The First Guillain-Barré Syndrome After SARS-CoV-2 Vaccination in Taiwan

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Abstract

Purpose: Guillain-Barré syndrome (GBS) is an immune-mediated disease of the peripheral nerves and could be fatal and has severe neurologic complications. This study herein reports the clinical course of the first patient of GBS after SARS-CoV-2 Oxford/AstraZeneca vaccination in Taiwan.

Case report: A 38-year-old woman who presented with progressive numbness and weakness of both upper and lower limbs over 1 week. Ascending patterns was noted, and bilateral leg were more severe with diffused absence of deep tendon reflex. Clinical examination and investigation findings confirmed with the diagnosis of GBS. Deterioration of muscle power and respiratory failure had developed during the hospitalization. She had no common GBS predisposing history, but she had received her first SARS-CoV-2 Oxford/AstraZeneca vaccination intramuscularly 10 days prior to her symptoms. Clinical symptoms had much improved after double filtration plasmapheresis.

Conclusion: Our case is the first case of GBS developed after AstraZeneca vaccine injection in Taiwan, presenting with atypical manifestation of early facial and bulbar involvement. The vaccination associated GBS should be closely monitored as other safety profile, since it may result in respiratory failure and severe neurologic complications.

Keyword: Guillain-Barré Syndrome, SARS-CoV-2 Vaccination.

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INTRODUCTION

Guillain-Barré syndrome (GBS) is an immune-mediated disease of the peripheral nerves and nerve roots, which is usually triggered by infections. These patients usually presented with weakness and sensory impairment, with great heterogeneous clinical features. Disease progression can be rapid with most patients reached its nadir within 2 weeks. About 20% of GBS developed respiratory failure and required mechanical ventilation[(1)]. Respiratory or gastrointestinal infection prior to the neuropathic symptoms about 1–3 weeks was usually

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found, and it's also associated with cytomegalovirus (CMV), influenza, Mycoplasma pneumoniae[2]. It had been reported that vaccine of swine flu and influenza might associated with the increased incidence of GBS, but no definite causal association was confirmed yet[3,4].

Due to the pandemic of coronavirus disease 2019 (COVID-19) caused by the SARS-CoV-2 infection, there are approximately 3.9 million deaths worldwide as of early July 2021 according to the World Health Organization (WHO)[5]. Vaccination of the COVID-19 had started globally from the very beginning of 2021. There were 156 cases of GBS had been reported from the European Union (EU)/ the European Economic Area (EEA) by the end of May 2021[6]. Taiwan started COVID-19 vaccination since March 2021, and here we would like to present the first case of GBS with a history of receiving first dose of the Oxford/AstraZeneca ChAdOx1 nCoV-19 vaccine (AZD1222) in Taiwan.

CASE PRESENTATION

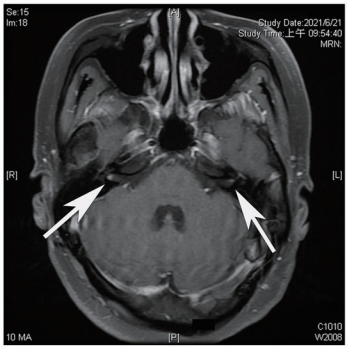
This 39-year-old female had four limbs progressive numbness for 1 week. The numbness was noted from distal parts of extremities and made her feel like floating when she walked. Four days later, she went to emergent department for help due to left facial palsy, where prednisolone and Cobamamide were given for suspected Bell's palsy. But ascending numbness, limbs weakness and dysphagia also developed. She couldn't walk without assistance at that time.

She has hypertension without regular medication, and she is an HBV carrier. There was no previous respiratory or gastrointestinal illness in recent 1 month, and she denied travel or trauma history as well. COVID-19 reverse transcription polymerase chain reaction (PCR) had been checked twice with negative finding. She had only received the first dose of AstraZeneca vaccine intramuscularly 10 days prior to her symptoms.

