



Letter to the Editor: New Observation

Variant Guillain–Barre Syndrome Following SARS-CoV-2 Vaccination: Case Report and Review of the Literature

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Guillain–Barre syndrome (GBS) is a rare, autoimmune neurologic condition that is preceded by an infection in most cases. Though gastrointestinal illness is the most common, a variety of infectious agents have been reported in association with GBS including SARS-CoV-2. Vaccination is an unusual inciting stimulus for GBS; however, there have been a few recent cases reported following SARS-Cov2 vaccination. We describe a case of variant GBS with facial paralysis and paresthesias as well as sixth nerve palsy occurring after AstraZeneca SARS-CoV2 vaccination. Our review of the current reported cases in the literature suggests that this specific GBS variant may be linked to SARS-CoV-2 adenoviral vaccination.

A 45-year-old man with a history of Crohn's disease received his first dose AstraZeneca SARS-CoV-2 vaccination. Twelve days later, he noticed weakness in the right side of his face and presented to a community hospital where a noncontrast CT head was normal and he was discharged home with a diagnosis of Bell's palsy. Over the next 2 days, he developed left facial weakness followed by bilateral severe muscle weakness to the point where he was unable to get out of bed. He had bilateral ascending paresthesias to the knee as well as the left upper limb. At this time, he presented again to hospital where he was admitted for investigations. Over the following days in hospital, he complained of diplopia and was noted to have a right sixth nerve palsy. MRI brain without gadolinium was interpreted as normal. Lumbar puncture showed highly elevated protein (2.0 g/L) with white blood cell count of 14. EMG findings were consistent with demyelinating polyradiculopathy. A diagnosis of GBS was made and treatment was initiated with IVIg. Two months later, he had regained most of the strength in his limbs. Facial paralysis and ocular motility showed only minimal improvement.

GBS is classically characterized by symmetric ascending paralysis and areflexia with a history of antecedent infection in 90% of cases, mostly commonly with *Campylobacter jejuni*.¹ Several clinical variants exist including Miller–Fisher syndrome, characterized by the triad of ophthalmoplegia, ataxia and areflexia, pharyngeal–cervical–brachial variant and bifacial weakness with paresthesias.² Symptoms develop a minimum of 3 and median of 10 days following infection³ and at least in some cases are hypothesized to result from molecular mimicry between bacterial lipopolysaccharides

and mammalian nervous system gangliosides.⁴ Viral triggers are also reported for GBS including cytomegalovirus, Epstein Barr and Zika virus^{5,6} and now COVID-19.⁷ Whether vaccination is conclusively linked to GBS is matter of some debate, however epidemiological evidence from influenza vaccination campaigns supports a very small risk following vaccine administration.

As mass vaccination campaigns are being carried out worldwide against SARS-CoV-2, reports of GBS are emerging (Table 1). Including the current report, we found 23 cases published in the literature, 21 (91%) of which occurred following AstraZeneca adenoviral vaccination (Table 1). Nineteen of these 21 (90%) cases had bilateral facial palsy and this finding was not present in the two cases following Pfizer messenger RNA (mRNA)-based vaccination. Three cases (13%) had involvement of at least one oculomotor nerve, with two cases of sixth nerve palsy and one of complete ophthalmoplegia. Respiratory symptoms were absent in 65% (15/23), and 17% (4/23) required mechanical ventilation.

Facial palsy is also a frequent finding in GBS following SARS-CoV2-related illness, reported in 42% of cases in a recent systematic review.⁸ GBS post-infection with SARS-CoV-2 appears to be more severe than when it follows vaccination, with 33% of cases requiring mechanical ventilation and 6% proving fatal. The pathophysiology of post-infectious and post-vaccination GBS in SARS-CoV-2 is unknown; however, if molecular mimicry between the virus and mammalian gangliosides is present it would have to be within the spike protein as this is the common target of all currently available vaccines.

Notably, a causative link is not present in all cases of GBS following COVID-19 or SARS-CoV-2 vaccination. One case of GBS occurred in the vaccine arm and one in the control arm in trials for the Johnson & Johnson adenoviral vaccine.⁹ A case of GBS 1 day following mRNA Pfizer SARS-CoV-2 vaccination is also reported, which is outside of the window of reported GBS cases being too rapid in onset. Large epidemiologic studies will be required to determine whether these reported cases are causatively linked.

