

CASE REPORT

Guillain–Barré Syndrome Associated with SARS-CoV-2 Infection in a Pediatric Patient

Carlos Henrique Michiles Frank, MAst,¹
Taynná Vernalha Rocha Almeida, PhD,² Elyana Almeida Marques, MD,³
Quezia de Sousa Monteiro, MD,⁴ Pablo Vinícius Silveira Feitoza, MSc,^{5,6}
Mayla Gabriela Silva Borba, MD,^{4,7} Heline Lira Vasconcelos, BPharm,¹
Michele de Souza Bastos, PhD,^{1,2} and
Marcus Vinicius Guimarães Lacerda, PhD⁸

¹Fundação de Medicina Tropical Dr. Heitor Vieira Dourado, Manaus, AM, 69040-000 Brazil

²Programa de Pós-graduação em Ciências da Saúde, Faculdade de Medicina, Universidade Federal do Amazonas, Manaus, AM, 69080-900 Brazil

³Fundação Alfredo da Mata, Manaus, AM, 69065-130 Brazil

⁴Hospital e Pronto Socorro Delphina Rinaldi Abdel Aziz, Manaus, AM, 69093-415 Brazil

⁵Departamento de Clínica Cirúrgica, Faculdade de Medicina, Universidade Federal do Amazonas, AM, 69080-900 Brazil

⁶Programa de Pós-Graduação em Medicina (Neurologia), Faculdade de Medicina de Ribeirão Preto, Universidade de São Paulo, Ribeirão Preto, SP, 14049-900 Brazil

⁷Universidade do Estado do Amazonas, Manaus, AM, 69055-010 Brazil

⁸Instituto Leonidas and Maria Deane, Fiocruz Amazonas, Manaus, AM, 69057-070 Brazil

Correspondence: Carlos Henrique Michiles Frank, FMT-HVD—Av. Pedro Teixeira—Dom Pedro, Manaus, Amazonas 69040-000, Brazil.
Tel: 55-92-9847-10667. E-mail <cahefrank@gmail.com>.

ABSTRACT

We report the case of a 15-year-old male patient presenting frontal headaches with retro-orbital pain accompanied by fever evolving to weakness and pain of the lower limbs, which ascended to upper limbs. A COVID-19 rapid test (IgG and IgM) and nasopharyngeal swab polymerase chain reaction (PCR) was positive for SARS-CoV-2. The blood tests, cerebral spinal fluid (CSF) analysis and CSF aerobic culture revealed no abnormalities. PCR testing of the CSF was negative for the most prevalent etiologies as well as for SARS-CoV-2. Electroneurography study was compatible with the acute motor axonal neuropathy variant of Guillain–Barré syndrome. No cases involving young patients have been presented to date. Therefore, this is the first reported pediatric case of SARS-CoV-2 infection associated with GBS. Evidence reveals that SARS-CoV-2 infection is not limited to the respiratory tract. Neurotropism could explain this important neurologic manifestation of COVID-19 in children.

LAY SUMMARY

We report the case of a 15-year-old male patient presenting frontal headaches with retro-orbital pain accompanied by fever evolving to weakness and pain of the lower limbs, which ascended to upper limbs. A COVID-19 rapid test and nasopharyngeal molecular test were positive for the SARS-CoV-2 virus. Neurological examination attested Guillain–Barré syndrome, a condition in which the immune system attacks the nerves and could be triggered by a bacterial or viral infection. The blood tests were normal and cerebral spinal fluid analysis was negative for the most common viruses related to GBS as well as for SARS-CoV-2. Although described in adults, no cases involving young patients have been presented to date. Therefore, this is the first reported case of GBS associated with SARS-CoV-2 in children.

KEYWORDS: neuromuscular diseases, Guillain–Barré syndrome, adolescent, pediatrics, SARS-CoV-2

INTRODUCTION

Healthcare systems worldwide are currently confronting the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and its associated disease COVID-19, which has been classified as Public Health Emergency of International Importance and, subsequently, as a pandemic by the World Health Organization. The virus infects human respiratory epithelial cells of the lungs through an interaction between the viral plasma glycoprotein (protein S) and the angiotensin-2-converting enzyme (ACE2) receptor present on the host cell [1]. ACE2 is widely expressed in several organ systems, including the cardiovascular, renal, pulmonary and cerebral systems. SARS-CoV-2 infects the central nervous system and is suspected of potentially developing into Guillain–Barré syndrome (GBS) [2]. The diagnosis of GBS remains based on clinical characteristics and ancillary laboratory investigations. The classic clinical manifestations of GBS are acute polyradiculoneuropathy with numbness, paresthesia, weakness, pain in the limbs or a combination of several of these symptoms [3]. Here, we report a pediatric case involving a progressive acute symmetrical paralysis of the lower and upper limbs, with an upward evolution, which was possibly related to SARS-CoV-2 infection.

