Journal of
Neurology and Neuro Toxicology

CASE REPORT

Guillain-Barré Syndrome associated with COVID-19 infection: A Case report and Review of Literature

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Abstract

Objective: Guillain–Barré syndrome is an acute, autoimmune, polyneuropathy that is often related to a previous infectious exposure. A surge of case reports around the world have identified a relationship between the occurrence of Guillain–Barré syndrome (GBS) and a history of a recent coronavirus (COVID-19) infection. Here we report a case of GBS associated with COVID-19 infection seen in our Neurology department, Dubai, United Arab Emirates.

Clinical Presentation: A 64-year-old man presented with five days history of fever and respiratory symptoms after which he developed acute progressive ascending lower limb weakness and numbness. He developed these symptoms within a week of testing positive for COVID-19. Nerve conduction study findings were consistent of severe generalized, mixed, mainly axonal sensori-motor poly radiculo-neuropathy. He was treated with intravenous immunoglobulin (IVIG) for a total of five days and showed significant improvement.

Conclusion: The diagnosis of GBS should be considered in known COVID-19 patients who develop weakness or sensorineural findings during the course of their illness, despite the presence of fever and respiratory symptoms at the onset of neurological symptoms. Though the syndrome is generally considered to be rare, early diagnosis and intervention can significantly improve outcomes and reduce the need of ventilatory support. The strength of the association of COVID-19 and GBS is still unclear but a high index of suspicion should be maintained during this pandemic.

Introduction

The coronavirus disease (COVID-19) first emerged in Wuhan, the capital of Hubei province, China. The news of this novel virus spread across the world within a few weeks. Initially it was described as a severe acute respiratory illness that mainly targets the respiratory system causing symptoms such as fever, cough, chest discomfort, and in severe cases dyspnea [1]. It soon became apparent that this virus is a cause of myriad of diseases across the body systems. As of late, the association of COVID-19 infection and the nervous system has become a matter of interest.

The neurological manifestations of the COVID-19 infection are varied. The virus has been noted to affect both the central nervous system and peripheral nervous system. Most notably being the loss of smell or taste, or other non-specific symptoms such as headache, dizziness, and altered levels of consciousness [2].

Recently, a surge of case reports have identified a relationship between the occurrence of Guillain–Barré syndrome (GBS) and a history of a recent COVID-19 infection [3-5]. It is hypothesized that the COVID-19 infection causes a post infectious dysregulation of the immune system resulting in GBS [6].

Guillain–Barré syndrome is an inflammatory disease of the peripheral nervous system and is the most common cause of acute flaccid paralysis, with an annual global incidence of approximately 1–2 per 100,000 person per year [7]. GBS occurs more frequently in males than in females and the incidence increases with age, although all age groups can be affected [7]. Patients with GBS typically present with weakness and sensory abnormalities in the lower limb that progress to the upper limb and cranial muscles. Though, it is important to note that the clinical presentation of the disease is heterogeneous and several clinical variants exist [8]. GBS includes a wide range of clinical variants that are based on the types of nerve fibers involved (motor, sensory, sensory and motor, cranial or autonomic), predominant mode of fiber injury (demyelinating versus axonal), and the presence of alteration in consciousness [9]. The classical form of GBS also known as acute inflammatory demyelinating polyradiculoneuropathy (AIDP) accounts for 90% of cases seen in the United States and Europe [10].

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Received: April 14, 2021; **Accepted:** April 29, 2021; **Published:** April 30, 2021

Other clinical variants of GBS that do not progress to the classic pattern of sensory loss and weakness include: Acute motor axonal neuropathy, Acute motor sensory neuropathy, Miller Fisher syndrome (MFS) and Bickerstaff's brainstem encephalitis (BBE). In general, GBS variants are rarely 'pure' and often overlap in part with the classic syndrome or show features that are typical of other variant forms [8,9].

The diagnosis of GBS is made based on clinical findings, cerebrospinal fluid analysis (CSF) and nerve conduction studies [10,11]. Treatment involves the administration of intravenous immunoglobulins, plasma exchange, continuous monitoring and supportive care. Although, the syndrome is generally considered to be rare, early diagnosis and intervention can significantly improve outcomes and reduce the need of ventilatory support [10,11].

Here we describe a patient diagnosed with COVID-19 infection, following which he developed Guillain–Barré syndrome (GBS).

