Neurology Asia 2022; 27(2) : 497 – 502

Guillain–Barré syndrome with weakness confined to the bilateral upper extremities after ChAdOx1-S/nCoV-19 vaccination

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Abstract

Currently, vaccination against coronavirus disease (COVID-19) is being conducted worldwide, and studies on its side effects are required to evaluate its safety. We report a case of Guillain-Barré syndrome (GBS) after vaccination with ChAdOx1/nCoV-19. A healthy 32-year-old man presented with mild weakness in his bilateral upper extremities 19 days after the vaccination. At 24 days after the vaccination, nerve conduction study showed demyelinating neuropathy in the bilateral upper and lower extremities. Intravenous immunoglobulin (IVIg) was administered over 5 days, and at the 2-week follow-up after finishing IVIg treatment, the weakness in the upper extremities was fully resolved. Although GBS is an uncommon side effect after COVID-19 vaccination, clinicians should be aware of its possible occurrence. When a patient complains of weakness after COVID-19 vaccination, clinicians should consider the possibility of GBS development.

Keywords: COVID-19, vaccine, Guillain–Barré syndrome, weakness, case report

INTRODUCTION

In South Korea, coronavirus disease 2019 (COVID-19) vaccination was commenced on February 26, 2021, and a large proportion of the population has been vaccinated with the ChAdOx1-S/nCoV-19 vaccine (CovishieldTM/Vaxzevria, AstraZeneca).[1] Reactogenicity symptoms, such as fever, chills, headache, and myalgia, occur in many individuals but mostly for short duration.[2,3] However, cerebral venous sinus thrombosis with thrombocytopenia has been reported as a serious adverse effect after ChAdOx1-S/nCoV-19 vaccination.[4]

Guillain–Barré syndrome (GBS) is an autoimmune disorder that is potentially triggered by vaccines.[5] A few studies have reported the occurrence of GBS or GBS variants after COVID-19 vaccination.[6-8]

CASE REPORT

A 32-year-old man, with no remarkable medical history (including no previous history of severe acute respiratory syndrome coronavirus 2 [SARS-CoV-2] infection), received his first dose of ChAdOx1-S/nCoV-19 vaccine on May 25th, 2021. At 19 days post vaccination, the patient presented with progressive motor weakness in the bilateral upper extremities. Five days later, he visited the peripheral nerve disorder clinic of a university hospital. Physical examination showed mild weakness in bilateral elbow flexion, wrist extension, and finger flexion; manual muscle testing (MMT) scores were grade 4. Weakness was not observed in the shoulder abductors or lower extremity muscles. There was no bulbar involvement and the extraocular movements were normal. Light touch sensation was impaired in both hands, and tendon reflexes (bilateral biceps, triceps, knee, and ankle jerks) were decreased. Cervical magnetic resonance imaging did not show any specific abnormality. The results of nerve conduction study indicate axonal neuropathy in the bilateral upper and lower extremities.[9] Compound motor action potentials (CMAPs) revealed decreased conduction velocity in all evaluated nerves, including the bilateral median, ulnar, radial, peroneal, and tibial nerves (nerves in upper extremities: 37–46 m/s; nerves in lower extremities: 38–39 m/s) (Table 1). Delayed distal latency was observed in the CMAPs of the bilateral median and peroneal nerves (median nerves,

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Date of Submission: 11 August 2021; Date of Acceptance: 18 February 2022

https://doi.org/10.54029/2022ywu

Table 1: Nerve conduction study results

Nerve (Normal Values)	Results	Nerve (Normal Values)	Results
Compound motor action potential			
Rt. median		**Lt. median**	
MNDL (<4.2), ms	**4.9**	MNDL (<4.2), ms	**4.9**
CMAP amp D/E (>5.0), mV	12.9/12.3	CMAP amp D/E (>5.0), mV	12.6/12.5
MNCV (>50), m/s	**37**	MNCV (>50), m/s	**39**
Rt. ulnar		**Lt. ulnar**	
MNDL (<4.2), ms	2.7	MNDL (<4.2), ms	2.7
CMAP amp D/E (>5.0), mV	17.7/17.3	CMAP amp D/E (>5.0), mV	15.7/15.1
MNCV (>50), m/s	**40**	MNCV (>50), m/s	**46**
Rt. radial		**Lt. radial**	
MNDL (<4.2), ms	1.5	MNDL (<4.2), ms	1.9
CMAP amp D/E (>5.0), mV	12.4/12.1	CMAP amp D/E (>5.0), mV	12.4/10.7
MNCV (>50), m/s	**43**	MNCV (>50), m/s	**42**
Rt. peroneal		**Lt. peroneal**	
MNDL (<6.0), ms	**6.5**	MNDL (<6.0), ms	**6.6**
CMAP amp D/K (>2.0), mV	4.8/4.3	CMAP amp D/K (>2.0), mV	4.8/4.8
MNCV (>40), m/s	**38**	MNCV (>40), m/s	**38**
Rt. tibial		**Lt. tibial**	
MNDL (<6.4), ms	3.8	MNDL (<6.4), ms	3.9
CMAP amp D/K (>2.6), mV	19.3/18.5	CMAP amp D/K (>2.6), mV	16.2/13.4
MNCV (>40), m/s	**39**	MNCV (>40), m/s	**39**
Sensory nerve action potential			
Rt. median SNAP amp (>20), μV	30	**Lt. median** SNAP amp (>20), μV	41
Rt. ulnar SNAP amp (>20), μV	45	**Lt. ulnar** SNAP amp (>20), μV	42
Rt. supf. peroneal SNAP amp (>10), μV	15	**Lt. supf. peroneal** SNAP amp (>10), μV	11
Rt. sural SNAP amp (>15), μV	30	**Lt. sural** SNAP amp (>15), μV	26
F-wave			
Rt. median latency (<30), ms	30	**Lt. median** latency (<30), ms	30
Rt. peroneal latency (<56), ms	58.0	**Lt. peroneal** latency (<56), ms	58.5

