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Case Report

Guillian-Barré Syndrome Following Vaccination with Covishield Vaccine: An Adverse Event of Special Interest

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ABSTRACT

Several formulations of vaccines against novel coronavirus have been launched. Thereby, increasing the plausibility of having one or more successful vaccines. India put in place the world's largest Covid-19 vaccination drive in January 2021. However, the side effects of these vaccines are slowly unfolding. Each new vaccine has potential adverse events of special interest (AESI) that warrant a focused evaluation. We report a very rare neurological complication Guillain-Barré syndrome, immediately following the first dose of COVID vaccination in a young female. An apparently healthy 35 years old female presented with acute onset lower backache, weakness of bilateral lower limbs 11 days after receiving the first dose of Covishield vaccine, which rapidly ascended to upper limbs over 5 days with symmetric motor weakness, power 1/5 in bilateral lower limbs, 3/5 in bilateral upper limbs, with absent deep tendon reflexes. Mild sensory involvement was seen. Evolving dysphagia and hoarseness of voice. Bladder/bowel function, respiratory pattern, and hemodynamics were unaffected. A provisional diagnosis of Guillain-Barre Syndrome was made on basis of clinical presentation, neurological examination, and nerve conduction studies suggesting axonal polyneuropathy. Gradual improvement of the muscle power over the next 2 weeks following Human Intravenous immunoglobulin was seen. The risk-benefit analysis for an individual should be considered prior to Covid-19 vaccination, including the implementation of a pre-vaccination screening checklist to ensure vaccine safety for every vaccine recipient. The vaccine continues to be far more beneficial than detrimental for the public at large. Nonetheless, increased awareness amongst healthcare professionals and the public regarding the potential adverse effects of the vaccine is warranted.

Introduction

In a desperate attempt to contain the wrath of the COVID-19 virus, several formulations of vaccines against novel coronavirus have been launched. Having a variety of vaccines in development increases the plausibility of having one or more successful vaccines safe and effective for the targeted populations [1]. India put the world's largest Covid-19 vaccination drive in January 2021. However, the side effects of these vaccines are slowly unfolding. Each new vaccine has potential adverse events of special interest (AESI) that warrant a focused evaluation [2]. Most adverse events are reported as mild to moderate in severity and self-limiting. Neurological complications have been rarely reported worldwide, primarily resulting from the hypercoagulable state triggered by the general inflammatory condition induced by COVID-19, with the attention now shifting to autoimmune-mediated disorders. GBS is an AESI that is very rare but the incidence increases with age. We report a very rare neurological complication GBS, immediately

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following the first dose of COVID vaccination in a young healthy female.

Case Report

A 35-year-old apparently healthy female presented to our hospital with complaints of lower backache, bilateral weakness, tingling, and numbness of lower limbs for the last four days. The symptoms were sudden onset, progressively increasing, and started with lower backache, followed by tingling and numbness and radiated bilaterally to the feet. She gave a history of receiving the first dose of ChAdOx1nCoV- 19 Corona Virus Vaccine (Recombinant) 15 days back. Post-vaccination on day 1, she had a fever that lasted for three days, followed by bilateral lower limb numbness and tingling sensation 11 days after vaccination. The patient complained of an inability to wear slippers or get up from a squatting position. There was no complaint of loss of touch, pain, or temperature. No bowel/bladder involvement seen. No loss of smell and vision seen. There was no complaint of headache, nausea, vomiting, seizures, head and neck injury, tinnitus, difficulty in chewing food, speech, tongue protrusion, and difficulty closing the eyes. The shoulder and bilateral upper limb's tone, power, and movements were adequate on examination. However, tone and power (3/5 Medical Research Council grade) was reduced in bilateral lower limbs. Bilateral upper and lower limb deep tendon reflexes were absent.