Case Presentation

Our patient was a 64-year-old man with a medical history significant for Hypertension, Dyslipidemia, Diabetes Mellitus Type 2 and lumbar disc herniation. Five days prior to his presentation to the emergency, the patient developed fever, cough, headache and generalized fatigue. He later tested positive for COVID-19 three days after his symptom onset and was advised for home isolation with supportive care which included oral hydration and vitamin C. Subsequently, over the next five days, the patient's fever and cough resolved however his headache and generalized fatigue persisted. He also noted new onset progressive lower back pain. This back pain was described as throbbing in nature, 7/10 in intensity (numeric rating scale) and not radiating elsewhere. One day prior to the admission, the patient woke up from sleep and noted weakness in his bilateral lower limbs. The weakness became progressively worse over the next few hours prompting him to present to our emergency department. He denied any new onset of numbness or any sensory abnormalities. He denied any loss of consciousness, changes in mental status, changes in vision and speech, difficulty swallowing, seizure-like symptoms, urinary or bowel incontinence. He denied any history of tick bites or trauma.

On physical examination, patient was vitally stable. He was oriented to time, person and place. Motor examination showed (5/5) muscle strength (Oxford Scale) in bilateral upper limbs. Motor examination in bilateral lower limbs showed moderate weakness with hip flexion (2/5) and mild weakness on hip extension, adduction and flexion (4/5). Distally, patient had severe weakness on knee extension and flexion (0/5). Deep tendon reflexes were mute in both upper and lower extremities. Sensation in the upper limb was diminished distally. Sensation in the lower limb was diminished distally with no sensation at all below the knee. He was admitted to the hospital as a case of Guillain–Barré syndrome (GBS) associated with COVID-19 infection.

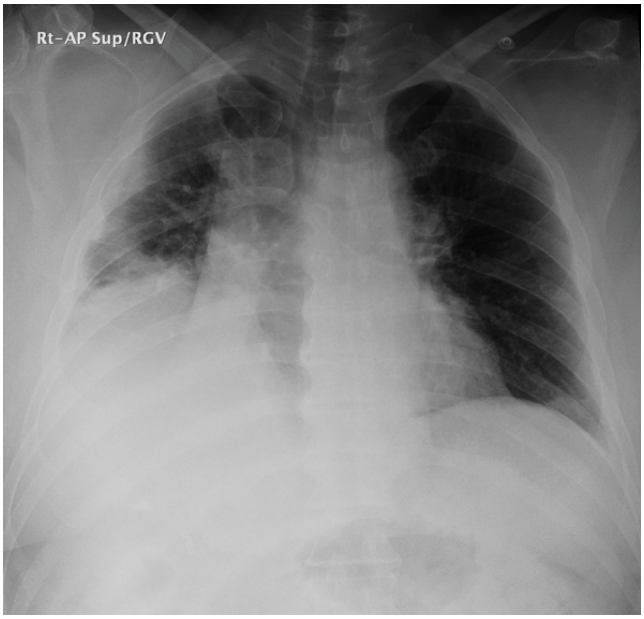

Figure 1. Chest X-ray Imaging showed right lower lung zone consolidation and peripheral based ground-glass consolidation in the right upper lung zone

1. Investigations

On the day of presentation, notable laboratory findings included a white blood cell count of 7.4 10^3/uL, C-reactive protein of 131.7 mg/L, vitamin B12 level of 283 pg/mL and thyroid stimulating hormone of 0.638 uIU/mL. Repeated COVID-19 PCR was still positive. Chest X-ray was ordered in light of his COVID-19 positive test and high C-reactive protein. (Figure 1)

2. Nerve conduction

In view of the patient's symptoms and working diagnosis of Guillain–Barré syndrome (GBS), nerve conduction studies of the left and right upper limb as well as the left and right lower limb were performed. Nerve conduction study findings revealed severe generalized, mixed, mainly axonal sensori-motor poly radiculo-neuropathy consistent of the Acute Inflammatory Demyelinating Polyneuropathy (AIDP) variant of GBS. (Table 1)

3. Management and Outcomes

The patient was admitted under the care of neurology team as a case of Guillain–Barré syndrome (GBS) associated with COVID-19 infection. He was immediately started on IVIG 50g (400mg per kg) over 3 hours for a total of five days. Patient required close observation which included cardiac and respiratory monitoring. Close follow up by chest and limb physiotherapists was also present. Infectious disease team was consulted in light of his positive COVID-19 PCR test and Chest X-Ray findings. He was started on methylprednisolone 80mg twice a day for seven days and favipravir 400mg three times daily for five days.

Table 1:

Nerve and Site	Latency	Amplitude	Segment	Latency Difference	Distance	Conduction Velocity
Median.L						
Wrist	6.7 ms	5.6 mV	Abductor pollicis brevis-Wrist	6.7 ms	mm	m/s
Elbow	13.9 ms	4.5 mV	Wrist-Elbow	7.2 ms	240 mm	33 m/s
Ulnar.L						
Wrist	5.3 ms	1.8 mV	Abductor digiti minimi (manus)-Wrist	5.3 ms	mm	m/s
Below elbow	11.4 ms	1.2 mV	Wrist-Below elbow	6.1 ms	235 mm	39 m/s
Ulnar.R						
Wrist	5.1 ms	1.0 mV	Abductor digiti minimi (manus)-Wrist	5.1 ms	mm	m/s
Below elbow	9.3 ms	0.5 mV	Wrist-Below elbow	4.2 ms	210 mm	50 m/s
Tibial.L						
Ankle	No response to stimualtion					
Popliteal fossa						
Peroneal.R						
Ankle	No response to stimualtion					
Fibula (head)						
Tibial.R						
Ankle	No response to stimualtion					
Popliteal fossa						
Peroneal.L						
Ankle	No response to stimualtion					
Fibula (head)						

