https://doi.org/10.22034/hmrj.2022.327300.1044

Case Report

Acute Motor and Sensory Axonal Neuropathy, a Variant of Guillain-Barre Syndrome, Following COVID-19: A Case Report

Azam Khalighi[1], Azam Honarmandpour [*2], Fatemeh Honarmandpour[3], Maryam Mohamadi[4]

[1] Department of Emergency Medicine, Shoushtar Faculty of Medical Sciences, Shoushtar, Iran
[2] Department of Midwifery, Shoushtar Faculty of Medical Sciences, Shoushtar, Iran
[3] Student Research Committee Shoushtar Faculty of Medical Sciences, Shoushtar, Iran
[4] Department of Neurology, School of Medicine, Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran

Abstract

Introduction
Acute motor and sensory axonal neuropathy (AMSAN) is a variant of Guillain–Barré syndrome (GBS), characterized by acute paralysis and the loss of reflexes and sensory symptoms. The emerging evidence is growing to confirm that SARS-CoV-2 infection may be associated with neurological complications, including acute peripheral nerve diseases. Here we reported a case of AMSAN following the COVID-19 diagnosis.

Case presentation
A 59-year-old man with severe cold symptoms and the oral plague was diagnosed three weeks before the SARS-CoV-2 positive test results. Then the AMSAN disorder was confirmed after hospitalization and more laboratory, clinical, and electrophysiological investigations. However, interestingly, the patient revealed no respiratory symptom.

Conclusion
GBS can also occur in patients with COVID-19 without respiratory symptoms. Since GBS syndrome can lead to patient mortality by involving the respiratory system, physicians should identify and treat early GBS and autonomic symptoms in coronavirus-affected individuals to prevent heart and respiratory failure. Accordingly, further studies on the early neurological symptoms of COVID-19 and their consequences are recommended.

Received: 30 January 2022
Revised: 19 September 2022
Accepted: 19 September 2022

Keywords: Guillain-Barre syndrome, COVID-19, Acute Motor and Sensory Axonal Neuropathy (AMSAN)

***Correspondence:** Azam Honarmandpour
Affiliation: Department of Midwifery, Shoushtar Faculty of Medical Sciences, Shoushtar, Iran
Email: honarmandpour.a@ajums.ac.ir

1. Introduction

Guillain-Barré syndrome is the most common and severe acute paralytic neuropathy [1]. The acute motor and sensory axonal neuropathy (AMSAN), as a variant of Guillain–Barré syndrome (GBS), is characterized by acute paralysis and the loss of reflexes and sensory symptoms [1,2]. Studies have revealed that motor and sensory axonal degeneration with antibody-mediated attacks to nerves and Ranvier nodes are involved in the pathogenesis of this disorder [2].

The coronavirus disease (COVID-19) is caused by a novel virus, called severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). The disease is a systemic infection usually accompanied by fever, fatigue, and respiratory failure resulting in dry cough, shortness of breath, chest pain, and interstitial pneumonia [3]. Although the clinical symptoms of COVID-19 are predominantly manifested as respiratory complications, neurological features are also detected and debated increasingly [4].

Many studies have declared that two-thirds of patients with GBS reveal an infectious disease, especially respiratory or gastrointestinal infections, two to four

weeks before the onset of neurological symptoms. [5-6]. On the other hand, there have also been reports on the neurotropic characteristics of coronavirus in some infected patients without fever and typical respiratory or gastrointestinal symptoms [7].

The emerging evidence is growing to confirm that SARS-CoV-2 infection may be associated with neurological complications, including acute peripheral nerve diseases [7-8]. Nevertheless, the respiratory and gastrointestinal manifestations of SARS-CoV-2 are well-described, and the neurological complications of COVID-19 have been continuously investigated and less expounded [9-10]. In this study, we reported a case of COVID-19 AMSAN.

