CLINICAL CASES received 8 December 2020 | accepted 26 January 2021 | published 5 March 2021

Doi: https://doi.org/10.31157/archneurosciencesmex.v26i01.258

Guillain-Barré syndrome associated with SARS-CoV-2 infection: A case report in Mexico

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Abstract

In December 2019, the first cases of COVID-19 were reported in Wuhan, China. Up to now, it has affected over 60 million people worldwide. COVID-19 is a multi-systemic disease; in addition to respiratory manifestations, various neurological complications have been identified, including encephalitis, stroke, and Guillain-Barré syndrome. Guillain-Barré syndrome is a condition of immune-mediated polyneuropathies frequently associated with infections. We present the case of a 41-year-old man that, after a 5-day history of non-productive cough, headache, muscle pain, joint pain, anosmia, ageusia, and non-quantified temperature rise; developed loss of tendon flexes and lower limbs weakness that progressed to walking disability, upper limbs weakness, and bilateral facial paresis. An oropharyngeal swab polymerase chain reaction confirmed SARS-CoV-2 infection, and the cerebrospinal analysis reported albuminocytologic dissociation. Nerve conduction studies showed acute inflammatory demyelinating polyradiculoneuropathy (AIDP). He received a 5-day course of intravenous immune globulin. There have been numerous reports of Guillain-Barré syndrome associated with SARS-CoV-2 infection worldwide; however, few cases have been reported in Latin America.

Keywords: *covid-19, sars-cov-2, guillain-barré syndrome*

Introduction

Guillain-Barré syndrome is a polyradiculoneuropathy of acute or subacute onset. It is characterized by ascending muscle weakness, areflexia or hyporeflexia in the affected limbs, paresthesias in hands and feet, pain, dysautonomia, and facial nerve paralysis.[1] Between 10-30% of cases present severe respiratory muscle involvement requiring invasive mechanical ventilation.[2] Several variants of the disease have been described, the most common being acute inflammatory demyelinating neuropathy, Miller-Fischer syndrome, and acute axonal motor neuropathy.

It has been proposed that the antecedent of infection induces an immune response, originating a cross-reactivity with the components of the peripheral nerves due to the presence of shared epitopes (molecular mimicry). The immune response is aimed directly at myelin (in the demyelinating form) or the axon of the peripheral nerves (in the axonal forms)[1].

Campylobacter jejuni infection has been most frequently associated with Guillain-Barré syndrome. Other viruses that have been identified are cytomegalovirus, Epstein-Barr virus, influenza A, Haemophilus influenzae, enteroviruses, human immunodeficiency virus, Zika virus, and more recently, SARS-CoV-2 virus.[3,4]

SARS-CoV-2 is a coronavirus family virus characterized by respiratory manifestations as the most recognizable symptoms. Some studies also report gastrointestinal, cardiac, renal, and neurological complications. Different neurological manifestations and complications specifically associated with SARS-CoV-2 have been reported, including anosmia, ageusia, ischemic cerebrovascular events, encephalitis, and Guillain-Barre syndrome.[5]

Presentation of the clinical history

A 41-year-old man with a history of grade I obesity and an old lacunar cerebral vascular event without sequelae or clinical repercussions. He came to the emergency department for a four-day evolution characterized by a progressive and ascending decrease in strength in the lower limbs; two days later he presented with an inability to ambulate and upper limb weakness of distal predominance and the same day of his admission, right facial paralysis was added, for which he requested hospital care.

The patient reported that five days before the onset of neurological symptoms he had a non-productive cough, headache, myalgia, anosmia, ageusia, and fever; he was managed on an outpatient basis with paracetamol with partial improvement of these symptoms.

On physical examination, the patient was conscious, oriented, and without dyspnea, with a heart rate of 103 beats per minute, respiratory rate of 22 breaths per minute, blood pressure of 150/90 mmHg, temperature of 36°C, oxygen saturation of 92% on room air. Right facial nerve palsy, both hemithoraxes with basal predominance cramp, decreased strength on Medical Research Council (MRC) scale in the upper extremities 4/5 in proximal and 3/5 in distal musculature, while in the lower extremities, proximal 3/5 and distal 2/5 muscle strength and generalized areflexia were found. Babinski negative bilaterally. No alterations in superficial or deep sensitivity and no signs of meningeal irritation were found.

