

# Case of Guillain-Barré syndrome following COVID-19 vaccine

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## SUMMARY

Guillain-Barré syndrome (GBS) is a rare immune-mediated disorder of the peripheral nerves. Although its cause is not fully understood, the syndrome often follows infection with a virus or bacteria, although in rare occasions, vaccination may precede GBS. We describe a case of a 62-year-old woman who presented with paraesthesia and progressive weakness of both lower limbs over 3 days. Clinical examination and investigation findings including lumbar puncture and nerve conduction studies were consistent with the diagnosis of GBS. She had no history of either diarrhoea or respiratory tract infections preceding her presentation. However, she had her first intramuscular dose of the Oxford/AstraZeneca COVID-19 vaccine 11 days prior to her presentation. Although no direct link could be ascertained, the purpose of this report is to highlight the incidence and consider this issue while evaluating any case of GBS in the light of the current pandemic and vaccination programme.

## BACKGROUND

The term Guillain-Barré syndrome (GBS) tends to be used interchangeably with acute idiopathic demyelinating polyneuropathy. The disease results in a severe and sometimes lasting paralysis; about one-third of patients develop respiratory failure requiring intensive care unit (ICU) admission and ventilation.<sup>1</sup> GBS is fatal in 3%–5% of patients, and about two-thirds have residual disability. A mild respiratory or gastrointestinal infection precedes the neuropathic symptoms by 1–3 weeks, sometimes longer in about 60% of the patients. In recent years, it has come to be appreciated from serologic studies that the enteric organism *Campylobacter jejuni* is the most frequent identifiable causative organism.<sup>2</sup> Other less common antecedent events or associated illness include cytomegalovirus, influenza, *Mycoplasma pneumoniae*, the flaviviruses including Zika and dengue viruses, and the alphavirus, chikungunya.<sup>3</sup> The administration of outmoded antirabies vaccines and a New Jersey (swine) influenza vaccine given in the late 1970s were associated with a slight increase in the incidence of GBS<sup>4</sup> and at least one subsequent influenza vaccination programme has been associated with a marginal increase.<sup>5</sup> However, no definitive causal associations have been proven despite these individual reports being widely recited.

Global cases of the COVID-19 respiratory illness caused by the SARS-CoV-2 have surpassed 131 million, with a death toll currently at a devastating number of >2.4 million. A worldwide mass vaccination programme to fight against this

raging virus has been started since the beginning of 2021 with variable side effects reported in clinical trials.<sup>6,7</sup> However, occurrence of GBS after COVID-19 vaccination has been reported only twice to date.<sup>8,9</sup> Here, we describe another case of GBS with a history of receiving first dose of the Oxford/AstraZeneca COVID-19 vaccine.

## CASE PRESENTATION

A 62-year-old woman presented to the acute medical unit with a 3-day history of gradual weakness of bilateral lower limbs preceded by paraesthesia and numbness. Initially, the distal muscles were involved which then progressed to involve the proximal muscles of both lower limbs and finally ascending to affect both the arms. She denied back pain, any history of spinal trauma and bowel or bladder dysfunction. She also reported of neuropathic pain in the posterior aspects of both legs. There was no recent history of respiratory or diarrhoeal illness before her presentation. Furthermore, she never tested positive for COVID-19 since outbreak of the pandemic. However, she received her first dose of the Oxford/AstraZeneca COVID-19 vaccine intramuscularly 11 days prior to her presentation. She did not suffer from pain at the injection site or influenza-like symptoms during this period. Her medical history was significant for bronchiectasis, asthma, osteoporosis and migraine. She had no known drug allergies. Her physical examination revealed normal vital signs apart from a blood pressure reading of 170/100 mm Hg indicating sympathetic over activity, with normal chest expansion and forced vital capacity. There was no postural drop in blood pressure. Neurological examination findings were consistent with a flaccid-type paraplegia of bilateral lower limbs. The power was noted to be 3/5 in the right leg and 2/5 in the left, both in the proximal and distal muscle groups. Muscle tone was reduced with absence of deep tendon reflexes and plantar response. There was no sensory involvement although she had some paraesthesia. Examination of the upper limbs revealed flaccid type of weakness with reduced power which was 4/5 in the right arm and 3/5 in the left, both proximally and distally. Jerks were diminished and there was no sensory involvement. There was absence of cerebellar signs and no evidence of cranial nerve abnormality pointing away from a diagnosis of Miller Fisher syndrome. Gait could not be examined due to weakness. Other systemic examinations were unremarkable.

