

Guillain-Barre Syndrome following COVID-19 Infection: First Case Report from Kuwait and Review of the Literature

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Keywords

Coronavirus · COVID-19 · Peripheral neuropathy · Guillain-Barre syndrome

Abstract

Objective: Guillain-Barré syndrome (GBS) is an acute immune-mediated polyradiculoneuropathy that is often related to a previous infectious exposure. GBS emerged as a potentially serious complication of coronavirus disease 2019 (COVID-19) since its declaration as a global pandemic. We report the first case from Kuwait, to the best of our knowledge. **Clinical Presentation:** A 72-year-old male presented with 3 weeks history of acute progressive and ascending lower limbs weakness. He developed these symptoms 3 weeks after testing positive to severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Electrophysiological studies showed acute demyelinating polyradiculoneuropathy and cerebrospinal fluid showed protein-cell dissociation. He was successfully treated with intravenous immunoglobulins (IVIGs). **Conclusion:** Neurologists should be aware of GBS as a potentially serious complication associated with COVID-19. Our patient had a favorable outcome with IVIG with no autonomic or respiratory affection.

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Introduction

Since the emergence of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in Wuhan, China, in December 2019, and the declaration of coronavirus disease 2019 (COVID-19) as a pandemic in March 11, 2020, several neurological manifestations have been associated with this disease. These manifestations involved both central and peripheral nervous systems and ranged from a simple headache and dizziness to a more sinister presentation such as encephalitis or cerebrovascular stroke [1].

Guillain-Barré syndrome (GBS) is an acute immune-mediated disease of peripheral nerves and nerve roots that is usually preceded by respiratory or gastrointestinal infection. It presents with progressive, ascending, symmetrical limb weakness, and paresthesia with diminished or absent deep tendon reflexes, with or without respiratory and cranial nerves involvement [2].

As of August 2020, 31 cases of GBS associated with COVID-19 have been reported in literature worldwide [3]. We present a case of a 72-year-old male who developed GBS 3 weeks after being diagnosed with COVID-19. This represents the first case report from Kuwait, to the best of our knowledge.

Case Presentation

A 72-year-old male, with a past medical history of well controlled hypertension and diabetes mellitus presented to the neurology department with 3 weeks history of acute inability to walk due to lower limbs weakness. The course was progressive and ascended to involve both upper limbs within 3 days. These symptoms occurred 3 weeks after testing positive for.

COVID-19 and 3 days after his discharge from the hospital, he has been diagnosed earlier with COVID-19 after developing cough, fever, generalized body ache, and occasional dyspnea with positive nasopharyngeal swab RT-PCR for SARS-CoV-2. Computed tomography of the chest showed bilateral and peripheral ground-glass opacities. He had no neurological involvement or anosmia at that time. He was admitted in a specialized institution for COVID-19 cases and received azithromycin 500 mg once daily for 5 days, amoxicillin/clavulanic acid 1,000 mg twice daily for 7 days, vitamin-C 1000 mg once daily for 2 weeks, zinc acetate 3 times daily for 2 weeks. His hospital stay was uncomplicated with no need for mechanical ventilation. He was discharged after complete resolution of his symptoms and after a negative nasopharyngeal swab.

On admission to our neurology facility, he had weakness of both distal and proximal lower extremities, associated with unsteady gait. He had with no sphincter affection or symptoms suggestive of dysautonomia. Physical examination showed normal temperature of 37°C, blood pressure 130/85 mm Hg, heart rate 70 beats/minute, respiratory rate 15/minute, and oxygen saturation of 99% on room air with no respiratory symptoms or signs. On neurological exam, the patient was alert, conscious, and oriented with normal speech and higher mental functions. Cranial nerves assessment was normal.

Motor examination showed normal tone, muscle strength examination weakness in 4 limbs with a Medical Research Council scale of grade 4/5 in proximal muscles, grade 4+/5 in distal muscles of the upper extremities, grade 3/5 in proximal muscles, and grade 4/5 in distal muscles of the both lower extremities. Deep tendon reflexes were absent all over, and planter response was down-going bilaterally. Sensory assessment showed glove and stocking hypoaesthesia with reduction in the vibration and fine touch sensation till the level of the clavicle with affection of sense of position and movement in both lower limbs with sensory ataxia in both upper and lower limbs. He was not able to walk without support with a characteristic stamping gait, suggestive of deep sensory affection.

