

Guillain–Barré syndrome associated with vaccines in Veracruz, Mexico

Dear Editor,

The main agents of Guillain–Barre syndrome (GBS) (the most common autoimmune disease of the peripheral nervous system, with an incidence of 1.1/100,000 worldwide) are infectious, predominantly *Campylobacter* and some neurotropic viruses such as dengue or Zika, which in past pandemics were one of the main agents suspected of conditioning outbreaks of the syndrome in this region of Southeastern Mexico endemic to arboviruses; however, there are other entities such as the application of vaccines that usually condition the appearance of the syndrome, with various case reports.^[1]

Within the history of vaccines, only one has shown a direct association with the development of GBS, being the swine influenza vaccine used in 1976 and 1977; other vaccines that have been associated with cases of the syndrome are tetanus toxoid and oral polio vaccine.^[2,3]

A recent meta-analysis shows a GBS rate of 2.77 cases per million people vaccinated for the influenza vaccine and 2.44 cases per million for the papillomavirus vaccine.^[4]

With the arrival of the COVID-19 pandemic and the accelerated efforts of universal vaccination, several cases

of the syndrome associated with vaccines against severe acute respiratory syndrome-coronavirus-2 have been reported, the main vaccines that have shown this incidence of cases are those of AstraZeneca, Pfizer, and Moderna, according to recent systematic reviews. However, there is evidence that vaccines with mRNA technology have a low incidence of this type of complication, which does not exceed the global incidence of the syndrome.^[5-7]

The main implicated vaccines are adenoviral vector vaccines (AstraZeneca, Janssen, and Sputnik V) according to a theory that the fact that adenoviruses can trigger stronger innate immune responses, such as interferons, compared to mRNA-based vaccines, can, in turn, stimulate a wide range of cells to increase their surface expression of Human leukocyte antigen (HLA), further setting the stage for a more rigorous immune response and leading to the onset of GBS.^[8]

A description is made of a series of cases of GBS associated with the administration of various vaccines presented in the state of Veracruz, in the Mexican southeast from 2019 to 2021.

Four cases of GBS associated with vaccines are reported, 75% are men, with an average age of 60 years; two patients

Table 1: Characteristics of the patients

	Case 1	Case 2	Case 3	Case 4
Genre/age (year old)	Female/54	Male/75	Male/70	Male/42
Origin	Veracruz	Boca del Rio	Lerdo de Tejada	Veracruz
Comorbidities	Diabetes Hypothyroidism	Cancer	Diabetes	-
Vaccine	Influenza/tetanus	COVID-Pfizer	COVID-Pfizer	COVID-Astra
Previous symptoms	Non	Gastrointestinal	Non	Gastrointestinal
Vaccine application time (weeks)	1	2	1	2
Time to diagnosis of GBS (days)	14	7	4	3
Variety of GBS	Classic	Classic	Cervico-pharyngo-brachialis	Classic
Cranial nerve involvement	Facial	No	Oculomotor and bulbar	Facial and bulbar
Neuroconduction	AMAN	AIDP	AMSAN	AIDP
Cerebrospinal fluid	-	Hyperproteinic	-	Hyperproteinic
Treatment	Intravenous immunoglobulin			
Hughes basal	4	4	4	4
Hughes end of treatment	4	3	4	4
MRC basal	4	4	4	3
MRC end of treatment	4	3	3	3
Complications	-	-	-	Pneumonia
Death	No	No	No	No

GBS: Guillain–Barré syndrome, MRC: Medical research council scale, AMAN: Acute motor axonal neuropathy, AIDP: Acute inflammatory demyelinating polyneuropathy, AMSAN: Acute motor-sensory axonal neuropathy

reported concomitant gastrointestinal symptoms; two patients had been vaccinated 2 weeks ago and two patients 1 week or less ago; one patient received two simultaneous vaccines (influenza and tetanus), two received the anti-COVID vaccine from Pfizer and one from AstraZeneca; the clinical variant of GBS was the classic one in three and one presented the cervico-pharyngo-brachial variant;

two presented concomitant sensory deficits, one ataxia, and two dysautonomias; one patient presented facial palsy, one oculomotor and bulbar palsy, and one facial and bulbar palsy; regarding the form of progression, two were classic and two were asymmetric and asynchronous; the neuroconduction velocity study reported one case of acute motor-sensory axonal neuropathy (AMSAN), one