During his stay, he was treated with human immunoglobulin at a dose of 0.4g/kg/day for five days. Due to the pulmonary pathology related to COVID-19, he received supplemental oxygen through nasal prongs at 5 liters per minute and dexamethasone 6mg/24h for ten days, in addition to nifedipine 30mg every 12 hours, enalapril 5mg every 12 hours and telmisartan 80mg every 24 hours, due to systemic arterial hypertension as part of dysautonomia secondary to Guillain Barré syndrome. The patient's clinical evolution within ten days of in-hospital follow-up progressed to greater muscle weakness in lower extremities MRC scale 1/5 distal and 2/5 proximal; no changes in upper extremity muscle strength reported on admission and bilateral facial paralysis that conditioned dysarthria.

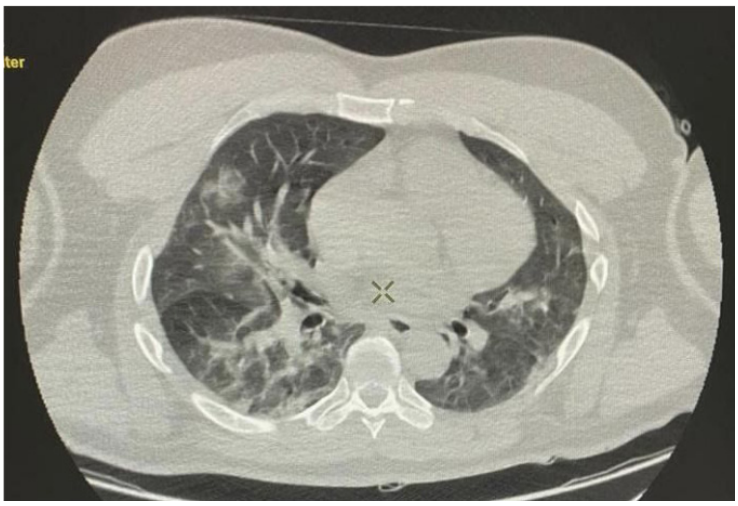
He was discharged 12 days after admission with a home rehabilitation program and at a two-month follow-up, he returned to ambulation; however, he was still unable to return to his usual activities.

Imaging and laboratory studies.

Oropharyngeal polymerase chain reaction (PCR): SARS-CoV-2 Positive.
Cerebrospinal fluid analysis 9 days after symptom onset: clear; protein 1174.0 mg/l; leukocytes 0.0 cells; Wright's, BAAR, GRAM, and India ink stain negative.
Hemoglobin 15.10 g/dL; white blood cell count 8.90 cells per microliter (neutrophils 5.40, lymphocytes 12.57); glucose 110.1 mg/dL; urea 13.7 mg/dL; creatinine 0.65 mg/dL; alanine aminotransferase 82 IU/L; aspartate aminotransferase 82 IU/L; sodium 133 mmol/L; potassium 3.9 mmol/L; chlorine 97 mmol/L; erythrocyte sedimentation rate.
30 mm/hour, C-reactive protein 3.6 mg/dL; Lactate

dehydrogenase 413 U/L; Ferritin 885.00 ng/mL. Simple cranial tomography: Hypodense rounded image in left temporal lobe of 6 x 6 mm, corresponding to old lacunar infarction. Plain chest CT scan: Increased attenuation in both lungs with mixed pattern in ground glass and areas of consolidation of patchy distribution. Findings compatible with COVID-19 pneumonia with moderate degree of involvement.

Figure 1. Chest computed tomography.



Neuroconduction study: Compatible with AIDP variant

Table 1. Neuroconduction study. Sensitive branches.