Initial laboratory investigations were as follows; white blood cells (WBCs) count of 8.0 cells per microliter (neutrophils = 63.2%; lymphocytes = 25.4%), RBCs of 4.72 million cells/mcL, hemoglobin 139 g/dL, and platelet count is 320,000 platelets/mcL. Erythrocyte sedimentation rate of 11 mm/h and C-reactive protein was 4 mg/L. His international normalization ratio was 1.34, serum glucose 7.4 mmol/L, BUN 4.6 mmol/L, Cr 84 umol/L, alanine aminotransferase 36 U/L, potassium 4.8 mmol/L, sodium 135 mmol/L, and HbA1c was 6.1%. Anti-GD1a and anti-GQ1b antibodies were negative.

Cerebrospinal fluid (CSF) analysis showed high protein; 543 mg/L, normal glucose levels: 4.3 mmol/L, no WBCs, negative culture and sensitivity, and gram stain for bacterial infection. Virology PCR screening for neurotropic viruses was negative in serum and CSF.

Neurophysiological study was performed and showed decreased velocity, decreased compound muscle action potential,

and less prominent focal slowing, yet very delayed late responses. The findings are compatible with acute demyelinating motor and sensory polyneuropathy (Table 1). Magnetic resonance imaging of the spine was normal apart from spondylodegenerative changes in lumbosacral spine.

Our patient received 0.4 g/kg/day of intravenous immunoglobulins (IVIG) for a duration of 5 days and he had marked improvement of his symptoms, and he could walk with unilateral support in the fifth day of infusion with no respiratory or autonomic manifestations on discharge. His follow-up assessment after 1 month showed muscle power of Medical Research Council grade 5/5 all over with marked improvement in deep sensation examination, and he could walk without support.

Discussion

SARS-CoV-2 is a novel coronavirus that was first detected in Wuhan, China, in December 2019 and is the causative pathogen for COVID-19. It primarily targets the respiratory system via fusion with angiotensin-converting enzyme 2 (ACE2) receptor; however, neurological involvement is not uncommon and can worsen clinical outcome [4]. This involvement can occur during the acute phase via direct viral cytopathy, probably through afferent branches of the olfactory and trigeminal nerve, para-infectious via cytokine release, or later as post-infectious, via immune-mediated phenomenon, classically manifested as GBS [5].

GBS is an acute, immune-mediated polyneuropathy that is usually preceded with infection. Several infectious agents have been associated with GBS, including *Campylobacter jejuni*, cytomegalovirus, Epstein-Barr, and Zika virus, and it was also reported following Middle East respiratory syndrome and severe acute respiratory syndrome caused by coronavirus [6, 7]. In our report, the patient developed the classical, postinfectious, demyelinating GBS phenotype, with protein-cell dissociation in CSF 3 weeks after testing positive for SARS-CoV-2.

As of August 2020, 31 cases of GBS or its variants in association with SARS-CoV-2 have been reported in literature. The first case of GBS following COVID-19 was reported by Zhao et al. [8] in a 61-year-old female who developed demyelinating polyneuropathy after traveling to Wuhan, China. Since then, the reporting is on the rise, and to our knowledge, 31 other cases were reported from China, Italy, Spain, Iran, France, the USA, and Switzerland [9, 10]. This is the first case to be reported from Kuwait. Most of the reported patients developed classical GBS presentation, while only 2 presented with Miller Fisher syndrome [11, 12].