CASE REPORT

In late April 2020, a 15-year-old boy experienced frontal headaches with retro-orbital pain accompanied by fever and intense sweating. By 5th May, the adolescent reported emetic episodes, weakness and

pain in the lower limbs, which ascended to his upper limbs. On 8th May, with no history of previous surgeries or hospitalizations, and no recent vaccinations reported, he was admitted to a local pediatric hospital. A COVID-19 rapid test (One Step COVID-19 TEST) was performed and showed a positive result for IgG and IgM. The initial blood tests and cerebral spinal fluid (CSF) analysis (cytometry, biochemistry) and CSF aerobic culture performed on admission revealed no abnormalities. The patient was initially treated with methylprednisolone, azithromycin, albendazole and, 3 days later, was transferred to the reference hospital COVID in the Amazon State, Brazil. On admission to our hospital, the adolescent was in good general condition with no respiratory symptoms. The neurologic examination revealed normal consciousness and speech, normal cranial nerve function, progressive symmetrical limb weakness (Medical Research Council score 3/5 for the upper limbs and 2/5 for the lower limbs), absent deep tendon reflexes, normal plantar response and no sensory loss.

Nasopharyngeal swabs analysed using polymerase chain reaction (PCR) tested negative for influenza and positive for SARS-CoV-2. Another cytometric and biochemical CSF analysis, approximately 2 weeks following the initial unspecific symptoms, presented results inside the normal parameters. PCR testing of the CSF (CDC Protocol [4]) was negative for the most prevalent etiologies (including Herpesvirus HSV1, HSV2, CMV, EBV, VZV; Zika virus; Dengue virus and Chikungunya virus), as well as for SARS-CoV-2. The chest tomography and the

TABLE 1. Motor nerve conduction studies

	Segment	Distal latency (ms)	Amplitude (mV)	NCV (m/s)	F latency (ms)
Left median nerve	Wrist	2.9 (normal ≤ 3.8)	0.45 (normal ≥ 4)	—	Absent (normal ≤ 30)
	Wrist–elbow	7.8	0.39	51.0 (normal ≥ 50)	
	Elbow–axilla	9.4	0.34	54.5	
Right median nerve	Wrist	2.8 (normal ≤ 3.8)	0.30 (normal ≥ 4)	—	Absent (normal ≤ 30)
	Wrist–elbow	7.6	0.28	52.6 (normal ≥ 50)	
	Elbow–axilla	9.2	0.25	54.5	
Left ulnar nerve	Wrist	3.8 (normal ≤ 3.8)	0.11 (normal ≥ 4)	—	Absent (normal ≤ 31)
	Wrist–below elbow	7.7	0.05	56.4 (normal ≥ 50)	
	Wrist	3.4 (normal ≤ 3.8)	0.43 (normal ≥ 4)	—	Absent (normal ≤ 31)
Right ulnar nerve	Wrist–below elbow	7.9	0.41	51.7 (normal ≥ 50)	
	Below elbow–above elbow	9.8	0.38	51.3	
	Above elbow–axilla	10.9	0.37	54.5	
Left peroneal nerve	Ankle	7.3 (normal ≤ 5.6)	0.15 (normal ≥ 2.8)	54.5 (normal ≥ 40)	Absent (normal ≤ 56)
	Ankle	4.6 (normal ≤ 5.6)	0.27 (normal ≥ 2.8)	—	Absent (normal ≤ 56)
Right peroneal nerve	Ankle–head of fibula	13.2	0.21	37 (normal ≥ 40)	
	Head of fibula–popliteal	15.4	0.17	37.2	
	Ankle	4.8 (normal ≤ 5.6)	0.31 (normal ≥ 3.6)	—	Absent (normal ≤ 56)
Left tibial nerve	Ankle–popliteal	17.4	0.23	34 (normal ≥ 40)	
	Ankle	5.3 (normal ≤ 5.6)	0.19 (normal ≥ 3.6)	—	Absent (normal ≤ 56)
	Ankle–popliteal	16.8	0.18	37.6 (normal ≥ 40)	

NCV, nerve conduction velocity.

