

# Guillain-Barré syndrome presenting with facial diplegia following COVID-19 vaccination in two patients

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## SUMMARY

In March 2020, the WHO declared COVID-19 to be a global pandemic and since December 2020, millions of vaccines have been administered. To date, cases of Guillain-Barré syndrome (GBS) following a COVID vaccine (Pfizer, Johnson & Johnson, Janssen, AstraZeneca) have been reported. A 61-year-old woman developed bilateral asymmetrical lower motor neuron (LMN) facial weakness followed by limb symptoms, 10 days after receiving the first dose of AstraZeneca COVID vaccine. The second patient was a 56-year-old man who, 9 days after receiving first dose of AstraZeneca COVID vaccine, developed bilateral asymmetrical LMN facial weakness with limb symptoms. Intravenous immunoglobulin was administered with rapid recovery. These cases of GBS following the AstraZeneca COVID vaccine add to cohort of patients reported. We flag up to raise awareness of this condition post-COVID-19 vaccine and highlight the prominent bifacial involvement. Early diagnosis and prompt treatment with intravenous immunoglobulin led to rapid recovery.

## BACKGROUND

All approved COVID-19 vaccines can cause minor side effects in the population with the most common being sore arm, fatigue and chills.<sup>1</sup> There have been some rare blood clotting cases with the AstraZeneca and Janssen vaccines, as well as cases of myocarditis following the Pfizer vaccine. A widespread study of the Pfizer vaccine found that the prevalence of acute side effects was the same in the treatment and control groups, but data since this study indicate that this may have been a biased result.<sup>2</sup> Given the dynamic nature of measuring vaccine side effects, this report aims to contribute to the literature by informing practitioners of an additional potential rare side effect.

Recently, the European Medicines Agency (EMA) and Food and Drug Administration (FDA) have listed Guillain-Barré syndrome (GBS) as a side effect of Janssen, AstraZeneca and Johnson & Johnson vaccines.<sup>3-5</sup> To date, there have been few case reports of GBS following COVID-19 vaccination reported whereas millions of vaccines have been administered in the UK.<sup>6,7</sup> Therefore, the causal link is not yet provable but given the severity of the cases involved, there is a need for awareness among the clinicians about this possible association. There is also no indication that COVID-19 vaccines should stop being administered and we fully support the current WHO recommendations. Our two cases

had received AstraZeneca vaccines. It is important that clinicians are aware of this condition occurring post-COVID-19 vaccine, as early diagnosis and treatment with intravenous immunoglobulin (IVIg) can improve clinical outcome as in our cases.

## CASE PRESENTATION

**Case 1:** a 61-year-old woman received the first dose of the AstraZeneca COVID-19 vaccine and, for the following 2 days felt unwell with general malaise. Ten days later, the patient noticed bifacial, left > right, weakness with prominent lower facial involvement. This was accompanied by asymmetrical, left > right, lower limb weakness and tingling in her feet and a day later in her hands. The patient's facial and limb weakness progressed over the next few days. One week after onset of symptoms, the patient went to the hospital for medical consultation. There was no respiratory involvement.

The patient has a history of multiple sclerosis, diagnosed 15 years ago but she had been asymptomatic since an episode of optic neuritis 11 years ago. She has never been on any disease-modifying treatment.

The patient had bilateral lower motor neuron facial weakness (House-Brackmann grade 4 on the left and grade 3 on the right side), and lower limb weakness (3/5 proximally and 4/5 distally). She also has decreased vibration sensation up to her ankles bilaterally and was areflexic with flexor plantar responses.

**Case 2:** a 56-year-old man received the first dose of the AstraZeneca COVID-19 vaccine and for 2 days experienced severe 'flu-like' symptoms. A week later, the patient developed sudden-onset severe back and lower limb radicular pain followed by waist down numbness and a sensation of heaviness in his legs. The following day, he developed tingling and numbness in his fingertips and weakness (left > right) with tingling and numbness on the face and was admitted to hospital. There were no bladder or bowel symptoms and no respiratory involvement.

