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Complex Interplay of COVID-19 ARDS with Guillain-Barré Syndrome and Cerebral Infarction: A Case Study

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Data Interpretation D
Manuscript Preparation E
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Patient: Male, 55-year-old
Final Diagnosis: COVID 19 infection • Guillain-Barré syndrome (GBS)
Symptoms: Dyspnea
Clinical Procedure: —
Specialty: Infectious Diseases • Neurology

Objective: Unusual clinical course

Background: Coronavirus disease (COVID-19) can cause various complications. We report a case of severe COVID-19 acute respiratory distress syndrome (ARDS) in a patient receiving veno-venous extracorporeal membrane oxygenation (V-V ECMO), complicated by Guillain-Barré syndrome (GBS) and cerebral infarction, as well as pulmonary embolism.

Case Report: A 55-year-old Japanese man with a history of ulcerative colitis was admitted for COVID-19. His respiratory status worsened and progressed to ARDS, requiring intubation on hospital day (HD) 3. On HD 16, contrast computed tomography revealed PE. On HD 18, his respiratory condition worsened, and V-V ECMO was initiated. On HD 23, V-V ECMO was successfully discontinued. He regained consciousness on HD 44, but he had quadriplegia. Deep-tendon reflexes were absent in all limbs. Cranial nerve involvement, specifically bilateral facial nerve weakness, was noted. Magnetic resonance imaging showed bilateral scattered cerebral infarctions on HD 76. Nerve conduction studies indicated severe axonal neuropathy. Cerebrospinal fluid examination showed albuminocytologic dissociation. The antibody to the ganglioside GD1a was positive. These findings were consistent with the diagnosis of GBS. He received immunoglobulin treatment on HD 89, and his neurological findings slightly improved.

Conclusions: This study emphasized that in COVID-19, neurological complications are not rare, are difficult to diagnose, and are prone to delays in detection.

Keywords: Cerebral Infarction • COVID-19 • Extracorporeal Membrane Oxygenation • Guillain-Barré Syndrome • Pulmonary Embolism • Respiratory Distress Syndrome

Full-text PDF: https://www.amjcaserep.com/abstract/index/idArt/944390

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Introduction

Coronavirus disease (COVID-19) can cause various complications. Neurological manifestations of COVID-19 have been reported in up to 36.4% of cases [1]. COVID-19 has been reported to be associated with various neurological symptoms, including dizziness, headache, confusion, myalgia, ageusia, and anosmia [1]. Several neurologic illnesses, such as encephalitis/encephalopathy, meningitis, and stroke, have reportedly occurred along with COVID-19 [1]. We report a case of severe COVID-19 acute respiratory distress syndrome (ARDS) complicated by neurological manifestations, including Guillain-Barré syndrome (GBS) and cerebral infarction, as well as pulmonary embolism (PE).

Case Report

A 55-year-old Japanese man with a history of ulcerative colitis (UC), hyperlipidemia, and hypertension was admitted to our hospital with dyspnea after 11 days of fever. He tested positive for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) RNA on reverse transcriptase polymerase chain reaction (RT-PCR) and was diagnosed with COVID-19. The patient's C-reactive protein level was 14.14 mg/dL. He was treated with ciclesonide, favipiravir, and methylprednisolone for COVID-19. His respiratory status worsened, and he developed ARDS, requiring intubation on hospital day (HD) 3. He received midazolam, propofol, and fentanyl for analog-sedation. On HD 8, he was able to grip with his hands and elevate his arms. Then, his respiratory condition worsened significantly. On HD 12, he developed a right pneumothorax, and a chest drain was inserted. He experienced anaphylactic shock, presumably due to xylocaine, during the insertion of a chest drain. Despite the insertion of a chest drain, oxygenation deteriorated. Therefore, a muscle relaxant, rocuronium, was added to his regimen to reduce breathing effort. Simultaneously, the dosage of propofol was increased, and on HD 14, his level of consciousness was GCS 1T1. On HD 16, contrast computed tomography revealed PE, and by HD 18, there was an added deterioration in respiratory status, presumably due to this PE, necessitating the initiation of veno-venous extracorporeal

