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COVID-19

Guillain-Barré syndrome following the first dose of Pfizer-BioNTech COVID-19 vaccine: case report and review of reported cases

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Abstract

Background Since the SARS-CoV-2 pandemic has started in December 2019, millions of people have been infected all over the world. Vaccination is the most efficient tool to end this pandemic, but vaccine surveillance is necessary to identify side effects. Some studies have shown that neurological complications after COVID-19 vaccination are rare and dominated by demyelinating disease.

Case presentation We present a case of a 67-year-old man who presented 7 days following his first dose of Pfizer-BioNTech COVID-19 vaccine a rapidly progressive ascending muscle weakness. The diagnosis of Guillain-Barré syndrome (GBS) was confirmed according to the clinical features, the albumino-cytological dissociation in the cerebrospinal fluid, and the electroneuromyography findings. The workup for all known infections associated with immune-mediated GBS was negative. The patient received treatment with intravenous immunoglobulin. Neurological examination 1 month after discharge showed full recovery and he regained his baseline functional status.

Conclusions As far as we know, this is the first reported case in Tunisia. Although extremely rare, neurologists should remain vigilant for acute inflammatory demyelinating polyradiculoneuropathy after COVID-19 vaccination.

Keywords Guillain-Barré syndrome (GBS) · COVID-19 vaccine · SARS-CoV-2 · Neurological complications

Introduction

Guillain-Barré syndrome (GBS) is the most common acute immune-mediated polyradiculoneuropathy in the world [1]. The classical clinical presentation of GBS is a bilateral weakness with hyporeflexia or areflexia with or without sensory symptoms [2]. The cause of GBS is unknown; it is believed that an autoimmune response plays a role in the pathogenesis of this disease [2]. The suggested pathophysiology is molecular mimicry following respiratory or gastrointestinal infections and extremely rare following vaccination [3]. Since the pandemic was caused by COVID-19, several vaccines were approved by the food and drug administration to control this pandemic and many side effects were reported ranging from fatigue, fever, and myalgia to more serious complications [3, 4]. We herein report a case of a patient who developed GBS 7 days after receiving the first dose of Pfizer-BioNTech COVID-19 vaccine. We report this case to increase awareness of acute inflammatory demyelinating polyradiculoneuropathy (AIDP) as a possible side effect of the COVID-19 vaccine and to understand if this syndrome is associated with a specific type of vaccine by an exhaustive reviewing of the literature.

Case report

A 67-year-old male, with a medical history of type II diabetes, was admitted for a weakness of the four limbs in July 2021. He presented 4 days before his admission complaints of progressive ascending weakness. He had received his first dose of COVID-19 (Pfizer-BioNTech) 7 days before presentation. He denied any history of recent fever, gastrointestinal, or upper respiratory tract illness. He denied also contracting

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COVID-19 infection. At physical examination on admission, his blood pressure was 124/80 mm Hg, his pulse was 76 bat/min, and his body temperature was 37.3 °C. Neurological examination showed a flaccid tetraparesis predominating in the lower limbs and weakness in distal lower limbs for foot and toes dorsiflexors. His upper limb power was a medical research council (MRC) grade 4/5 and his lower limb power was MRC grade 3/5. There was a generalized areflexia, with intact superficial and vibratory sensation. Examination of the cranial nerves was normal. No bowel or bladder dysfunction was reported.

Routine blood tests revealed a hemoglobin rate of 12.4 g/dL, a platelet count of 361000/µL, and a white blood cell count of 6780/µL. He had a C-reactive protein of 4 mg/dL.

Electroneuromyography performed 1 day after admission showed typical features of AIDP. Reviewing the neurophysiological criteria of Rajabally et al. [5], there is a prolonged F response in the left median and left tibial nerves. Table 1 summarizes the results of the electroneuromyography.

