



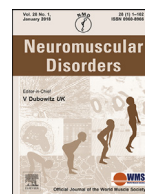
Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Elsevier hereby grants permission to make all its COVID-19-related research that is available on the COVID-19 resource centre - including this research content - immediately available in PubMed Central and other publicly funded repositories, such as the WHO COVID database with rights for unrestricted research re-use and analyses in any form or by any means with acknowledgement of the original source. These permissions are granted for free by Elsevier for as long as the COVID-19 resource centre remains active.



Contents lists available at ScienceDirect

Neuromuscular Disorders

journal homepage: www.elsevier.com/locate/nmd

Bilateral facial palsy with paresthesias, variant of Guillain-Barré syndrome following COVID-19 vaccine: A case series of 9 patients

J.I. Castiglione^{a,*}, J.M. Crespo^{a,b,c,d}, L. Lecchini^b, F.O. Silveira^c, M.B. Luis^d, N. Cotti^e, C.J. Simison^f, F. Aguirre^f, M.A. Piedrabuena^e, R.N. Alonso^d, C.L. Azcona^c, P.S. Sosa^c, E. Maldonado^b, F. Barroso^a

^a Neurology Department, Raul Carrea Institute for Neurological Research (FLENI), Montañeses 2325, Buenos Aires 1428, Argentina

^b Hospital Nacional Alejandro Posadas, Argentina

^c Hospital Italiano de Buenos Aires, Argentina

^d Sanatorio Güemes, Argentina

^e Sanatorio de los Arcos, Argentina

^f Hospital J.M. Ramos Mejía, Argentina

ARTICLE INFO

Article history:

Received 10 October 2021

Revised 24 April 2022

Accepted 9 May 2022

Keywords:

Guillain-Barré Syndrome (GBS)

Bilateral Facial Palsy (BFP)

Facial diplegia

COVID-19 vaccine

ABSTRACT

Several cases of Guillain-Barré Syndrome (GBS) associated with COVID-19 vaccination have been reported, including the rare subtype known as Bilateral Facial Palsy with paresthesias (BFP). To date, it is not known whether a causal relationship may exist between the two. We report 9 cases of BFP in patients vaccinated against COVID-19 in the previous month. Nerve conduction studies revealed demyelinating polyneuropathy in 4 patients, and 5 presented bilateral, focal facial nerve involvement, exclusively. Ganglioside antibody panel was positive in 4 patients (anti-GM1=2, anti-GD1a=1 and anti-sulfatide=1). Seven patients received intravenous immunoglobulin treatment, one plasma exchange, and one patient died from sudden cardiac arrest following arrhythmia before treatment could be administered. Rates of BFP following COVID-19 vaccination, did not differ from those reported in previous series. Epidemiological studies are essential to determine whether a causal relationship may exist between this rare form of GBS and COVID-19 vaccination.

© 2022 Elsevier B.V. All rights reserved.

1. Introduction

In the context of mass worldwide COVID-19 vaccination programs conducted to control the pandemic, several cases of Guillain-Barré Syndrome (GBS) developing within 4 weeks immunization against the virus have recently been reported [1–5]. Current evidence suggests these are overlapping, concurrent events, with no causal relationship between them [6].

We report a series of 9 cases of the GBS variant known as Bilateral Facial Palsy with Paresthesias (BFP), admitted to six different hospitals in the city of Buenos Aires, Argentina, within a six-month period (February/2021–August/2021).

1.1. Case 1

A 56-year-old woman developed bilateral facial weakness and distal paresthesia in all 4 limbs, 19 days after the first dose

of Sputnik V vaccine. Sensory examination and reflexes were normal.

1.2. Case 2

A 55-year-old male was admitted to hospital due to bilateral facial palsy and paresthesias in both hands and feet. Twenty-eight days prior to symptom onset, he had received the first dose of Sputnik V vaccine. Patient referred no pain. Reduced bicipital and patellar reflexes were observed.