She was admitted to the ward and was provisionally diagnosed to have GBS. She was started on human intravenous immunoglobulin (IVIg) treatment at 2 grams per kilogram body weight. CSF examination done on the fourth day of symptoms showed a normal white blood cell count with 0.37gram/Litre of protein and sugar of 0.58gram/Litre. The patient underwent nerve conduction studies, and the report was suggestive of sensory-motor axonal polyneuropathy. Over three days, she gradually deteriorated Single Breath Test count and power in both upper (3/5) and lower limbs (2/5). After that, she was shifted to the Intensive Care Unit (ICU) for further care. Her single breath count was 20 initially, and when she was shifted to the ICU, it had deteriorated to 16 and continued to remain between 16 and 20 throughout the course of her ICU stay.

On day 2 of ICU admission, she developed difficulty in speech and a weak cough, but the breathing pattern was typical. Her vitals and saturation of peripheral blood on room air were stable. The IVIg was continued for five days. The patient was closely monitored for single breath count, arterial blood gas, negative inspiratory pressure, respiratory rate, pattern, motor power, and deep tendon reflexes (Table 1-2). She was also put on methylcobalamin therapy at 1000 micrograms/day. The patient had a normal tone and power in the bilateral upper limbs at presentation. Over the next five days, power reduced to 3/5 in bilateral upper limbs and 1/5 in bilateral lower limbs over two days. Power improved to 3/5 in lower limbs over 13 days and 4/5 in upper limbs over 12 days. In all the sixteen days of follow-up, her deep tendon reflexes of bilateral upper and lower limbs were absent. She was shifted to the ward with stable vitals on room air.

Table 1- Monitoring of Power during ICU stay (Medical Research Council (MRC) Grading)

Days of Presentation	Limb	Right	Left
1	Upper	5	5
	Lower	3	3
2	Upper	4	4
	Lower	1	1
3	Upper	4	4
	Lower	1	1
4	Upper	4	4
	Lower	1	1
5	Upper	3	3
	Lower	1	1
6	Upper	3	3
	Lower	1	1
7	Upper	3	3
	Lower	2	2
8	Upper	3	3
	Lower	2	2
9	Upper	3	3
	Lower	2	2
10	Upper	3	3
	Lower	2	2
11	Upper	3	3
	Lower	2	2
12	Upper	4	4
	Lower	2	2
13	Upper	4	4
	Lower	3	3
14	Upper	4	4
	Lower	3	3
15	Upper	4	4
	Lower	3	3
16	Upper	4	4
	Lower	3	3
17 (Discharged)	Upper	5	5
	Lower	4	4

Investigations

The patient's hemogram, coagulation profile, and renal and liver function tests were within normal limits, except that her AST began to rise twice to thrice the normal value after stopping IVIg. Her blood and urine cultures were sterile. CSF examination was done on the fourth day of symptoms, and the total protein level was 37milligram/decilitre. A nerve conduction study showed sensory-motor axonal polyneuropathy. (Table 3-5)

Treatment

The patient received five days of IVIg at 2 grams per kilogram body weight, 120 grams with 24 grams per day. Analgesia with intravenous paracetamol on an SOS basis. Tablet Methylcobalamine 1000 micrograms per oral once daily was added. Incentive spirometry and deep breathing

exercises were explained and demonstrated to the patient, and she remains compliant with them. She is also undergoing physical rehabilitation with physiotherapy; compression stockings were installed for prophylaxis against Deep Venous Thrombosis.

Outcome

Signs of neurological improvement were seen after completion of the course of IVIg [1]. Motor power in the lower limbs showed improvement, and the progression of paralysis in the upper limbs was arrested. Breath-holding time improved along the course. The patient felt "much better" than before, in her own words. She was shifted from the ICU to the general ward after her motor power in the bilateral upper limb improved to 4/5 and bilateral lower limbs improved to 3/5. Complaints of dysphagia resolved, and she well-tolerated oral nutrition. Hoarseness of voice and weak cough had also resolved. She started to walk with support. Eight months since her first presentation motor weakness continues to improve progressively, although she still requires support to ambulate.

