Case Series

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Guillan-barre syndrome during COVID-19 pandemic: a case series from Syria

Ibrahim Labbad, MD*, Ibrahim Shammas, MD, Aram Abbas, MD, Ibrahim Alorfhli, MD, Mohamad S. Agha, PhD

Background: The Coronavirus was first discovered in December 2019 and quickly it turned into a pandemic called coronavirus disease 2019 (COVID-19). The main symptoms of infection with this virus were constitutional and respiratory symptoms. However, one-third of COVID-19 patients also developed neurologic manifestations, including Guillan-Barre syndrome (GBS), which was one of the most critical complications.

Case presentation: In this paper, the authors present seven patients who suffered from GBS after being infected with the Coronavirus or in conjunction with the infection. Nerve conduction studies showed axonal type in four patients, and demyelinating type in three patients. Neurological symptoms were the initial symptoms in two patients and the presence of COVID-19 was later discovered. Most of the patients had an excellent recovery.

Conclusion: In the medical literature, many articles have mentioned the association of GBS with the Coronavirus, and it is considered the most common peripheral neurologic complication for the virus, but this article is considered one of the very few articles that were published from the Middle East, especially from Syria. Guillain-Barre's occurrence after infections is known, and the Coronavirus is one of the most important viruses of the era, which incited an increase in the number of Guillain-Barre patients.

Keywords: Guillan-barre syndrome–COVID-19, neurological complication, peripheral neuropathy, SARS-CoV-2

Background

In December 2019, a new Coronavirus was discovered in Wuhan, China, called Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2)[1]. Within a few weeks, this virus swept all countries of the world to become the pandemic of the century[2]. This virus uses the human angiotensin-converting enzyme II as an entry receptor[3,4]. The previous receptor is present in several human tissues, including the lungs, heart, thyroid gland, adipose tissue, and kidneys. As a result the virus is able to infect cells from all these tissues causing a variety of symptoms[5,6]. Although respiratory symptoms are the most common symptoms of the Coronavirus, more than 35% of patients developed neurological symptoms[7]. One of the important neurological complications that occurred after coronavirus disease 2019 (COVID-19) was Guillan-Barre Syndrome (GBS)[8], which is an acute inflammatory demyelinating polyradiculoneuropathy[8]. GBS is an autoimmune disease, that manifests with symmetric ascending progressive weakness[9]. In this article, we present seven patients from Syria who suffered from GBS during their infection with the Coronavirus or later after infection, and we specify their clinical pictures, laboratory findings in addition to treatment efficacy.

HIGHLIGHTS

- One-third of coronavirus disease 2019 patients developed a variety of neurologic manifestations.
- One of the important neurological complications that occurred during the coronavirus disease 2019 pandemic was Guillan-Barre Syndrome. The primary mechanism is molecular mimicry.
- In this case series, we present seven patients from Syria who suffered from Guillan-Barre syndrome in conjunction with their infection with the Coronavirus or later after infection.
- In our cases, only one case needed a mechanical ventilator and there were no deaths. All our patients were treated with plasmapheresis with clear improvement in six cases and limited improvement in one case.
- All our seven patients did not received any type of severe acute respiratory syndrome coronavirus 2 vaccinations previously.

Case presentation

Case one

In July 2020, a 55-year-old man with no medical history was admitted to the ICU for respiratory failure. On admission, his vital signs were unstable; therefore, he required a mechanical ventilator. His family stated that he had suffered from lower extremities weakness, which progressed to the upper extremities

Faculty of Medicine, Damascus University, Damascus, Syria

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**Corresponding author. Address: SYRIAN ARAB REPUBLIC. Tel.: +00963988532628. E-mail: dribrahimlabbad@outlook.com (I. Labbad).*

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3 days before admission in the ICU. One week before, he had a fever and cough. On admission, his strength was 2/5 in all his extremities using the Medical Research Council (MRC) scale, with the absence of reflexes without any upper motor neuron signs. His nerve conduction study (NCS) showed marked sensory and motor decreased amplitudes, which confirmed acute motor and sensory axonal neuropathy, which is a rare subtype of GBS. Cerebrospinal fluid (CSF) analysis showed an elevated protein of 325 mg/dl, glucose of 75 mg/dl, and total white blood cell count of 0. Due to the previously occurrence of fever and cough in the pandemic, serum COVID-19 antibodies (IgM and IgG) were requested and the results were positive. He was treated with five sessions of plasmapheresis. After the third session, he was weaned off the ventilator and after the fifth session he was discharged with some improvement in his muscles weakness (strength 3/5) and physical therapy was started.