Abbreviations: CMAP, compound motor action potential; amp, amplitude; D, distal; E, elbow; MNCV, motor nerve conduction velocity; MNDL, motor nerve distal latency; K, knee; SNAP, sensory nerve action potential; supf, superficial; Rt., right; Lt., Left.

Normal values are presented in parentheses.

Abnormal values are shown in bold.

both: 4.9 ms; peroneal nerves, right: 6.5 ms, left: 6.6 ms). The CMAP and SNAP amplitudes were within the normal range. F-wave latencies were delayed in the bilateral median (30 ms) and peroneal nerves (right: 58 ms; left: 58.5 ms). Electromyography (EMG) did not reveal any denervated potentials. A cerebrospinal fluid study showed no abnormal findings (white blood cells: 0 cells/μL; protein: 41.11 mg/dL). Anti-GM1 (IgM and IgG) and anti-GD1b antibodies (IgM) were not found in the blood. The result of a SARS-CoV-2 polymerase chain reaction was negative. The patient was diagnosed with GBS and treated with intravenous immunoglobulin (IVIg) 140 g (2 g/kg) over 5 days.

There were no complications observed during and after the treatment. At 2 weeks follow-up after IVIg treatment, the weakness in the upper extremities had fully resolved.

DISCUSSION

The development of GBS after vaccination might be due to the generation of host antibodies cross-reacting with proteins in the myelin of peripheral nerves.[6] The causal antibodies might be generated

Table 2: Summary of previous reports on the occurrence of Guillain–Barré syndrome after COVID-19 vaccination

First author	Number of patients	Type of vaccine	Interval vaccine-GBS symptoms	Symptoms	CSF study	NCS	Treatment	Outcome
Waheed[8]	1	Pfizer (1st dose)	14 days	Mild bilateral hip flexor weakness	Albuminocytologic dissociation +	No information	IVIg for 5 days	No information
Maramattom[7]	7	AstraZeneca (1st dose)	14 days	Quadriplegia with facial paresis: 7 patients Respiratory failure: 6 patients	Albuminocytologic dissociation +: 5 patients No information: 2 patients	Demyelinating neuropathy: 6 patients, axonal neuropathy: 1 patient	IVIg: 7 patients Plasmapheresis: 2 patients	Full recovery: 1 patient Poor outcome: 6 patients
Allen[6]	4	AstraZeneca (1st dose)	11–22 days	Facial weakness with limb paresthesia: 4 patients Mild quadriplegia: 1 patient Mild weakness confined to bilateral lower extremities: 1 patient	Albuminocytologic dissociation +: 1 patient Lymphocytosis and elevated protein level: 2 patients No information: 1 patient	Reduced CMAP in bilateral facial nerves: 1 patient Normal: 2 patients No information: 1 patient	Oral prednisolone 60 mg for 5 days: 2 patients IVIg: 1 patient No treatment: 1 patient	No information
Hasan[13]	1	AstraZeneca (1st dose)	11 days	Quadriplegia	Albuminocytologic dissociation +	Demyelinating sensorimotor neuropathy	IVIg (2 g/kg) for 5 days	Poor outcome: tracheostomy and mechanical ventilation
Razok[20]	1	Pfizer (2nd dose)	20 days	Weakness confined to bilateral lower extremities	Albuminocytologic dissociation +	Bilateral absent H-reflexes in the gastrocnemius muscles	IVIg (2 g/kg) for 5 days	Full recovery
Nasuelli[18]	1	AstraZeneca (1st dose)	10 days	Gait ataxia with distal paresthesia	Albuminocytologic dissociation +	Demyelinating neuropathy on motor nerves	IVIg (2 g/kg) for 5 days	No information
McKean[16]	1	AstraZeneca (1st dose)	10 days	Facial weakness, quadriparesis, paresthesia	Lymphocytosis and elevated protein	Multifocal sensorimotor demyelinating polyneuropathy	IVIg (2 g/kg) for 5 days	Good outcome