Lumbar puncture revealed an albumino-cytological dissociation with 0.8 g/L of protein, 4 WBC/mm^3, and normoglucorrachia. Cerebrospinal fluid (CSF) cytology was unremarkable. Extensive infectious and inflammatory workup of serum and CSF which included HIV antibodies, hepatitis B and C serologies, *Campylobacter jejuni* serology, Lyme titers, CMV titers, EBV titers, and anti-nuclear antibodies were all negative. Ganglioside antibodies GM1, GD1a, GD1b, GQ1b, and GM2 were negative. COVID-19 PCR from a nasopharyngeal swab was negative.

Based on the previous workup, and according to the Brighton criteria [6], the diagnosis of GBS was made with the highest level of diagnostic certainty, and an intravenous immunoglobulin (IVIG) treatment was started. He was given IVIG in the standard recommended dose (0.4 g/kg/day) for 5 days with rehabilitation. After 1 week of hospitalization, his strength began to improve. He was seen in the neurology clinic, outpatient department of the hospital 4 weeks after discharge, where neurological examination showed full recovery and he regained his baseline functional status.

Table 1 Summary of electromyography and nerve conduction studies

Tests	Normal value	Right	Left
Motor nerve conduction			
DML (ms)			
Median	≤3.8	**4.3**	**4.1**
Ulnar	≤3.2	2.2	2.5
Peroneal	≤5	4.9	**5.6**
Tibial	≤4.5	**5.7**	**6.5**
F waves (ulnar)	≤30	33.5	34.3
F waves (median)	≤30	28.8	**37.5**
F waves (tibial)	≤50	55.3	**61.3**
CMAP (mV)			
Median			
Wrist	≥6	**0.7**	**1.2**
Ulnar			
Wrist	≥6	**1.2**	**3.9**
Below elbow		**1.7**	**3**
Above elbow		**0.7**	**1.3**
		Proximal conduction block	**Proximal conduction block**
Peroneal	≥3	**2.5**	3.5
Tibial	≥6	**0.2**	**0.4**
MCV (m/s)			
Median	≥45	57.6	51.6
Ulnar	≥45	55.3	56
Peroneal	≥42	42.6	41
Tibial	≥42	40.3	45.4
Sensory nerve conduction			
SNAP (mV)			
Ulnar	≥10	13	14
Median	≥15	7	7.5
Radial	≥15	11	15
Sural	≥10	6.4	11
Musculocutaneous	≥10	19	15
SCV (m/s)			
Ulnar	≥45	56.3	57.8
Median	≥45	43.8	48.6
Radial	≥45	64.6	62.4
Sural	≥40	42	45.5
Musculocutaneous	≥40	54.3	57.4

DML, distal motor latency; *CMAP*, compound muscle action potential; *MCV*, motor nerve conduction velocity; *SNAP*, sensory nerve action potential; *SCV*, sensory conduction velocity; values marked in bold are above or below normal; values marked in bold underlined meet Rajabally's criteria

Discussion

This paper reported a case of GBS in a patient who recently received the Pfizer-BioNTech vaccine. This vaccine is a synthetic messenger RNA vaccine (mRNA). Inside the human body, mRNA enters the human cell and produces the spike protein found on the surface of the virus. Our bodies recognize this protein as an invader and produce antibodies against it [4]. In some cases, this immune response can trigger autoimmune processes that lead to the production of antibodies against the myelin and cause GBS. This syndrome is an immune-mediated syndrome that involves a variety of demyelinating conditions: AIDP like in our case, acute motor-sensory axonal neuropathy (AMSAN), acute motor axonal neuropathy (AMAN), and Miller Fisher syndrome [7].

The immunological pathophysiology of GBS was reinforced by many reported cases following vaccination against