## INVESTIGATIONS

Following admission, routine tests including full blood counts, C reactive protein, urea and



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electrolytes, calcium, magnesium, phosphate, liver function tests and clotting profile were within normal limits. An initial chest X-ray to look for infective changes was unremarkable. A urine dipstick test was negative for leucocytes or nitrites. A 12-lead ECG showed normal sinus rhythm. COVID-19 PCR test for SARS-CoV-2 RNA came back negative as a part of routine hospital admission screen.

Basic peripheral neuropathy screen including HbA1c, glucose level, vitamin B<sub>12</sub> level, folate level, copper level, thyroid function tests, protein electrophoresis, paraprotein level, syphilis, HIV test and hepatitis screen were performed. The results of these tests were unremarkable. Antinuclear antibody (ANA) was negative. Antineutrophil cytoplasmic antibody (ANCA) as well as C3 and C4 levels were done as a part of vasculitis screening and results were within normal limits.

Owing to the high clinical suspicion of an acute flaccid type of polyneuropathy, a lumbar puncture (LP) was planned. However, before proceeding to perform an LP, a non-contrast CT scan of the head was performed as per hospital protocol to rule out occult intracranial pathologies. The findings, as expected, came back unremarkable.

LP was performed and cerebrospinal fluid (CSF) analysis revealed albumin-cytological dissociation. CSF protein was 0.9g/L (reference range: 0.2–0.4) and CSF white blood cell count was 1×10<sup>9</sup>/L (reference range: 0–5). Analysis of CSF did not detect bacterial and viral pathogens on BioFire PCR panel.

Following this, a non-contrast MRI of the whole spine was performed to rule out spinal pathologies explaining the clinical presentation. The findings from MRI was unremarkable apart from collapse of the T8 vertebral body without bony infiltration. There was no evidence of spinal cord compression, transverse myelitis, spinal cord infarction or spinal stenosis.

Nerve conduction study (NCS) was performed thereafter which showed marked, demyelinating, sensorimotor polyneuropathy (figure 1). There was some sural sparing with no evidence of acute denervation on electromyography at that time. Ultrasound imaging showed normal nerve cross sectional area measurements at the wrist and arm but evidence of C5 root swelling. All these findings were consistent with the diagnosis of GBS.

**DIFFERENTIAL DIAGNOSIS**

Given the initial presentation of acute flaccid polyneuropathy and an obvious trigger in the form of recent vaccination, the most likely diagnosis was GBS. Spinal cord compression from degenerative disc disease, spinal cord infarcts, transverse myelitis and spinal stenosis needed to be ruled out. The fact that she had no bowel or bladder involvement and the absence of back

pain made the possibility of spinal cord compression less likely. In addition, cord compression and transverse myelitis present as spastic paraparesis in contrary to the patient in our case. However, MRI of whole spine was warranted to confidently rule these out. Peripheral neuropathy was another important differential in our case as it presents as flaccid paraparesis or quadriparesis. However, the acute nature of the presentation and normal peripheral neuropathy screen could rule this out, as neuropathy due to metabolic causes usually have a gradual course. Negative ANA and ANCA with normal complement levels ruled out the possibility of other autoimmune disorders or vasculitis (ANCA positive vasculitis) as a cause of this acute flaccid neuropathy. There was no history of intake of any potential drugs which could cause neuropathy. In addition, there was no history of exposure to heavy metals or toxins. Our patient denied drinking excessive alcohol or recent tick and insect bites. The classic CSF findings of albumin-cytological dissociation and NCS findings of demyelinating, sensorimotor polyneuropathy confirmed the diagnosis of GBS.<sup>1</sup>