2. Case presentation

A 59-year-old man with a medical history of hypertension and hyperlipidemia was admitted to the emergency department of the Khatamalanbia Hospital, Shoushtar, Southwest of Iran, on July 5, 2021. The patient represented the main tingling, murmurs, and paraplegia symmetry of the lower extremities started one day ago. He started suffering from severe cold symptoms (fever and chills, lethargy, and body aches) about three weeks ago, and at the same time, he was treated on Cefixime 400 mg tablets for a week to cure his oral plaque. The physician prescribed mesalacin (calcinevine) with prednisolone 5 mg for one week after refractory to treatment. Then he suffered from pain in the sole and paresthesia in the lower limbs. According to the doctor's prescription, the drug consumption was stopped, and he was referred to the hospital emergency department.

On physical examination, the patient was completely conscious (GCS=15/15) and had a normal cranial nerve examination. The sensation on both sides of the face was symmetrical and normal. The patient's tone was also normal, with no hoarseness. More evaluations showed that the patient had a normal gag reflex, heart sounds, symmetrical and complete pulses, and no shortness of breath or chest pain.

Moreover, the abdomen was completely soft without tenderness, and his lower limbs were colder to the touch. At the emergency department, admission body temperature, Blood pressure, pulse rate, respiratory rate, and oxygen saturation were 37 °C, 120/80, 84, 20, and 95%, respectively. The arterial blood gas analysis demonstrated pO2 = 63.3 mmHg with normal p/f ratio 95, PH=7.45, (normal = PH=7.35-7.45) IU/L, PCO2=35 mmHg (normal= 40), HCO3=24.9, (normal= 24).

The cerebrospinal fluid (CSF) examination revealed normal cell count, and the protein level was 115 mg/dl. The serological tests using the ELISA technique indicated SARS-CoV-2 Abs IgM =10.8 U/mL and IgG= 50.5 U/mL.

The tonicity and strength of the upper limbs, lower limbs, and fore muscles were 5/5, 5/5, and 4/5, respectively. The patient was admitted to the ICU, and a day later, his SARS-CoV-2-RNA test using RT-PCR on the nasopharyngeal swab was positive. Although he displayed no respiratory symptom, he had been experiencing severe cold symptoms since about three weeks ago (fever and chills, lethargy, and body aches). The investigations of Brain MRI, CT scan, EMG, and NCV (for measuring the normal function of neurons) exhibited no pathological finding, and laboratory parameters, including Hb, Hct, MCV, MCH, MCHC, PLT, WBC, RBC, neutrophils, lymphocytes, Na, K, BS, BUN, and Cr, were all normal. Hepatic and renal function tests, C-reactive protein, and the erythrocyte sedimentation rate were also normal.

According to a cardiologist, the echocardiography and ECG indicated no evidence in favor of embolic causes. The bedside ultrasound of the abdominal and thoracic aorta was completely normal, and the echocardiography of the heart appeared with no pathological lesion. No pathological lesions were observed on the whole leg ultrasound. Subsequently, The MRI and CT scans of the brain were performed, and the patient's documentation and history with suspicion of GBS were reexamined to consult a neurology service.

The progression of extremity weakness to four extremities (4.5 at the proximal and 2.5 in the distal), facial plasy, and fluctuations in blood pressure were observed the day after admission. The patient's status improved eight days after the intravenous immunoglobulin (IVIG) prescription.

The face deviation and paresthesia disappeared; however, the lower limbs' muscle tone remained at 2.5, and the left eyelid movement was still exited. As mentioned, the patient had no respiratory symptom caused by coronavirus throughout his illness. According to clinical findings, the AMSAN disorder was diagnosed (Table 1).

The patient was finally referred to the neurology ward after 12 days in the ICU and discharged 15 days after hospitalization (on July 19). The medical recommendations for this patient included three sessions of physiotherapy and daily gabapentin tablets. The patient follow-up was performed one week after discharge, and the results showed that the upper and lower limb muscle tone was 5, and that the muscle force was 4 for the upper and 3 for the lower limb, respectively. The remaining facial palsy, the slight paresthesia of the upper extremities, swallowing, and voice tone were normal.