First author	Number of patients	Type of vaccine	Interval vaccine-GBS symptoms	Symptoms	CSF study	NCS	Treatment	Outcome
Scendoni[21]	1	Pfizer (2nd dose)	14 days	Quadriparesis	Albuminocytologic dissociation +	Demyelinating sensorimotor neuropathy	IVIg (2 g/kg) for 5 days	Slight improvement
García-Grimshaw[12]	7	Pfizer (1st dose)	4–28 days	Quadriparesis: 6 patients Facial weakness 1 patient Respiratory failure: 1 patient	Albuminocytologic dissociation +: 3 patients Increased WBC with normal protein level: 1 patient Normal findings: 1 patient Not performed: 2 patients	AIDP: 4 patients AMAN: 3 patients	IVIg: 7 patients	Good outcome: 1 patient Poor outcome (unable to walk independently): 5 patients Death: 1 patient
Tutar[22]	1	Sinovac (2nd dose)	14 days	Quadriparesis	No information	AMSAN	-	-
Min[17]	2	AstraZeneca (1st dose)	3-4 days	Sensory deficit	Case 1: albuminocytologic dissociation + Case 2: no information	Case 1: decreased amplitude of SNAP in both sural nerves, absent CMAP in the right peroneal nerve Case 2: normal	No information	No information
Introna[15]	1	AstraZeneca (1st dose)	10 days	Quadriparesis, facial weakness, paresthesia	Albuminocytologic dissociation +	Sensorimotor mixed polyneuropathy (demyelination with predominant axonal changes)	IVIg (2 g/kg) for 5 days	Good outcome
Hughes[14]	1	Pfizer (1st dose)	2 days	Quadriparesis, facial weakness	Albuminocytologic dissociation +	Prolonged lower extremity F- waves	IVIg	Good outcome
Prasad[19]	1	Janssen	15 days	Quadriparesis, facial weakness, paresthesia	Albuminocytologic dissociation +	Demyelinating neuropathy	IVIg (2 g/kg) for 5 days	Full recovery

Abbreviations: CSF, cerebrospinal fluid; NCS, nerve conduction study; CMAP, compound motor action potential; AIDP, acute inflammatory demyelinating polyneuropathy; AMAN, acute motor axonal neuropathy; AMSAN, *acute motor* sensory *axonal neuropathy*

by an immunologic response to the SARS-CoV-2 spike protein or adenovirus vector components.[6]

Although a few studies have reported the occurrence of GBS following SARS-CoV-2 infection, this association has not been fully established.[10-12] Furthermore, an increase in GBS incidence after COVID-19 vaccination has not been reported.

To date, several studies have reported the occurrence of GBS after COVID-19 vaccination (Table 2).[6-8, 13-23] Waheed *et al*.[8] reported a patient with GBS 2 weeks after the first Pfizer COVID-19 vaccine dose. The patient showed bilateral hip flexor weakness (MMT: 4). However, the study did not present the nerve conduction velocity (NCV) and EMG results. Considering that electrodiagnostic studies (NCV and EMG) are essential for diagnosing GBS, we believe that the diagnosis cannot be confirmed. The GBS cases in the other two reports occurred after ChAdOx1-S/nCoV-19 vaccination. Maramattom *et al*.[7] reported seven patients with severe GBS that developed within 2 weeks after the first ChAdOx1-S/nCoV-19 vaccine dose. All seven patients had quadriplegia with facial paresis, and six patients required mechanical ventilation for respiratory failure. The diagnosis of GBS was confirmed following an electrodiagnostic study.[24] Allen *et al*.[6] reported four patients with a GBS variant. All four patients had bifacial weakness accompanied by limb paresthesia and mild quadriparesis, which developed 11–22 days after receiving the first ChAdOx1-S/nCoV-19 vaccine dose. In addition to the above three reports, many cases of GBS after COVID-19 vaccination have been reported.[13-23] The patients' symptoms included quadriparesis (or paraparesis), facial weakness, and/or sensory abnormality with an interval of 2–28 days between vaccination and the onset of GBS symptoms. In contrast to the patients in previous reports, our patient showed weakness limited to bilateral upper extremities and not in the lower extremities or facial muscles. Although the NCV study revealed mildly slowed conduction velocities in the evaluated peripheral nerves in the lower extremities, no weakness was observed. This may be due to the nerve damage was not severe enough to cause neurologic symptoms.

Herein, we reported a case of GBS occurring after COVID-19 vaccination (ChAdOx1-S/nCoV-19 vaccine) that presented with mild weakness confined to the bilateral upper extremities. Clinicians should consider the possibility of GBS when a patient complains of weakness after COVID-19 vaccination. Robust national surveillance would be required in order to better understand the association between GBS and COVID-19 vaccination.

DISCLOSURE

Financial support: This study was supported by the National Research Foundation of Korea Grant funded by the Korean government, No. NRF2021R1A2C1013073.

Conflict of interest: None

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