**TREATMENT**

The patient on diagnosis was transferred under the care of neurology team and commenced on intravenous immunoglobulin at a dose of 2g/kg body weight divided over 5 consecutive days. Unfortunately, her condition gradually deteriorated over couple of days with persistently falling oxygen saturations on pulse oximetry and forced vital capacity <1.5L (<20mL/kg body weight). She also started experiencing difficulty in speech and swallowing due to bulbar involvement, necessitating nasogastric feeding. Neuropathic pain was managed by gabapentin and paracetamol. She was urgently transferred to ICU for monitoring on day 4 of her treatment. During her stay there, she developed sepsis secondary to aspiration pneumonia for which she was started on intravenous antibiotics. Considering rapidly worsening ascending paralysis and to protect the airways, she was intubated, followed by a tracheostomy and put under mechanical ventilation.

**OUTCOME AND FOLLOW-UP**

At the time of writing of this report, the patient remains in the ICU and is making slow improvement with regards to sepsis on intravenous antibiotics. She has also made some progress in terms of improvement of lower limb weakness. However, she remains mechanically ventilated and is under close monitoring.

**Sensory Nerve Conduction Studies**

SNCS					
Nerve	pLat ms	Amp uV	CV m/s	Dur ms	Stim. Int. mA
<b>Hand Screen Sensory Right</b>					
R Index - Wrist	--	--			32.8
<b>Sural Sensory Right</b>					
Mid. lower leg - Ankle	5.00	1.78	25.5	1.96	24.6

**Motor Nerve Conduction Studies**

MNCS							
Nerve	Lat ms	Amp mV	Amplitude Diff %	Duration ms	Duration Diff %	Velocity m/s	Stim. Int. mA
<b>Median Motor Right</b>							
Wrist - APB	5.54	3.6		9.2			34.6
Elbow-Wrist	13.7	2.4	-33.3	8.4	-8.7	27.0	49.8
<b>Peroneal Motor Right</b>							
Ankle - EDB	9.60	0.86		9.0			60.8
Fib. head-Ankle	26.8	0.53	-38.4	10.8	20.0	18.0	94.4

**F-Wave**

Right Median FResponse			
	F Lat ms	M-Lat ms	F-M Lat ms
Wrist - APB	51.8	5.5	46.4

Right Tibial FResponse			
	F Lat ms	M-Lat ms	F-M Lat ms
Ankle - Abd hal	37.5	8.5	29.0

Figure 1 Nerve conduction study (NCS) shows marked, demyelinating, sensorimotor polyneuropathy.

## DISCUSSION

GBS is a rare immune-mediated neurological disorder that affects the peripheral nerves and nerve roots, triggered by certain infections such as *C. jejuni*, cytomegalovirus, hepatitis E virus, *M. pneumoniae*, Epstein-Barr virus and Zika virus.<sup>13–16</sup> Numerous case reports and studies have linked GBS to COVID-19 caused by the SARS-CoV-2.<sup>11–16</sup> Vaccines are very rarely associated with GBS. There have been reports of increased incidence of GBS following swine influenza vaccinations in 1976. There have been studies showing that there is a small risk of developing this condition after yearly influenza/influenza vaccines at about 1–2 cases per million influenza vaccine doses administered.<sup>5, 17–19</sup> A case report by Waheed *et al*<sup>8</sup> described the first case of GBS after the initial dose of the Pfizer–BioNTech COVID-19 vaccine.

