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Guillain-Barré Syndrome Related to the application of Vaccine Against Sars-CoV2 and Seasonal Influenza. Case Report

López-Hernández Juan Carlos[1,2] | López-Alderete Jorge[3] | Escamilla-Ramírez Ángel[3] | Rosiles-Abonce Artemio[3] | Violante-Villanueva Arturo[1] | Gutiérrez-Romero Alonso[4] | Vargas-Cañas Steven[2]

1. Department of Neurological Emergencies. National Institute of Neurology and Neurosurgery Manuel Velasco Suarez
2. Neuromuscular Diseases Clinic National Institute of Neurology and Neurosurgery Manuel Velasco Suarez
3. Department of Neurology National Institute of Neurology and Neurosurgery Manuel Velasco Suarez

Correspondence

Juan Carlos López Hernández
National Institute of Neurology and Neurosurgery. Av. Insurgentes Sur 3877, Col. La Fama. CP 14269, Mexico City.

juanca9684@hotmail.com

Abstract

Summary: Guillain-Barré Syndrome (GBS) is the principal cause of acute flaccid paralysis in the world. During mass vaccination campaigns, implemented in previous decades for the influenza virus and currently for the SARS-CoV2 virus, an increase in GBS cases has been reported. Recently, both vaccines have been implemented in adult immunization schedules. **Objective**: to report a case of GBS with a history of vaccination against seasonal influenza and SARS-CoV2 in a short period of time. **Results**: A 53-year-old woman with no previous infectious disease received a trivalent inactivated seasonal influenza vaccine [Virus A (A/Victoria/2570/2019(H1N1pm09), Virus A (A/Cambodia/e0826360/2020(H3N2), Virus B (B/Washington/02/2019(B/Victoria line)] and a SARS-CoV2 vaccine (Oxford/AstraZeneca, ChAdOx1-S) 22 days apart. The patient then developed progressive and ascending symptoms of weakness predominantly in the lower extremities, with areflexia. **Paraclinical examinations**: lumbar puncture with albuminocytological dissociation, nerve conduction study fulfilling criteria for AIDP variant, classifying for GBS with level of certainty 1 by Brighton criteria. **Conclusion**: due to the SARS-CoV2 pandemic, mass vaccination schedules against this virus were implemented, which coincide with vaccination against seasonal influenza virus in the winter season; consequently, cases of GBS may occur with a history of recent application of both vaccines.

Keywords: *SARS-CoV2, influenza, Guillain-Barré syndrome, vaccination, AIDP*.

Introduction

Guillain Barre Syndrome (GBS) is the leading cause of acute flaccid paralysis in the world. In 70% of the cases, the mechanism of peripheral nerve damage is attributable to an aberrant immune response after infection. Other cases have been related to the application of certain vaccines, for example, against seasonal influenza, hepatitis B and hepatitis A, to name a few.[1] Even when patients are diagnosed and treated promptly (immunoglobulin human G or plasma exchanges), 20-40% present short term severe disability (non-independent gait).[1,2]

The main electrophysiological variants are acute inflammatory demyelinating polyradiculoneuropathy (AIDP) and acute motor axonal neuropathy (AMAN).

The AIDP variant is more frequent in European countries and in the USA, and is related to viral infections (e.g., cytomegalovirus) and post-vaccination. The AMAN variant is the most frequent in some Latin American countries, such as Mexico, and in Asia; this variant is related to gastrointestinal infection by the agent Campilobacter jejuni.[1,2]

In 2011, as a consequence of the increase in GBS cases linked to different vaccines, a group of experts created the Brighton Criteria, which offer recommendations to define GBS cases related to vaccination, and classify them in levels of diagnostic certainty.[3]

Currently, due to the SARS-CoV2 pandemic, health systems in all countries have implemented mass vaccination against this virus. Worldwide, secondary reactions to vaccines against the SARS-CoV2 virus have been reported, ranging from mild symptoms such as fever, myalgia and flu-like symptoms, to cases of GBS.[4] However, it should be noted that there are few cases of GBS related to vaccination against SARS-CoV2.[5] In addition, during the winter season and in accordance with WHO recommendations, countries such as Mexico implement vaccination against seasonal influenza with a trivalent inactivated virus vaccine in the adult population.[6]

To our knowledge, there is little information on cases of GBS with a history of vaccine application against two respiratory viruses. In this work we report the case of a patient who presented GBS after receiving the vaccines against seasonal influenza and the SARS-CoV2 virus in a short period of time.