1.3. Case 3

An 87-year-old man presented with bilateral facial weakness, 17 days after the first dose of Sputnik V vaccine. Patient experienced distal paresthesias in all four limbs, but denied having pain. On physical examination, lower cranial nerve involvement and deep tendon reflexes were decreased in all four limbs. Five days after admission, the patient died as a result of sudden-onset arrhythmia before any treatment was administered.

* Corresponding author.

E-mail address: jicastiglione@fleni.org.ar (J.I. Castiglione).

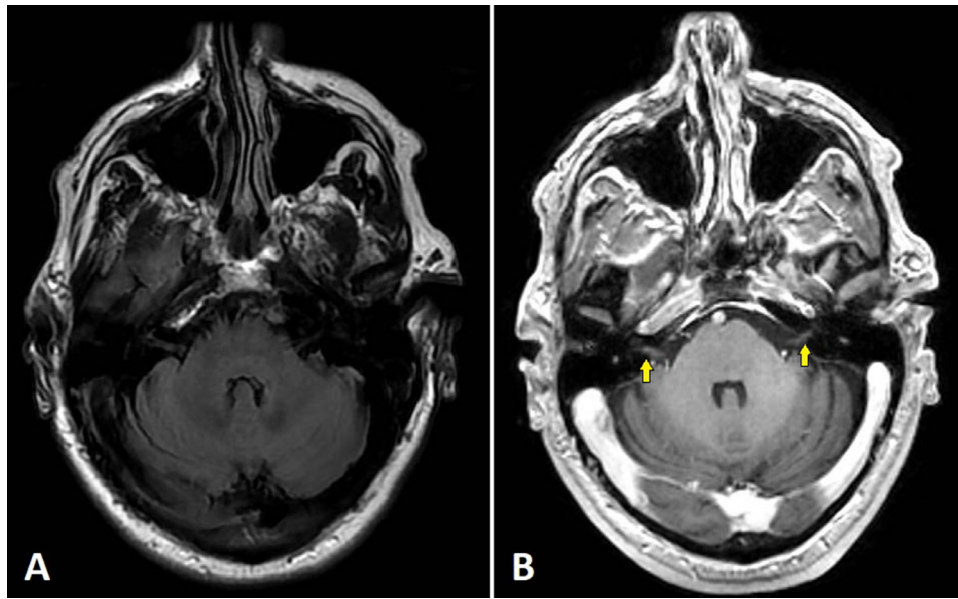


Fig. 1. (A) T2-FLAIR weighted and (B) postcontrast T1-weighted axial images of the brain. (A) Normal appearance of brain parenchyma, ventricles and subarachnoid space, on the T2-weighted image. (B) Post-contrast T1-weighted image shows smooth contrast enhancement on both facial nerves (arrows).

Table 1
Demographics, results, treatments and clinical outcomes.

Case	1	2	3	4	5	6	7	8	9
Gender	F	M	M	M	M	M	F	M	M
Age (years)	56	55	87	50	39	42	52	43	65
Covid-19 vaccine	Sputnik V	Sputnik V	Sputnik V	Astra- Zeneca	Sputnik V	Astra- Zeneca	Astra- Zeneca	Sputnik V	Astra- Zeneca
Number of doses	1st	1st	1st	1st	1st	1st	1st	2nd	2nd
Days from vaccine to GBS	19	28	17	20	10	28	13	13	13
Pain	No	No	No	Yes	No	Yes	Yes	Yes	Yes
CSF protein (mg/dl)	43	580	293	116	85	112	156	108	128
CSF white cells (mm3)	2	2	5	0	0	0	0	12	2
HIV serology	Negative	Negative	Negative	Negative	Negative	Negative	Negative	Negative	Negative
Chest X-Ray	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal
Anti-Ganglioside antibodies	Negative	Negative	GD1a positive	Negative	Sulfatide positive	-	GM1 positive	Negative	GM1 positive
Brain MRI	Normal	Normal	-	Normal	Normal	Normal	Normal	Normal	Normal*
Electrophysiological Classification	FDNF	FDNF	AIDP	AIDP	FDNF	FDNF	AIDP	AIDP	FDNF
Days from GBS to NCS	8	28	3	18	23	10	20	53	7
Treatment	IVIg	IVIg	Nil	IVIg	IVIg	IVIg	PE	IVIg	IVIg
Outcome	Clinical improvement	Clinical improvement	Sudden death	Clinical improvement	Clinical improvement	Clinical improvement	Clinical improvement	Clinical improvement	Clinical improvement

