Causality or coincidental: The first case report of acute inflammatory demyelinating polyneuropathy following COVID-19 vaccination in the Philippines

Introduction

Guillain-Barre’ Syndrome (GBS) is the most common cause of acute or subacute generalized paralysis in clinical practice, affecting children and adults of all ages, with a slight male predominance. In almost two thirds of cases, mild respiratory or gastrointestinal infection precede neuropathic symptoms by one to three weeks [1]. While most cases of GBS are preceded by infection, a modest risk of GBS has been attributed to vaccinations such as the yearly influenza vaccine and meningococcal vaccine [1,2]. This raises concern that the current worldwide COVID-19 vaccination campaign can lead to increased incidence of GBS. Indeed, there have been case reports of GBS attributed to COVID-19 vaccines (Johnson and Johnson, Pfizer, AstraZeneca) that have been published in United States, United Kingdom, Israel, Egypt, Austria and Qatar. Based on these published case reports, the onset from the time of vaccination to the development of neuropathic symptoms can be as short as one day to as much as twenty-one days [3-9,1]. To date, there have been no published case reports in the Philippines regarding COVID-19 vaccine and the development of neuropathic symptoms attributed to AIDP. Here we report the first case of AIDP in the Philippines after receiving the first dose of AstraZeneca COVID-19 vaccine.

Case report

A 45-year old female with good baseline functional capacity who was independent on all her activities of daily living, with a history of essential hypertension was given her first dose of AstraZeneca vaccine on May 24, 2021. She remained well without any respiratory or gastrointestinal symptoms until 10 days after vaccination when she started experiencing severe holocranial band-like headache, which eventually resolved with bedrest and as needed pain reliever. The next day (11 days after vaccination), she then noted paresthesia over both hands and feet with weakness of the proximal bilateral upper and lower Extremities. She would have difficulty raising her arms above her head and ascending up the stairs. By the next day, there would be persistence of Weakness of the proximal bilateral upper and lower Extremities, where she would eventually seek Emergency care consults at two local hospitals Where work-ups (complete blood count, Electrolytes, cardiac enzyme, thyroid function tests, Renal and liver function tests, plain whole Abdominal CT scan, cranial CT scan with contrast) Were unremarkable and she was managed as a Case of hypertensive urgency. Her blood pressure Ranges during this time was 160-180/100. She was discharged with dual antihypertensive medications (Amlodipine and Losartan) without improvement of symptoms. Interim, there would be worsening of symptoms for which she now required assistance when ambulating, now with generalized body
The patient did not show any signs of respiratory compromise (light touch, pinprick, temperature, vibration) involving the dorsal and palmar aspect of both hands (until the wrist area), and the dorsal and plantar aspect of both feet (until the ankle area). No dysmetria nor dyschokinesia was noted. Reflex testing shows hyporeflexia in the bilateral upper extremities and areflexia in the bilateral lower extremities. Routine labs showed euvolemic hypotension secondary to syndrome of inappropriate ADH secretion. RTPCR for SARS-CoV2 was negative on admission. Lumbar puncture was not performed due to patient refusal. Cranial MRI with contrast was normal while whole spinal MRI with contrast showed unremarkable results. She was admitted to the progressive care unit and electrophysiologic studies done one day after admission showed absent bilateral sensory median response while median and ulnar motor studies showed slowed conduction velocity and prolonged distal motor latency, conduction block in the bilateral ulnar and left peroneal nerve, diffuse low amplitude responses, absent F responses, increased insertional activity in the left deltoid with all muscles showing reduced recruitment. These findings are compatible with the electrophysiologic criteria of Acute Inflammatory Demyelinating Polyneuropathy (AIDP). She was then treated with intravenous Immunoglobulin (2 g/kg over 5 days) starting on June 12, 2021 (18 days after onset of neuropathic symptoms). She was referred to outpatient Neurology Clinic for follow-up electrophysiologic studies to be done in four weeks.