Table 1. Electrophysiological findings showing demyelinating polyneuropathy

Motor nerve conduction studies						
Nerve	CMAP onset, μ (ms)	CMAP duration, ms	Amplitude, mV	Distance, mm	CV, m/s	F-M lat, ms
<i>Fibular-peroneal motor left</i>						
Ankle-EDB	4.45	6.3	8.1			62.8
Ab.Knee-BL.knee	14.9	11.5	2.8	80.0	36.4	
Bl.knee-ankle	12.7	10.3	2.9	320	38.8	
<i>Fibular-peroneal r motor right</i>						
Ankle-EDB	6.36	13.2	4.6			
Bl.knee-ankle	14.7	15.1	1.29	330	39.6	
Ab.Knee-BL.knee	17.4	12.2	1.25	70.0	25.9	
<i>Median motor LT</i>						
Wrist-APB	3.47	12.1	6.3			31.1
Elbow-wrist	8.31	10.6	5.4	225	46.5	
Axilla-elbow	12.4	12.8	6.1			
Erb's axilla	16.3	13.4	3.7			
<i>Median motor RT</i>						
Wrist-APB	4.38	8.5	8.2			
Elbow-wrist	9.83	8.5	6.0			
Axilla-elbow	12.9	10.6	4.4			
Erb's axilla	17.2	13.2	3.8			
<i>Peroneal-TA motor LT</i>						
Be.Fibrular head	2.76	18.7	3.7			
Lat.popliteal fossa Be.Fibrular head	4.85	17.4	3.2	70.0	33.5	
<i>Peroneal-TA motor RT</i>						
Be.Fibrular head	2.71	15.5	3.1			
Lat.popliteal fossa Be.Fibuar head	4.54	15.4	3.2	70.0	33.5	
<i>Post-tibial motor left</i>						
Med.ankle-Abd.hal	4.14	14.9	9.3			71.9
Pop.fossa-med.ankle	14.9	15.2	2.0	390	36.2	
<i>Post.tibial motor right</i>						
Med.ankle-Abd.hal	5.57	12.9	8.5			73.9
Pop.fossa-med.ankle	16.1	12.9	1.90	390	37.0	
<i>Ulnar motor RT</i>						
Wrist-ADM	2.30	9.7	9.2			36.1
BL.elbow-wrist	7.16	8.8	5.6	230	47.3	
Ab.elbow-wrist						
Ab.elbow-BL.elbow	9.34	8.8	4.8	100	45.9	
Axilla-Ab.elbow	12.8	9.2	3.1			
Erb's axilla	15.4	63.5	1.75			
Sensory nerve conduction studies						
Nerve	Start Lat, ms	Peak Lat, ms	Amp, μ V	Distance, mm	CV, m/s	
<i>Suralis sensory RT</i>						
Mid.lower leg-Lat.Malleolus	2.75	2.79	11.9	130	47.3	
<i>Median sensory LT</i>						
Wrist-Dig II	2.63	3.33	21.2	140	53.2	
<i>Median sensory RT</i>						
Wrist-Dig II	2.88	2.92	15.7	140	48.6	
<i>Ulnar sensory RT</i>						
Wrist-Dig V	2.49	2.99	22.3	120	48.2	
H-reflex study						
Recording site		Stimulation site	M-latency, ms	H-latency, ms	H-latency, ms ^a	
<i>Side to side difference</i>						
RT soleus		Tibial-Mid popliteal fossa	5.2	40.0		
LT soleus		Tibial-Mid popliteal fossa	5.0	41.0		

CMAP, compound muscle action potential. ^a Side to side difference.

Toscano et al. [13] reported 5 patients from Italy; 3 with axonal variant of GBS and 2 with demyelinating neuropathy. However, most published cases so far had demyelinating polyneuropathy on electrophysiological studies with axonal neuropathy in only 4 patients [14]. Similar to our case, a common comorbidity was found in some of these patients which is diabetes mellitus (DM) [14, 15]. It is known that underlying DM can worsen the clinical and electrophysiological features of coexisting peripheral neuropathies, including GBS. The exact mechanism underlying the DM-induced exacerbation is not clear; however, it might be related to chronic inflammatory conditions associated with DM in addition to neurovascular compromise of peripheral nerves [16].

Three cases in the literature so far have reported autonomic complications, 2 with sphincter dysfunction and 1 with hypertension [9]. However, in our case and the 5 cases reported from Italy, there were no symptoms suggestive of autonomic system affection [13]. It is noteworthy that several cases of GBS post-COVID-19 had followed a para-infectious course, in addition to the classic postinfectious pattern [8].

The mechanism of GBS in association with COVID-19 is still unclear. GBS is an immune-mediated disease and molecular mimicry could play a role [17]. COVID-19 produces inflammatory cytokines and might be responsible for antibodies production against specific antigens associated with GBS [18]. Moreover, some viruses, such as cytomegalovirus and varicella zoster virus, can cause peripheral neuropathy via direct attacks on the nerves [19]. Whether this is the case in COVID-19, through angiotensin-converting enzyme 2 (ACE2) receptors on neuronal tissues, is yet to be investigated [20].

Our patient showed significant improvement after 5 days of IVIG course. In literature, 15/19 GBS patients were treated with IVIG, and 8 (all with classical Guillain-Barré syndrome) needed admission to intensive care unit

for ventilator support. Those 8 patients had classical GBS features of whom 2 have died. Twelve showed improvement, while 5 had residual disability at discharge [8].

Conclusion

Neurologists should be aware of GBS as a rare complication associated with COVID-19. Diagnosis can be challenging and delayed, especially in asymptomatic patients or those with mild respiratory infection weeks earlier. Early diagnosis and management can improve clinical outcome. Most of the literature consist of case reports or case series, and further larger studies are needed to assess the causal relationship between COVID-19 and GBS.

Statement of Ethics

The patient gave written consent to share his case.

Conflict of Interest Statement

The authors declare that they have no conflicts of interest to disclose.

Funding Sources

The authors received no special funding.

Author Contributions

W.A.K.: treating physician, and wrote the case report. I.I.I.: wrote the initial manuscript, performed literature review, and helped in treating the patient. J.Y.A.: supervised and critically revised the manuscript.

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