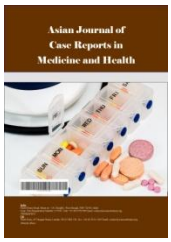

Asian Journal of Case Reports in Medicine and Health

8(2): 24-30, 2022; Article no.AJCRMH.89690

GBS, Breaking the Stereotypes of Clinicians' Minds: A Case Study of Atypical Presentation of GBS, Caused by COVID-19 Vaccination?

Rabia Arshad [a*#], Zoha Fatima [b†], Ujala Abdul Rashid [b†] and Umara Nasim [b†]

[a] Department of Emergency and Critical Care (DEC), Holy Family Hospital, Rawalpindi, Pakistan.
[b] DEC, Holy Family Hospital, Pakistan.

Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

Article Information

Open Peer Review History:
This journal follows the Advanced Open Peer Review policy. Identity of the Reviewers, Editor(s) and additional Reviewers, peer review comments, different versions of the manuscript, comments of the editors, etc are available here: https://www.sdiarticle5.com/review-history/89690

Case Study

Received 09 June 2022
Accepted 13 August 2022
Published 22 September 2022

ABSTRACT

The clinicopathologic spectrum of Guillain Barré Syndrome (GBS) has expanded to include both inflammatory injuries that lead to demyelination and axonal loss forms that cause the motor and sensory loss. However, GBS may also have atypical presentations, that intrigue the clinicians' interest. COVID-19 vaccines and their adverse effects are an emerging topic in medicine. While GBS has been reported as a rare complication of COVID-19 infection as well as after the meningococcus, influenza, polio, and rabies vaccine; a definitive association with the COVID-19 vaccine is yet to be established.

Keywords: Guillain Barré Syndrome (GBS); COVID-19; vaccine; pandemic.

1. INTRODUCTION

Guillain-Barré syndrome (GBS) is an immune-mediated peripheral neuropathy with an estimated annual incidence of 1–2 cases per 100,000 worldwide [1]. It is a collection of clinical syndromes that manifests as an acute inflammatory polyradiculoneuropathy with resultant weakness and diminished reflexes [2]. Although traditionally, the hallmark of GBS is

[#] Senior Medical Officer,
[†] House Officer,
**Corresponding author: E-mail: uja.arashid69@gmail.com;*

demyelinating neuropathy with ascending paralysis; many clinical variants have been documented.

Typically, a patient with GBS presents 2-4 weeks following a relatively benign respiratory or gastrointestinal illness. Most common complaints at presentation include finger dysesthesias and proximal muscle weakness of the lower extremities [3]. The weakness then progresses over hours to days to involve the arms, truncal muscles, and muscles of respiration. Ventilatory failure with required respiratory support occurs in up to one-third of patients at some time during their disease [4]. Patients not only manifest motor symptoms but also autonomic and sensory disturbances, as well as cranial nerve involvement are equally common, which may cause facial droop, diplopia, dysarthria, dysphagia, ophthalmoplegia, and pupillary disturbances.

Paresthesia generally begins in the toes and fingertips, progressing upward but is usually limited to wrists or ankles. The pain, often aching or throbbing in nature, is most severe in the shoulder girdle, back, buttocks, and thighs and may occur with even the slightest movements. Autonomic disturbances in GBS can cause cardiovascular instability, facial flushing, anhidrosis and/or diaphoresis, and urinary retention [5].

COVID-19 has become a global pandemic. While it mostly affects the respiratory system, the neurologic manifestations of COVID-19 infection like ischemic stroke, GBS, and headache have become widely recognized [6]. With the other challenges brought by the pandemic, one of the major concerns is the vaccine against the disease. Several vaccines were approved by FDA and reported side effects ranging from pain at the site of injection, myalgia, fatigue, and fever to more serious ones including anaphylaxis were reported [7]. A few cases have been reported where patients present with neurological manifestations mimicking GBS after getting the COVID vaccine. The presumed pathophysiology is that it is an immune-mediated peripheral neuropathy triggered by molecular mimicry [8].

We report this unusual and interesting case to not only highlight the varied ways in which GBS can present among patients but also the possible association of the COVID-19 vaccine with the neurological manifestations mimicking GBS.

2. CASE REPORT

We describe the case of 42 years old lady who presented to Medical Emergency with complaints of neck pain, headache, and paresthesia of hands and feet. The patient has been known hypertensive for the last 4 years. She has been taking oral antihypertensive medications with poor compliance and control.

The patient had received the CanSino COVID-19 vaccine 2 months before presentation. After six weeks, the patient had an acute respiratory infection with productive cough and fever. COVID-PCR was performed which came out to be negative (Fig. 1) and she was treated at home conservatively. Two weeks later, the patient experienced acute progressive symmetrical weakness of bilateral upper limbs involving both proximal and distal muscle groups. This was preceded by a sudden headache associated with difficult and painful neck movements and multiple episodes of vomiting. The patient deteriorated over the next few hours with an altered level of consciousness, labored breathing, and limb weakness progressing to quadriparesis. The patient was shifted to the critical care unit for ventilatory support.

