A Case Report of Guillain-Barré Syndrome In Association with SARS-CoV-2 Vaccination in Malaysia

Hoe Leong SII, Sin Hui NG, Voon Fei WONG, Wan Chung LAW

Abstract

Purpose: Guillain-Barré Syndrome (GBS) associated with SARS-CoV-2 vaccine administration is very rare. Early recognition of GBS at early stage could prevent extensive nerve damage with potential respiratory and autonomic failure.

Case report: We report a case of paraparetic spectrum of GBS in a 53-year-old lady who presented with rapidly progressive acute flaccid paralysis involving both lower extremities with areflexia eight days after the first dose of Sinovac vaccine for SARS-CoV-2 in Malaysia. Cerebrospinal fluid (CSF) albuminocytological dissociation was seen and nerve conduction study (NCS) revealed sensory neuropathy. The diagnosis of GBS was made based on the Brighton criteria. Patient responded well to intravenous immunoglobulin (IVIG).

Conclusion: Though there is currently no convincing evidence of any causation between GBS and SARS-CoV-2 vaccination, clinicians should remain vigilant and consider GBS in the differential diagnosis for patient who presents with weakness with reduced or absent deep tendon reflex after vaccination against SARS-CoV-2.

Keywords: **Guillain-Barré Syndrome, SARS-CoV-2 vaccination, intravenous immunoglobulin, Malaysia**

Acta Neurol Taiwan 2023;32:207-211

INTRODUCTION

Guillain-Barré Syndrome (GBS) is an immune-mediated, inflammatory, polyradiculoneuropathy, characterised by rapidly progressive motor weakness with reduced or absent reflexes. The reported global incidence of GBS is 0.81-1.91 cases per 100,000 person-years with a mortality rate of approximately 5% [(1)].

Common antecedent triggers of GBS include upper respiratory or gastrointestinal tract infection, surgery, immunotherapy and even vaccination [(1)]. The association between vaccination and GBS was first noted during the

From the Department of Medicine, Hospital Sibu, KM 5 1/2, Jalan Ulu Oya, 96000 Sibu, Sarawak, Malaysia; Department of Medicine, Hospital Sibu, KM 5 1/2, Jalan Ulu Oya, 96000 Sibu, Sarawak, Malaysia; Department of Medicine, Hospital Sibu, KM 5 1/2, Jalan Ulu Oya, 96000 Sibu, Sarawak, Malaysia; Neurology Unit, Department of Medicine, Sarawak General Hospital, Jalan Hospital, 93586 Kuching, Sarawak, Malaysia; Department of Medicine, Hospital Sibu, KM 5 1/2, Jalan Ulu Oya, 96000 Sibu, Sarawak, Malaysia

Received April 18, 2022. Revised June 24, 2022.
Accepted August 1, 2022.

Correspondence to: Dr Sii Hoe Leong, Department of Medicine, Hospital Sibu, KM 5 1/2, Jalan Ulu Oya, 96000 Sibu, Sarawak, Malaysia.

National Influenza Immunization Programme against swine influenza in 1976, although studies later have shown that the risk is very low, at approximately one case per million vaccination [2]. With the SARS-CoV-2 pandemic and ongoing massive vaccination campaigns, SARS-CoV-2 vaccine administration has been temporally associated with GBS cases. However, this remains controversial as a causal relationship has not been established. GBS is considered vaccine-associated if the onset of symptoms occurs within 4 weeks of vaccination [1]. The first case of GBS following SARS-CoV-2 vaccination was reported in February 2021 in United States after an 82-year-old lady received the first dose of the Pfizer vaccine [3].

To date, there have been more cases reported after SARS-CoV-2 infection than after vaccination and the benefits of SARS-CoV-2 vaccination outweigh the adverse effects in view of the ongoing pandemic with high morbidity and mortality. We report a case of GBS following SARS-CoV-2 vaccination with initial presentation of flaccid weakness of both lower extremities associated with paraesthesia, coupled with typical cerebrospinal fluid (CSF) and nerve conduction study (NCS) findings.

CASE PRESENTATION

A 53-year-old lady with underlying hypertension, presented with rapidly progressive, ascending weakness of both lower extremities associated with paraesthesia for one week. She was unable to stand and ambulate upon admission. On further questioning, she reported receiving her first dose of SARS-CoV-2 vaccine (Sinovac) 8 days prior to the current presentation. She denied fever, respiratory symptoms, recent history of trauma or fall, back pain, urinary or bowel incontinence or symptoms of connective tissue disease such as hair loss, rashes, oral ulcer and joint pain.

