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A CASE SERIES: DIFFERENT VARIANTS OF GUILLAIN-BARRE SYNDROME ASSOCIATED WITH DIFFERENT COVID-19 SCENARIOS

General Medicine

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ABSTRACT

Covid19 has multisystem manisfestation amongst which neurological disease like Gullain Bairre syndrome (GBS) is an important one . More than 220 cases of GBS have been reported post COVID and 500 cases post COVID vaccination . We share our experience of three cases of GBS of which two occurred post COVID 19 infection and the one occurred post COVID 19 vaccination . All cases had clinical signs suggestive of GBS and were proven by nerve conduction study and cerebrospinal fluid examination . Post treatment with IV Immunoglobulins they were discharged with stable vitals and static or improving neurological parameters . We are publishing this case series to add to this growing body of evidence of link between covid-19 infection , covid vaccination and GBS and henceforth increase awareness amomgst clinicians to have high index of suspicion of GBS , initiate early treatment and get more favorable outcomes.

KEYWORDS

Covid19, Guillain barre syndrome and Covid vaccination.

INTRODUCTION

In December 2019, a novel coronavirus was identified as the cause of a cluster of pneumonia cases in Wuhan, China. The disease rapidly spread and, in February 2020, the World Health Organization designated the disease COVID-19 (coronavirus disease 2019)[1] and declared COVID-19 a pandemic on March 11, 2020[2]. The virus was designated as Severe Acute Respiratory syndrome-Coronavirus-2 (SARS-CoV-2).Since the outbreak of the pandemic it became clear that the virus not only involves lungs but affects other organs like central and peripheral nervous system , kidneys, intestines and heart[3-5]. Neurologic complications are common in hospitalized patients[6-13].

GBS result from an immune response to preceding infection that cross-reacts with peripheral nerve components like myelin or axon because of molecular mimicry resulting in demyelinating and axonal Variants. Till date 220 cases of GBS linked with Covid19 have been reported[14-17]. Though a definite causal association is not confirmed, there are cases of GBS following vaccination against COVID 19, reported in many countries and warning has been issued to raise awareness of GBS following vaccination[18-20]. 550 such cases have been reported till date[18-20].

CASES:

CASE:1

A 75 year male presented with sudden onset symmetrical weakness involving both lower limb since 12 days and bilateral upper limb since 10 days. Patient had contact history with COVID Positive 25 days back. On admission patient was vitally stable. Neurological examination revealed hypotonia of all limbs with power in both UL 3/5 and both LL 1/5 with neck flexor 3/5 & extensor 3/5 with generalised areflexia. Single breath count (SBC) was 13/ min. CSF examination showed albumino-cytologic dissociation. SARS cov2 RT-PCR was negative. HRCT- Thorax suggested CORADS-5 and CT sevearity score of 8/25. Nerve conduction velocity (NCV) study was done and it suggested AMSAN (ACUTE MOTOR SENSORY AXONAL NEUROPATHY) variant of GBS. Patient was treated with IVIG for 5 days along with other supportive treatment. Patient eventually improved and on discharge his power in both UL 4+/5 and both LL 4/5 with neck flexor 4/5 and neck extensor of 5/5. SBC was improved to 28/min.

CASE : 2

A 66 year male patient presented with bilateral progressive asymmetrical weakness of both lower limbs since 5 days followed by upper limb weakness since 4 days . Patient had history of COVID 19 , 30 days back (RT PCR COVID 19 positive and CT severity of 10/25) for which he required hospital admission and was treated with oxygen therapy , iv steroids and anticoagulants for ten days. On evaluation of vital signs , patient had hypertension and his saturation was 88 % on Room air . On neurological examination patient had hypotonia in all four limbs , he had 4/5 power in right upper limb at shoulder and elbow joint and 3/5 power in left upper limb at shoulder and elbow joint with grip weakness in both hands . He had power 1/5 in both lower limbs at all possible joints . He was also unable to sit or turn in the bed and had power of neck flexor sand extensors was 3/5 . Single breath holding count was 12 . Patient had generalised areflexia with normal sensory system examination examination . There was no involvement of bowel or bladder NVC study suggestive of AMSAN (acute motor plus sensory axonal neuropathy) variant GBS however CSF examination did not reveal albumin-cytologic dissociation . Arterial blood gas analysis was suggestive of type 1 respiratory failure . Repeat computed tomography scan of lungs revealed severity score of 17/25 . Patient was given iv gamma therapy for 5 days, o2 therapy , and anticoagulants . On discharge his single breath count 30 , his upper limb power was 4/5 and lower limb power was 4/5 and had stable vitals.