On presentation, the patient was vitally stable with a GCS of 12/15. Pupils were bilateral round & reactive. She had an unremarkable cranial nerve examination and no visible facial weakness or asymmetry was appreciated. No visual disturbances were seen. Motor examination revealed normal bulk and tone in all four limbs. Power in both upper limbs was 3/5 while 5/5 in lower limbs using the Medical Research Council Scale, which progressively reduced to complete paralysis on subsequent examinations. Deep tendon reflexes were absent. Planters were downgoing. Sensory examination was unremarkable in all four extremities. Signs of meningeal irritation were negative. Autonomic dysfunction was present with sphincter disturbances and cardiovascular instability. No cerebellar dysfunction was noted.

Fundoscopy showed grade I bilateral papilledema. CT scan Brain was performed that showed diffuse cerebral edema with grey-white matter differentiation preserved (Fig. 2). CSF R/E showed cytoalbuminologic dissociation (WBC count= 2, Proteins=147.7 g/dl). CSF findings were not consistent with meningitis. Nerve Conduction Study (NCS) was performed which

showed normal conduction velocities with absent F waves. Electromyography (EMG) revealed normal resting activity (Fig. 3). These findings pointed toward the diagnosis of Acute Inflammatory Demyelination Polyneuropathy variant of GBS (AIDP-GBS). Hematological, biochemical, urine, and stool analyses were unremarkable. SARS Cov-2 PCR was negative. Thyroid profile and serum B12 levels were within the normal range.

National Institute of Health

Virology & Immunology, National Institute Of Health,Islamabad , info@nih.org.pk
Contact:+92519255112,+92519255113

MR #:	[redacted]	**Visit No:**	[redacted]
Lab Ref No :	61663	**Booking:**	March 14, 2022
Patient Name:	[redacted]	**CNIC:**	[redacted]
Age | Gender:	42 Y/ Female		
Order From:	NIH Virology & Immunology		

SARS-CoV-2 PCR

Test	Result Mar 20, 22
Result	Negative

Comments : On the testing with the Real time RT-PCR panel.The sample is Negative for the SARS Cov-2 (NovelCorona Virus). In view of the recent travel and contact history we may contact you for follow-up regarding your general health. The negative result must be interpreted along with clinical observation, patient history and epidemiology information.

Booking: Mar 14, 17:28 **Result Processed:** Mar 20, 13:58

Method:

The Test was performed after RNA Extraction (Qiagen Viral RNA Mini Kit) on ABI 7500 Real Time RT-PCR detection system with internal and external positive controls using the SARS-CoV-2 protocol.

This is an electronically verified report, no signatures are required

Fig. 1. COVID PCR Report, showing negative results

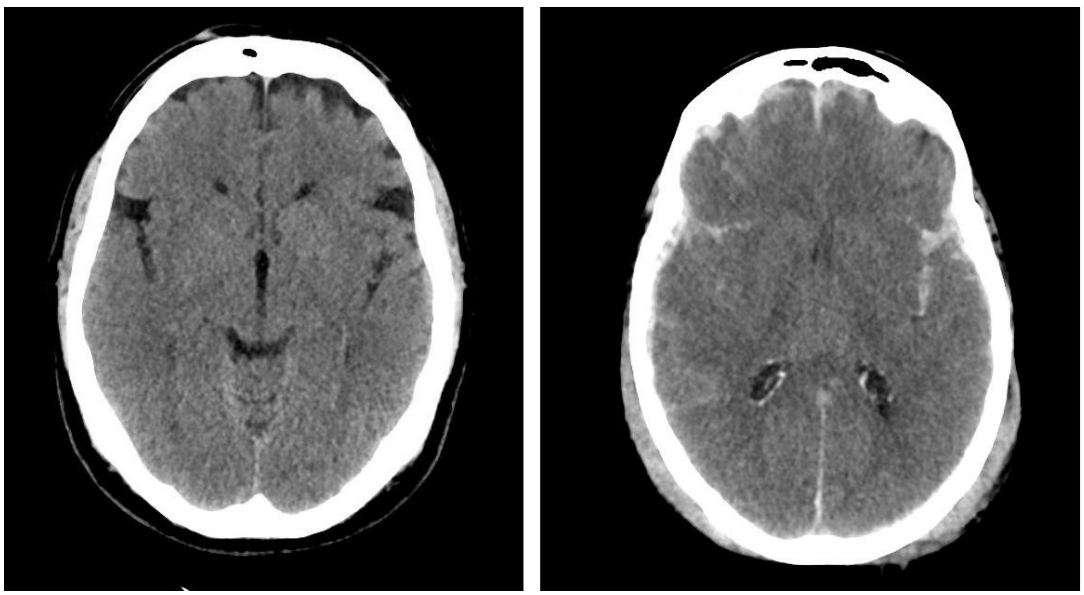

Fig. 2. CT Scan brain (Plain) showing diffuse cerebral edema, an unusual finding in GBS