On examination, the patient was alert and oriented. Bilateral lower extremities were hypotonic. Power was graded 2 on 5 for hip flexion/extension/abduction/adduction and 3 on 5 for knee flexion/extension and plantar flexion/extension based on the modified medical research council (mRC) scale. She had absent ankle and knee reflexes with loss of pin-prick and vibration sensation as well as proprioception over the distal aspect of lower extremities. Plantar responses were downgoing . With respect to upper extremities, all power were 5 on 5 on mRC scale, tone and reflexes were normal with loss of pin-prick sensation over distal aspect of upper extremities. Her cranial nerve and cerebellar examination were normal. Anal tone was normal.

Blood investigations such as thyroid function and serum electrolytes were unremarkable. Blood cultures were sterile. SARS-CoV-2 polymerase chain reaction (PCR) was negative. Viral screening for HIV, hepatitis B and C, Venereal Disease Research Laboratory test (VDRL) were negative. Lumbar puncture was performed with normal opening pressure of 19 cm H2O. Analysis of CSF showed albuminocytologic dissociation (elevated protein of 1.1 mg/mL with normal white cell count of 0 cell/uL), elevated glucose at 5.6 mmol/L (normal 2.5-4.5 mmol/L) (serum glucose of 10.1 mmol/L). Otherwise, no abnormality was detected on CSF gram stain, cryptococcal antigen test, Indian ink, acid-fast bacillus stain, VDRL as well as cytology. Anti-ganglioside antibodies test was not routinely performed at our center.

No acute intracranial abnormalities were found on the CT of her head. MRI of the spine did not reveal evidence of intramedullary cord lesion. NCS demonstrated reduced ulnar sensory nerve action potential (SNAP) on the left compared to the right and normal sural SNAP, in keeping with a sural sparing pattern. Motor studies suggested conduction block in both tibial nerves (Table 1). Based on the GBS single-study electrodiagnostic criteria by Uncini et al, the patient's NCS was abnormal but did not meet either demyelinating or axonal criteria, making the electrodiagnosis equivocal.

According to Brighton case definition of GBS, the diagnostic certainty of GBS for our patient reached the highest level with the presence of bilateral and flaccid weakness of limbs, areflexia in weak limbs, CSF cell count of <50/ul and protein concentration > normal range, and presence of sensory neuropathy on NCS. We initiated intravenous immunoglobulin (IVIG) with a dose of 0.4g/kg daily for 5 days. Power of lower extremities improved to 3 on 5 for hip flexion/extension/abduction/adduction as well as 4 on 5 for knee flexion/extension and plantar flexion/extension respectively. Patient was discharged home with follow-up as an outpatient at Physiotherapy Unit and Medical Outpatient Clinic. After a careful risk-

Table 1. Nerve conduction study (NCS) demonstrated reduced ulnar sensory nerve action potential (SNAP) on the left compared to the right and normal sural SNAP, whereas motor studies suggested conduction block in both tibial nerves.

Nerve/ Sites	Latency (ms)	Peak Amplitude (μV)	Distance (cm)	Velocity (m/s)
Sensory NCS				
Left Median - Digit II				
Wrist	3.33	16.6	13.0	39.0
Right Median - Digit II				
Wrist	2.97	13.7	13.0	43.8
Left Ulnar - Digit V				
Wrist	2.24	8.7	11.0	49.1
Right Ulnar - Digit V				
Anterior elbow	1.93	18.0	11.0	57.1
Left Radial - Thumb				
Forearm	2.24	11.3	10.0	44.7
Right Radial - Thumb				
Forearm	1.61	29.6	10.0	61.9
Left Sural – Lateral Malleolus				
Calf	2.50	34.1	14.0	56.0
Right Sural – Lateral Malleolus				
Calf	2.92	19.3	14.0	48.0
Motor NCS				
Left Median - APB				
Wrist	4.43	10.9	6.5	
Elbow	8.65	10.9	21.5	51.0
Right Median - APB				
Wrist	3.07	8.7	6.5	
Elbow	8.23	6.9	21.5	41.7
Left Ulnar - ADM				
Wrist	2.81	7.3	6.5	
B. Elbow	6.04	5.6	20.0	61.9
A. Elbow	7.81	4.4	10.0	56.5
Right Ulnar - ADM				
Wrist	2.45	9.1	6.5	
B. Elbow	6.15	6.8	21.5	58.1
A. Elbow	7.40	5.9	10.0	80.0
Left Radial - EIP				
Forearm	2.50	4.9	7.0	
Right Radial - EIP				
Forearm	2.19	7.4	7.5	
Left Common Peroneal - EDB				
Ankle	4.79	4.4	7.0	
Fib Head	12.66	2.4	3.1	39.4
Knee	13.80	2.5	7.0	61.1
Right Common Peroneal - EDB				
Ankle	4.74	4.4	7.0	
Fib Head	11.30	3.3	30.0	45.7
Knee	12.40	3.4	8.0	73.1
Left Tibial - AH				
Ankle	5.63	14.7	7.0	
Knee	19.22	1.4	34.0	25.0
Right Tibial - AH				
Ankle	4.11	10.8	8.0	
Knee	15.83	2.8	32.0	27.3