Classically, GBS presents as acute sensorimotor neuropathy which usually starts with distal paraesthesia followed by weakness of the legs and arms. It is the most common cause of acute flaccid paralysis with an incidence of about 2 in 100 000 people/year.<sup>1</sup> Incidences can increase with the advent of disease outbreaks as seen in the Zika virus epidemics. The main key findings on investigations are raised CSF protein with a normal cell count, often termed as albumin-cytological dissociation along with abnormal neurophysiological studies.<sup>1</sup> Antiganglioside antibodies can be detected in a subgroup of patients. Intravenous immunoglobulin at a dose of 2 g/kg divided over 5 days and plasmapheresis 200–250 mL/kg for five sessions are the only treatments available currently to treat GBS. Respiratory functions in the form of forced vital capacity have to be monitored in all patients with GBS as this disorder can be potentially life threatening due to the involvement of respiratory muscles leading to respiratory failure in 20% cases requiring admission to ICU and mechanical ventilation. Autonomic nervous systems can be involved in some cases leading to fluctuations in blood pressure, cardiac arrhythmias as well as bladder and bowel dysfunction. Mortality rates in these cases can range between 3% and 5%. Relapse after treatment is not very common at around 2%–5% of cases.<sup>1</sup>

COVID-19 is caused by the SARS-CoV-2 which was first detected in Wuhan, China in 2019. Since then, it has spread worldwide leading to a pandemic. This virus can cause severe respiratory disease leading to high mortality and morbidity. The main purpose of the UK COVID-19 vaccination programme was to protect the population, especially the most vulnerable from this disease. Three vaccines have been currently approved for use by the Committee on Vaccination and Immunisation and the Medicines and Healthcare Regulatory Authority in the UK. The BNT162b2 vaccine by Pfizer and BioNTech, the ChAdOx1 nCoV-19 (AZD1222) by the University of Oxford and AstraZeneca as well as the COVID-19 Vaccine Moderna have been approved in the UK for use in adults aged  $\geq 18$  years.

The Oxford/AstraZeneca ChAdOx1 nCoV-19 (AZD1222) COVID-19 vaccine is composed of a single recombinant chimpanzee adenovirus (ChAdOx1) vector containing DNA encoding the S glycoprotein/spike protein of SARS-CoV-2. This genetic code of the SARS-CoV-2 spike protein is introduced to the host cell which then produces these spike proteins. The S glycoprotein/spike protein of SARS-CoV-2 is responsible for stimulating immune response in the individual. Results from trials across the UK and Brazil showed that the Oxford/AstraZeneca COVID-19 vaccine can prevent about 70% of COVID-19 cases.<sup>20</sup> The most common reported side effects from trials of this vaccine in the UK, Brazil and South Africa were pain and tenderness at the site of injection, fever, chills, malaise, fatigue, myalgia, arthralgia, nausea and headache. There were very few reported cases of

anaphylaxis, reduced appetite, lymphadenopathy, dizziness and abdominal pain.<sup>20</sup> Recently, there have been growing concerns regarding vaccine-associated thromboembolism with thrombocytopenia.<sup>21</sup> So far, only one case of GBS has been reported following the Oxford/AstraZeneca vaccine.<sup>9</sup> Over 37 million doses of vaccine have been administered in the UK including the most vulnerable of people to protect them from this virus.<sup>22</sup> There is no vaccine which is 100% effective or without risks. However, the safety of COVID-19 vaccines need to be rigorously monitored and side effects need to be immediately reported to the respective bodies. In the current situation, based on data, the benefits of the approved COVID-19 vaccines in preventing COVID-19 and its complications far outweigh their side effects.<sup>23–25</sup>

## Learning points

- ▶ In light of the current COVID-19 pandemic and vaccination programme, complications such as Guillain-Barré syndrome (GBS) need to be looked out for. Prompt diagnosis and management is needed in such cases as it may affect outcomes.
- ▶ COVID-19 vaccines are potentially associated with development of acute sensory motor neuropathy but more association studies are required to establish this theory.
- ▶ GBS related to COVID-19 vaccination can progress rapidly to involve the respiratory and bulbar muscles leading to neuromuscular respiratory failure, requiring intensive care admission.
- ▶ GBS could be an extremely rare complication of the COVID-19 vaccines, but benefits of currently approved vaccines significantly outweigh their risks.

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