Table 2 Review of the literature

Publications Date/country	Number of cases	Sex/age (years old)	Vaccine/technique	Interval vaccine-GBS symptoms (days)	Neurological examination	Electromyography	CSF	Brain and spinal MRI	Treatment	Evolution
Waheed et al. [9] February 2021/USA	1	F/82	Pfizer (first dose)/mRNA	14	Flaccid paraplegia	Not performed	Albumino-cytological dissociation (proteins 0.88 g/L)	Enhancement of cauda equina nerve roots	IVIG	Favorable
Razok et al. [10] May 2021/Qatar	1	M/73	Pfizer (second dose)/mRNA	20	Flaccid tetraplegia	AIDP	Albumino-cytological dissociation (proteins 0.8 g/L)	Bilateral nerve root enhancement in the lumbar region and the upper part of the cauda equina	IVIG	Favorable
Ogbebor et al. [11] April 2021/USA	1	F/86	Pfizer (first dose)/mRNA	1	Flaccid paraplegia	Not performed	Albumino-cytological dissociation (proteins 1.62 g/L)	Normal	IVIG	Favorable
Azam et al. [12] May 2021/UK	1	M/67	AstraZeneca (first dose)/viral vector	19	Flaccid tetraplegia + bilateral peripheral facial palsy	AIDP	Albumino-cytological dissociation (proteins 3.9 g/L)	Bilateral enhancement of the facial nerve	IVIG	-Autonomic complications of GBS (hyponatremia) -Favorable
Patel et al. [13] April 2021/UK	1	M/37	AstraZeneca (first dose)/viral vector	14	Flaccid tetraplegia + ataxia	Normal	Albumino-cytological dissociation (proteins 1.77 g/L)	Bilateral thickened of the cauda equina nerve rootlets, particularly at the level of S1	IVIG	Respiratory distress and neuropathic pain
Loza et al. [14] April 2021/USA	1	F/60	Johnson & Johnson/viral vector	10	Bilateral facial palsy + flaccid paraplegia + diplopia	AIDP	Albumino-cytological dissociation (proteins 1.4 g/L)	Enhancement of the cauda equina	IVIG	Favorable

Table 2 (continued)

Publications Date/country	Number of cases	Sex/age (years old)	Vaccine/technique	Interval vaccine-GBS symptoms (days)	Neurological examination	Electromyography	CSF	Brain and spinal MRI	Treatment	Evolution
Allen et al. [15] May 2021/UK	4	M/54	AstraZeneca (first dose)/ viral vector	16	Bilateral facial palsy + distal dysesthesia in his feet and hands	Facial NCS showed severely reduced compound muscle action potential amplitude responses and normal terminal latencies bilaterally. Sensory and motor NCS were normal in the upper and lower limbs.	Mild lymphocytosis (19 cells/mL) and elevated proteins (1,626 g/L)	Subtle enhancement bilaterally in the distal facial nerves at the internal auditory canal	Oral prednisolone 60 mg for 5 days	No improvement
		M/20	AstraZeneca (first dose)/ viral vector	26	Dysesthesia in his distal lower limbs + facial diplegia	Facial NCS showed borderline normal amplitude responses and normal terminal latencies bilaterally. Sensory and motor NCS were normal in the upper and lower limbs.	Mild lymphocytosis (14 cells/mL) and elevated proteins (1,232 g/L)	Normal	Oral prednisolone 60 mg for 5 days	No improvement
		M/57	AstraZeneca (first dose)/ viral vector	21	Flaccid tetraplegia + diplopia	Normal	Mild lymphocytosis (8 cells/mL) and elevated proteins (2,471 g/L)	Normal	IVIG	Unspecified
		M/55	AstraZeneca (first dose)/ viral vector	29	Bilateral thigh paresthesias + facial diplegia	Not performed	Albumino-cytological dissociation (proteins 0.890 g/L)	Enhancement of the facial nerve within the right internal auditory canal	No treatment	Spontaneous improvement

Table 2 (continued)