Site	NR	Peak (ms)	P-T Amp (μV)	Site1	Site 2	Dist (cm)	Vel (m/s)
Right median nerve (2nd finger)							
Wrist	NR	NR	NR	Wrist	2nd finger	14.0	
Elbow	NR	NR	NR	Elbow	Wrist	26.0	
Right radial nerve (1st finger posterior aspect)							
Wrist		2.5	19	Wrist	1st finger	10.0	40.0
Right ulnar nerve (5th finger)							
Wrist	NR	NR	NR	Wrist	5th. finger	14.0	
Elbow	NR	NR	NR	Elbow	Wrist	24.0	
Left median nerve (2nd finger)							
Wrist	NR	NR	NR	Wrist	2nd. finger	14.0	
Elbow	NR	NR	NR	Elbow	Wrist	26.0	
Left radial nerve (1st finger, posterior aspect)							
Wrist		2.5	18	Wrist	1st. figer	10.0	40.0
Left ulnar nerve (5th toe)							
Wrist	NR	NR	NR	Wrist	5th. finger	14.0	
Elbow	NR	NR	NR	Elbow	Wrist	24.0	
Right superficial peroneal nerve (lateral malleolus anterior face)							
14 cm	NR	NR	NR	14 cm	Lat mal ant	14.0	
Right sural nerve (lateral malleolus)							
Leg		5.1	8	Leg	Lat mal	14.0	36.0
Left superficial peroneal nerve (lateral malleolus, anterior aspect)							
14 cm	NR	NR		14 cm	Lat mal ant	14.0	
Left sural nerve (lateral malleolus)							
Leg		4.9	12	Leg	Lat mal	14.0	38.0

Table 2. Neuroconduction study. Motor branches.

Site	Start (ms)	O - P	Site 1	Site 2	Dist (cm)	Vel (m/s)
Right median nerve (abductor pollicis brevis of the thumb)						
Wrist	8.5	7.3	Elbow	Wrist	22	41
Elbow	13.9	7.0	Axilla	Codo	17	44
Axilla	17.8	6.4				
Right radial nerve (Extensor of the index finger)						
8 cm	4.0	3.8	Arm	8 cm	18.0	35
Arm	9.1	4.3	Axilla	Arm	19.0	633
Axilla	8.8	3.0				
Right ulnar nerve (abductor of the little finger)						
Wrist	6.3	5.8	Post Elbow	Wrist	22.0	37
Post Elbow	12.2	5.0	Ant Elbow	Post Elbow	5.0	9
Ant Elbow	17.8	3.8	Axilla	Ant Elbow	16.0	43
Axilla	21.5	3.3				
Left median nerve (Abductor pollicis brevis of the thumb)						
Wrist	8.0	10.3	Elbow	Wrist	22	45
Elbow	12.9	10.0	Axilla	Elbow	19	39
Axilla	17.8	10.0				
Left radial nerve (Extensor of the index finger)						
8 cm	3.1	5.7	Arm	8 cm	18.0	41
Arm	7.5	4.2	Axilla	Arm	19.0	380
Axilla	8.0	6.4				
Left ulnar nerve (Little finger abductor)						
Wrist	5.1	7.1	Post Elbow	Wrist	22.5	36
Post Elbow	11.3	5.3	Ant Elbow	Post Elbow	5.0	14
Ant Elbow	15.0	5.2	Axilla	Ant Elbow	17.0	61
Axilla	17.8	4.3				
Right peroneal nerve (extensor digitorum brevis)						
Ankle	8.3	1.5	Ankle	Ankle	30.0	37
Post Fibula	16.4	1.2	Post Fibula	Post Fibula	9.5	30
Popliteal fossa	19.6	1.1				
Right tibial nerve (Abductor of the thumb)						
Ankle	8.2	3.2	Rodilla	Ankle	41	28
Knee	22.9	1.9				
Left peroneal nerve (Extensor digitorum brevis)						
Ankle	8.8	2.1	Ankle	Ankle	31.0	40
Post Fibula	16.6	1.4	Post Fibula	Post Fibula	9.0	31
Popliteal fossa	19.5	1.3				
Left tibial nerve (Abductor of the thumb)						
Ankle	10.5	2.3	Knee	Ankle	42.0	34
Knee	22.7	1.4				

Table 3. Neuroconduction study. F-wave study.

