Acute inflammatory demyelinating polyneuropathy induced by sars cov-2 viral infection.

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Abstract

Introduction: Guillain Barre Syndrome (GBS) in SARS- CoV-2 is estimated to be around 15 cases per 100,000 and most cases occur after active infection is resolved. We present a case where GBS occurredconcurrently during anactiveinfection, raisinga broad clinical question aboutitsimmuno-mimicking or modulating properties and genetic susceptibility predisposing certain individuals.
Case: A forty-one-year-old male presented with acute weakness in his bilateral lower extremities. The patient had ongoing flu-like symptoms. He was not vaccinated and tested positive for SARS-CoV-2. Past medical history was significant for acute inflammatory demyelinating polyneuropathy two years ago, with similar presentation as above shortly after influenza A. Neurological exam revealed bilateral lower leg weakness with reduced strength. Lumbar puncture showed elevated proteins. The patient was started on plasmapheresis and noted significant improvement after treatments for five days.
Discussion: A review of literature demonstrated that SARS-CoV-2 is responsible for multiple autoimmune disorders. Hyperstimulation of the immune system occurs due to viral entry triggering cytokine storms, and production of multiple gamma globulins. This is one of the proposed mechanisms where low levels of antibody were already present in individuals and hypergammaglobulinemia precipitated autoimmunity. The similarity in primary sequence between humans and components of SARS-CoV-2 explains molecular mimicry as a second causative factor. Neutrophil Extracellular Traps activation produces extracellular fibers that traps and degrades organisms using elastase and proteases. This can cause the deimination of self-proteins, making them autoreactive. However, further research is warranted to study the underlying mechanism of autoimmunity.

Keywords: Severe Acute Respiratory Syndrome Coronavirus 2, Guillain Barre Syndrome, Auto immunity, acute inflammatory demyelinating polyneuropathy, Neutrophil extracellular traps.

Introduction

Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) has proven to affect various organ systems in different ways. Previously reported cases have linked SARS-CoV-2 to myocarditis [1], arrhythmias [2], coagulopathies, and various neurological manifestations apart from acute respiratory distress syndrome [3]. Neurological manifestations vary from simple anosmia and dysgeusia to encephalitis and hemorrhagic encephalopathy, indicating that the virus is neuroinvasive in nature [4]. Prevalence of GBS in SARS- CoV-2 is estimated to be around 15 cases per 100,000 and most cases after active infection [5]. We bring a case of SARS-CoV-2 that illustrates one of its rare neurological presentations, Guillain Barre Syndrome (GBS), which occurred concurrently during an active infection, raising a broad clinical question about its immuno-mimicking or immuno-modulating properties and genetic susceptibility predisposing certain individuals.

Case

A forty-one-year-old male presented to us with complaints of weakness in his bilateral lower extremities leading to difficulty in walking over the course of one day. The patient reported that he has ongoing flu-like symptoms, including fevers, chills, and sweats, a few days before developing his lower extremity weakness. Workup revealed a positive SARS CoV-2 on a Polymerase Chain Reaction. The patient was not previously vaccinated or was infected with SARS CoV-2. The patient denied any respiratory distress at the initial presentation. His past medical history was significant for acute inflammatory demyelinating polyneuropathy two years prior, and it presented similarly as above with bilateral lower extremity weakness a few days after testing positive for influenza A. Lumbar puncture showed elevated proteins and he received Intravenous immunoglobulin (IVIG) infusion and the symptoms resolved.

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On physical examination, He was noted to be alert and oriented with no signs and symptoms of respiratory distress. His respiratory capacity on admission was evaluated by obtaining a negative inspiratory force (NIF), which on admission was -46 cm of water (H2O), indicating some loss of capacity despite being clinically asymptomatic. His neurological exam showed no acute abnormalities in any cranial nerves. Motor exam revealed bilateral motor weakness with findings described in Table 1. There was decreased sensation to light touch in all extremities, more pronounced distally. Muscle tone was noted as normal in all limbs.

Lab workup, including a complete blood count and a comprehensive metabolic panel, was within normal limits. C-reactive protein was elevated at 43 milligram/Liter (normal <10 mg/L). The electrocardiogram showed normal sinus rhythm. Magnetic resonance imaging of the head and lumbar and cervical spine was obtained, which showed no signs of acute intracranial abnormalities or cord lesions. A lumbar puncture was performed, and cerebrospinal fluid (CSF) analysis revealed normal protein at 42 milligrams/ deciliter (normal 15-60 mg/dL), glucose at 73 milligrams/ deciliter (normal 50-80 mg/dL), cell count of less than 5, and cultures showed no growth. Based on the CSF analysis, infectious etiology was ruled out. Considering the patient's past medical history, it was suspected that the patient had SARS CoV-2-induced acute inflammatory demyelinating polyneuropathy. The patient was immediately started on plasmapheresis and was noted to have significant improvement in his strength after daily treatments for five days. His respiratory capacity improved, indicated by a NIF greater than 60 in repeat testing. No respiratory distress was noted throughout his treatment course. He was subsequently discharged to rehabilitation.