Clinical Case

A 53-year-old woman with a diagnosis of type 2 diabetes mellitus and systemic arterial hypertension, had been on treatment for a year with losartan 50 mg every 12 h and metformin 500 mg every 12 h with adequate control. She denied any gastrointestinal or respiratory infection in the last 4 weeks. She was vaccinated against seasonal influenza with a trivalent inactivated virus vaccine [Virus A (A/Victoria/2570/2019 (H1N1pm09)), Virus A (A/Cambodia/e0826360/2020 (H3N2)), Virus B (B/Washington/ 02/2019 (line B/Victoria))], and 22 days later, she received the third vaccine against the SARS-CoV2 virus (Oxford / AstraZeneca, ChAdOx1-S [recombinant] vaccine). That same day, 8 hours later, the patient presented distal paresthesias in the upper extremities, adding in the following days progressive weakness of the four extremities, predominantly in the lower extremities, until requiring a wheelchair to move. The patient was admitted to the emergency department 14 days after symptom onset. In the general physical examination, vital signs were in normal parameters, without fever, and no pathological findings in the lung fields. At neurological examination, the patient showed no abnormalities in the cranial nerves. Regarding the motor system, muscle strength —quantified with the MRC scale— was 4/5 in the upper limbs (deltoid, biceps and hand extensor muscles), 1/5 in the lower limbs (iliopsoas muscle, quadriceps and tibialis anterior), with a score of 4 on the Hughes scale. Muscle stretch reflexes were found to be generally abolished. She had no alterations in sensitivity. General tests (hematic cytometry, blood chemistry, serum electrolytes, liver function tests, CPK levels, TSH) were within normal ranges; serologies for HIV, HCV and HBV were negative; C-reactive protein 1.1 mg/l; chest CT with no data of pulmonary interstitial infiltrates. Lumbar puncture was performed, which reported 243 mg/dL of protein, 0 cells, 80 mg/dL of glucose. Nerve conduction studies of 4 limbs revealed the AIDP variant, according Hadden criteria[7] (Figure 1 and Table 1). Using the Brighton criteria, GBS was concluded,[3] for which the patient received treatment with human immunoglobulin G at a dosage of 2 g/kg, divided into 5 days. She remained hospitalized for 6 days, without in-hospital complications or dysautonomia, with improved recovery of functionality, and she was discharged home having a Hughes scale score of 3.

Revision

Both the vaccine against the influenza virus and the SARS-CoV2 virus have been related to the increase in GBS cases in the last decades, which has been controversial. Recently, the vaccine against the SARS-CoV2 virus was added to the vaccination schemes already implemented in the population, as well as the application of the seasonal influenza vaccine in the winter period.

Guillain-Barré syndrome (GBS) is the most common cause of acute flaccid paralysis in the world, with an incidence of 0.81 to 1.91 cases per 100,000 inhabitants.[1] In its classic form, GBS is a post-infectious autoimmune disease, in two thirds of cases symptomatic respiratory or gastrointestinal infections precede the onset of GBS symptoms; other triggering factors that have been described are vaccines.[1] The AIDP electrophysiological variant is the most frequently reported in some populations, and has been related to symptomatic infections by certain viruses, for example: cytomegalovirus, Epstein-Bar, Influenza A virus, Hepatitis B. The lack of a serological study for these viruses in our patient is a shortcoming of our report.[1]

Since 1976, an increase in cases of Guillain Barre syndrome has been reported linked to vaccination against the seasonal influenza virus, notably increasing the risk during the vaccination period of that year. During these vaccination campaigns, GBS cases peaks have been reported that reached high incidences, of 1 per 100,000 vaccinated.[8]

Figure 1. Nerve conduction recordings of motor nerves: A) left median nerve presents prolonged distal latency (arrow); B) Tibial nerve (left and right), in both nerves there is prolongation of the distal latencies (arrows).