Patients presenting with bilateral facial palsy should be asked about the recent SARS-CoV-2 vaccination and also be tested for serologic evidence of infection so that the diagnosis of GBS may be considered. Cases without other classic features of this

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Table 1: Guillain–Barre syndrome following SARS-CoV-2 vaccination

Author	Age	Sex	Vaccine	Facial palsy	Other cranial	Respiratory	Symptom onset (days)	Limb paresthesias	Antibodies	Motor
Waheed [1]	82	F	Pfizer	None	None	None	8-14	Yes	ND	Areflexia, limb weakness
Razok [2]	73	M	Pfizer	None	None	None	16-17	NS	ND	Areflexia, limb weakness
Present	45	M	AstraZeneca	Bilateral	R sixth nerve pals	None	12	Yes	GM1 negative	Areflexia, limb weakness
Hasan [3]	62	F	AstraZeneca	None	Dysphagia, Dysarthria	Yes, ventilated	8	Yes	ND	Areflexia, limb weakness
Bonifacio [4]	66	M	AstraZeneca	Bilateral	Tongue, mouth numbness	None	7	Yes	Negative	Absent R ankle jerk only
Bonifacio	43	M	AstraZeneca	Bilateral	Dysphagia, dysgusia, tongue paraesthesia	None	11	Yes	Negative	Areflexia
Bonifacio	51	M	AstraZeneca	Bilateral	None	None	7	NS	GM3 positive, GM4 borderline	None
Bonifacio	71	F	AstraZeneca	Bilateral	Dysgusia	None	12	NS	Negative	Areflexia, limb weakness
Bonifacio	53	M	AstraZeneca	Bilateral	Facial, perioral paraesthesia	None	8	Yes	ND	Areflexia
Patel [5]	37	M	AstraZeneca	None	Dysphagia	Mild, no ventilation	14	Yes	ND	Areflexia, limb weakness
Nasuelli [6]	59	M	AstraZeneca	Bilateral	None	None	10	Yes	Negative	Areflexia
Maramattom [7]	43	F	AstraZeneca	Bilateral	None	Yes, ventilated	10	NS	ND	Areflexia, limb weakness
Maramattom	67	F	AstraZeneca	Bilateral	R abducens palsy, bulbar palsy	Yes, ventilated	14	Yes	Negative	Areflexia, limb weakness
Maramattom	53	F	AstraZeneca	Bilateral	R face and tongue numbness	Yes, ventilated	12	NS	Negative	Areflexia, limb weakness
Maramattom	68	F	AstraZeneca	Bilateral	Facial numbness, bulbar palsy	Yes	14	NS	Negative	Areflexia, limb weakness
Maramattom	70	M	AstraZeneca	Bilateral	Bulbar palsy	Yes	11	NS	ND	Areflexia, limb weakness
Maramattom	69	F	AstraZeneca	Bilateral	Bulbar palsy, complete ophthalmoplegia	None	12	NS	ND	Areflexia, limb weakness
Maramattom	69	F	AstraZeneca	Bilateral	Bulbar palsy	Yes	13	NS	ND	Areflexia, limb weakness
Allen [8]	54	M	AstraZeneca	Bilateral	None	None	12	Yes	Negative	None
Allen	20	M	AstraZeneca	Bilateral	None	None	23	Yes	Negative	None
Allen	57	M	AstraZeneca	Bilateral	Dysarthria	None	15	Yes	Negative	Areflexia, limb weakness
Allen	55	M	AstraZeneca	Bilateral	None	None	22	Yes	Negative	None
McKean [9]	48	M	AstraZeneca	Bilateral	None	None	10	NS	Negative	Areflexia, limb weakness

ND: not done; NS: not specified.

syndrome may otherwise be missed, as initially occurred in the current case, or facial palsy may be the only complaint reported. Correct diagnosis is essential so that patients are monitored for signs of respiratory compromise. In addition, reporting of all suspected cases will help to determine whether there is a true causative link between SARS-CoV-2 vaccination and GBS.

Supplementary Material. To view supplementary material for this article, please visit <https://doi.org/10.1017/cjn.2021.492>

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