On examination, he had bilateral lower motor neuron facial weakness (House-Brackmann grade 4 on the left and grade 3 on the right side) and decreased vibration sensation at the ankles. He was areflexic with flexor plantar responses.

## INVESTIGATIONS

**Case 1:** Cerebrospinal fluid (CSF) was acellular with a protein level of 1.64 g/L. Motor nerve conduction



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**Table 1** Selected motor nerve conduction studies

Motor nerve	DML (ms)			Amplitude (mV)			Minimum 'F' wave latency (ms)			Conduction velocity (m/s)		
	C1	C2	NR	C1	C2	NR	C1	C2	NR	C1	C2	NR
L facial (nasalis)	5.01	5.01	2.5–3.2	1.0	1.47	1–2						
R facial (nasalis)	4.58	4.28		1.0	1.7							
R median (Abductor pollicis brevis)	5.38	4.29	2.5–3.7	7.5	11.0	≥5	37.0	35.0	26–31	44.4 (forearm)	41.7 (forearm)	≥50
L ulnar (Abductor digiti minimi)	3.08	3.14	2.2–3.2	8.9	9.7	≥5	37.0	37.2	27–31	38.0 (forearm)	44.0 (forearm)	≥50
R tibial (Abductor hallucis)	9.05	4.04	3.2–4.5	5.2	6.2	≥3	78.1	56.8	48–56			
L common peroneal (Extensor digitorum brevis)	6.99	5.25	3.8–5.5	2.3	6.7	≥2	70.9	55.6	47–55	31.0 (ankle–knee)	41.9 (ankle–knee)	≥40

C1 refers to case 1 studies done 2 weeks after the onset of symptoms, C2 refers to case 2 studies 10 days after the onset of symptoms. There were neither conduction blocks nor temporal dispersions.

NR, normal range.

studies fulfilled the criteria for demyelinating polyneuropathy (table 1). Sensory nerve studies were within normal limits. There were no acute denervation potentials on needle electromyogram (EMG) studies.

Case 2: CSF showed a protein level of 1.6 g/L and two lymphocytes only. Motor nerve conduction studies fulfilled the criteria for demyelinating polyneuropathy. Sensory nerve studies were within normal limits (table 1). There were no acute denervation potentials on needle EMG studies.

All blood tests including serological tests for other causes of peripheral neuropathy were within normal limits/negative in both cases.

**TREATMENT AND OUTCOME**

Case 1: patient reached level 1 of Brighton criteria for diagnostic certainty of GBS.<sup>8</sup>

The patient received a course of IVIg 0.4 g/kg/day for 5 days. By the third day of IVIg, the patient started to notice improvement in the facial and limb weakness. At 3 weeks, the patient still had mild residual proximal muscle weakness (4/5).

Case 2: patient reached level 1 of Brighton criteria for diagnostic certainty of GBS.

The patient received a course of IVIg 0.4 g/kg/day for 5 days. From the third day of treatment onwards, the patient made a rapid improvement of all his symptoms with complete recovery within 10 days.

**DISCUSSION**

In December 2019, the first case of SARS-CoV-2 was reported in Wuhan, China. On 11 March 2020, the WHO declared COVID-19 to be a global pandemic. Acute inflammatory demyelinating polyneuropathy (AIDP) type of GBS along with rarer variants such as Miller Fisher syndrome, polyneuritis cranialis, bilateral facial palsy with paraesthesia and isolated oculomotor neuropathy have been reported in association with COVID infection.<sup>9–11</sup> Abu-Rumeileh *et al* performed a systematic review of 73 cases of COVID associated neuropathy of which five patients had bilateral facial palsy with paraesthesia.<sup>10</sup> Epidemiological and cohort study by Keddie *et al* suggests that there is no evidence that COVID-19 triggers GBS.<sup>12 13</sup> However, a multicentre study in Northern Italy by Filosto *et al* proposes a pathological link as there was increased incidence of GBS during the COVID-19 pandemic; the predominant subtype was AIDP type of GBS.<sup>14</sup>