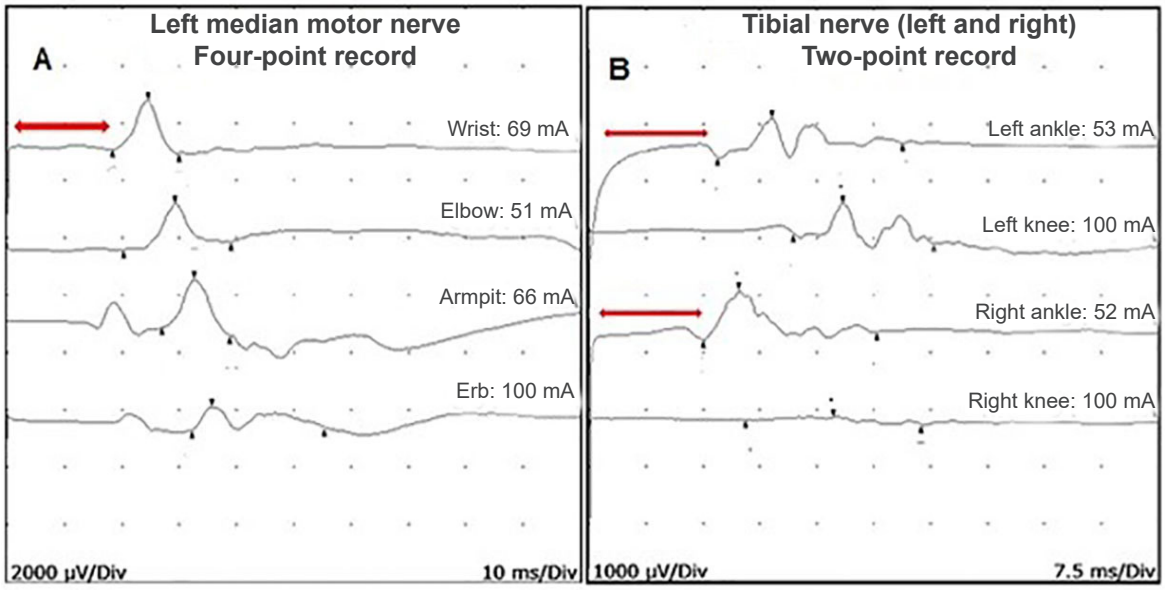

Table 1. Nerve conduction recordings of motor nerves.

	Distal latency (ms)	Conduction velocity (m/s)	Distal CMAP (mIV)
Motor nerves			
Medium	18.4	33	0.9
Ulnar	4.6	34	2.9
Tibial	15	59	0.7
Peroneal	11.1	40	0.4
Sensory nerves			PANS (µV)
Medium	NR	NR	NR
Sural	3.4	41	11.8

CMAP: compound muscle action potential; SNAP: sensory nerve action potential; NR: no record; mIV: millivolts; µV: microvolts

Due to the SARS-CoV2 virus pandemic, mass vaccination systems were established. Currently, several cases of GBS have been reported related to vaccination against SARS-CoV2, particularly with vaccines designed with adenovirus vectors,[9] consequently, the mechanisms of association have been investigated, without finding conclusive evidence.[9] During 2021, a total of 833 GBS cases were reported worldwide in patients who were vaccinated with AstraZeneca, out of a total of 592 million vaccinated.[7] In the Mexican population, a study reported 8 cases of GBS after vaccination against SARS- CoV2, 2 of which were linked to the application of the AztraZeneca vaccine.[4]

Within the different case series published on the GBS association related to vaccination against SARS-CoV2, and the seasonal influenza vaccine, it is mentioned that the majority of cases present the classic sensory-motor clinical variant of GBS and the electrophysiological variant of AIDP, as in the case of our patient.[4,10]

Despite the fact that previous studies indicate problems with the safety of the vaccines, there is still no conclusive evidence on the association between SARS-CoV2 vaccines and GBS. The risk of developing GBS after vaccination is low compared to other vaccines, such as influenza, suggesting that SARS-CoV2 vaccines are safe. On the other hand, the benefit its application outweighs the risk of contracting the infection.[5,11]

Analyzing the case of the influenza vaccine, during the swine influenza pandemic in 1976, a massive vaccination program was carried out in the United States of America, reporting an increased risk of presenting GBS after receiving the vaccine.[12] Since then, studies have been published assessing the risk of GBS after vaccination, finding an increased relative risk of up to 1.7 (95% CI, 1.0 - 2.8).[13] However, over time, it was documented that the risk of presenting GBS after influenza infection is higher compared to the application of the vaccine.[14]

According to the Brighton criteria —created by a panel of experts to classify patients with GBS into certainty levels—, our patient classified into certainty level 1. In addition, these criteria establish a time frame of 6 weeks to relate a case of GBS with a history of vaccination.[3] In the case of our patient, both vaccines were applied in a period of 22 days.

Due to the current SARS-CoV2 pandemic, mass vaccination against this virus was implemented using different types of vaccines, jointly with the reinforcement of the vaccination against the seasonal influenza virus in the winter season. These modifications in the vaccination schedules cause a modification in the population characteristics, consequently, it will be more common for monophasic autoimmune disease models such as GBS to develop in patients with a history of applying both vaccines, even with a temporal period of up to 6 weeks from the vaccine application and the onset of symptoms, without implying an association. In addition, as mentioned previously, we consider that there is a higher risk of GBS in the population not vaccinated against seasonal influenza. Regarding the SARS-CoV2 vaccine, we believe that epidemiological studies of large populations are necessary to establish a correlation with the increase of GBS cases.[14]

Conclusion

Currently, the global population is being vaccinated as a consequence of the SARS-CoV2 pandemic, in parallel, vaccination schemes against the seasonal influenza virus are being reinforced in the winter season, which causes certain population to have a particular clinical history. We report the case of a patient with AIDP variant GBS, with a history of vaccine application for the SARS-CoV2 virus and for seasonal influenza.

Conflicts of interest

The authors of this study have no conflicts of interest to disclose.

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