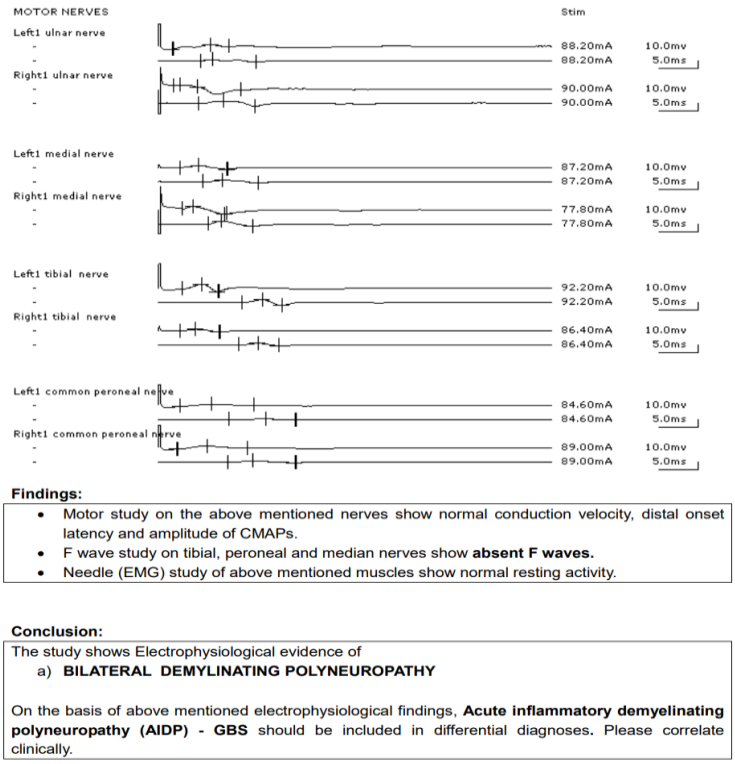

Fig. 3. Nerve Conduction Studies (NCS) and Electromyography (EMG) findings, consistent with Acute Inflammatory Demyelinating Polyneuropathy (AIDP-GBS)

After confirmation of GBS, plasmapheresis was initiated. Clinical improvement was seen after 3 sessions and a total of 5 sessions were done. The patient remained on ventilatory support for 2 months due to respiratory failure. Meanwhile, the patient was also managed on the lines of cerebral edema. Intravenous steroids and mannitol were administered for three days, with permissive hyperventilation and head end elevation. During the hospital stay, the patient developed hyponatremia and was treated for SIADH secondary to GBS. Her routine chest and limb physiotherapy was also assured. The patient was discharged with follow-up advice after 1 month. On her follow-up visit, her complete physical examination was done and NCS was performed, which showed good recovery from GBS with minimal residual paralysis. She was sent home with the advice of continued limb physiotherapy and general care.

3. DISCUSSION

COVID-19 is still an ongoing pandemic that is caused by SARS-CoV-2; originating at the end of 2019, disseminating worldwide, and engulfing every aspect of daily lives. As of June 2022, the disease has already afflicted 544 million people all over the world and has caused 6.33 million deaths worldwide, according to World Health Organization (WHO) [9]. A few months into the pandemic, scientists began their research to find possible counteractive weapons to deal with the problem. To the utmost disappointment, most of the therapeutic interventions have only proved to be partly effective in combating the disease symptoms, halting the transmission, and reducing mortality. The main point of focus, however, has been the primary prevention.

Ever since the pandemic, scientists have tried their best to make multiple COVID-19 vaccines, each one with an improved safety profile and better efficacy than the former. Currently, the FDA-approved vaccines that are most commonly administered are Pfizer-BioNTech, Moderna, Janssen, and CanSino in decreasing order of frequency [10]. With increasing awareness and rapid transmission of the infection, the use of the vaccine is becoming more common day by day. Due to these reasons, thorough and in-depth studies of the novel side effects that might be associated with the newer vaccines have become a dire need of the day. The healthcare

providers and authorities have always shown a special and justified interest in the side effects and complications associated with these vaccines. The commonly reported side-effects include both local and systemic manifestations, in addition to asymptomatic laboratory abnormalities. The side effects that develop locally at the administration site include pain, redness, and edema, which are mostly administrator-dependent. Systemic complications include fever, body aches, and malaise. Some COVID-19 vaccines may also produce benign and asymptomatic changes in biochemical parameters, which include anemia, derangement of liver enzymes (i.e., transaminases), and hyperbilirubinemia [11].