Case two

An 82-year-old man was admitted to the neurology department in July 2020 complaining of weakness in his upper and lower extremities that had been progressing over the past 2 days without other complaints. Two weeks before, he had had upper respiratory symptoms and a loss of smell and taste, which suggested a Coronavirus infection with a positive nasal swab. On admission, he could not walk alone. A physical examination demonstrated lung crackles on auscultation. His strength was 4/5 in the upper extremities and 3/5 in the lower extremities with absent reflexes and flaccid muscle tone. The cranial nerves exam was intact. His NCS showed absence of F-waves with conduction velocity slowing and prolongation of distal latency. The CSF study showed elevated protein (78 mg/dl) with normal cell count (albuminocytologic dissociation). The diagnosis was an acute inflammatory demyelinating polyneuropathy (AIDP) subtype of GBS. He was treated with five sessions of plasmapheresis, which led to an obvious improvement. On discharge, he was able to walk again.

Case three

A 60-year-old woman with a history of hypertension, was admitted to the neurology department in September 2020, due to generalized weakness that had started 10 days earlier with intact urinary function. On physical examination, she was conscious with normal vital signs. Her higher cortical functions were intact. Motor examination revealed normal bulk with hypotonia in all four extremities, with a strength of 4/5 in the upper extremities and 2/5 in the lower extremities (both proximally and distally). She could not walk alone and her reflexes were absent. However, her cranial nerves and respiratory muscles were intact. One month earlier, she had suffered from respiratory symptoms including fever, cough, and loss of smell and taste and COVID-19 anti-bodies IgG were positive. The NCS displayed normal sensory nerves, but decreased motor nerves amplitude with normal velocities, which correlated with the acute motor axon neuropathy (AMAN) subtype of GBS. CSF analysis showed 10 WBC and 53 mg/dl protein. All other laboratory studies were normal. She was treated with three sessions of plasmapheresis because after around two weeks of the onset of symptoms she could walk alone, so we decided to stop the plasmapheresis.

Case four

In December 2020, a 50-year-old woman without past medical history presented with weakness and numbness in the lower extremities that started 5 days before admission and then progressed to include the upper extremities with intact bladder and bowel sensation. She provided a history of fever and chills 3 weeks back. She also had a dry cough, myalgia, headache, and anosmia. She was started on paracetamol 1000 mg orally two times daily and azithromycin 500 mg orally once daily for 5 days. Upon examination, she had difficulty standing from a sitting position. She had bilateral facial nerve palsy. Power of lower limbs was 3/5 proximally and 4/5 distally. Power of bilateral upper limb was 4/5. Deep tendon reflexes were absent. The bilateral plantar reflex was flexor. NCS showed a pattern consistent with AIDP. Lumbar puncture and CSF analysis revealed 10 WBC and 65 mg/dl protein. Upon admission, COVID-19 antibodies IgM and IgG were positive. She was treated with five sessions of plasmapheresis, and discharged on physical rehabilitation. She had obvious improvement and could walk alone on discharge.

Case five

During mid-February 2021, a 75-year-old man was admitted to the neurology department for progressive general weakness with lower limb dominance which for 4 days. Previous symptoms such as ageusia, anosmia, and dry cough were reported 2 weeks before. A nasal swab for SARS-CoV-2 was performed, and it was positive. On examination, his strength was 4/5 in the upper extremities and 3/5 in the lower extremities with absent reflexes. The laboratory tests showed normal count blood cells, electrolytes, lactate dehydrogenase, and creatine phosphokinase. There was mildly elevation in D-Dimer. NCS indicated AMAN. The CSF analysis contained zero WBC and 164 mg/dl protein (protein-cytological dissociation), which was consistent with GBS. He was treated with five sessions of plasmapheresis with a good response. He could walk without help on discharge.