References:

GBS= Guillain-Barré syndrome; F= Female; M= Male; CSF= Cerebrospinal fluid; HIV= Human immunodeficiency virus; AIDP= Acute inflammatory demyelinating polyneuropathy; FDNF= Focal demyelination of facial nerves; NCS= Nerve conduction study; IVIg= Intravenous immunoglobulin; PE= Plasma exchange.

* Smooth contrast enhancement on both facial nerves.

1.4. Case 4

A 50-year-old male developed bilateral facial palsy 20 days following vaccination with the first dose of Covishield/AstraZeneca vaccine. He presented generalized areflexia and paresthesias, but no pain.

1.5. Case 5

A 39-year-old man presented with a 5-day history of severe bilateral facial weakness, altered taste and paresthesias in both feet. Ten days prior to symptom onset, he had received the first dose of Sputnik V vaccine.

1.6. Case 6

A 42-year-old man referred bilateral facial weakness, paresthesias and radicular pain, 28 days after vaccination with the first dose of Covishield/AstraZeneca vaccine. Physical examination showed generalized hyporeflexia.

1.7. Case 7

A 52-year-old female came to the emergency department with bilateral facial palsy 13 days after the first dose of Covishield/AstraZeneca vaccine. At initial evaluation, hypoesthesia and absent deep tendon reflexes were observed. Paresthesias were present in all four limbs.

1.8. Case 8

A 43-year-old male experienced bilateral facial weakness 13 days following vaccination with the second dose of Sputnik V vaccine. Lower cranial nerve involvement was confirmed. Patient referred radicular pain and paresthesias. Deep tendon reflexes were depressed.

1.9. Case 9

A 65-year-old man presented with a 2-week history of severe cramping pain in his legs starting one week after receiving the Covishield /AstraZeneca vaccine. Three days later, patient developed numbness in his feet and hands, spreading proximally to the ankles. One week prior to admission, he had developed progressive right facial weakness, which evolved to become severe and bilateral after 5 days. On examination, bilateral facial weakness was confirmed, the rest of the neurological exam was normal.

2. Discussion

We present 9 cases of bilateral facial palsy with paresthesias in all four limbs, 5 of which referred pain during the acute phase. Routine laboratory and HIV tests as well as chest X-rays were obtained in all cases. No evidence of underlying systemic disease was found. Lumbar puncture performed to rule out infection showed albuminocytological dissociation (ACD) was present in 7. Brain magnetic resonance imaging (MRI) available in eight patients, showed smooth contrast enhancement of both facial nerves in one case, with no other signs of brain injury (Fig. 1).

Sensory and motor nerve conduction studies performed on all patients, using a standard method investigating both facial nerves and all four limbs [7] showed two different patterns on nerve conduction studies (NCS). One group of patients ($n = 4$) presented demyelinating polyneuropathy, and the other ($n = 5$) showed focal amplitude involvement and distal latencies along both facial nerves. No abnormalities were detected in peripheral nerves, nor were significant differences observed between groups with respect to clinical presentation or delay to NCS.

Ganglioside antibody panel was positive in 4 patients (two anti-GM1, two anti-GD1a and one anti-sulfatide antibody, respectively). Seven patients received intravenous immunoglobulin, and in one patient plasma exchange was performed. Clinical improvement was observed in all cases, with the exception of case number 3, who died following sudden onset of arrhythmia and cardiac arrest, before treatment could be administered. Test results, treatments and outcomes are summarized in Table 1.