3. Discussion

This case study presented the temporal evolution of the neurological manifestations of GBS following infectious diseases with severe cold symptoms and the oral plague three weeks before neurological symptoms using the SARS-CoV-2 positive test for the diagnosis. According to the findings, regarding the disease onset and experienced symptoms, GBS could be a post-infectious complication of COVID-19; hence, an association between AMSAN and SARS-CoV-2 infection is likely. In this regard, some cases of GBS in patients with COVID-19 have been recently reported in other countries [11-12].

Neurological complications, including headache, dizziness, alteration of consciousness, smell and taste disorder, weakness, strokes, and seizures, are common in COVID-19 patients. In this regard, more neurological complications are represented in sevely ill patients (8,13). Mao et al. also illustrated the neurological symptoms

Table 1. Nerve conduction study parameters in GBS patient

Nerve Stimulated	Stimulation Site	Recording Site	Amplitude motor=mV Sensory= µV	Latency (ms)	conduction Velocity(m/s)	Fwave Latency (ms)
			RT LT NL	RT LT NL	RT LT NL	RT LT NL
Median (m)	Wrist antecubital fossa	APB APB	NR NR ≥4 NR NR	NR NR ≤4.4 NR NR	NR NR ≥49	NR NR ≤31
Ulnar (m)	Wrist below elbow above elbow	ADM ADM ADM	NR NR ≥6 NR NR NR NR	NR NR ≤3.3 NR NR NR NR	NR NR ≥49 NR NR ≥49	NR NR ≤32
Median (S)	Wrist	Index finger	NR NR ≥20	NR NR ≤3.5	NR NR ≥50	
Ulnar (S)	Wrist	Little finger	NR ≥17	NR ≤3.1	NR ≥50	
Tibial (m)	Ankle Popliteal Fossa	AHl AHl	0.75 0.8 ≥4 0.68 0.63	5.8 5.6 ≤5.8 11.7 11.6	42 41 ≥41	NR NR ≤56
Peroneal (m)	Ankle below fibula lateral popliteal fossa	EDB EDB EDB	NR NR ≥2 NR NR NR NR	NR NR ≤6.5 NR NR NR NR	NR NR ≥44 NR NR ≥44	NR NR ≤56
Sural (s)	Calf	Posterior Ankle	20.45 23.85 ≥6	3.45 3.35 ≤4.4	39.08 40 ≥40	

APB: Abductor pollicis brevis, ADM: Abductor digiti minimi, AHL: Abductor hallucis longus, EDB: Extensor digitorum brevis, NR = no response, Sensory= µV, m = motor study, s = sensory study, RT = right, LT = left, ms: mili second, m/s: metre/second, mV: milli volt.

of COVID-19 infection (4). Despite previous studies, it is unclear whether these neurologic manifestations are particular to COVID-19 or whether there is comorbidity.

It has been proved that both SARS and COVID-19 attach to the angiotensin-converting enzyme 2 receptors [5,14] in the cell membrane of human organs, including the lung, kidney, liver, nervous system, and skeletal muscles [15]. SARS-CoV-2 can initiate an excessive immune reaction with the increased levels of various inflammatory cytokines, including Interleukin-6 (IL-6) produced by activated leukocytes. This would stimulate the inflammatory cascade and cause extensive tissue damage [7-8,16]. These immunological processes are supposed to be responsible for the major part of organ manifestations, including neurological complications [4].

GBS is also an immune-mediated disorder, and molecular mimicry is a mechanism of autoimmune disorder involved in the disease pathogenesis [15]. It is an acute monophasic paralyzing disorder, usually provoked by a primary infection at all age groups worldwide [17]. GBS can be caused by an aberrant autoimmune response to a preceding infection that evokes a cross-reaction against ganglioside-components of the peripheral nerves (18). Sharing cross-reactive epitopes (molecular mimicry) leads to acute polyneuropathy, and this immune response can be directed toward the axon of the peripheral nerves [17].

On the other hand, GBS pathology demonstrated multifocal inflammatory demyelination started at the level of the nerve roots, which in the earliest changes occur at the Ranvier nodes. Moreover, both the cellular and humoral immune responses participate in the GBS pathologic process [17, 19]. Accordingly, patients with severe COVID-19 and rapid clinical deterioration are more susceptible to developing serious neurological disorders. Nevertheless, the GBS occurrence mechanism in COVID-19 patients is a challenging issue not investigated yet.