Table 2. Sensitive nerve conduction studies

	Segment	Latency 1 (ms)	Amplitude (μ V)	NCV (m/s)
Left median nerve	Wrist–finger	2.5 (normal \leq 2.5)	37 (normal \geq 20)	55.1 (normal \geq 50)
Right median nerve	Wrist–finger	2.4 (normal \leq 2.5)	35 (normal \geq 20)	57.7 (normal \geq 50)
Left ulnar nerve	Wrist–finger	2.5 (normal \leq 2.5)	38 (normal \geq 20)	51.6 (normal \geq 50)
Right median nerve	Wrist–finger	2.1 (normal \leq 2.5)	30 (normal \geq 20)	57.7 (normal \geq 50)
Left radial nerve	Forearm	2.0 (normal \leq 2.1)	22 (normal \geq 14)	60 (normal \geq 50)
Right radial nerve	Forearm	2.0 (normal \leq 2.1)	24 (normal \geq 14)	56.1 (normal \geq 50)
Left sural nerve	Leg	2.2 (normal \leq 2.6)	14 (normal \geq 6)	49.1 (normal \geq 40)
Right sural nerve	Leg	2.4 (normal \leq 2.6)	18 (normal \geq 6)	45.1 (normal \geq 40)
Left superficial peroneal nerve	Leg	2.8 (normal \leq 2.8)	18 (normal \geq 5.6)	42.3 (normal \geq 40)
Right superficial peroneal nerve	Leg	2.6 (normal \leq 2.8)	17 (normal \geq 5.6)	46.9 (normal \geq 40)

NCV, nerve conduction velocity.

cranial, thoracic and lumbar spine magnetic resonance imaging (MRI) revealed no abnormalities. Blood tests, including blood count, serum glucose, C-reactive protein, electrolytes, kidney function and liver enzymes were within normal range (see [Supplementary Appendix](#)). The serology for hepatitis B and C, human immunodeficiency virus and Venereal Disease Research Laboratory tests were negative. Electroneurography revealed normal sensory nerve action potential, though severe reduction of the nerve compound muscle action potential amplitude in all motor nerves studied, with relatively preserved conduction velocities. F waves were absent in the studied nerves. These abnormalities are therefore compatible with the acute motor axonal neuropathy (AMAN) variant of GBS. See [Tables 1](#) and [2](#) for a summary of the results of the nerve conduction studies ([Supplementary Appendix](#)).

Given the patient's clinical history of a rapidly progressive symmetrical weakness with supporting electroneurography findings, a recent SARS-CoV-2 infection confirmed through the PCR test, negative microbiologic results for other etiologies in CSF and normal MRI, a diagnosis of GBS associated with COVID-19 was made. On 15th May, the patient was started on 400 mg/kg/day of intravenous immune globulin (IVIG) therapy for a planned 5 days course. Despite some improvement after IVIG therapy, weakness in the upper and lower extremities

persisted, however, and he is currently undergoing motor physiotherapy.

DISCUSSION

According to the most recently published systematic review on neurological manifestations in patients with COVID-19, studies have shown data ranging from common, non-specific symptoms to more complex and life-threatening conditions, such as cerebrovascular diseases, encephalopathies and GBS [5]. Nineteen reports demonstrated variant forms of GBS associated with SARS-CoV-2 and one of them presenting five cases from Italy ([Supplementary Appendix](#)). No cases involving younger patients have been presented to date. Therefore, this is the first reported pediatric case of SARS-CoV-2 infection associated with GBS.

In general, diagnosis of GBS is based on the patient history, electrophysiological and CSF analysis. Electrophysiological studies can distinguish among the subtypes of GBS, to determine AMAN, acute inflammatory demyelinating polyradiculoneuropathy and acute motor sensory axonal neuropathy [3]. The first published study of neurological symptoms associated with COVID-19 were reported by Mao *et al.* [2], who presented 78 of 214 cases from hospitalized patients with confirmed SARS-CoV-2 infection. The most evident neurological manifestations were acute

cerebrovascular diseases (5.7%), decreased level of consciousness (14.8%) and skeletal muscle injury (19.3%). These findings demonstrate that neurological deficits may be in progress without being noticed.

Until now, few studies reported pediatric neurological symptoms of COVID-19. Thus, the present case highlights the possibility of a rare but important neurologic manifestation of COVID-19 in children. Dugue *et al.* [6] reports a 6-week-old male infant presenting fever, cough and two brief 10–15 s episodes of upward gaze and bilateral leg stiffening. In a North American case, an 11-year-old child manifested status epilepticus which required four anticonvulsant medications. The CSF examination suggested viral encephalitis as the cause [7]. Regarding the other types of coronavirus, a 5-year-old boy had progressive lower extremity weakness and pain 3 days prior to onset of unilateral peripheral facial palsy, during a Middle East respiratory syndrome (MERS) coronavirus in 2015 [8]. In fact, it is well known that GBS and related syndromes are associated with emerging infections including arboviruses, such as Zika.