Increasing numbers of BFP cases have been identified in the last 6 months. This appears to be in contrast with levels in previously published GBS series, in which the BFP subtype usually corresponds to less than 5% of the total [8].

One possible explanation for this discrepancy may be increased patient monitoring and therefore greater GBS detection, in the context of the current COVID-19 pandemic. Social distancing could

also play a significant role in decreasing circulation of other classic infectious agents triggering GBS. One recent series described 5 cases of BFP, 7–12 days after administration of the AstraZeneca vaccine [ChAdOx1-S] [9].

In our series, BFP was diagnosed in 9 cases after vaccination against COVID-19 (Sputnik V = 5 and AstraZeneca = 4). Clinical presentation was similar to previously published findings. Further surveillance and epidemiological studies will be necessary to better establish vaccine safety, and rule out a possible causal relationship between vaccination and this rare form of GBS.

Ethical publication statement

Authors confirm having read the Journal's position on issues involved in ethical publication and affirm this report is consistent with those guidelines.

Funding information

No targeted funding reported.

Declaration of Competing Interest

The authors declare no conflicts of interest.

Acknowledgment

Teaching and Research Committee, Raúl Carrea Institute for Neurological Research (FLENI).

References

- [1] Waheed S, Bayas A, Hindi F, Rizvi Z, Espinosa PS. Neurological complications of COVID-19: Guillain-Barre syndrome following Pfizer COVID-19 vaccine. *Cureus* 2021;13(2):e13426 Feb 18.
- [2] Patel SU, Khurram R, Lakhani A, Quirk B. Guillain-Barre syndrome following the first dose of the chimpanzee adenovirus-vectored COVID-19 vaccine, ChAdOx1. *BMJ Case Rep* 2021;14(4):e242956 Apr 22.
- [3] Goss AL, Samudralwar RD, Das RR, Nath A. ANA investigates: neurological complications of COVID-19 vaccines. *Ann Neurol* 2021;89(5):856–7 May.
- [4] Rossetti A, Gheihman G, O'Hare M, Kosowsky JM. Guillain-Barré syndrome presenting as facial diplegia after COVID-19 vaccination: a case report. *J Emerg Med* 2021;61(6):e141–5 Epub 2021 Aug 7. PMID: 34538679; PMCID: PMC8346349. doi:10.1016/j.jemermed.2021.07.062.
- [5] Introna A, Caputo F, Santoro C, Guerra T, Ucci M, Mezzapesa DM, Trojano M. Guillain-Barré syndrome after AstraZeneca COVID-19-vaccination: a causal or casual association? *Clin Neurol Neurosurg* 2021;208:106887 Sep.
- [6] Lunn MP, Cornblath DR, Jacobs BC, Querol L, van Doorn PA, Hughes RA, Willison HJ. COVID-19 vaccine and Guillain-Barré syndrome: let's not leap to associations. *Brain* 2021;144(2):357–60 Mar 3.
- [7] Kimura J. *Electrodiagnosis in diseases of nerve and muscle: Principles and practice*. 4th ed. Oxford University Press; 2001.
- [8] Jacobs BC, van den Berg B, Verboon C, Chavada G, Cornblath DR, Gorson KC, Harbo T, Hartung HP, Hughes RAC, Kusunoki S, van Doorn PA, Willison HJ, G.O.S. Consortium. International Guillain-Barré syndrome outcome study: protocol of a prospective observational cohort study on clinical and biological predictors of disease course and outcome in Guillain-Barré syndrome. *J Peripher Nerv Syst* 2017;22(2):68–76 Jun.
- [9] Bonifacio GB, Patel D, Cook S, Purcaru E, Couzins M, Domjan J, et al. Bilateral facial weakness with paraesthesia variant of Guillain-Barré syndrome following Vaxzevria COVID-19 vaccine. *J Neurol Neurosurg Psychiatry* 2022;93(3):341–2 Epub 2021 Jul 14. PMID: 34261746. doi:10.1136/jnnp-2021-327027.