CASE REPORT

Guillain-Barré Syndrome in a 28-Year-Old Female with Antecedent COVID 19 Infection: A Case Report

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Abstract:

Various neurological manifestations have been observed throughout the SARS-CoV-2 disease (COVID-19) pandemic. However, few cases of Guillain-Barré syndrome (GBS) in association with COVID-19 have been described. We submit a unique case of a previously healthy 28-year-old woman who presented with ascending weakness including facial diplegia, areflexia and respiratory compromise consistent with GBS Miller Fisher variant in the setting of recent COVID-19 infection one month prior to symptom onset.

Introduction:

COVID-19, a disease caused by the novel betacoronavirus (SARS-CoV-2), has rapidly become a global pandemic threat with rapidly evolving data due to unprecedented efforts by the medical and scientific community. While COVID-19 primarily affects the respiratory system, increasing evidence points to multisystem effects of the virus with significant morbidity and mortality. Neurological manifestations have been described involving both central and peripheral nervous systems that range in clinical severity and timing of onset, including headache, dizziness, hyposmia, hypogeusia and cognitive dysfunction (1). There have also been reports of COVID-19 infection associated with severe neurological manifestations such as acute cerebrovascular disease, meningitis/encephalitis, acute necrotizing hemorrhagic encephalopathy, and acute Guillain–Barré syndrome. (2)

Guillain-Barré syndrome (GBS) is an immune-mediated polyradiculoneuropathy with diagnosis typically preceded by respiratory or gastrointestinal infection (1). Clinical presentation involves progressive, ascending, symmetrical limb weakness, and paresthesia with diminished or absent deep tendon reflexes, with or without respiratory and cranial nerve involvement (3). The classic subtypes of GBS include acute inflammatory demyelinating polyneuropathy (AIDP), acute motor axonal neuropathy (AMAN), acute motor sensory axonal neuropathy (AMSAN), and Miller Fisher syndrome (MFS) (4). The development of neurological symptoms following infection is the classic phenotype of GBS. Many infectious agents have been associated with GBS including the Epstein–Barr virus, cytomegalovirus, *Campylobacter jejuni*, human immunodeficiency virus (HIV), and ZiKa virus. (5).

The polyneuropathy in GBS involves cross-immunity against epitopes of peripheral nerve components that are shared epitopes on the cell surface of pathogens causing the antecedent infection. Although several viral and bacterial pathogens have been identified in case-control studies, the specific factors that induce the immune-mediated destruction of the nerve tissues remain unclear. Furthermore, the cross-immunity between viral antigens and peripheral nerve glycolipids have not been well-documented (3).

Although the precise mechanism is yet to be elucidated, the link between coronaviruses and GBS is thought to be related to direct neuroinvasive capacity via ACE2 receptors on neuronal tissues, or through indirect inflammatory mechanisms (5). It is well described that SARS-CoV-2 infection causes an immune reaction with an increased level of interleukin-6 (IL-6), which stimulates the inflammatory cascade leading to tissue damage, suggesting an important role in the organ dysfunctions of patients with COVID-19 infection (2) Furthermore, SARS-CoV-2 has structural similarity to SARS-CoV, both with binding capacity to the angiotensin-converting enzyme 2 (ACE2) receptor to allow entry to human cells. Neurons and glial cells that express ACE2 may act as targets, rendering them susceptible to infection by SARS-CoV-2 (2, 6). In addition, SARS-CoV-2 RNA has been detected in a cerebrospinal fluid specimen of patients with COVID-19 (7), supporting the theory of neurotropic involvement of SARS-CoV-2 (8, 2).

With increasing concern over the possible linkage between COVID-19 and GBS,

clinical reports are of value to better understand the precise clinical manifestations and epidemiological link. Although there exists biological plausibility for the neuropathogenic effect of SARS-CoV-2 via expression of ACE2 as well as through a deregulated immune response, a limited number of case reports of patients with COVID-19-associated MFS have been reported to date. Here we present a unique case of 28-year-old female with MFS in the setting of recent COVID-19 infection one month prior to symptom onset.

Case:

The patient is a 28-year-old woman with no past medical history who presented as a transfer to our emergency department with a chief complaint of progressive numbness and weakness beginning four days prior to presentation. Symptoms started with numbness in her feet bilaterally which evolved over the next several days to include her upper legs. She initially presented to another Emergency Department and discharged home the same day. The day prior to admission the patient also noted weakness in bilateral upper extremities, also associated with severe back pain and shortness of breath. Notably, one month prior to presentation the patient tested positive for COVID-19 after exposure to a known infected individual. She was symptomatic for one day with headache and upper respiratory like symptoms, however she never required oxygen therapy nor pharmacologic therapies, and managed her disease course at home. On the morning of her admission, the patient was unable to ambulate or raise her arms to hold her child so EMS was called. Outside hospital CT head was unremarkable and she was transferred for further workup and management.

On admission, she was tachycardic and dyspneic while talking, with respiratory rates to the 30s, and the inability to complete full sentences. Neurologic and musculoskeletal examination was notable for intact orientation, language, reactive pupils and extra-ocular movement. Bilateral facial weakness was present with other cranial nerves being normal. Neck flexion was found to be 4+/5, neck extension 5/5, with the inability to lift bilateral upper extremities against gravity. Individual muscle groups: 2/5 hip flexion, 3/5 knee extension/flexion, 1/5 dorsiflexion/plantar flexion, decreased sensation, vibration, and temperature roughly below the T4 level. Reflexes revealed mute plantars, widespread areflexia, and absent clonus.

Laboratory investigation on admission demonstrated a CBC and BMP reflective of dehydration, but a normal lactic acid and TSH. Initial chest x-ray demonstrated low lung volumes and atelectasis, and a total MRI was performed on the day of admission which demonstrated a normal MR appearance of the spinal cord without evidence of mass lesion or abnormal enhancement.

The patient was initially admitted to general neurology service, however due to autonomic instability, manifesting as sinus tachycardia and bradycardia intermittently accompanied by oscillations in blood pressure, as well as marginal negative vital capacity (VC) breaths and negative inspiratory forces (NIFs), she was transferred to our Neuro Critical Care unit for closer monitoring. A 5 days course of intravenous immunoglobulin (IVIG) 0.4mg/kg was initiated. On hospital day two she had difficulty with worsening bulbar symptoms along with increased work of breathing and was intubated for respiratory failure. Lumbar puncture was deferred due to classical presentation, however anti-GQ1b

ganglioside antibody studies were sent off for evaluation.

On hospital day four the patient developed a low-grade fever of 38.5, mild leukocytosis, increasing oxygen requirement on her ventilator, and sustained tachycardia into the 120-140s. A CTA was obtained that did not show evidence of pulmonary emboli however bilateral pleural effusions were appreciated as well as concern for multifocal pneumonia. Bronchoscopy was performed with bronchial-alveolar lavages reveling *S. aureus.* She was treated appropriate for a hospital acquired pneumonia with intravenous antibiotics. Her autonomic instability was addressed with the addition propranolol and midodrine with satisfactory results. Surveillance venous dopplers were performed due to her immobility and found to be negative.

On hospital day 12 the patient underwent an uneventful bedside percutaneous tracheostomy placement followed by a bedside percutaneous endoscopic gastrostomy for nutrition. She also developed a catheter related *E. coli* urinary tract infection. Over the next two weeks, ventilator support was weaned with the patient tolerated trach collar during the day and ventilator support at night. She was discharged to a skilled nursing facility on hospital day 36 with improved but not yet baseline sensation in upper and lower extremities, 1/5 muscle strength in both upper and lower extremities, and residual cranial nerve seven weakness.

Discussion:

Although Drs. Guillain, Barré, and Strohl, first described the syndrome of acute autoimmune neuropathies, typically manifesting as peripheral polyneuropathies, which may or may not involve the cranial nerves, it wasn't until 1956 Dr. Miller Fisher first described a series of patients with the constellation of ophthalmoplegia, ataxia, and arflexia (9), later dubbed Miller Fisher syndrome (MFS). Antibodies against GQ1b ganglioside are present in 85-90% of patients with MFS and is strongly associated with involvement of oculomotor nerves (10). About 25% of patients will also develop symmetrical ascending weakness, however there are phenotype variabilities including acute ophthalmoplegia without ataxia, and acute ataxic neuropathy without ophthalmoplegia (11), that later of which fits the clinical presentation of our patient. Anti-GQ1b antibodies block acetylcholine release from the nerve terminal of the ganglioside, however their presence is not a necessary component for diagnosis of MFS, and may in fact be absent of ophthalmic involvement is lacking. MFS is a clinical diagnosis based on history and presenting symptoms, accompanied by normal findings on imaging and cerebral spinal fluid albuminocytological dissociation.

As of August 2020, 31 cases of GBS have been reported in association with COVID-19 (12) with only two published cases of MFS (13, 14), however to our knowledge this this is the first case without significant opthalmoplegia. Our case is also notable for the classic autonomic dysfunction often observed in typical GBS presentations as well. It is not surprising that COVD-19 induced GBS is being described given the overall disease burden of this pandemic as well as cases being previously described with Middle East respiratory syndrome (MERS) and severe acute respiratory syndrome (SARS-CoV-1) (15). Acute neurologic involvement from active COVID-19 infection is most likely secondary to direct viral cytopathy via the afferent branches of the olfactory and trigeminal nerve, however later, post-infectious involvement is probably

via immune-mediated phenomenon typical for other post viral GBS infections (16), as in this case.

As the diversity of presenting symptoms and complications of COVID-19 continues to expand, it is crucial to elucidate the potential multi-system effects of the virus in view of developing effective preventive measures, rehabilitation techniques, and clinical management strategies.
From the clinical perspective, it is of value for physicians to be aware of the symptoms, signs, and biomarkers present in patients previously affected by COVID-19 in order to potentially intervene with COVID-19 progression and minimize the risk of chronic effects beyond the acute respiratory phase of the illness. Based on increasing evidence and case reports such as this one, attention should be drawn to the risk of neurological involvement in patients with COVID-19 and a diagnosis of SARS-CoV-2 should be considered in patients presenting with non-specific neurological findings during the current pandemic era.

Conclusions:

GBS should be considered as rare but a major neurological complication in patients with previous COVID-19 infection. Early diagnosis along with supportive management can improve clinical outcomes including rapid initiation of immunoglobulin therapy.

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