Discussion

AZD1222 Vaxzevria by AstraZeneca is a recombinant, replication-deficient chimpanzee adenovirus vector encoding the SARS -CoV-2 Spike (S) glycoprotein. CoviShield is a ChAdOx1_nCoV-19 AstraZeneca vaccine manufactured by Serum Institute of India. The other available vaccines like The Pfizer-BioNTech and Moderna vaccines are nucleoside-modified mRNA vaccines encoding the spike glycoprotein of SARS-CoV-2, the virus that causes COVID-19. Janssen Vaccine is a replication-incompetent Ad26 vector encoding the spike glycoprotein of SARS-CoV-2. Sinopharm and Sinovac are inactivated whole virus vaccines [1]. These had been approved and listed under Emergency Use Listing (EUL) [3] due to the widespread nature of the Covid-19 pandemic without going through rigorous, long-term trials, the side-effects profile is unfolding gradually.

The most common side-effects of ChAdOx1_nCoV-19 are usually mild to moderate and self-limiting [4]. Some rare but severe side effects have been reported, including Immune Thrombocytopenia (ITP), Thrombosis with Thrombocytopenia Syndrome (TTS), myocarditis, and pericarditis [5]. Overall, symptoms were more frequent and severe following the second dose of the vaccine and among adolescents and young adults compared with older people [6]. Headache is the most commonly reported neurological symptom following COVID vaccination [7]. The European Medicines Agency (EMA) added Guillain Barre Syndrome (GBS) to this list as an infrequent side effect and added a warning in the product information [8].

The Association of GBS has been proven with vaccination against Influenza A [9], but the risk was higher with influenza infection [10]. The potential association between GBS and SARS-CoV-2 infection was studied [11]. This raises caution regarding the GBS spike parallel to the ongoing COVID-19 pandemic and mass vaccination [12].

Guillain- Barré Syndrome (GBS) is a rare heterogeneous condition characterized by rapidly progressive, symmetrical limb weakness with hyporeflexia or areflexia, sensory disturbances, and cranial nerve deficits in some patients. Primary infection is usually identified, resulting in GBS, pathogenesis likely explained by molecular mimicry, antiganglioside antibodies, and complement activation.

The Brighton criteria identify GBS with four levels of diagnostic certainty, from level 1 (highest) to level 4 (lowest) [13]. Clinical diagnosis of GBS can be supported by additional investigations [10]. Nerve conduction study provides diagnostic strength to GBS. The CSF value is an optional criterion for diagnosing GBS according to the level 2 diagnostic certainty of the Brighton Criteria for diagnosis of Guillain- Barré Syndrome [10,13]. The CSF study for this patient was done within seven days of onset of symptoms; thus, it probably was within normal limits. However, we did not repeat a CSF study, as it would not have altered the course of management for the patient. Intravenous immunoglobulin and plasma exchange have been established as efficacious treatments. Our patient showed a clinical response on received IVIg, distributed over five days [3].

Cases of GBS after COVID-19 vaccination are being increasingly reported worldwide. In India, 7 cases have been reported in Kerala by Maramattom et al. [14]. GBS may be associated with the COVID-19 vaccine; however, more studies are needed to establish this relation.

It is interesting to note that patients with a history of GBS were not precluded from receiving COVID-19 vaccination, also for the second dose despite developing GBS with the first vaccine dose [14]. Though the increasing incidence of GBS has sparked a change in approach, and history of GBS has now been included in the pre-vaccination screening checklist [15]. The pre-vaccination screening checklist has been formulated to ensure vaccination safety in the vaccine recipients, and informed consent is obtained from the recipient. High-risk recipients should be aware of the potential adverse effects to facilitate their early recognition.

The risk-benefit ratio of the vaccination should be assessed for a given patient population, and for the particular individual and the decision-making should be done accordingly. Neurological complications are substantially higher after infection than after vaccination [16]. A population-based cohort and self-controlled case series analysis by Xintong Li et al. [17] studied the association between covid-19 vaccination, SARS-CoV-2 infection, and risk of immune-mediated neurological events and found no safety signal was observed between

covid-19 vaccines and the immune-mediated neurological events including Guillain-Barré syndrome, an increased risk, however, observed for people with SARS-CoV-2 infection.