Discussion

Autoimmunity has been linked to genetics, environmental and hormonal factors [6, 7]. The exact mechanism and pathogenesis are unknown, but multiple factors play a critical role in the development of autoimmune conditions, and novel SARS CoV-2 has proven to be one of those factors.

A comprehensive review of medical literature demonstrated that SARS-CoV-2 is responsible for multiple autoimmune disorders. The receptors for viral invasion, Angiotensin-Converting Enzyme-2 (ACE-2), and transmembrane serine proteases are expressed in type 2 alveolar pneumocytes and endothelial cells [8]. Hyperstimulation of the immune system occurs due to viral entry inside the host cells triggering the production of inflammatory cytokines and interleukins, including IL-6, IL-1B, IL-10, IL-17, TNF, and GM-CSF; this leads to cytokine storm, resulting in the production of multiple gamma globulins by plasma cells [9]. The inflammation and secondary cytokine release is known to cause Acute Respiratory Distress Syndrome (ARDS). However, various cases have been reported in the medical literature where robust polyclonal B cell proliferation and antibody production caused new onset autoimmune diseases [10-12].

Recent studies demonstrated a similarity in primary sequence between humans and components of SARS-CoV-2 [13]. Therefore, any alterations in the form of mutations, additions, or deletions of genes cause autoimmunity due to molecular mimicry [14,15]. Coagulopathy associated with COVID-19 also has multiple proposed mechanisms, and anti-phospholipid antibody formation is one of them. Beta 2 glycoprotein 1 and anticardiolipin antibodies were found in hospitalized patients with severe infection [16-18]. Antinuclear Antibodies (ANA) titers were elevated in patients with severe COVID-19 infection, and were directly proportional to their CRP levels [19]. This raises the question on whether the antibodies were alreadypresent in those individuals in lowtiters (asymptomatic) and the viral infection precipitated APLA syndrome. Notably, Anti-heparin platelet factor 4 was found in patients without prior exposure to heparin, suggesting its autoimmune nature and coagulopathy. Finally, Neutrophil Extracellular Traps activation, a.k.a NETosis, is the third proposed mechanism for autoimmunity. This innate immunity is led by neutrophil, which produces a network of extracellular fiber that contains DNA and chromatin, trapping pathogenic organisms and degrading them using elastase and proteases. This process can sometimes cause the deimination of self-proteins, making them autoreactive [20]. This is similar to the citrullination of amino acids that has been studied in rheumatoid arthritis and systemic lupus erythematosus [21, 22].

In our case, based on the onset of clinical presentation, negative imaging and normal protein in CSF analysis. We think that the most likely mechanism of GBS development during ongoing SARS-CoV-2 infection is that preexisting low levels of Anti-Ganglioside D3 antibodies from prior episodes triggered more antibody formation and precipitation of GBS during active infection. Table. 2 describes various autoimmune phenomena as described in medical literature. However, further research is warranted to study mechanisms of autoimmunity seen in SARS CoV-2 infection [23-38].

Table 1. *Lower Extremity Strength of SARS CoV 2 infection.*

Lower Extremity Strength (Grade 0 to 5)		
	Right	**Left**
Hip Flexion	0/5	0/5
Knee Extension	5-Feb	5-Feb
PlantarFlexion	0/5	5-Feb
Dorsiflexion	5-Mar	5-Mar

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Table 2. *Various autoimmune phenomena demonstrated with SARS CoV 2 infection.*

New onset of autoimmune diseases	Antibodies	References
Autoimmune Thyroid disease	Anti- TPO, Anti TG, Anti TSHR	[23-25]
Type 1 Diabetes	Anti Glutamic acid decarboxylase	[26-28]
Kawasaki's disease	Unknown etiology, vasculitis	[29-30]
Autoimmune hemolytic anemia	IgG and IgM	[31-33]
Immune thrombocytopenic purpura	GPIb, GPIIbIIIa, GPV	[34-35]
Systemic lupus erythematosus	ANA, atypical ANCA	[36-37]
Posterior Orthostatic Tachycardia Syndrome	No antibodies found	[38]

Conclusion

A male patient aged is 52 years old from Deoli district Wardha was admitted to pediatric ward AVBRH on 2 may 2021 with the complaints of Difficulty in breathing Breathlessness, Difficulty in swallowing, Restlessness, profuse sweating, fever. He is diagnosed for Acute Respiratory Failure after covid-19 on Report of HRCT scan of Thorax score 15/25 on date 20 may 2021. As soon as the patient was admitted in AVBRH All the required investigation were done and appropriate treatments were started.

The patient is on symptomatic treatment. The patient and his family underwent psychological stress, which was resolved on an extent by being an active listener and providing proper counseling.

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