Rare occurrence of Guillain-Barré syndrome after Moderna vaccine

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SUMMARY

A Caucasian man in his 60s with a medical history significant for ruptured left middle cerebral artery aneurysm status post clipping 2005 with residual right eye blindness and right leg weakness with gait instability presented with loss of balance, weakness of his legs and fatigue for 3 days. No other antecedent event was identified other than receiving Moderna COVID-19 vaccine 4 weeks before the presentation and 3 days before symptom onset. CT head and CT angiogram of the head and neck were performed and demonstrated no acute intracranial bleeding and no vascular abnormalities. With the findings of diffuse hyporeflexia and cerebrospinal fluid showing albumino-cytological dissociation, Guillain-Barré syndrome was high on the differentials. Electromyogram showed evidence of demyelination. He was treated with intravenous immune globulin (IVIG) and was discharged to rehab with complete symptom resolution.

BACKGROUND

Guillain-Barré syndrome (GBS) is an autoimmune disorder of the peripheral nervous system that typically manifests as a rapidly progressive ascending paralysis, with or without sensory and autonomic dysfunction, following an antecedent event. Since poliomyelitis has nearly been eliminated, GBS is currently the most frequent cause of acute flaccid paralysis worldwide.[1] Common antecedent events identified include upper respiratory tract infections, gastroenteritis and less commonly ganglioside administration, surgery, vaccinations and immune-checkpoint inhibitor therapy.[2] Heightened surveillance of GBS associated with vaccine administration was prompted by reports of an increased risk of GBS (approximately 1 in 100 000 vaccinations) in individuals receiving the H1N1 1976 influenza vaccine.[3]

Infection with the novel pathogen SARS-CoV-2), also referred to as COVID-19, was first reported in Wuhan, China in December 2019 and declared a pandemic by the WHO in March 2020.[4]

In the USA, the first Food and Drug Administration (FDA)-approved vaccine was the Pfizer-BioNTech COVID-19 Vaccine (mRNA vaccine BNT162b2) on the 11 December 2020. This was followed by the approval of the Moderna COVID-19 Vaccine (mRNA-1273 vaccine) and the Janssen COVID-19 Vaccine (Ad26.COV2.S vaccine). The two vaccines, in particular, Pfizer and Moderna have demonstrated over 90% efficacy with a favourable safety profile.[5] Most adverse events have been mild and resolved spontaneously without permanent deficit.[6] Cases of neurological symptoms related to SARS-CoV2 vaccinations have been uncommon. So far, cases of GBS have been reported after receiving the Moderna, Janssen, AstraZeneca (ChAdOx1-S (recombinant) vaccine), Pfizer vaccine.[7–13] We present a case of GBS that developed 4 weeks after receiving the first dose of Moderna vaccine (mRNA-1273).

CASE PRESENTATION

We present the case of a Caucasian man in his 60s with a past medical history significant for ruptured Left Middle Cerebral Artery aneurysm status post clipping 2005 with residual right eye blindness and right leg weakness with gait instability who presented with complaints of loss of balance, weakness of his legs and fatigue for 3 days. He was in his usual state of health before receiving his second Moderna vaccine injection. In the evening after receiving his second injection, he was unable to fall asleep and, when he tried to get out of bed, noticed that his balance was off and he had an episode of urinary incontinence. The next day he was fatigued and unable to walk to the bathroom. At baseline, he rarely uses a cane for his gait instability but since his symptoms began, he was weak to the point where he relied on his cane for walking. Later that day he lost his balance and fell in his kitchen, but did not injure himself or lose consciousness. On the third-day postvaccination, as his symptoms failed to improve, he presented to the emergency department (ED) on the advice of his primary care physician (PCP).

On presentation to the ED the patient's vital signs were stable and his cardiovascular and respiratory exams were unremarkable. He denied any recent fever, chills, runny nose, sore throat, nausea, vomiting, diarrhoea or headache. His neurological examination was notable for bilateral and symmetric 3/5 strength in the following muscle groups: biceps, triceps, wrist flexors and extensors, and iliopsoases. He had trace right biceps reflex, but the remainder of his deep tendon reflexes (DTRs) were absent across triceps, brachioradialis, ankle and knee reflex. Babinski reflex was mute bilaterally. His sensory examination to light touch and pinprick was intact across bilateral medial and lateral aspects of lower extremities. He was noticed to have a loss of vibration sense below dermatomes T11 on the left, L2 on the right. On coordination testing, he was noticed to have dysmetria on finger-to-nose. No dysmetria or ataxia on heel-to-shin. Slow rapid alternating hand movements.