During the physical examination, there was no obvious abnormalities including the vital signs and no respiratory distress. Neurologic examination revealed left peripheral facial palsy, and decreased pin-prick sensation over four limbs and trunk without sensory level. Impaired joint position and vibration sensation were noted over the extremities. The muscle strength (grading by MRC scale) was 3 of the left side proximal lower limb, and 4 of all others. There was generally decrease of deep tendon reflex while no cerebellar signs nor limitation of eye movement. The magnetic resonance imaging (MRI) of brain showed unremarkable finding in brain parenchyma but contrast enhancement at bilateral facial nerves (figure 1A). The CSF analysis showed albuminocytological dissociation (CSF protein level: 239.7 mg/dL, Leukocyte count 2 uL) without evidence of CNS infection.

Her bilateral upper and lower limbs muscle strength dropped prominently to 2 after admission. Demyelinating sensory-motor polyneuropathy with conduction block and sural sparing was revealed by the nerve conduction study (figure 1B&C). We therefore conducted the double filtration plasmapheresis (DFPP). However, respiratory

A



B

Nerve Conduction Studies

Anti Sensory Summary Table

NERVE	Recording Site	Onset latency (ms)	Amplitude (uV)	NCV (m/s)
Ulnar	5th Digit	2.2	6.8	43
Median	2nd Digit	NR		
Sural	Lat Malleolus	2.5	25.3	32

Motor Summary Table

NERVE	Stimulation Site	Recording Site	Onset latency (ms)	Amplitude (mV)	NCV (m/s)	F-wave Latency (ms)
Median	Wrist	APB	8.8	1.0	----	42.3
Ulnar	Wrist	ADM	5.1	1.5	----	34.6
Deep Peroneal	Ankle	EDB	11.1	1.4	----	52.8
Tibial	Ankle	AH	8.0	6.5	----	53.0
Facial	StyloMastoid foramen	Orbic Oculi	4.9	0.2		
H-(Left)	Pop fossa	Soleus	NR			

C

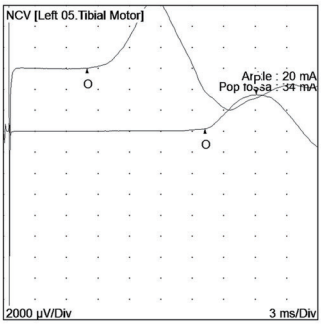


Figure 1. (A)Axial T1-weighted image with contrast of the brain demonstrating enhancements at bilateral facial nerves(arrows). (B) Nerve conduction study(NCS) shows marked, demyelinating, sensorimotor polyneuropathy. (C) Left tibial nerve NCS with conduction block.

failure with CO_2 retention occurred during hospitalization, at the 10th day after symptoms onset. Intubation with mechanical ventilator was done and she was transferred to intensive care unit for further management.

We had done some investigations for the possible etiology. We checked the hemogram, C-reactive protein, electrolytes, liver and renal function routinely, and they were normal except leukocytosis which was favored related to the previous steroid use before the hospitalization because of suspected Bell's palsy. As for the polyneuropathy workup, we checked the glycohemoglobin, protein electrophoresis in CSF, and showed unremarkable findings. Possible predisposing factor of the GBS was also checked, which showed no evidence of recent infection of CMV, Varicella-Zoster Virus (VZV), campylobacter, mycoplasma and human immunodeficiency virus (HIV). Polyneuropathies related antibodies GQ1b, GT1b, GD1a, GD1b, GM1, GM2 and GM3 also showed negative results. The only positive finding of serology was the positive detection of serum Herpes simplex virus (HSV)-1 IgG and HSV IgM (HSV-IgG titer: 62.2, Positive: > 2.1; HSV –IgM titer: 2.1, Positive: >1.1). However, no HSV-IgM nor HSV DNA was detected in the CSF, and there were also no vesicles, rash nor pain over her ear and face. No tinnitus nor any hearing impairment occurred to her before or during hospitalization.

After 2 courses DFPP, muscle power of her bilateral arm was improving from 2 to 3 gradually, and extubation was done smoothly after 4 courses DFPP. By the time of mid-July, almost one month after symptoms onset, although she was still hospitalized for further rehabilitation, her bilateral leg muscle power was improved to 3 and bilateral arm had recovered to full power after completed 5 courses of DFPP.