NR	F-Lat (ms)	M-Lat (ms)	FLat-MLat (ms)
Right median nerve (Mrkrs) (Abductor pollicis brevis of the thumb)			
	4.3	8.2	35.6
Right ulnar nerve (Mrkrs) (Little finger abductor)			
	52.9	6.1	46.8
Left median nerve (Mrkrs)(Abductor pollicis brevis of the thumb)			
	42.3	7.8	34.5
Left ulnar nerve (Mrkrs) (Little finger abductor)			
	50.2	6.2	32.4
Right peroneal nerve (Mrkrs) (extensor digitorum brevis)			
	73.4	7.0	66.4
Right tibial nerve (Mrkrs) (Thumb abductor)			
	85.1	7.8	77.3
Left peroneal nerve (Mrkrs) (short extensor of the fingers)			
	73.6	7.1	66.5
Left tibial nerve (Mrkrs) (Abductor of the thumb)			
	83.2	10.4	72.8

Discussion

It has been described that a probable association of Guillain-Barré syndrome with SARS-CoV-2 infection requires the onset of neurological disease within 6 weeks of acute infection; SARS-CoV-2 RNA detected in any specimen or antibody evidence of acute SARS-CoV-2 infection; and absence of evidence of other commonly associated causes.[6] Based on the National Institute of Neurological Disorders and Stroke (NINDS) criteria and the Brighton criteria for the diagnosis of Guillain-Barré syndrome; our patient was diagnosed by presenting with classic neurologic symptoms five days after the onset of respiratory symptoms, albuminocytologic dissociation, and findings on neuroconduction studies compatible with the AIDP variant; likewise, there was no progression after eight weeks from the onset of clinical Guillain Barré syndrome, which ruled out the diagnosis of chronic inflammatory demyelinating polyneuropathy. Additionally, SARS-CoV-2 infection was confirmed by oropharyngeal PCR.

The onset of symptoms associated with Guillain-Barre syndrome five days after the onset of respiratory symptoms associated with SARS-CoV-2 suggests the possibility of a parainfectious presentation, as opposed to a postinfectious presentation where there is a longer period between the clinical presentation and the triggering event. The parainfectious course has been described in Guillain-Barré syndrome associated with Zika virus and also in some cases associated with SARS-CoV-2.[7,8]

The exact pathophysiology by which the SARS-CoV-2 virus triggers Guillain-Barré syndrome is unknown. The SARS-CoV-2 virus binds to respiratory epithelial cells through the spike (S) protein which binds to angiotensin-converting enzyme receptor 2 found in vascular endothelium, brain, and smooth muscle; it also binds to glycoproteins and gangliosides which may act as antigens in patients with neuropathies. Because the spike protein of SARS-CoV-2 interacts with the GaiNAc residue of GM1 and ganglioside dimers, there is the possibility of cross-reactivity between the ganglioside epitopes to which SARS-CoV-2 binds and the surface glycolipids of peripheral nerves.[4]

Regarding the variant of Guillain Barré syndrome, according to the electrodiagnostic study, based on Uncini's criteria, it is classified as acute inflammatory demyelinating demyelinating polyneuropathy (AIDP). This variant was the most commonly reported (81.3%) in the 73 clinical cases of SARS-CoV-2-associated Guillain-Barré syndrome analyzed by Abu-Rumeileh et al. in agreement with previous reports in Europe and the United States.[7] However, some authors agree that the pathophysiology of Guillain-Barré syndrome is dynamic and that serial studies allow a more accurate diagnosis of the subtypes.[9]

Finally, the patient returned to ambulation two months after the onset of Guillain-Barré syndrome. It has been reported that 20% of patients with Guillain-Barré syndrome can walk

without assistance at four weeks, and 80% and 84% can walk independently at six and twelve months, respectively.[10]

Conclusion

Currently, numerous cases of patients with Guillain-Barré syndrome associated with SARS-CoV-2 have been reported,[7,8] and this would be one of the first reported in Mexico. It is important to be aware of the suspicion of SARS-CoV-2 infection in patients presenting clinical data of Guillain-Barré syndrome to perform confirmatory tests to carry out isolation and timely management measures to avoid progression and complications associated with both diseases. Neurological complications associated with the SARS-CoV-2 virus can cause lifelong disability, so long-term follow-up of these patients is required to determine whether their evolution is different from cases of Guillain-Barré associated with other etiologies.[11]

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Article with no conflict of interest