F Waves

Nerve	Min F Latency (ms)	Max F Latency (ms)	Mean F Latency (ms)
Left Median - APB	24.79	25.00	24.85
Left Ulnar - ADM	24.79	25.10	24.92
Right Median - APB	24.79	24.79	24.79
Right Ulnar - ADM	25.57	25.99	25.85
Left Tibial - AH	32.97	36.15	34.41
Left Common Peroneal - EDB	29.48	30.10	29.88
Right Tibial - AH	34.06	37.03	34.85
Right Common Peroneal - EDB	26.82	30.68	29.63

benefits discussion, she was advised not to receive further dose of SARS-CoV-2 vaccination. Her muscles power gradually recovered to pre-morbid level with intensive physiotherapy and occupational therapy. She is now able to carry out activities of daily living (ADL) independently.

DISCUSSION

GBS is the commonest cause of acute, severe flaccid paralysis globally and the diagnosis remains based on the clinical presentation and ancillary CSF and NCS findings [(1)]. In classical GBS, flaccid weakness involve bilateral extremities in an ascending pattern with reduced or absent deep tendon reflexes, and there may be presence of additional clinical features such as mild sensory symptoms or signs, cranial nerve involvement, autonomic dysfunction, albumin-cytologic dissociation on CSF analysis and electrophysiological evidence of neuropathy [(1)].

Till January 2022, Malaysia had recorded 2.7-million confirmed SARS-CoV-2 cases with an overall fatality rate of approximately 1.1% [(5)]. Neurological sequelae of SARS-CoV-2 include headache, anosmia and dysgeusia to serious events such as stroke, meningoencephalitis and GBS [(6)]. In particular, GBS was reported in 73 patients with preceding SARS-CoV-2 infection, and most of them developed GBS manifestation within 2 weeks from disease onset [(7)]. SARS-CoV-2 associated GBS is likely triggered by an aberrant autoimmunity against the ganglioside components of the peripheral nerves, which then affects various antigens in the axonal subtypes of GBS, resulting in peripheral axon or myeline nerve damage [(6)]. This mechanism is coined as humoral molecular mimicry and has been proven in various infection caused by bacterial and viral pathogens, commonly Campylobacter jejuni sp., Haemophilus influenzae sp., Influenza virus and Epstein-Barr virus [(6)].

Similar to SARS-CoV-2 infection, SARS-CoV-2 vaccination related GBS has been reported. The first global SARS-CoV-2 vaccination programme was initiated in December 2020 as a response to SARS-CoV-2 pandemic with Malaysia began its vaccination programme in February 2021. As of January 2022, Malaysia has vaccinated approximately 80% of its total population and nearly 30% of them has received a third or booster dose [5]. SARS-CoV-2 vaccines demonstrate an efficacy of at least 90% against symptomatic disease in different clinical trials participated by several countries [(8)]. While the potential link between immunisation against SARS-CoV-2 and GBS has not yet been fully proven, it is postulated that SARS-CoV-2 vaccines trigger antibody cross-reaction when the vector containing DNA encoding the S glycoprotein/ spike proteins of SARS-CoV-2 bind to sialic acid-containing gangliosides on cell surfaces [(9)].