F-Wave Studies

Nerve	M-Latency	F Lat Min	F Lat Max	F-M Lat Min	F-M Lat Max	%
Median.L	5.9	40.6	43.3	34.7	37.4	100.0
Ulnar.L	3.7	42.6	44.0	38.9	40.3	45.5
Ulnar.R	7.3	34.0	39.1	26.7	31.8	50.0
Peroneal.L	3.7	Not obtained				
Tibial.R	7.3					
Peroneal.R	3.7					
Tibial.L	7.3					

On the second day of admission, patient's blood oxygen saturation dropped to 92%. As per the recommendation of the infectious disease team, he was started on oxygen therapy at the rate of 4 L/min O2 flow via nasal cannula to maintain his blood oxygen saturation above 94%.

Over the course of the week, the patient showed significant improvement in his lower limb weakness. Motor examination in bilateral lower limb showed improved proximal weakness (4/5) as well as improved distal weakness (4/5). Sensation in the upper limb improved but sensation in the lower limb remained diminished.

The patient was discharged after two weeks of admission and only required minimal support while mobilizing. His COVID-19 infection settled with improvement of his Chest X-Ray findings and inflammatory markers. He was maintaining adequate blood oxygen saturation on room air and did not require any invasive ventilation throughout his admission.

Discussion

Guillain–Barré syndrome (GBS) is generally described as a post-infectious syndrome characterized by a delayed onset of neurological symptoms due to a mechanism that is distinct from the infection. The classical description of post-infectious GBS picture is known with Clostridium jejuni infection where the onset of GBS occurs approximately one week after the onset of the infection [12]. One of the largest reviews of published case reports on GBS associated with COVID-19, described 37 patients in which the mean time to onset of neurological symptoms was 11 days from the onset of COVID-19 infection. The majority of patients (31 of 37, 84%) developed GBS while still experiencing ongoing symptoms from COVID-19 [13]. This could be due to the longer duration that the COVID-19 associated symptoms may take to resolve. Most of the patients in the review were over the age 50 years old and were of the male gender [13]. This likely reflects the demographic profile of the COVID-19 pandemic where older age groups and male gender are risk factors for a more severe COVID-19 infection [14,15]. Likewise, the incidence of GBS also rises with age [7].

Similar results were also observed in another review of case reports on GBS associated with COVID-19. The review included 48 patients, with the mean age of 56 years old, the majority of which were male (31 of 48, 65%) [16].

Among the GBS variants, the classic Acute Inflammatory Demyelinating Polyneuropathy (AIDP) variant accounted for the majority of patients in both reviews. [13, 14]

Although the neurological symptoms have been reported to develop during the infectious state, it is unlikely that the neurological damage is due to direct virus invasion. CSF for COVID-19 by RT-PCR was found to be negative in COVID-19 associated GBS patients. Post-mortem brain tissues from COVID-19 patients had not shown any evidence for viral invasion on immunohistochemical studies. This indicates that the disease pathogenesis is likely due to anti-ganglioside antibodies or a hyperinflammatory response to COVID-19 infection [17, 18]. This is supported by few reviews showing positive antiganglioside antibodies in such patients [13, 14]. This highlights the need for early initiation of immunomodulatory treatment including IVIG or PLEX as just treatment of the infection alone will not suffice.

Conclusion

Our patient presented with a history of fever and respiratory symptoms for five days following which he developed rapidly progressive ascending quadriparesis and numbness. The age and gender of our patient support the previous described notion of male and elderly population being more affected by GBS. He had a mixed pattern of sensorimotor polyneuropathy, likely due to pre-existing diabetic neuropathy as well. He started having rapid improvement after initiation of IVIG which supports an immune mediated etiology for the neuropathy rather than direct viral invasion or critical illness neuromyopathy.

Diagnosis of GBS should be considered in known COVID-19 patients who develop weakness or sensorineural findings during their course of their illness, despite the presence of fever and respiratory symptoms at the onset of neurological symptoms. In certain cases, it may be the only manifestation during an otherwise asymptomatic infection. The strength of the association of COVID-19 and GBS is still unclear but a high index of suspicion should be maintained during this pandemic.

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Citation: Lootah M, Sarathchandran P (2021) Guillain-Barré Syndrome associated with COVID-19 infection: A Case report and Review of Literature. J Neurol Neuro Toxicol. 5(1): 001-004.