Case six

A 60-year-old man with a previous medical history of hypertension and type 2 diabetes mellitus of recent diagnosis controlled with medication, presented to the neurology department in April 2021, with progressive generalized weakness for 5 days, which gradually progressed to an inability to walk. On day 1 of admission, blood pressure was 165/85 mmHg, heart rate was regular (74 beats per min), respiratory rate was 18 breaths per min and SaO2 was 95% on room air. Neurological examination showed absent reflexes, and strength was 3/5 in all his extremities using the MRC scale. No bulbar muscles involvement was observed. One day after admission, he developed a fever and a dry cough. His fever was 38.5 and his blood saturation became 91%. A chest computed tomography scan showed bilateral infiltration. His nasopharyngeal swab reverse transcription-polymerase chain reaction (PCR) was positive for SARS-COVID-19 infection. NCS indicated AMAN subtype of GBS. Additionally, CSF results were consistent with GBS with normal WBC and elevated protein (75 mg/dl). Thus, plasmapheresis was indicated and the patient showed improvement on discharge after five sessions.

Case seven

During May 2021, a 41-year-old woman with no previous medical history admitted to the hospital complaining of tingling and paresthesia in her lower limbs, which had progressed to the upper limbs within a week. She did not have any respiratory symptoms. On clinical examination, the patient was conscious and oriented to time, place, and person. Higher mental functions were normal. In a motor system examination, she had a power of 4/5 proximally and distally in all her extremities. She also had a diminished pinprick sensation in her feet. Her reflexes were +1 bilaterally. No bowel and bladder involvement were observed. There was no evidence of cranial nerve involvement. Count blood cells, liver function tests, and renal function tests were within normal limits. Serum C reactive protein was 200 mg/dl. NCS was suggestive of demyelinating polyradiculoneuropathy with prolonged distal motor latencies, slow nerve conduction velocities, and increased F-wave latencies, which are consistent with the AIDP variant. CSF showed albuminocytologic dissociation (3 white cells and 92 mg/dl protein). A chest radiograph showed infiltrations in both lungs. COVID-19 IgM antibodies were positive. The patient was diagnosed with GBS concomitant with COVID-19. After three plasmapheresis sessions, her strength improved and became 5/5 using the MRC scale, so she was discharged from the hospital (Table 1).

Discussion

COVID-19 disease is caused by SARS-CoV-2 virus infection, which mainly affects the respiratory system, but neurological, cardiologic, gastrointestinal, and much more complications have been reported[10]. Neurological complications are divided into two groups: central nervous system manifestations (headache, cerebrovascular disease, acute disseminated encephalomyelitis), and peripheral nervous system manifestations (taste and smell impairment, peripheral neuropathies, muscular manifestations)[11]. One of these complications is GBS. GBS is classically diagnosed by its clinical characteristics, which consist of symmetrical distal limb weakness and/or paresthesia following a respiratory or gastrointestinal viral infection[12]. GBS is an autoimmune disorder, and the expected pathological mechanism is the molecular mimicry[12]. This mechanism is supported by the normal white blood cells counts and negative COVID-19 PCR in CSF analysis[6]. Complement activation and infiltration of macrophages are typical characteristics of affected peripheral nerves and nerve roots in patients with GBS[13]. The incidence of GBS can increase during outbreaks of infectious illnesses that trigger the disease, like the Zika virus epidemics[14]. In 1976, flu vaccination against the influenza H1N1 antigen led to an increased incidence of GBS. Later, studies estimate that developing GBS after a flu infection is up to seven times more likely than developing GBS after a vaccination[15]. The first reported case of GBS linked to COVID-19 was a woman , which presented with generalized weakness and distal hypoesthesia, with no signs or symptoms of COVID-19 until the eighth day when she developed cough and fever, and a PCR was positive for SARS-CoV-2[16]. GBS is the most common cause of acute or subacute, flaccid weakness worldwide; however, other disorders may mimic GBS like critical illness neuropathy and myopathy, tick paralysis, acute intermittent porphyria, HIV infection, toxic neuropathies, and spinal cord disorders[12], but the accurate diagnosis is based on clinical history and neurological examination, and is supported by investigations such as CSF analysis and electrodiagnostic studies. Based on the NCS, GBS has multiple variants: axonal type (AMAN, acute motor and sensory axonal neuropathy), and AIDP[12]. A systematic review of 109 cases showed that the predominant electromyography variant was the AIDP[17]. In our series, cases 2, 4, and 7 showed demyelinating neuropathy, while case 1, 3, 5, and 6 showed axonal neuropathy. The mean duration between the COVID-19 infectious symptoms and GBS was 2 weeks in the systematic review previously mentioned[16], but in some cases the symptoms appear after the onset of GBS symptoms[17], like the case number 6 in our paper, or GBS occurs without any initial infectious symptoms like case number 7, emphasizing that physicians should think about SARS-CoV-2 despite of the absence of any respiratory symptoms[11]. Patients' ages in our series range from 41 to 82. Nonetheless, multiple studies have reported an association between SARS-CoV-2 and GBS in younger ages, and children[18]. The male to female ratio in the literature was 2.5:1[17], which is higher than what is reported in typical GBS. In our series, there were four male patients and three female patients. The disease course is frequently severe with high rates of respiratory dysfunction and ICU admission[19], whereas in our cases only one case needed a mechanical ventilator. All our patients were treated with plasmapheresis with clear improvement in six cases and limited improvement in one case, with unfortunately no use for intravenous immunoglobulin to

Table 1

Summarize patients' information

Patient number	Age	Sex	Time of the onset of GBS after infection	GBS subtype	Clinical symotoms	Admitted in ICU	Protein in CSF (mg/dl)	Plasmapheresis	Outcome
1	55	Male	One week	AMSAN	Areflexia, generalized weakness, respiratory failure.	Yes	325	5	Good
2	82	Male	Two weeks	AIDP	Areflexia, generalized weakness.	No	78	5	Excellent
3	60	Female	One month	AMAN	Generalized weakness, areflexia.	No	53	3	Excellent
4	50	Female	Three weeks	AIDP	Bilaterally facial nerve palsy, generalized weakness, numbness, areflexia.	No	65	5	Excellent
5	75	Male	Two weeks	AMAN	Generalized weakness, areflexia.	No	164	5	Excellent
6	60	Male	Presenting symptom	AMAN	Generalized weakness, areflexia.	No	75	5	Excellent
7	41	Female	Presenting symptom	AIDP	generalized weakness, paresthesia, diminished pinprick sensation, diminished reflexes.	No	92	3	Excellent

Table 2

Comparison between our series and several case series.

Case series	Country	Patients number	Age years	Sex Male: Female	Facial involvement	Time of the onset of GBS after infection	GBS sub-types	Protein in CSF mg/dl
Our series	Syria	7	> 41	4:3	1	Presenting symptom-a month	Axonal > demyelinating	53–325
Monica Chan et al[20]	United States	2	> 68	2:0	1	18-23 days	NA	67–226
Kendal Carpenter et al[21]	United States	3	> 46	2:1	0	5 days 2 months	Axonal	103–415
N. Cerón Blanco et al[22]	Colombia	12	> 38	8:4	3	1–45 days	Demyelinating > axonal	52.8–280
Ayman Ahmed et al[23]	Sudan	6	> 41	2:4	0	2–17 days	Demyelinating	NA
Tagrid Ahmad et al[24]	Syria	2	> 34	2:0	1	10 days 3 weeks	Axonal	51–182

make a comparison between the two treatment strategies. We provide a summary table to list several case reports (Table 2).

We should mention that all our seven patients did not receive any type of SARS-CoV-2 vaccinations previously. Finally, our case series is one of the very few reported case series about GBS related to COVID-19 from the Middle East.

Conclusion

GBS should be assessed as a significant neurological complication of COVID-19. This paper describes the clinical picture of GBS and wide neurophysiology findings in patients who have a previous history of COVID-19. Besides, therapy should be initiated by the time GBS is diagnosed in order to achieve better outcomes. Future studies should be conducted to achieve better understand of the molecular mechanism regarding the relation between GBS and COVID-19.

The PROCESS 2020: This work has been reported in line with the PROCESS 2020 criteria[25].

Ethical approval

This case is exempted from ethnical approval in my institution and patients identifying knowledge was not presented in the report.

Consent

Written informed consent was obtained from the patients for publication of this case series. A copy of the written consents are available for review by the Editor-in-Chief of this journal on request.

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Author contribution

I.L., I.S., and M.S.A. contributed to the study concept and design. I.A., I.L., A.A., and M.S.A. participated in the data acquisition and analysis. I.L., I.S., I.A., and A.A. contributed to the drafting of the manuscript.

Conflicts of interest

Authors declare no conflict of interest.

Research registration unique identifying number (UIN)

NA.

Guarantor

Dr Ibrahim Labbad.

Data availability statement

The data that support the findings of this study are available from the corresponding author I.L., upon reasonable request.

Provenance and peer review

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