The more serious and concerning, yet uncommon complications include cardiovascular and neurologic issues, including myocarditis, Vaccine-associated Immune Thrombosis and Thrombocytopenia (VITT), and Guillain-Barré syndrome (GBS) [12]. Vaccine-associated myocarditis has shown a specific predilection for adolescents and young adults, while VITT shows no age association [13]. Rather, studies have shown that it follows the immune-mediated pathways and has a preference for intracerebral vessels [14].

Even though COVID vaccines have been linked to GBS, however COVID-19 infection itself causes neurological manifestations one of which is GBS. In scenarios similar to our case study, it is quite challenging to identify the actual culprit of GBS. Multiple cases have been described which indicate that the disease and its vaccine both are related to the development of GBS, as there is no reliable tool to differentiate between the two.

Guillain-Barré syndrome (GBS) is an immune-mediated disorder and encompasses a variety of demyelinating conditions which include Acute Inflammatory Demyelinating Polyradiculopathy (AIDP), which predominantly affects the myelin sheath; Acute motor axonal neuropathy, Acute motor-sensory axonal neuropathy, and Miller Fisher syndrome [15]. It has become one of the leading non-traumatic causes of Acute Flaccid Paralysis (AFP), especially in developed countries [16]. The annual incidence of GBS in Pakistan is 1.1/100,000 to 1.8/100,000 per year. The incidence of GBS seems to increase with advancing age as it has been estimated that after the age of 50 years, the incidence rises from 1.7/100,000 to 3.3/100,000 per year [17].

GBS typically presents with ascending weakness and areflexia with or without accompanying sensory symptoms, like paresthesia and numbness. Descending paralysis with papilledema, and raised intracranial pressure is a rare phenotype of GBS. Similarly features like ptosis, neck stiffness, proximal muscle weakness, and post-infection SIADH is all atypical findings of GBS.

The commonly employed diagnostic modalities include a lumbar puncture followed by a CSF routine examination to not only rule out meningitis but also demonstrate the hallmark of GBS, the albuminocytological dissociation. Nerve Conduction Studies are conducted to further augment the diagnosis as they show peripheral neuropathy and can classify the subtype as demyelinating or axonal in origin.

Due to the consistent finding that GBS occurs after certain types of infections, “molecular mimicry” has become widely accepted as the underlying pathophysiology. It was suggested that some infectious agents, like *Campylobacter jejuni,* can trigger the formation of certain cross-reactive antibodies that, in turn, react with the myelin sheath around the nerve trunks, leading to immune-mediated peripheral neuropathy, thereby producing the neurological manifestations of the disease [18]. This same mechanism is also responsible for causing the comparably similar symptom complex after certain other vaccines like meningococcus, polio, rabies, influenza, hepatitis A, etc. [19]. The testified cases of GBS following vaccination further supported this theory, however proving a causal relationship between vaccines and GBS on the molecular level remains a challenge to this date.

The COVID-19- vaccine-associated GBS was first suspected in 2021 in the USA when the typical neurological signs and symptoms were seen two weeks after the vaccination [20]. This alarmed the clinicians about GBS being one of the possible uncommon untoward effects of the COVID vaccine. Ever since, multiple similar cases have been reported in literature time and again, but the overall incidence amounts to approximately 1 in a million confirming the rarity of the issue [21]. To this day, no definitive hypothesis has been formulated that could confirm the COVID-19 vaccine as one of the definitive causes of GBS.

Considering the uncertainty of the causal relationship between vaccines and GBS and the inability to prove that relation on a molecular basis, it is suggested that thorough and large-scale research are conducted before asserting or ruling out an association between GBS and the COVID-19 vaccine.

4. CONCLUSION

GBS presents in myriads of ways. Our case represents GBS with its rare manifestations of descending paralysis and raised intracranial pressure. Failure to recognize GBS with atypical presentation may lead to an erroneous diagnosis, inappropriate treatment, and significant morbidity. Appropriate diagnosis requires a combination of a detailed history and examination and accurate interpretation of diagnostic testing, but cause evaluation still remains a dilemma after the COVID-19 vaccine.

CONSENT

The authors declare that informed written consent was taken from the patient before data collection and no personal patient data appear in this report. The authors also declare that they have followed the protocols of their work center on the publication of patient data.

ETHICAL APPROVAL

As per international standard or university standard written ethical approval has been collected and preserved by the author(s).

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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DOI:https://doi.org/10.1001/JAMANETWORKOPEN.2022.8879

Peer-review history:
The peer review history for this paper can be accessed here:
https://www.sdiarticle5.com/review-history/89690