So far, the vaccination has been substantially more advantageous than detrimental for the general public. Nonetheless, continuous vaccine safety surveillance is needed to increase awareness among healthcare professionals. The vaccinated people are warranted to timely recognize and treat the potential adverse effects and rule out other causes.

Table 2- Monitoring of Patient Vitals during ICU stay

Day of ICU stay	pCO2 (mmHg)	Breath Holding Time (seconds)	Peak Inspiratory Pressure (cmH2O)	Neck Muscle power	Respiratory Rate (breat-hs/ min)	Heart rate (bpm)	Blood pressure (systolic/diast-olic in mmHg)
3	27	15	-20	Able to lift head	18	76	118/61
4	26.8	16	-17	Able to lift head	16	71	112/58
5	24.8	15	-20	Able to lift head	17	68	120/62
6	28.4	20	-20	Able to lift head	18	65	119/71
7	25	26	-20	Able to lift head	20	66	122/67
8	27	22	-20	Able to lift head	16	61	121/70
9	25.7	18	-20	Able to lift head	21	64	114/59
10	21.7	20	-21	Able to lift head	22	71	123/63
11	21.0	21	-20	Able to lift head	18	68	121/68

Table 3- Sensory Nerve Conduction Study

Nerve/Sites	Rec. Site	Peak Lat ms	PP Amp µV	Segments	Distance mm	Velocity m/s	Comment
L Median – Dig II (Antidromic)							
Wrist	Index	NR	NR	Wrist - Index	140	NR	
L Ulnar – Dig V (Antidromic)							
Wrist	Dig V	NR	NR	Wrist – Dig V			
R Sural - (Antidromic)							
Calf	Ankle	NR	NR	Calf - Ankle			
L Sural - (Antidromic)							
Calf	Ankle	NR	NR	Calf - Ankle			

Table 4- Motor Nerve Conduction Study

Nerve/ Sites	Muscle	Latency (ms)	Amplitude (mV)	Rel. Amp. (mV)	Dur.	Segment	Distance (mm)	Velocity (m/s)	Diff (ms)	Area (mV.ms)
R Median – APB										
Wrist	APB	6.94	2.5		12.3	Wrist - APB			7	0.0
Elbow	APB	12.65	1.5	58.1		Elbow - Wrist	220	39	13	0.0
L Ulnar – ADM										
Wrist	ADM	4.90	1.8	100	9.0	Wrist – ADM			5	0.0
B Elbow	ADM	9.96	1.6	86.5	8.5	B Elbow – Wrist	230	45	10	0.0

R Peroneal – EDB Ankle	EDB	8	1.4	100	8.2	Ankle – EDB			8	0.0
B Fib Head	EDB	18.21	0.3	18.4	10.7	B Fib Head – Ankle	340	33	18	0.0
L Peroneal – EDB Ankle	EDB	10.17	0.3	100	9.4	Ankle - EDB			10	0.0
B Fib Head	EDB					B Fib Head - Ankle				0.0
R Tibial – AH Ankle	AH	9.27	0.7	100	7.3	Ankle – AH			9	0.0
Knee	AH	21.58	0.3	38.5	6.4	Knee - Ankle	400	32	22	0.0
L Tibial – AH Ankle	AH	8.90	0.5	100	6.1	Ankle – AH			9	0.0
Knee	AH	23.50	0.3	54.6	5.6	Knee - Ankle	400	27	24	0.0

Table 5- F Waves

Nerve/Sites	Rec. Site	Peak Lat ms	PP Amp µV
R Peroneal – EDB		7.3	
R Tibial – AH		7.7	
L Tibial – AH			
R Median – APB			
L Ulnar – ADM	0.0	5.0	5.0

Conclusion

The risk-benefit analysis should be considered before the Covid-19 vaccination, including implementing a pre-vaccination screening checklist to ensure vaccine safety for every vaccine recipient. The vaccine continues to be far more beneficial than detrimental for the public at large. Nonetheless, continuous vaccine safety surveillance coupled with increased awareness amongst healthcare professionals and the public regarding potential adverse effects of the vaccine is warranted.

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