Case : 3

A 50 year old male patient presented with acute asymmetric gradually progressive weakness of both lower limbs for 7 days and drooling of food from both angles of mouth for 3 days. Patient did not have any recent history of infection. Patient had COVISHIELD vaccination 1 month back. Initial examination revealed power 2/5 in both lower limbs at all joints in all possible movements with bilateral lower motor neuron type facial nerve palsy and absent vibratory and proprioceptive senses at toes. Reflexes +2 in both upper limbs and absent in both lower limbs. MRI of brain and whole spine was unremarkable. CSF analysis was consistent with GBS (Albuminocytological dissociation, total cells - 5 cells/mm^3, CSF protein - 144 mg/dl). NCV study showed acute inflammatory demyelinating polyneuropathy . IVIG was given over a period of 5 days. Patient was discharged after vitals stabilized.

DISCUSSION:

Since the first reported GBS case in January 2020 in a COVID-19 patient from Wuhan21, association between COVID-19 and GBS has proven to be a topic of much discussion and dilemma. This could be because incompletely understood pathophysiology of GBS and complexity of the immune response and multisystem involvement in COVID-19.

Although the epidemiological evidence on post-infectious GBSs is equivocal22, approximately two-thirds of total GBSs cases are due to

antecedent infections like Campylobacter jejuni, Mycoplasma pneumoniae Haemophilus influenzae, cytomegalovirus (CMV), influenza, enteroviruses, Epstein−Barr virus, herpes simplex virus, hepatitis, human immunodeficiency virus and Zika virus23-26. So, hypothetically SARS COV 2, being a respiratory virus can cause GBS. Now it is established that immune system abnormalities are common in COVID-19, like cytokine storm27. This raises the possibility of autoimmune response mediated nerve damage. Many previous systematic review have shown that COVID-19 manifestations consistently precede GBSs symptoms (median interval 14 days, interquartile range 7–20) and support further the hypothesis of a post-infectious aetiology.

According to studies , the number of published GBSs cases in COVID-19 did not exceed estimated cases amongst general population, except in Italy28. One cohort study carried out in London have even observed decrease in number of cases during pandemic. This might be due to lack of 'causal' association between SARS-CoV-2 and GBSs or might be due to the reduced transmission of common infective GBSs triggers following the implementation of lockdown and public hygiene measures29. Systematic review and meta-analysis, carried out in Greece, estimated overall GBSs prevalence of 0.15 inCOVID-19 against GBSs in the general population (≈2/100,000)19. Studies carried out in Europe have suggested the same.

There are many cases of GBS following vaccination against influenza , hepatitis A and tetanus30,31. Pathogenesis in vaccine induced GBS is thought to be immunological like post infection GBS. So, possibility of GBS cannot be ruled out in vaccine against SARS-COV-2, eg 227 cases of GBS had been reported from the EU with Vaxzevria by 27 June 202130, 100 cases have been reported with Johnson & Johnson (Janssen) COVID-19 vaccine in US as of 30 June31 and the WHO global database of Individual Case Safety Reports (ICSR), which indicated 164 unconfirmed cases in countries outside the EEA and US for Astrazeneca (Vaxzevria and Covishield) vaccines and a warning was issued to raise awareness of GBS following vaccination18-20.

Considering the uncertainty of the causal relation between vaccines and GBS and the inability to prove that relation on a molecular basis32, further studies are required before establishing a conclusion. We would like to express our opinion that the reduction in morbidity and mortality achieved by vaccination outweighs the risks of the reported adverse events and extensive research is required before asserting or ruling out a causal relation between COVID-19 vaccine and GBS.

In case 1 though patient did not have any complain suggestive of COVID-19, patient was advised HRCT thorax as there was haziness on roentgenograph and also having contact history (wife) 20 to 25 days back. It is possible that patient had asymptomatic COVID-19 7-10 days after exposure(incubation period) and patient developed GBS 2 weeks after that.

Case 2 had moderate severity COVID-19 with CT score of (10/25) and required O2 therapy but patient did not have any neurological complication during the course of covid19 . But presented with GBS 30 days after infection . So cause can be attributed to COVID-19.

Case 3 had no comorbidities , no recent history of infection but He was vaccinated for the COVID-19 4 weeks back which is the same duration required for maximum antibody response after 1st dose of vaccine19. There is increasing data of GBS in population vaccinated for COVID-19 20. So, vaccination can be considered the causative factor.

CONCLUSION:

On the basis of this study we conclude that GBS can present as any variant of GBS as well as GBS in COVID-19 is not related to clinical feature or severity of COVID-19 and mechanism for GBS in COVID-19 is immune mediated rather than Para infectious course or direct damage, because all the three cases developed GBS 2-3 weeks after antigen exposer which favours our observation.

We suggest that more data should be collected and published to support link between COVID-19 and GBS, so that clinicians are aware of this association to avoid delays in diagnosis and to promote early initiation of treatment and supportive care for a condition associated with significant morbidity and mortality.

We also suggest that the neurological system is included in history taking and examination to ensure neuromuscular causes are not missed, as clinicians are at risk of confirmation bias when assessing patients with shortness of breath during the COVID-19 pandemic.

Further research is needed to investigate whether the GBS phenotype associated with COVID-19 follows a para infectious as opposed to the classically post-infectious course.

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