INVESTIGATIONS

Basic labs including complete blood count, basic metabolic panel were within normal limits. His ECG demonstrated a normal sinus rhythm. With

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a high suspicion for stroke, CT head and CT angiogram head and neck were performed and demonstrated no acute intracranial bleeding and no vascular abnormalities other than a 50% stenosis of the proximal left internal carotid artery. Given the generalised weakness and diffusely absent DTRs, we had high suspicion for GBS, and neurology was consulted for further evaluation. To help with the diagnosis, we obtained a lumbar puncture. Cerebrospinal fluid (CSF) analysis was significant for albumino-cytological dissociation with a protein of 90 mg/dL and white cell count (WCC) of 0 cells x 10^6/L.

Electromyogram (EMG) with nerve conduction study showed evidence of demyelination with prolonged distal latency of above 130% of the upper limit of normal with slowed conduction velocity below 75% of the lower limit of normal (LLN) of the right fibular motor response. The conduction velocity of the left fibular and right ulnar motor responses was slowed to approximately 80% of the LLN.

TREATMENT

With the above workup indicating probable GBS, our patient was immediately started on IVIG 0.4 g/kg daily for 5 days. During his hospital course, the patient's negative inspiratory force and vital capacity were serially monitored without evidence of respiratory compromise. He completed his IVIG treatments without complication.

OUTCOME AND FOLLOW-UP

His strength showed marked improvement, 5/5 throughout except for 4/5 right wrist extension and he continued to have areflexia except in the right bicep's tendon. From his acute hospitalisation, he spent 1 week in inpatient rehabilitation before being discharged home. At PCP follow-up 3 weeks following his initial ED presentation he was back to his functional baseline with no residual weakness.

DISCUSSION

Based on the history, physical examination and testing including CSF analysis and EMG results this patient's clinical presentation is most consistent with the diagnosis of GBS. On review of his medical record, he had no preceding respiratory or gastrointestinal illnesses in the preceding 6 months and no vaccinations in that time other than his COVID-19 vaccine. Since he did not have any history or symptoms suggestive of other known antecedents, his precipitating event is hypothesised to be the first dose of Moderna vaccination which he received 4 weeks before the presentation. The second vaccine dose is unlikely to have been the precipitating event as he developed symptoms on the same day.

GBS is an acute inflammatory neuropathy characterised by a spectrum of symptoms affecting myelin or the axons of the peripheral nervous system.[14] GBS has a global incidence of 1–2 cases per 100 000 people per year.[15] The classical ascending motor and sensory polyneuropathy is the most common presentation[14] and the patients often present with relatively symmetrical muscle weakness that begins in the lower limbs and progress cranially to affect other muscle groups. Other symptoms include respiratory muscle weakness, facial nerve palsy and oculomotor weakness, hand and foot paresthesia, and dysautonomia symptoms such as cardiac arrhythmias, urine retention and ileus. Deep tendon responses are frequently absent or depressed when the relevant muscle groups are examined physically. Causative associations with the infections such as Campylobacter jejuni, cytomegalovirus, Epstein-Barr virus and Mycoplasma pneumoniae exist with strong evidence.[14] The theorised mechanism of GBS is molecular mimicry, with an antecedent infection eliciting an immune-inflammatory response that later cross-reacts with peripheral nerve components such as the Schwann cell surface membrane or myelin through cross-reacting epitomes. This results in multifocal inflammatory demyelination, with the initial alterations occurring most frequently at Ranvier nodes. Although GBS is a clinical diagnosis, several findings can aid in the diagnosis. Albuminocytological disassociation is defined as elevated protein levels and normal WCC in CSF fluid analysis and has is present in up to 50% of patients with the GBS during the first week of illness, with rising up to 75% in the third week.[1] Abnormal EMG results include decreased motor nerve conduction velocity, prolonged distal motor latency, increased F wave latency, conduction blocks, temporal dispersion (in demyelinating forms of GBS) or decreased distal motor and/or sensory amplitudes (in axonal form).[16]

Treatment of GBS is primarily supportive and treatment decisions are based on the trajectory of symptom progression. Patients who present with quickly progressing paralysis within 4 weeks of the onset of symptoms can be treated with either immunoglobulin (IVIG) or plasma exchange. Patients' respiratory state should be monitored closely to assess for impending respiratory failure. Autonomic dysfunction can increase the risk for cardiac arrhythmias, a reason for continuous telemetry monitoring.[17]