The incidence of GBS is approximately 1.1–1.8 cases per 100 000 people per year but this may vary after exposure to infectious agents known to cause GBS. Triggering pathogens include viruses (eg,

Cytomegalovirus, Epstein-Barr virus, Influenza A, Hep E, measles, Zika) and bacteria (eg, *Campylobacter jejuni*, *Mycoplasma pneumoniae* and *Haemophilus influenza*). Postinfectious and autoimmune pathogenic mechanisms have been described and other associations with immunisation, surgery and malignancy have also been reported.<sup>11 12 14</sup>

Both patients described in this report had bilateral facial weakness at presentation. In the literature, facial diplegia is described only in 0.25%–0.8% of all patients with GBS at presentation although facial nerve paralysis may subsequently be seen in 27%–50% of GBS cases.<sup>15 16</sup> In COVID-19 associated GBS, bilateral facial palsy was described in 20% of cases.<sup>13</sup>

The prevalence of GBS in recipients of any vaccine is rare and is reported as 0.07–0.46 cases per 100 000. During the H1N1 pandemic in 2009, an excess case rate of 0.8 cases per million vaccinations was observed.<sup>17</sup> The pathophysiological mechanisms by which vaccination may cause GBS remain uncertain. They are hypothesised to be immune-mediated or autoimmune reactions, which are related to the production of autoreactive antibodies induced by vaccine epitopes.<sup>18</sup> In our two cases, the rapid improvement in symptoms in response to IVIg treatment supports immune-mediated cause. Symptoms of GBS have usually occurred up to 6 weeks after a vaccine dose although some authors suggest the consideration of a longer time frame.<sup>17 18</sup> Due to a lack of case-controlled data, the Institute of Medicine could not refute nor confirm the causal relationship between GBS and various vaccines.<sup>18</sup>

Since the United States FDA and various other national healthcare organisations approved certain COVID-19 vaccines in December 2020, there have been cases of GBS reported post vaccination. Waheed *et al* described a case of GBS following a first dose of the Pfizer vaccine and George *et al* reported a case of GBS after a singular dose of the Johnson & Johnson vaccine in a clinical trial participant who recovered after IVIg.<sup>19 20</sup> Recently, the EMA has reported that around 51.4 million doses of Vaxzevria AstraZeneca AB had been given to people in the European Union/European Economic Area by 20 June 2021 and 227 cases of GBS had been reported by 27 June 2021.<sup>3</sup> A few more case reports of GBS following COVID vaccination have been reported lately. Nasuelli *et al* has reported a case of acute demyelinating polyradiculoneuropathy with bilateral facial palsy after AstraZeneca chimpanzee adenovirus vectored vaccine ChAdOx1 nCoV-19 vaccine.<sup>6</sup>

The two patients we report here were of similar ages and presented within 1 week of each other, this may be a result of the age-specific vaccination scheme in the UK.

Given that millions of vaccinations have been administered this does not imply any strong causality between COVID-19 vaccines and GBS, nor does it suggest that vaccinations should be halted. However, the epidemiology of this disease and any vaccination side-effects are still emerging and so we should remain alert to address these issues.<sup>14</sup>

We report these cases in order to raise the awareness of GBS occurring post-COVID-19 vaccine as early diagnosis and prompt treatment with IVIg can rapidly reduce morbidity as shown in our cases. However, we reiterate that association does not imply causation itself and therefore we require more observed cases and a natural experiment study to determine the possibility of causality.

### Learning points

- ▶ Guillain-Barré syndrome (GBS) can present following COVID-19 vaccination. The patients described add to the cohort of patients with GBS reported after AstraZeneca vaccination. These observations raise the question about casual relationship between the two facts about which healthcare professional should be aware.
- ▶ Lower motor neuron facial weakness can present as GBS following COVID-19 vaccination.
- ▶ Early diagnosis and prompt treatment with intravenous immunoglobulin as in our cases lead to rapid recovery.

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