According to a recent systematic review of 39 SARS-CoV-2 vaccination associated GBS cases, the commonest clinical GBS variants is the classic form, reported in more than half of cases, followed by bilateral facial palsy with paraesthesia (~30%), paraparetic form (~10%) and GBS-Miller Fisher syndrome overlap variant (<1%) [(10)]. On the other hand, AIDP is the commonest electrophysiological features of SARS-CoV-2 vaccination associated GBS [(10)]. The clinical presentation of our patient with ascending bilateral lower extremities weakness without the involvement of upper extremities would suggest the paraparetic GBS spectrum. The NCS findings of our

patient was equivocal and did not fulfil a specific subtype of GBS. Previous cohort study of patient with GBS who underwent NCS (n=440) also reported a forty-two percent of normal or equivocal NCS [11]. The clinical features of our patient remained the hallmark of the diagnosis of GBS.

Majority of patients recovered with or without neurological deficits after treatment with intravenous immunoglobulin or plasmapheresis with approximately one-fifth required mechanical ventilation during hospitalisation after the diagnosis of SARS-CoV-2 vaccination associated GBS [10]. Early recognition and subsequent treatment of GBS could have prevented the rapid progression of the disease course and our patient was discharged and able to ambulate again after received treatment with IVIG.

There is still no clear evidence on temporal association between SARS-CoV-2 vaccination and GBS. To the best of our knowledge, this is the first published case report of SARS-CoV-2 vaccine associated GBS in Malaysia and does not imply any causation. Clinicians should remain vigilant and consider GBS in the differential diagnosis of patient who presents with rapidly progressive, symmetric weakness of extremities with reduced or absent deep tendon reflexes, with or without sensory deficits post SARS-CoV-2 vaccination. The benefits of SARS-CoV-2 vaccination far outweigh the risks and this case report should not be seen as a deterrent to the public to receive the vaccination.

CONCLUSION

GBS is temporally associated with SARS-CoV-2 vaccination, however, the evidence is not established yet. Acute limbs weaknesses with reduced or absent deep tendon reflexes following vaccination should alert clinicians a differential diagnosis of GBS. Early recognition and treatment of SARS-CoV-2 vaccination-related GBS with intravenous immunoglobulin (IVIG) can reduce morbidity and mortality.

ACKNOWLEDGEMENT

Authors would like to thank all healthcare staffs involved in the management of the patient's care till her discharge from hospital.

REFERENCES

1. Shahrizaila N, Lehmann HC, Kuwabara S. Guillain-Barré syndrome. The Lancet. 2021.
2. Koike H, Chiba A, Katsuno M. Emerging Infection, Vaccination, and Guillain–Barré Syndrome: A Review. Neurology and Therapy. 2021:1-15.
3. Waheed S, Bayas A, Hindi F, Rizvi Z, Espinosa PS. Neurological complications of COVID-19: Guillain-Barre syndrome following Pfizer COVID-19 vaccine. Cureus. 2021;13(2).
5. COVIDNOW in Malaysia: Ministry of Health Malaysia 2022 [Available from: https://covidnow.moh.gov.my/.
6. Tawakul AA, Al-Doboke AW, Altayyar SA, Alsulami SA, Alfahmi AM, Nooh RT. Guillain-Barré Syndrome in the COVID-19 Pandemic. Neurology International. 2022;14(1):34-48.
7. Abu-Rumeileh S, Abdelhak A, Foschi M, Tumani H, Otto M. Guillain–Barré syndrome spectrum associated with COVID-19: an up-to-date systematic review of 73 cases. Journal of neurology. 2021;268(4):1133-70.
8. Swan DA, Bracis C, Janes H, Moore M, Matrajt L, Reeves DB, et al. COVID-19 vaccines that reduce symptoms but do not block infection need higher coverage and faster rollout to achieve population impact. Scientific reports. 2021;11(1):1-9.
9. López-Hernández J, Lisette B-R, de Saráchaga Adib J, Eunice M-J, Elizabeth L-M, Erika G-L, et al. Guillain-Barré syndrome following SARS-CoV-2 vaccination: Is there a real association? Neuroimmunology Reports. 2022;2:100050.
10. Shao S-C, Wang C-H, Chang K-C, Hung M-J, Chen H-Y, Liao S-C. Guillain- Barré Syndrome Associated with COVID-19 Vaccination. Emerging infectious diseases. 2021;27(12):3175.
11. Fokke C, van den Berg B, Drenthen J, Walgaard C, van Doorn PA, Jacobs BC. Diagnosis of Guillain-Barré syndrome and validation of Brighton criteria. Brain. 2014;137(1):33-43.