Post-COVID-19 vaccine Guillain-Barré syndrome; first reported case from Qatar.

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Abstract

Guillain-Barré syndrome is an immune-mediated neuropathy that was reported following multiple vaccines. We present the case of a gentleman who developed GBS 20 days after the second dose of COVID-19 vaccination. It is important to mention that more research is needed to establish an association between COVID-19 vaccine and GBS.

Introduction:

Guillain–Barré syndrome (GBS) is an immune-related disorder with an estimated annual incidence of 1-2 cases per 100,000 worldwide. It is the most common cause of acute non-trauma related paralysis in the developed world[1]. It manifests as acute, rapidly progressing polyradiculoneuropathy due to inflammation and demyelination of the peripheral nervous system, resulting in a classically symmetrical and ascending weakness, often in association with hyporeflexia or areflexia[2]. The exact cause of Guillain–Barre syndrome is still unknown, but the suggested pathophysiology is molecular mimicry following respiratory and gastrointestinal infections.

After the first case was reported in Wuhan, China in December 2019, the global pandemic caused by SARS-CoV-2 brought many challenges including the manufacturing and administration of vaccine. Several vaccines were approved by FDA and reported side effects ranged from pain at the site of injection, myalgia, fatigue, and fever to more serious ones including anaphylaxis[3,4]. GBS was linked with some vaccines namely, rabies, hepatitis A and B, polio and influenza[5]. However, a causative relationship was not established.

Case history:

A 73-year-old gentleman, active smoker, with medical history of hypertension and well-controlled rheumatoid arthritis, presented to the emergency department with 3-4 days' complaints of progressive bilateral lower limb weakness which prevented him from carrying out his activities of daily living. He previously had an excellent functional status and denied any history of recent trauma, fever, upper respiratory or gastrointestinal tract illness. There was no weight loss, night sweats or change in bowel habits. He had received the second dose of COVID-19 vaccine (Pfizer) 20 days prior to his presentation.

On physical examination, the patient was vitally stable, afebrile and on room air with no signs of distress. Neurological examination showed intact sensation in both upper and lower limbs. Motor strength according to Medical Research Council grade was 5/5 in upper limbs and 3/5 in both lower limbs, proximally and distally. The patient was not able to walk or maintain sitting posture on his own. His reflexes were absent in the ankles, reduced in the knees bilaterally (1/4) and normal in the upper limbs. There was no nystagmus or dysdiadochokinesia. Examination of the cranial nerves and other systems was normal.

Investigations:

Complete blood count showed mild leukocytosis of 11.9 x 10^3/uL (reference range 4-10 x 10^3/uL) with neutrophilic predominance, and normal hemoglobin and platelet count. His renal, hepatic and coagulation profile were normal. C-reactive protein was elevated at 54 mg/dl (reference range 0 - 5 mg/dl). COVID-19 PCR from a nasopharyngeal swab was negative. Computed tomography (CT) and magnetic resonance imaging of the brain were negative for any acute insult in the cerebellum and brainstem. A lumbar puncture was performed, and cerebrospinal fluid analysis showed normal glucose in addition to normal white and red blood cell counts. Additionally, CSF analysis showed elevated protein at 0.8 gm/L (reference range 0.15 - 0.45 gm/L) and elevated albumin at 421 mg/L (reference range 0 - 350 mg/L). Gram stain and culture of the fluid were negative. Oligoclonal band from the CSF was negative as well. Computed tomography (CT) and MRI of the brain were negative for any acute insult in the cerebellum and brainstem. MRI of the spine showed bilateral nerve root enhancement in the lumbar region and the upper part of the cauda equina (Figure 1). Nerve conduction study (NCS and electromyogram (EMG) showed bilateral absent H reflexes in the gastrocnemius muscles consistent with early polyneuroradiculopathy.

Outcome and follow up:

Based on the previous work up a diagnosis of GBS was made. The patient had a stable forced vital capacity (FVC) above 80% throughout his stay in the hospital. He received human intravenous immunoglobulin (IVIG) at a dose of 0.4 gm/kg/day for 5 days, after which he showed signs of improvement in ambulation and overall function. As he remained stable and responded well to IVIG, he was transferred to an inpatient rehabilitation facility for physiotherapy and is planned to have regular follow-ups in the neurology clinic after discharge.

Discussion:

Guillain-Barré syndrome (GBS) encompasses a variety of demyelinating conditions which include acute inflammatory demyelinating polyradiculoneuropathy (AIDP), acute motor axonal neuropathy, acute motor-sensory axonal neuropathy and Miller Fisher syndrome[6]. The annual incidence of GBS in the United States has been estimated as 1.65-1.79 case per 100,000[7]. The incidence of GBS seems to increase with advancing age and is higher in males than females with a ratio of 1.5:1. GBS has become one of the leading non-traumatic causes of acute flaccid paralysis (AFP), especially in developed countries. The classical presentation of GBS is bilateral symmetric weakness and decreased deep tendon reflexes with or without accompanying sensory symptoms such as numbness or tingling. The most helpful investigations include a lumbar puncture with CSF analysis demonstrating albuminocytological dissociation and electrophysiological studies showing peripheral neuropathy which is either demyelinating or axonal in origin[8]. The post-infectious occurrence of GBS led to the reinforcement of the molecular mimicry theory as the underlying pathophysiology. It was postulated that certain infectious agents such as *Campylobacter jejuni* can lead to the formation of cross-reactive antibodies that target gangliosides which constitute a part of the myelin sheath encircling the peripheral nerves[9]. The axonal neuropathy observed in rabbits following their injection with ganglioside-like structures extracted from the bacterial cell wall of *C.jejuni* further support this theory[10].

The immunological pathogenesis of GBS was further reinforced by the reported cases following vaccination against multiple pathogens. The influenza vaccine was the most notorious, however others such as hepatitis A and tetanus were also on the list of possibly associated vaccines[11,12]. Despite a relatively large number of reported cases of post-vaccination GBS, a definite causal association was not strongly confirmed. The increased cases of GBS following the administration of the swine influenza vaccine between 1967 and 1977 did point towards a possible causality, however this was negated in further studies conducted in the years after. The same applied for the oral polio and tetanus vaccines. Earlier studies suggested possible causality; however, the results were contradicted by large multicenter epidemiological studies performed later[13].

The first case of GBS following COVID-19 vaccination was reported in February 2021 in the USA in an elderly female who presented 2 weeks after the first dose of the vaccine. The patient presented with fatigue and bilateral symmetric weakness of the lower limbs. CSF analysis showed albuminocytological dissociation and she was started on IVIG which led to improvement in the weakness. The patient recovered successfully

and was discharged to a rehabilitation institute thereafter[14].

Considering the uncertainty of the causal relation between vaccines and GBS, a temporal association is a possibility. However 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.

Key clinical message:

We hope that our case will serve as a bridge to further research on this subject and will alarm healthcare workers to consider GBS as a diagnosis in patients who present with acute flaccid paralysis after receiving the COVID-19 vaccine.

Declarations:

Consent for publication**:** Written informed consent was obtained from the patient for publication of this case report and the accompanying image. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

Availability of data and materials: The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

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Figures and captions :

Figure 1:

Magnetic resonance image of the spine with intravenous gadolinium showing bilateral contrast enhancement of the nerve roots in the lumbar region and the upper part of the cauda equina (as indicated by the arrows).