**Case Report**

**Guillain Barre’ Syndrome– A post-infectious sequele of COVID-19 in postnatal period & its treatment modality: A case report**

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**Abstract:**

We present a case of 26 years old lady, who was diagnosed as GBS in her postpartum period after being infected with COVID-19. Initially she had mild sore throat and cough but was diagnosed with COVID-19 after undergoing normal vaginal delivery which was done as a part of routine investigation. Later she developed sudden blurring of vision, severe headache along with quadriplegia, areflexia, slurring of speech with nasal voice. On the basis of this she was diagnosed as a case of GBS clinically and was treated with IVIG. She was taken care under critical care medicine department for a week where she improved clinically but still her quadriplegia persisted with diminished reflex.

**Keywords:** COVID-19, Neurological complications, GBS, Respiratory failure, Pandemic.

**Introduction:**

The SAR-CoV-2 (COVID-19) propagated very swiftly all over the world, causing significant morbidity & mortality,1,2, causing a dreadful impact on world health care system, creating a pandemic. It is caused by a newly discovered virus species of the Betacoronavirus genus, where other species are known to cause common cold, severe acute respiratory syndrome (SARS) and Middle East respiratory syndrome (MERS).3 This new virus is named as Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2), which is recognised to be the cause of an outbreak of a respiratory illness in Wuhan city, Hubei Province, China, in December 2019.4 The WHO named the disease as ‘Coronavirus disease 2019’ (COVID-19) and finally in March 2020 announced the COVID-19 outbreak as a ‘pandemic’.5

As cases are increasing with time, researchers are including more pathophysiology in order to better explain the disease process. Commonly COVID-19 patients presents with fever along with respiratory illness. With passage of time more systems are also recognized to be involved e.g., myocarditis and hypercoagulibility state6, neurological symptoms, e.g., dizziness, headache, confusion, myalgia, loss of taste and smell. Severe neurological symptoms accompanying COVID-19 also extend to stroke, impaired consciousness and encephalopathy.

Recent research showed that two-third of GBS cases occur after being infected by upper respiratory infection or enteritis.9 Also from the perspective of virus genus, SARS-CoV-2 has similar features to SARS & MERS coronavirus, where MERS was detected with Guillain Barre’ Syndrome (GBS) in two cases.10 Here we describe a case of GBS following COVID-19 infection.

**Case Report:**

Mrs. X, 26 years, was admitted to our COVID-HDU of our hospital on 27/12/20 as a diagnosed case of GBS during her 3rd postnatal day. She is normotensive, non diabetic and a diagnosed case of psoriasis with no extradermal manifestations. Patient underwent normal vaginal delivery on 18/12/20. Three days later she developed blurring of vision, gradual increasing of weakness in lower limbs. The weakness also spreaded to her upper limbs and eventually she developed areflexia, slurring of speech and nasal voice. This was first detected by her husband who was also a physician himself. Then she was immediately admitted to National Institute of Neurosciences & Hospital (NINSH) and was diagnosed as a case of GBS clinically on 27/12/20. During her treatment in NINSH she also tested positive for COVID-19 during her routine investigation. At that time nerve conduction test was not done for any COVID positive patient in any centre. She received her first dose of IV IG at NINSH and was promptly referred to COVID-HDU of United Hospital Ltd (UHL) for further management. Upon arrival she was found to have significant difficulty in deglutition and blurring of vision. For closure monitoring and protection of airway she was then shifted to COVID-ICU.

On Admission she was hemodynamically stable, anemic and her SpO2 was 96% at room air, RR- 23 br/min, temperature-98.4°F, BP- 110 mmHg, HR- 122 beats/min, skin- psoriatic...
plagues with silver scaling (on scalp, thigh, breast & vulva). Her higher psychic function was normal, GCS 15/15, weakness of eye muscle and throat muscle were noted. Her gag reflex was impaired and nasal intonation was noted. Muscle tone was diminished in both upper & lower limb, significantly more in lower limb. All deep tendon reflexes were absent. Her initial inflammatory markers were high, CRP- 26 mg/L, ESR- 120 mm/hr, D-dimer- 1210 mcg/L. Cerebrospinal fluid (CSF) -Albuminocytological dissociation, Protein- 502.88 mg/dl, WBC- 02 cells/mm³. Her nerve conduction study (NCT) could not be arranged as she was COVID-19 positive. Chest X-ray findings were unremarkable. She was started on IV Human Immunoglobulin, IV Remdesivir, IV LMWH(low molecular weight heparin), IV Methyl Prednisolone followed by IV Dexamethasone, IV antibiotics and other symptomatic management along with topical steroid ointment for psoriasis.