As expected for the age, our patient presented with mild symptoms, which were restricted to headache and fever, with no respiratory symptoms and normal chest CT imaging. Apparently, the severity of COVID-19 in children may have no direct relationship with the incidence of neurological manifestations, such as GBS. Despite being more prevalent in pediatric groups, the variant AMAN, which may evolve to respiratory failure, has not been observed in our patient so far. The Erasmus GBS Respiratory Insufficiency Score (EGRIS) indicates a moderate risk (EGRIS 4–35%) of mechanical intervention. *Campylobacter jejuni* enteritis has a prominent role in the pathogenesis of AMAN. The cross-reaction between the *C. jejuni* antibodies and myelin sheath results in the neurological damage observed in GBS. Despite an isolated emetic episode, our patient did not present with any gastrointestinal symptoms. Notably prevalent in northern Brazil, arboviruses (especially the Zika virus) are also related to the increase in GBS cases. However, the negative serology and PCR results for the most prevalent arboviruses combined with

incompatible signs and symptoms for these diseases, reduce the probability necessary to consider this etiology for polyradiculoneuropathy.

Genomic analysis has shown that SARS-CoV-2 belongs to the beta-coronavirus (β CoV) genera as do MERS-CoV and SARS-CoV, and it shares a highly homologous sequence with SARS-CoV [1]. Most coronavirus infections (CoVs) have similarities in their structures and mode of infection. Therefore, it is assumed that the infection mechanisms previously found for other CoVs may also be applicable to SARS-CoV-2. Evidence indicates that neurotropism is a common feature of CoVs and most β CoVs are not limited to respiratory tract infections and can invade the central nervous system, inducing neurological diseases [9]. In the context of the current pandemic, pediatric neurological manifestations are rare and have not yet been adequately studied; therefore, further research and data acquisition are needed to clarify the pattern of GBS associated with SARS-CoV-2 in children.

SUPPLEMENTARY DATA

Supplementary data are available at *Journal of Tropical Pediatrics* online.

FUNDING

The research was supported by Fundação de Amparo à Pesquisa do Estado do Amazonas (FAPEAM), Programa Primeiros Projetos/Conselho Nacional de Desenvolvimento Científico e Tecnológico—Edital 016/2014 [grant number 06201105/2017].

REFERENCES

1. Wrapp D, Wang N, Corbett KS, *et al.* Cryo-EM structure of the 2019-nCoV spike in the prefusion conformation. *Science* 2020;367:1260–3.
2. Mao L, Jin H, Wang M, *et al.* Neurologic Manifestations of Hospitalized Patients With Coronavirus Disease 2019 in Wuhan, China [published online ahead of print, 2020 Apr 10]. *JAMA Neurol.* 2020;77(6):1–9. doi:10.1001/jamaneurol.2020.1127
3. Dimachkie MM, Barohn RJ. Guillain-Barré syndrome and variants. *Neurol Clin* 2013;31:491–510.
4. Centers for Disease Control and Prevention. 2019–Novel Coronavirus (2019-nCoV) Real-time rRT-PCR Panel Primers and Probes. US Centers for Disease Control and Prevention. Atlanta, GA, 2020, 2–3. <https://www.cdc.gov/>

- coronavirus/2019-ncov/lab/rt-pcr-panel-primer-probes.html.
5. MUNHOZ R P, PEDROSO J L, NASCIMENTO F A, et al. Neurological complications in patients with SARS-CoV-2 infection: a systematic review. *Arq Neuro-Psiquiatr* 2020; 78:290–300.
 6. Dugue R, Cay-Martinez KC, Thakur K, et al. *Neurologic manifestations in an infant with COVID-19. Neurology* 2020; 94:1100–2.
 7. McAbee GN, Brosgol Y, Pavlakis S, Agha R, Gaffoor M. Encephalitis Associated with COVID-19 Infection in an 11-Year-Old Child [published online ahead of print, 2020 Apr 24]. *Pediatr Neurol.* 2020;doi:10.1016/j.pediatrneurol.2020.04.013.
 8. Sharma K, Tengsupakul S, Sanchez O, Phaltas R, Maertens P. Guillain-Barré syndrome with unilateral peripheral facial and bulbar palsy in a child: A case report. *SAGE Open Med Case Rep.* 2019;7:2050313X19838750. Published 2019 Mar 21. doi:10.1177/2050313X19838750
 9. Li YC, Bai WZ, Hirano N, et al. *Coronavirus infection of rat dorsal root ganglia: ultrastructural characterization of viral replication, transfer, and the early response of satellite cells. Virus Res* 2012;163:628–35.