In the present study, the patient's clinical and electrophysiological findings were consistent with the AMSAN diagnosis during the benign clinical course; however, no respiratory symptom was manifested. AMSAN is an acute motor and sensory axonal neuropathy form of GBS, which is mainly prevalent in Asia and America and may be detected as a common variant of GBS in other countries [20]. Axonal neuropathies cause signs and symptoms related to axon loss, which may be caused by a wide spectrum of systemic illnesses [21]. Neurologic appearance is the major form of clinical presentation, following a temporal febrile respiratory or gastrointestinal infection [21]. Lower extremity symmetric weakness may ascend over hours to days to involve the respiratory arms and muscles in severe cases [21]. In cranial neuropathy, the facial nerve is mainly affected, leading to bilateral facial weakness [20]. Moreover, autoantibodies joining gangliosides at the Ranvier nodes activate complement and disrupt sodium-channel clusters and axoglial junctions, thereby resulting in nerve conduction failure and muscle weakness [22]. According to our observations, GBS should be considered in patients with progressive limb weakness. However, the chest imaging findings were not associated with respiratory insufficiency.

Moreover, since GBS cases have been described in COVID-19 involvement [16,23], GBS is assumed to be an infrequent complication of COVID-19. In this regard, Toscano also identified five cases of GBS using a SARS-CoV-2 positive test in Italy [16]. Although the SARS-CoV-2 infection mainly causes fever, severe respiratory syndrome, and other organ manifestations in the heart and kidney [7-8], further research on coronaviruses are recommended to detect whether these viruses can develop neurotrophic and neuroinvasive characteristics [5].

In short, the causal relationship between GBS and COVID-19 remains speculative. However, given that GBS has already been described as a post-infectious complication of other coronaviruses (SARS-severe acute respiratory syndrome and MERS-middle east respiratory syndrome), this relationship is highly likely [24]. Accordingly, further etiologic studies on the effects of COVID-19 on GBS initiation and underlying mechanisms are suggested.

4. Conclusion

According to the findings, GBS can also occur in

patients with COVID-19 without respiratory symptoms. Since GBS syndrome can arouse patient mortality by involving the respiratory system, physicians should identify and treat early GBS and autonomic symptoms in coronavirus-affected individuals to prevent heart and lung failure. Further studies on the early neurological symptoms of COVID-19 and their consequences are recommended.

Funding

The study was approved by. of the Medical Ethics Committee of the university (Code: IR.SHOUSHTAR.REC.1400.011). This research received no specific grant from funding agencies in the public, commercial, or non-profit sectors.

Conflicts of Interest

The authors declared no conflict of interest.

Acknowledgement

We thank the patient for his consent to publish the case report. The authors would like to give a special thank you to the colleagues at Khatamalanbia Hospital, shoushtar faculty of Medical Sciences, for his guidance and encouragement.