On day three of IV IG therapy her weakness started to decrease, limb reflexes started to reappear (at first, right sided biceps reflex reappeared), blurring of vision and difficulty in deglutition subsided over the next two days. She completed her IV Ig therapy at COVID-ICU. Throughout her stay under critical care she didn’t require any oxygen support and respiration remained normal.

On 01.01.21 her RT-PCR for COVID-19 turned negative and then she was transferred under Neurology department on 02.01.21 as a step down process. She was managed with conservative approach and was uneventful. On 04.01.21 she was discharged on request in a clinically stable condition, with limb reflexes still being diminished. At home she was on daily physiotherapy. Finally she regained all her limb reflexes and returned to normal daily activities after two months.

Discussion:

GBS is an autoimmune condition, followed by a recent infection or immune stimulus, i.e., vaccination, which creates an autoimmune reaction affecting the nervous system due to molecular mimicry. As observed in this case report it affected the spinal roots and peripheral nerves, giving the features of quadriaparesis and areflexia. Covid-19 causes an accelerated immune response which present with fever, high inflammatory markers and pro-inflammatory cytokines. Since COVID-19 causes immune reaction, it is also thought to increase the risk of immune mediated disease such as GBS.

Overall incidence of GBS worldwide was reported only to be 1.1-1.8/100,000 in a literature review of the epidemiology of GBS, so in this case also it is very much unlikely that GBS occurred due to pregnancy. However an important aspect according to pathophysiology is to differentiate whether GBS following COVID-19 is a para-infectious response or a true post infectious immune mediated response. There are few theories which explain why the virus has a strong affinity for nervous system. Studies show that the virus first infect a peripheral neuron then reach cell body across synapse via a retrograde transport mechanism and ultimately reach the brain. The parainfectious process is thought due to previous GBS cases presenting along with ZIKA virus, another previous viral disease outbreak. While parainfectious neuropathies can be undertaken due to unusual hyperimmune response leading to direct toxic effect or Neuropathy.

The post infectious mechanism of GBS is supported by the evidence of autoantibodies resulting from an immune response against infectious agent, cross reacting with a similar epitope of peripheral nerve, causing damage to peripheral nervous system. SARS-CoV-2 bind to cell surface via viral spike (S) protein, which also binds to angiotensin-converting enzyme 2 and also to gangliosides with sialic acid residues, e.g. the GalNAc residue of GM1. This suggests that cross-reactivity between the viral protein- associated gangliosides and peripheral nerve can be due to molecular mimicry.

The first case of COVID-19 presenting with neurological symptoms was reported in the case series By Mao et al in Wuhan, China. It showed that the more severe the COVID-19 disease was, the more likely patients would present with neurological symptoms. Previously GBS was detected two-thirds of adult cases, preceded by respiratory or gastrointestinal infection, which was also thought to trigger immune response causing neuropathy. In supporting to the above contrary, couple of other infectious agent are also recognised in case-control studies, including bacteria, e.g. Campylobacter jejuni and viruses, e.g. Ebstein-Barr & Cytomegalovirus. Studies concluded that the severity of GBS is also linked with the causative organism, manifested by severe axonal damage after Campylobacter jejuni infection.

In this case the patient also developed significant neurological symptoms, only after one week of having sore throat and dry cough as mild COVID symptoms. With all the above discussions and the case that we have presented, favors more towards the theory as GBS being a post infectious sequelae of COVID-19.

Disease modifying therapy for GBS include high dose of IVIG and plasmapheresis. Both IV IG and PLEx (Practical Aspects of Therapeutic Plasma Exchange) are suggested as treatments for the COVID-19 as it can directly remove cytokines during cytokine storm and is able to create a less anti-inflammatory cellular and cytokine marker. With these treatment eighty-five percent of patients showed good functional recovery, twenty-percent of patients had long-term complications, e.g. severe disability, pain & fatigue and five percent was the mortality rate. Nevertheless PLEx is challenging to be used in haemodynamically unstable patient in critically ill patients and exposes clinicians and health care workers to SARS-CoV-2 infected patients over a longer duration. So at present it is preferred to treat GBS in COVID-19 patients with IV IG unless patients have contraindication, e.g. severe coagulopathy. Our patient of this case also showed drastic clinical improvement by IV IG.

Newer treatments of COVID-19 pneumonitis includes dexamethasone and other immunomodulatory medications which has an impact on prevalence and time of onset of GBS in SARS-CoV-2 infected patients.
Potential life threatening complication of our case could arise from bulbar dysfunction, which could lead to aspiration pneumonia causing respiratory failure, requiring intubation and mechanical ventilation (in 20% - 30% of patients). Since both COVID-19 and GBS increase the chance of respiratory failure requiring intensive care support, it is advisable for the clinicians to improve more awareness in keeping GBS in mind while treating COVID-19 patients, as more new cases of GBS are emerging with time in this era of COVID-19 pandemic.

References: