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Guillain-Barré Syndrome Following AstraZeneca COVID-19-Vaccination: Two Cases Report Study

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Abstract

Guillain-Barré syndrome (GBS) is an immune-mediated polyradiculoneuropathy. It is recognized as a serious condition, because it includes dysautonomia and respiratory affection. In fact, there have been an increasing number of reports about GBS vaccine-related vaccinations as the COVID-19 vaccination campaign goes on. Here, we report two cases of Guillain-Barré syndrome (GBS) following the first dose of the Oxford/AstraZeneca COVID-19 vaccine. Symptoms appeared 21 days after vaccination, with acute progressive bilateral symmetric ascending flaccid tetra-paresis. The electromyography was compatible with a motor demyelinating polyneuropathy, confirming the diagnosis of the Guillain-Barré syndrome. Management with intravenous immunoglobulin was prescribed, with favorable outcomes. Clinical and laboratory tests confirmed the Guillain-Barré syndrome and the period from the date of vaccination to the appearance of initial symptoms, added to the absence of other causes, allowed to assume that the vaccination could be the cause. The literature is still unable to determine the pathogenesis of GBS due to COVID-19 vaccination. However, the findings underscore the importance of continuous surveillance and investigation into potential adverse effects of COVID-19 vaccines, emphasizing the need for informed decision-making and vigilant monitoring in vaccination campaigns.

Subject Areas

Neurology, Pharmacology

Keywords

Guillain-Barré Syndrome, AstraZeneca, COVID-19 Vaccine, Electrophysiological Study

1. Introduction

Guillain-Barré syndrome (GBS) is an immune-mediated acute polyradiculoneuropathy that typically include acute ascending paralysis, areflexia, and albumin-cytologic dissociation cerebrospinal fluid (CSF) analysis [1]. Approximately half of those affected by GBS have a history of an identified infection and two-thirds have previous infectious symptoms. The most common triggering infection in the world is gastroenteritis caused by *Campylobacter jejuni* [1] [2]. Acute polyradiculoneuropathy is one of the most commonly reported adverse events following immunization in adults [1].

Coronavirus disease 2019 (COVID-19) is a worldwide pandemic associated with 113,820,168 confirmed cases, including 2,527,891 deaths [3]. World Health Organization (WHO) was engaged in the development of a safe and effective vaccine within a time frame of 6 to 18 months [4]. Between the 19 vaccines, we found the Oxford AstraZeneca vaccine, which was developed by the University of Oxford. It contains the CoV-2 surface protein (nCoV-19) in a vector from the chimpanzee adenovirus (ChAdOx1) [5]. Multiple side effects have been reported, including fatigue, headache and fever [5]. A recent review suggests that AstraZeneca was the most-reported vaccine associated with GBS (52 cases) followed by Pfizer (20 cases). GBS following COVID-19 vaccination may be associated with the first dose of the vaccine, especially DNA vaccines [6]. Clinical features were similar to regular GBS [6]. Considerable short-term recovery in response to treatment with IVIG was noticed [6]. We report two cases of GBS following the first dose of the Oxford/AstraZeneca COVID-19 vaccine.

2. Cases Report

2.1. Case 1

A 70-year-old woman presented to the emergency department with acute progressive bilateral symmetric ascending flaccid tetraparesis and bladder dysfunction. Patient history included allergy to penicillin, hypertension, and degenerative osteoarthritis of the knee.

Seven weeks before admission, neurological manifestations started with tingling of the toes, progressive acute weakness of the distal lower extremities, and urinary retention. Three weeks prior to these symptoms, the patient received the first dose of the ChAdOx1 vaccine.

On admission, she was afebrile, and her vital signs were as follows: blood pressure, 132/85 mmHg; respiratory rate, 17 cycles/min; oxygen saturation, 99% on room air; heart rate, 96 bpm. Physical examination revealed a normal mental

status and speech. Motor examination demonstrated muscular weakness with a Medical Research Council scale of 3/5 proximally in the lower limbs, and 4/5 proximally and distally in the upper extremities. The distal strength in the bilateral upper extremities was 5/5. The deep tendon reflexes were reduced with bilateral areflexia of the patellar, bicipital, and tricipital reflexes. Sensory deficits were not observed. No signs of an upper motor neuron disorder or meningeal irritation were observed. Magnetic resonance imaging of the entire neuroaxis, with and without contrast, was unremarkable for any acute or chronic pathology that may correlate with her symptoms.

Laboratory investigations revealed a hemoglobin of 13.9 g/dl with a hematocrit of 40%, leukocyte count of 6910/mm^3, erythrocyte sedimentation rate at the first hour was 25 mm, and electrolyte, renal, and hepatic functions were within normal limits. Tests for HIV, syphilis, HVB, and HVC were also normal. Covid-19 PCR were negative. Cerebrospinal fluid examination revealed clear fluid, normal opening pressure, glucose 0.78 g/L (glycemia 1.71 g/L), and albumin-cytologic dissociation with proteins of 1.25 g/l and white blood cells < 2/mm^3. Electrophysiological studies of motor nerve conduction have shown delayed distal latencies and the absence of F waves. The sensory nerve conduction was within the normal range (Table 1). Based on physical examination, cerebrospinal fluid findings, and electrophysiological study, a diagnosis of acute demyelinating polyradiculoneuropathy consistent with Guillain–Barre syndrome was made.

Intravenous immunoglobulin was administered at a dose of 0.4 g/kg for 5 days with physical therapy sessions, and no complications were observed during or after the treatment. The National Center of Pharmacovigilance was notified of this complication associated with the ChAdOx1 vaccine. After 6 months of follow-up, satisfactory evolution was noticed, without motor or sensory sequelae. Given the good outcome, it was not necessary to perform an EMG control.

2.2. Case 2

A 68-year-old woman with a history of hypertension and no reports of any travel or infectious episodes presented to the emergency department with symptoms of descending, symmetrical, and synchronous tetraplegia, preceded 4 days before by diffuse headaches with impairment of multiple cranial nerves and bladder dysfunction.

One week before admission, the initial neurological manifestations were diffuse headaches, diplopia, and facial paralysis. The clinical picture progressively deteriorated over two days with severe dysphonia and dysphagia to solids and liquids. The evolution was marked thereafter by paresthesias in the extremities, with descending, symmetrical weakness rapidly evolving over four days beginning in her arms, then lower limbs, and urinary retention. Three weeks before these manifestations occurred, the patient benefited from the first dose of the ChAdOx1 vaccine.

Table 1. Electrophysiological study.

Case 1							
MNCV Data				SNCV Data			
Nerve	Latency	Amplitude	Velocity	Nerve	Latency	Amplitude	Velocity
R Ulnaris							
Wrist	4.01	3.9	-	**R Ulnaris**	5.52	3.8	20
Elbow	7.50	3.9	66				
L Ulnaris							
Wrist	3.33	2.5	-	**L Ulnaris**			
Elbow	7.61	2.4	50				
R Medianus							
Wrist	10.68	2.5	-	**R Medianus**	6.82	16.9	12
Elbow	15.94	2.3	37				
L Medianus							
Wrist	16.93	0.9	-	**L Medianus**	3.59	2.6	36
Elbow	22.50	0.1					
R Peroneus							
Ankle	15.68	0.5	32	**R Suralis**	2.76	14.8	33
Fibular Head	25.42	0.2					
L Peroneus							
Ankle	15.21	1.5	-	**L Suralis**	3.02	38.6	33
Fibular Head	16.46	1.2					
R Tibial nerve	10.78	2.4					
L Tibial nerve	8.96	2.0					
Case 2							
R Ulnaris							
Wrist	12.0	0.4	-	**R Ulnaris**	2.0	15.7	66.3
Elbow	18.4	0.3	35.4				
L Ulnaris							
Wrist	5.78	4.6	-	**L Ulnaris**	3.01	12.4	52.4
Elbow	13.9	1	21				
R Medianus							
Wrist	27.2	0.4	-	**R Medianus**	3.0	7.4	41.5
Elbow	36.0	0.0	27.3				
L Medianus							
Wrist	27.4	0.5	-	**L Medianus**	3.3	10.9	43.0
Elbow		0.5					
R Peroneus							
Ankle	13.9	0.6	39.8	**R Suralis**	3.4	7.0	41.0
Fibular Head	22.3	0.5					
R Peroneus							
Ankle	12.6	0.6	32.1	**L Suralis**	2.3	6.4	60.3
Fibular Head	23.2	0.5					
R Tibial nerve	7.1	0.3	42.3				
L Tibial nerve	10.1	0.3	38				

On admission, the patient was asthenic, and initial vital signs were as follows: heart rate, 98 beats/min; respiratory rate, 20 breaths/min; blood pressure, 138/84 mmHg; temperature, 37.4˚C, saturation 96% on room air.