Publications Date/country	Number of cases	Sex/age (years old)	Vaccine/technique	Interval vaccine-GBS symptoms (days)	Neurological examination	Electromyography	CSF	Brain and spinal MRI	Treatment	Evolution
Nasuelli et al. [16] July 2021/Italy	1	M/59	ChAdOx1 nCoV-19 vaccine (first dose)/viral vector	10	Gait ataxia+ global areflexia + and distal paresthesia in the four limbs	AIDP	Albumino-cytological dissociation (proteins 1.4 g/L)	Normal	IVIG	Worsening (cranial nerve palsy: bilateral facial palsy)
Garcia-Grimshaw et al. [17] July 2021/ Mexico	7	M/33	Pfizer (first dose)/mRNA	28	Facial diplegia and loss of deep tendon reflexes	AIDP	Albumino-cytological dissociation (proteins 0.67 g/L)	Unspecified	IVIG	Favorable
		M/25		12	Symmetric weakness and paresthesia of hands and feet	AIDP	Albumino-cytological dissociation (proteins 0.64 g/L)			Partial improvement
		F/53		6	Quadriparesis and loss of deep tendon reflexes.	AMAN	Albumino-cytological dissociation			No improvement
		M/72		4	Quadriparesis and decreased deep tendon reflexes	AMAN	Not performed			No improvement
		M/31		4	Symmetric weakness and loss of deep tendon reflexes	AIDP	Not performed			Partial improvement
		F/67		5	Quadriparesis, loss of deep tendon reflexes, and respiratory failure	AMAN	Proteins: 0.30 g/L			Dead
		F/81		4	Asymmetric weakness and loss of deep tendon reflexes	AIDP	Albumino-cytological dissociation (proteins 0.414 g/L)			No improvement
Trimboli et al. [18] August 2021/Italy	1	F/25	Pfizer (second dose)/mRNA	5	Flaccid paraplegia + areflexia in lower extremities	AIDP	Normal	Not performed	IVIG	Favorable

Table 2 (continued)

Publications Date/country	Number of cases	Sex/age (years old)	Vaccine/technique	Interval vaccine-GBS symptoms (days)	Neurological examination	Electromyography	CSF	Brain and spinal MRI	Treatment	Evolution
Our case Tunisia	1	M/67	Pfizer (first dose)/mRNA	7	Flaccid tetraparesis	AIDP	Albumino-cytological dissociation (proteins 0.8 g/L)	Normal	IVIG	Favorable

F, female; *M*, male; *IVIG*, intravenous immunoglobulin; *NCS*, nerve conduction studies; *AIDP*, acute inflammatory demyelinating polyneuropathy; *AMAN*, acute motor axonal neuropathy

multiple pathogens. The influenza vaccine was the most offending, also hepatitis B and A, tetanus, and polio vaccines can cause GBS [8]. The first case of GBS following COVID-19 vaccination was reported by Waheed et al. [9] in February 2021 in the USA, in a 82-year-old female, 14 days after the first dose of Pfizer-BioNTech.

Reviewing the literature, at the time of writing this paper, 19 cases of GBS after COVID-19 vaccination were reported in the world (Table 2). All patients described in the literature had not a history of COVID-19 or current infection, as in our patient. Many types of vaccines with different mechanisms of action have been implicated in the development of GBS (Table 2): eleven cases after Pfizer-BioNTech vaccine, six cases after AstraZeneca vaccine, one case after ChAdOx1 nCoV-19 vaccine, and one case after Johnson & Johnson vaccine. All reported cases presented GBS after receiving the first dose of COVID-19 vaccine, only one case after the second dose.

Our patient developed, 7 days after receiving the first dose of Pfizer-BioNTech vaccine, as far as our known this is the first reported case in Tunisia. However, despite a relatively large number of reported cases of GBS in post-vaccination, a temporal association is a possibility and a definite causal association was not confirmed considering the inability to prove that relation on a molecular basis. The classical clinical manifestation of GBS is bilateral symmetric weakness and decreased deep tendon reflexes. The CSF analysis demonstrates albumin-cytological dissociation, like the findings in our patient and electrophysiological studies mainly showing AIDP. The treatment of GBS is based on plasma exchange (PE) or IVIG. Our patient and the majority of cases described in the literature underwent IVIG, because it is easier to manage than PE and has substantially fewer complications, only 2 cases were treated by prednisolone (Table 2).

Conclusion

We describe a case of GBS following vaccination against SARS-COV-2. We report this case to increase awareness of GBS as a possible complication of this vaccine, but further extensive studies are required to adequately determine the link between vaccination and GBS.

Declarations

Conflict of interest The authors declare no competing interests.

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