DISCUSSION

GBS developed after COVID-19 infection, has been reported in several studies already[7-10]. The viral spike protein, which binds to angiotensin-converting enzyme 2 (ACE2), plays a role of entry cells and triggering disease. The cells expressing ACE2, such as neurons and glial cells, hence became the possible targets of SARS-CoV-2 infection. Another possible mechanism is the post-infectious "molecular mimicry" of the autoantibody[8]. In addition to ACE2, the viral spike protein also binds to sialic acid–containing glycoproteins and gangliosides on cell surfaces[11]. The cross-reactivity between epitopes within the COVID-19 spike-bearing gangliosides and signature sugar residues of surface peripheral nerve glycolipids is likely attributed to the neuron injury[11].

The first report of GBS after vaccination was a case receiving the first dose of Pfizer–BioNTech COVID-19 vaccine in America[12]. There were 156 cases of GBS after receiving AstraZeneca vaccine had been reported, under the circumstances that around 40 million doses of AstraZeneca vaccine had been administered in EU/EEA until 21 May 2021[6]. In the United Kingdom, not only typical GBS was reported but also four cases of GBS variant, presenting with bifacial weakness with paraesthesia after AstraZeneca vaccine injection[13,14]. Two of the four patients had contrast enhancement of facial nerve in brain MRI study[14], which is similar to our case.

In Asia, there were 7 cases reported in India, where the AstraZeneca vaccine started injection since January 2021. Six out of seven cases developed respiratory failure, and only one of them had recovered to ambulatory condition. All of the seven patient had bilateral facial palsy, which not occurs commonly in GBS patients[15].

The AstraZeneca vaccine contains a chimpanzee adenovirus vector that codes for the S glycoprotein of SARS-CoV-2. After vaccination and the vector entering cells, it stimulates the spike glycoprotein export to the cell surface, provoking the production of antibodies to induce the immunity effect[13]. The mechanism of vaccination associated GBS is possible due to the molecular mimicry response induced antibodies against neuronal myelin sheaths[13]. Another vaccine which also contains recombinant adenovirus vector expressing the SARS-CoV-2 spike protein, Johnson & Johnson's coronavirus vaccine, had its label updated by the Food and Drug Administration of the United State to warn of the possible increased risk of GBS on 8th July, 2021[16]. However, further studies and investigation are necessary since the causal relationship is not yet established despite the temporal association.

The association of HSV and GBS was rarely observed and only a few case reports were published[17-21], which included encephalitis and demyelinating neuropathy with

direct CNS infection[17-18] or overlapping syndromes with Bickerstaff's brainstem encephalitis(BBE)[19-20]. The overlapping features of BBE reported had prominent ophthalmoplegia and pupil involvement[20-21], with a significant association with anti-GQ1b IgG[19-20].

According to the guideline and instruction of laboratory test in diagnosing HSV infection, low level of HSV-IgM antibodies may occasionally persist for more than 12 months post-infection and is not recommended as a means to establish recent or acute infection alone[22-23]. In our case, the negative serology finding in CSF indicated no primary CNS infection, and no vesicles, rashes, pain of face and periauricular area had been noted. There were also no limitation of eye movement or pupil involvement in our patient with negative finding of serum anti-GQ1b IgG. Since her clinical manifestation was quite different from the phenotypes of HSV induced GBS/BBE overlapping syndrome and the absent of the anti-GQ1b IgG induced by the antecedent HSV infection, we therefore considered that HSV infection is less likely to be the most possible etiology of GBS in our patient.

In Taiwan, AstraZeneca vaccination has started since March 2021. A few neurologic disorders after vaccination had been reported, which included facial palsy, seizures, transverse myelitis, acute disseminated encephalomyelitis and cerebral venous thrombosis by the end of June 2021[24]. Around 1.84 million doses of AstraZeneca vaccine were done, and no causality has been confirmed yet.

Our case is the first case of GBS developed after AstraZeneca vaccine injection in Taiwan. And her clinical presentation shared some similarities with the previous reports after the AstraZeneca vaccination. The early facial and bulbar involvement noted in our patient, which were rarely seen in GBS, were also found among the post-vaccination patients reported previously[14-15]. Despite monitor the safety profile of vaccine closely all around the world, COVID-19 vaccination associated GBS should be highly alert and should not be overlooked, since it may result in respiratory failure and severe neurologic complications[25]. But still, approved vaccines provide great benefits in preventing COVID-19 infection and its complications[26-28], which is crucial during the ongoing pandemics compared to its side effects.

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