Examination revealed several cranial neuropathies including facial diplegia, bilateral oculomotor paralysis, bilateral soft palate paralysis and abolition of the pharyngeal reflex. Motor examination revealed hypotonia in all four limbs, with weakness estimated to be 2/5 in the proximal and distal muscles. The patient exhibited generalized areflexia.

There were no sensory impairments or upper motor neuron involvements. The biological assessment revealed no abnormalities. Brain MRI was normal. Coronavirus Cov-2 PCR results were negative. Analysis of cerebrospinal fluid (CSF) showed albumin-cytologic dissociation (protein of 1.22 g/l and WBC of 3). ENMG performed on the same day of hospitalization showed acute inflammatory axonal and demyelinating polyradiculoneuropathy (**Table 1**).

Immunoglobulin was started on the fourth day of hospitalization (0.4 g/kg for 5 days) without any significant complications. Clinical improvement was observed on the third day of treatment. This case was also reported to the National Pharmacovigilance Center. After 6 months of follow-up, the patient regained strength in both upper and lower limbs, so as cranial nerves functions. Given the good outcome, it was not necessary to perform an EMG control.

3. Discussion

Guillain-Barré syndrome is an autoimmune disease usually associated with a previous infection that can cause cross-reactions between peripheral nerve components, leading to inflammatory demyelination [1]. It is uncommon, with an incidence of 0.4 to 2 cases per 100,000, but flare-ups and seasonal variations have been observed [7]. Approximately half of those affected by GBS have a history of an identified infection and two-thirds have previous infectious symptoms [8].

Many publications have described an association between Guillain-Barré syndrome and COVID-19 DNA vaccines [9] [10]. In a recent literature review, 52 patients with GBS associated with ChAdOx1 were reported [11]. They found that the majority of reported cases occurred after the first dose of the vaccination in middle-aged and elderly people (mean age: 54.5 years). The mean time from vaccination to the onset of neurological symptoms was extremely inconstant (2 - 30 days; 13.9 ± 7.41 days) [6]. Classical GBS is the main clinical form [6] [10] [11]. Our two cases matched perfectly with the literature data. Favorable outcome was noticed in many cases, only few patients had partial recovery and poor outcomes. Good prognosis with a high chance of response to IVIG therapy was in line with our two cases [6] [11].

The Oxford/AstraZeneca vaccine uses a single recombinant replication-deficient chimpanzee adenovirus vector (ChAdOx1) to get inside the cell and encode the spike protein of the SARS-CoV-2 virus, which is then transferred to the cell surface to activate the immune cells. Antibodies against the spike protein may cross-react with gangliosides to cause GBS [6] [11]. Nevertheless, GBS cases that occur after COVID-19 vaccination have a low positive rate of anti-ganglioside

antibodies (20%), which suggest that gangliosides are not the antigenic target for GBS that appears after COVID-19 vaccination [11]. Molecular mimicry antigens may be structurally related to adenoviral vectors, abnormal splice variants or contaminated proteins [12]. However, accurate antigenic targets remain to be further investigated [6] [10] [11].

Our study sheds light on the possible association between the risk of GBS and the first dose of the ChAdOx1 vaccine. However, it is not yet possible to establish a reliable causal relationship between ChAdOx1 and GBS occurrence, especially with an unclear pathophysiological mechanism [11]. The risk of post-vaccination GBS due to COVID vaccine is much lower than the reference (0.26 cases of GBS per 1 million doses of COVID vaccine) [11]. The GBS/CIDP Foundation also states that there is no clear evidence that COVID-19 vaccination increases the risk of GBS [11] [13].

4. Conclusion

Many cases of GBS after ChAdOx1 vaccination have been reported, yet the physio-pathological mechanisms are not completely elucidated and the risk appears to be lower according to the literature. Therefore, we continue to promote COVID-19 vaccination, along with population surveillance, to facilitate the detection and management of GBS that may occur after COVID-19 vaccination.

Conflicts of Interest

The authors declare no conflicts of interest.

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