. A lumbar puncture was performed, and CSF analysis showed elevated protein to 110 mg/dL with no cells. Anti-ganglioside antibody was negative. The patient had 5 sessions of plasmapheresis, and his strength improved in all extremities. Finally, he was able to be weaned from the ventilator.

Discussion

Acute SARS-CoV-2 infection and many other acute viral infections can cause a severe increase in pro-inflammatory cytokines5,6,7. During infection, SARS-CoV-2 enters cells of the body--especially nasal ciliary, upper bronchial epithelial, and type II alveolar cells—by spike-protein binding with cells' angiotensin-converting-enzyme receptors8. Viral entry into the cell ignites an acute inflammatory response that can lead to a state of autoimmunity. This state of autoimmunity can exacerbate pre-existing neurological conditions including myasthenia gravis, an autoimmune neuromuscular disorder that can—even on its own—cause impaired ventilation, further compromising the ventilation-perfusion balance of an already-compromised patient in respiratory failure9. Serial neurological evaluations and early consultation with Neurology should be considered for prompt diagnosis and rapid intervention, to decrease a patient's number of days on mechanical ventilation, thus improving survival and decreasing further exacerbations of comorbidities. Electrodiagnostic studies may be helpful to diagnose a new-onset neurological pathology associated with COVID-19 infection, but in many parts of the world this technology may not be readily available or practical. In these areas, lumbar puncture, clinical acumen and serial examination suffice for diagnosis. If electrodiagnostic study is performed, a pattern consistent with axonal degeneration of motor nerves without sensory involvement is most consistent with GBS as neurological sequela of COVID-1910. In the above case, our patient had no prior neurological comorbidities, lumbar puncture, careful physical exam, clinical reasoning were adequate to detect GBS in this COVID-19 patient, who had no other reason to fail multiple SBTs.

GBS is commonly preceded by any number of bacterial or viral infections, but a causal link is thought to exist between preceding Campylobacter jejuni or Epstein-Barr Virus infections and GBS due to molecular mimicry between gangliosides of the peripheral nerves and antigens of C. jejuni and EBV10,11,12,13. In these cases, autoimmune-response antibodies are generated against those gangliosides12. Multiple studies suggest that patients with COVID-19-associated GBS tend to be negative for anti-ganglioside antibodies, though this is not always the case3,10,13. It is important in

understanding our patient, because it helps rule out a more familiar cause of GBS, like a recent infection with C. jejuni, and thus points to COVID-19 as the culprit of our patient's neurological pathology.

Management of acute GBS consists of immunomodulatory measures such as intravenous immune globulin (IVIG) or plasma exchange (PE) in combination with standard supportive ICU care12. Both therapies can improve outcome and recovery. To wean a patient such as this from ventilation, one must consider both ventilatory considerations as well as neurological considerations of the patient. Ventilatory considerations include ease of ventilation, vital capacity, negative inspiratory force (NIF) measurements, and spontaneous breathing trials, while neurological considerations include repeat neuro exams to assess improving strength not only while being ventilated at the usual settings, but also during weaning trials. Our patient required aggressive therapy and inpatient rehab following extubation. Several studies have shown an increased number of GBS patient in the COVID-19 surges showing the association of SARS – CoV-2 inflammatory response triggering autoimmunity and GBS.

Conclusion

COVID-19-induced pro-inflammatory cascade can produce autoantibodies leading to muscle weakness and prolonging a patient's time on the ventilator. High clinical suspicion and serial neurological examinations are needed to identify the cases that will improve with plasma exchange or intravenous immunoglobulin. Lumbar puncture, imaging and neurological consultation—as well as electrodiagnostic, when available--should be part of the multidisciplinary approach to treating such a patient. Serial monitoring of ventilatory capacity such as with NIF test, SBT, and CPAP trials, as well as testing of extremity strength is all crucial to document the degree of improvement in response to therapy. This type of patient, if able to be extubated, should have aggressive physical therapy afterwards. For the patient that fails weaning trials even after treatment for GBS, consider tracheostomy and admission to a long-term care ventilator facility. The coincidence of GBS and COVID-19 may be a result of autoimmunity or a result of direct damage of the virus to the nervous system. Further study is needed to better understand the relationship between COVID-19 and GBS. The immune system can be idiosyncratic, and SARS-CoV-2 continues to mutate despite increased vaccination rates in developed countries, opening up the possibility of a variant with an even greater affinity for the cells of the nervous system. Therefore, to prevent further morbidity and mortality to those infected with COVID-19, GBS should maintain a position on the differential for difficult-to-extubate COVID-19 patients.

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