### Discussion

Guillain-Barre Syndrome (GBS) is associated with numerous bacterial and viral infections [1]. The pathogenesis involves the production of an immune response secondary to antecedent infection or vaccination, which in turn cross-reacts with peripheral nerve components because of sharing of cross-reactive epitopes (molecular mimicry). Immune response can be directed against the myelin or the axon, the latter of which cause the axonal variants of GBS which are associated with a worse prognosis and slower recovery time [2]. The Brighton criteria is a diagnostic tool that can in the diagnosis of GBS (Figure 1) [11]. The most important diagnostic aids in GBS include Cerebrospinal Fluid (CSF) analysis and electrophysiologic studies. CSF analysis will show normal pressure, acellular or few lymphocytes and increased CSF protein secondary to widespread inflammatory disease of the nerve roots. This is compatible with albuminocytologic dissociation seen in GBS. Electrophysiologic criteria of GBS include prolonged distal motor latency, slowed conduction velocity, absent F responses and conduction block. At least three of the four electro physiologic criteria are needed for the diagnosis of GBS [1,2,11]. Spinal MRI with gadolinium contrast will show enhancement of the nerve roots of the cauda equine [2]. Since the start of the global COVID-19 pandemic in December 2019, global mass vaccination campaigns have been done to mitigate the spread of COVID-19 infection. The FDA-approved COVID-19 vaccines are either inactivated or live messenger RNA vaccines that enter the human cell to allow identification of the spike protein found on the surface of SARS-CoV2 virus [3]. The

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#### Table 1: Brighton Criteria In the context of global mass vaccination campaigns, it is difficult to conclude that a particular case is associated with the vaccine. Many people will develop GBS by coincidence and by chance alone within a few weeks after receiving a vaccination. A vaccine clinical trial showed that one of their participants developed GBS days after receiving a placebo, supporting a coincidental association [3]. Nevertheless, the Center for Disease Control has created a Vaccine Adverse Effect Reporting System (VAERS) that allows clinicians and patients receiving the vaccine to report any adverse effect seen within sixty days after receiving the COVID-19 vaccine [12]. Clinicians must properly educate their patients and reassure the public regarding the safety of COVID-19 vaccinations and that the benefits of vaccination outweigh the risks associated with COVID-19 infection.

<table>
<thead>
<tr>
<th>Diagnostic criteria</th>
<th>Level of diagnostic certainty</th>
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<tbody>
<tr>
<td>Bilateral and flaccid weakness of limbs</td>
<td>+</td>
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<tr>
<td>Decreased or absent deep tendon reflexes in weak limbs</td>
<td>+</td>
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<tr>
<td>Monophasic course and time between onset-radii 12 h to 28 days</td>
<td>+</td>
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<td>CSF cell count &lt; 50/μL</td>
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<td>CSF protein concentration &gt; normal value</td>
<td>+</td>
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<tr>
<td>NCS findings consistent with one of the subtypes of GBS</td>
<td>+</td>
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<tr>
<td>Absence of alternative diagnosis for weakness</td>
<td>+</td>
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+ present; − absent; +/− present or absent;
NCS = nerve conduction studies; GBS = Guillain-Barre syndrome.

a If CSF is not collected or result not available, nerve electrophysiologic results must be consistent with the diagnosis Guillain-Barre syndrome.
human body then produces antibodies that recognize and kill the virus. In a small subset of patients, this immune response leads to the production of antibodies against myelin and axon, thereby causing GBS. The proposed pathophysiology of vaccine associated GBS is an immune-mediated. Hypersensitivity to the solvent (polyethylene glycol) [5]. GBS may be seen in patients within six weeks after receiving a first dose of 10 weeks after a second dose [3]. Because of the limited case reports, no guidelines on the optimal treatment of vaccine-associated GBS are available. Most cases have been treated with IVIG (2 g/kg over 3-5 days) [3,5-10].

**Conclusion**

In summary, we report the first case of COVID-19 post vaccine associated GBS in the Philippines. Rare occurrences of COVID-19 vaccine-related neuromuscular complications are possible. Any serious adverse reaction must be reported to facilitate continuous safety evaluation and to minimize vaccine hesitancy. It is important to emphasize to patients and to the public that temporal association does not always imply causality. Further studies are needed to better elaborate the neurological complications after COVID-19 vaccination and whether a causal relationship between vaccination and neurological complications can be established. With the ongoing pandemic and worldwide mass vaccination campaigns, it is important for clinicians to recognize the other adverse effects associated with COVID-19 vaccination. Lastly, it is important to highlight that the benefits of COVID-19 vaccination outweigh the risks and possible adverse effects associated with vaccination in order to limit and mitigate the further spread of COVID-19 infection.

**Declarations**

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