In the USA, three COVID-19 vaccines have been approved by FDA for emergency use which includes the Pfizer, Moderna and Janssen COVID-19 vaccine. Until now, just a few cases of GBS following COVID-19 vaccination have been documented, with the first case being published in February 2021 by Waheed *et al*.[18] The majority of GBS cases have been recorded after receiving the Janssen COVID-19 vaccine, prompting the FDA to issue a safety warning for an elevated risk of GBS 42 days after getting the vaccine. However, a small number of cases have recently been reported in relation to other COVID-19 vaccines,[7–13] which leaves us again with the question about the incidental or causal occurrence.

The Moderna COVID-19 vaccine is a modified messenger RNA (mRNA) vaccine formulated in lipid nanoparticles that allows RNA delivery into host cells to allow expression of the SARS-CoV-2 spike (S) antigen and elicit both neutralising antibody and cellular immune response to S antigen, promoting active immunisation against COVID-19 caused by SARS-CoV-2 virus. Injection site reactions, lethargy, headache, myalgias, fever, chills and back pain[18 19] are the most common adverse effects reported.

GBS after immunisation is frequently an incidental occurrence. Its previous association with swine influenza vaccination in 1976 has been questioned,[18] and data on its association with influenza vaccination is inconsistent among influenza seasons. If there is an elevated risk of GBS after influenza vaccination, it is minimal, on the order of one to two more GBS cases per million influenza vaccine doses delivered.[20]

Mass vaccination campaigns play important role in controlling pandemics such as the ongoing SARS-CoV-2 pandemic. It is expected that there will be some number of GBS cases occurring coincident with these vaccinations. However, causality is not always clear, and is difficult to establish if these cases are a rare vaccine side effect or unrelated to the vaccination. After approximately 12.5 million doses, 100 cases of GBS were reported among Janssen vaccination recipients—a rate of 1 case per 125 000 vaccinated individuals, nearly five times the background rate over a 42-day window postvaccination.[21 22] Among approximately 51 million administered doses, 277 cases were

reported with other vaccinations that are not approved in the USA, such as Oxford/AstraZeneca COVID-19 vaccine.[6] Early in their deployment, no cases of GBS were attributed to the mRNA vaccines, but with the ongoing mass vaccination campaigns, a report of few cases of GBS associated with mRNA vaccine Pfizer-BioNTech COVID-19 vaccine[23–25] have been reported. To our knowledge, only a handful of cases have been reported with the Moderna vaccines.[9 11–13] We contribute to the literature by reporting a case of GBS associated with the first dose of the Moderna vaccine. We postulate that even though causality is hard to establish but the reporting of these cases can be used as a contribution to the database that tracks the safety of these vaccines.[26] Data on these immunisations are still developing, and the potential causal relationships should be investigated. Controlling the COVID-19 pandemic, with its high morbidity and mortality, necessitates vaccination. Based on the available information the benefits of these vaccines outweigh the risks, as supported by most public health authorities.[27]

Patient's perspective

'I am glad that these vaccine side effects are being discussed. I do not want anyone else to have a similar experience.

When I noticed the weakness in my legs, I thought I was having a stroke. I spoke to my doctor who asked me to go to the emergency room. In the hospital, the brain scans were done which looked fine. I was then checked out thoroughly, only to reveal that I was having these symptoms as a side effect of the COVID-19 vaccine. My family and I were very scared that my paralysis was permanent. However, with the treatments that I received, I had a miraculous recovery. I doubt I will ever be able to fathom the courage to receive any vaccination again.'

Learning points

- Guillain-Barré syndrome (GBS) can present not only following COVID-19 infection but also after vaccination.
- Cases of patients developing GBS after mRNA vaccines are less frequently reported when compared with AstraZeneca, Janssen.
- The patient described above developed symptoms after the first dose of the Moderna vaccine. There are case reports of GBS following both the first and second dose of the Moderna vaccine.
- Early diagnosis and treatment IVIG as in our case lead to rapid recovery.
- Recent vaccine exposure should be recorded in neurological presentations and GBS should be considered, even in the context of complex neurological medical history.

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Case reports provide a valuable learning resource for the scientific community and can indicate areas of interest for future research. They should not be used in isolation to guide treatment choices or public health policy.

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