Table 2: Neuroconduction studies performed on patients

	Patient 1		Patient 2		Patient 3		Patient 4	
	Right	Left	Right	Left	Right	Left	Right	Left
MNC								
MNC median nerve								
Distal latency (ms)	7.1	NR	3.5	3.4	4.0	3.5	11.7	8.9
Amplitude (mV)	0.52	NR	5.35	4.13	4.39	4.26	1.37	1.22
Neuroconduction velocity (m/s)	41	-	56	56	48	46	33	41
Latency maximum of F (ms)	NR	NR	28.3	28.2	34.2	31.6	NR	NR
Persistence of F (%)	-	-	31	50	81	44	-	-
MNC ulnar nerve								
Distal latency (ms)	4.4	3.9	3.4	3.1	3.6	3.2	4.8	4.7
Amplitude	0.21 uV	0.18 uV	2.18 mV	3.14 mV	5.96 mV	5.18 mV	2.02 mV	2.63 mV
Neuroconduction velocity (m/s)	48	48	54	55	45	53	42	21
Latency maximum of F (ms)	NR	NR	32.6	31.1	36.5	30.4	NR	NR
Persistence of F (%)	-	-	19	69	100	81	-	-
MNC tibial nerve								
Distal latency (ms)	5.5	7.6	4.6	4.2	3.8	4.6	6.3	8.5
Amplitude	0.09 uV	0.22 uV	2.65 mV	2.31 mV	3.38 mV	7.11 mV	0.97 mV	1.17 ms
Neuroconduction velocity (m/s)	28	-	29	36	26	32	33	34
Latency maximum of F (ms)	NR	NR	63.5	64.8	67.9	67.1	NR	NR
Persistence of F (%)	-	-	100	75	100	100	-	-
MNC peroneal nerve								
Distal latency (ms)	6.9	6.9	6.9	6.4	NR	5.2	9.4	13.1
Amplitude	0.26 uV	0.10 uV	0.76 mV	0.56 mV	NR	0.96 mV	0.66 mV	0.67 mV
Neuroconduction velocity (m/s)	-	-	40	42	NR	37	34	36
Latency maximum of F	NR	NR	-	-	-	-	NR	NR
Persistence of F	-	-	-	-	-	-	-	-
MNC facial nerve								
Latency	6.5 ms	NR	-	-	-	-	7.0	NR
Amplitude	0.24 uV	NR	-	-	-	-	0.06 mV	NR
NCV	-	-	-	-	-	-	-	-
SNC								
SNC median nerve								
Distal latency (ms)	3.4	3.4	2.5	2.5	2.7	2.6	NR	NR
Amplitude (uV)	26.0	38.59	19.02	19.50	17.3	20.10	NR	NR
Neuroconduction velocity (m/s)	41	42	56	56	52	54	-	-
SNC ulnar nerve								
Distal latency (ms)	3.0	3.4	2.8	2.7	2.9	2.4	NR	NR
Amplitude (uV)	37.86	26.84	3.92	13.97	6.39	16.15	NR	NR
Neuroconduction velocity (m/s)	47	41	50	51	48	57	-	-
SNC sural nerve								
Distal latency (ms)	3.5	3.5	NR	3.5	3.1	3.2	3.4	3.7
Amplitude (uV)	16.49	13.58	NR	6.26	1.07	1.08	4.41	4.33
Neuroconduction velocity (m/s)	43	47	-	40	44	45	65	41
Pathophysiological mechanism	Axonal degeneration and moderate evidence of demyelination (AMAN)		Demyelination superimposed on Axonal degeneration (AIDP)		Axonal degeneration but shows proximal demyelination in lower extremities (AMSAN)		Demyelination with secondary axonal degeneration (AIDP)	

MNC: Motor neuroconduction, SNC: Sensory neuroconduction, AMAN: Acute motor axonal neuropathy, AIDP: Acute inflammatory demyelinating polyneuropathy, AMSAN: acute motor-sensory axonal neuropathy, NR: Non reactive, NCV: Neuroconduction velocity

case of AMAN, and two cases of acute inflammatory demyelinating polyneuropathy (AIDP); cerebrospinal fluid analysis reported hyperproteinorrachia in two cases; all were treated with intravenous immunoglobulin; the initial Hughes scale was four in all cases and at the end of treatment only one presented Hughes 3, the rest remained at 4; one patient developed pneumonia and none died [Tables 1 and 2].

This small series of cases alludes to the increase in cases of GBS associated with vaccines coupled with the great vaccination campaign against COVID-19, being only anecdotal cases in this region of the Mexican southeast do not translate into a health alarm, highlighting that, as in other case reports, the most frequent variety was the sensory-motor (AMSAN), in the same way, it highlights that influenza and tetanus vaccine can be one of the main promoters of the appearance of this syndrome, in addition to the vaccines adenoviral for COVID-19.^[9,10]

The incidence of GBS associated with vaccines is relatively low, but it is a possibility that exists during vaccination campaigns and one must be alert to the presence of neurological symptoms for early diagnosis and timely initiation of treatment, limiting neurological sequelae of the illness.

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Conflicts of interest

There are no conflicts of interest.

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