References

1. De Andrade da Silva R, Carvalho Cremaschi R, Rebello Pinho JR, Bosco de Oliveira J, Morgadinho Coelho F. Guillain–Barré syndrome—the challenge of unrecognized triggers. Neurol Sci. 2019; 40(11):2403–2404.
2. Van Doorn PA, Ruts L, Jacobs BC. Clinical features, pathogenesis, and treatment of Guillain-Barrè syndrome. Lancet Neurol. 2008; 7:939–950.
3. Guan WJ, Ni ZY, Hu Y, Liang WH, Ou CQ, He JX, et al. Clinical characteristics of coronavirus disease 2019 in China. N Engl J Med. 2020; 382(18):1708–20.
4. Mao L, Wang M, Chen S, et al. Neurological manifestations of hospitalized patients with COVID-19 in Wuhan, China: a retrospective case series study. MedRxiv. 2020 Jan 1.
5. Sedaghat z, Karimi N. Guillain Barre syndrome associated with COVID-19 infection: A case report. J Clin Neurosci. 2020; 76: 233–235.
6. Jacobs BC, Rothbarth PH, van der Meché FG, Herbrink P, Schmitz PI. The spectrum of antecedent infections in Guillain-Barré syndrome: a case-control study. Neurosci. 1998; 51(4):1110–1115.
7. Carod-Artal FJ. Neurological complications of coronavirus and COVID-19. Rev Neurol. 2020; 70(9):311-322.
8. Helms J, Kremer S, Merdji H, Clere-Jehl R, Schenck M, Kummerlen C, et al. Neurologic features in severe SARS-CoV-2 infection. N Engl J Med. 2020. 4; 382(23):2268-2270.
9. Chen L, Liu HG, Liu W, Liu J, Liu K, Shang J, Deng Y, Wei S, et al. Analysis of clinical features of 29 patients with 2019 novel corona virus pneumonia. Zhonghua Jie He He Hu Xi Xi Ji Bing Za Zhi 2020 .6; 43(0): E005.
10. Wang D., Hu B., Hu C., Zhu F., Liu X. Clinical Characteristics of 138 Hospitalized Patients with 2019 Novel Coronavirus-Infected Pneumonia in Wuhan, China. JAMA. 2020; 323(11):1061-1069.
11. Cao-Lormeau VM, Blake A, Mons S, Lastère S, Roche C, Vanhomwegen J, et al. Guillain-Barré Syndrome outbreak associated with Zika virus infection in French Polynesia: a case-control study. Lancet. 2016; 387:1531–1539.
12. Zhao H, Shen D, Zhou H, Liu J, Chen S. Guillain-Barré syndrome associated with SARS-CoV-2 infection: causality or coincidence? Lancet Neurol. 2020; 19:383–384.
13. Koralnik IJ, Tyler KL. COVID-19: a global threat to the nervous system. Ann Neurol. 2020 Jul;88(1):1-1.
14. Sahin AR, Erdogan A, Mutlu Agaoglu P, Dineri Y, Cakirci AY, Senel ME, et al. 2019 Novel Coronavirus (COVID-Outbreak: A Review of the Current Literature. Eurasian J Med Oncol. 2020; 4(1):1-7.14.
15. Huang C, Wang Y, Li X, Ren L, Zhao J, Hu Y. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. Lancet. 2020; 395(10223):497–506.

16. Toscano G, Palmerini F, Ravaglia S, Ruiz L, Invernizzi P, Cuzzoni MG, et al. Guillain–Barré syndrome associated with SARS-CoV-2. N Engl J Med. 2020; 382:2574-2576. doi: 10.1056/NEJMc2009191.
17. Yuki N, Hartung HP. Guillain-Barré syndrome. N Engl J Med 2012; 366(24):2294-304.
18. Willison HJ, Jacobs BC, van Doorn PA. Guillain-Barre syndrome. Lancet [Internet]. 2016 Feb [cited 2020 Jun 2];388(10045):P717-27.
19. Kieseier BC, Kiefer R, Gold R, Hemmer B, Willison HJ, Hartung HP. Advances in understanding and treatment of immune-mediated disorders of the peripheral nervous system. Muscle & Nerve. 2004 Aug;30(2):131-56.
20. Khadilkar SV, Yadav RS, Patel BA. Acute Motor Axonal Neuropathy. In: Neuromuscular Disorders. Springer, Singapore. 2018.
21. Shang P, Zhu M, Wang Y, Zheng X, Wu X, Zhu J, et al. Axonal variants of Guillain–Barré syndrome: an update. J Neurol. 2021;268:2402-19. Doi:10.1007/s00415-020-09742-2
22. Kuwabara S, Yuki N. Axonal Guillain-Barré syndrome: concepts and controversies. Lancet Neurol 2013;12(12):1180-1188.
23. Ghosh R, Roy D, Sengupta S, Benito-León J. Autonomic dysfunction heralding acute motor axonal neuropathy in COVID-19. J Neurovirol. 2020;26:964–966.
24. Kim JE, Heo JH, Kim HO, Song SH, Park SS, Park TH, et al. Neurological complications during treatment of Middle East respiratory syndrome. J Clin Neurol. 2010;13(3):227–233.