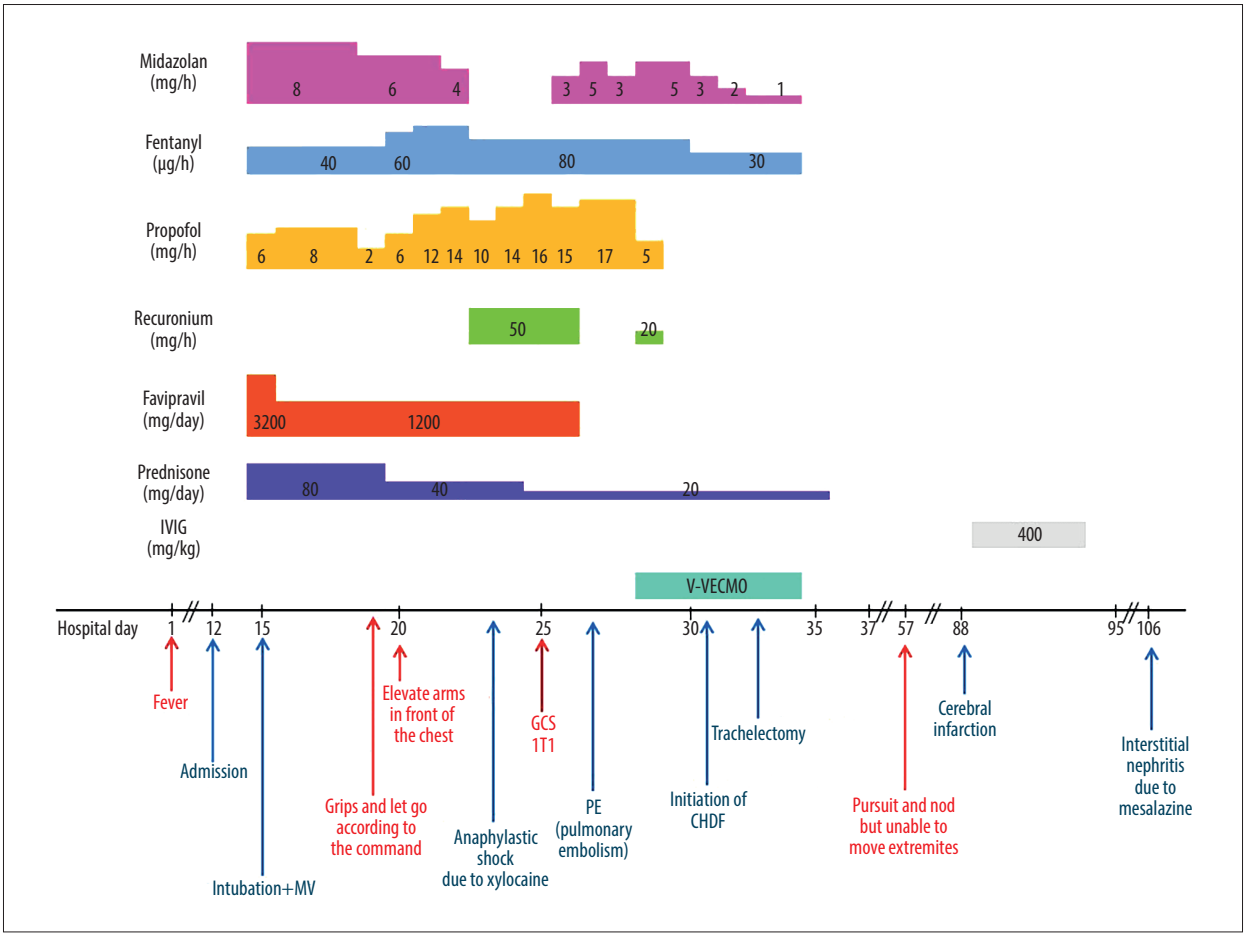

Figure 1. Clinical course of case related to treatment. MV – mechanical ventilation; GCS – Glasgow Coma Scale; PE – pulmonary embolism; V-V ECMO – veno-venous extracorporeal membrane oxygenation; IVIG – intravenous immunoglobulin.

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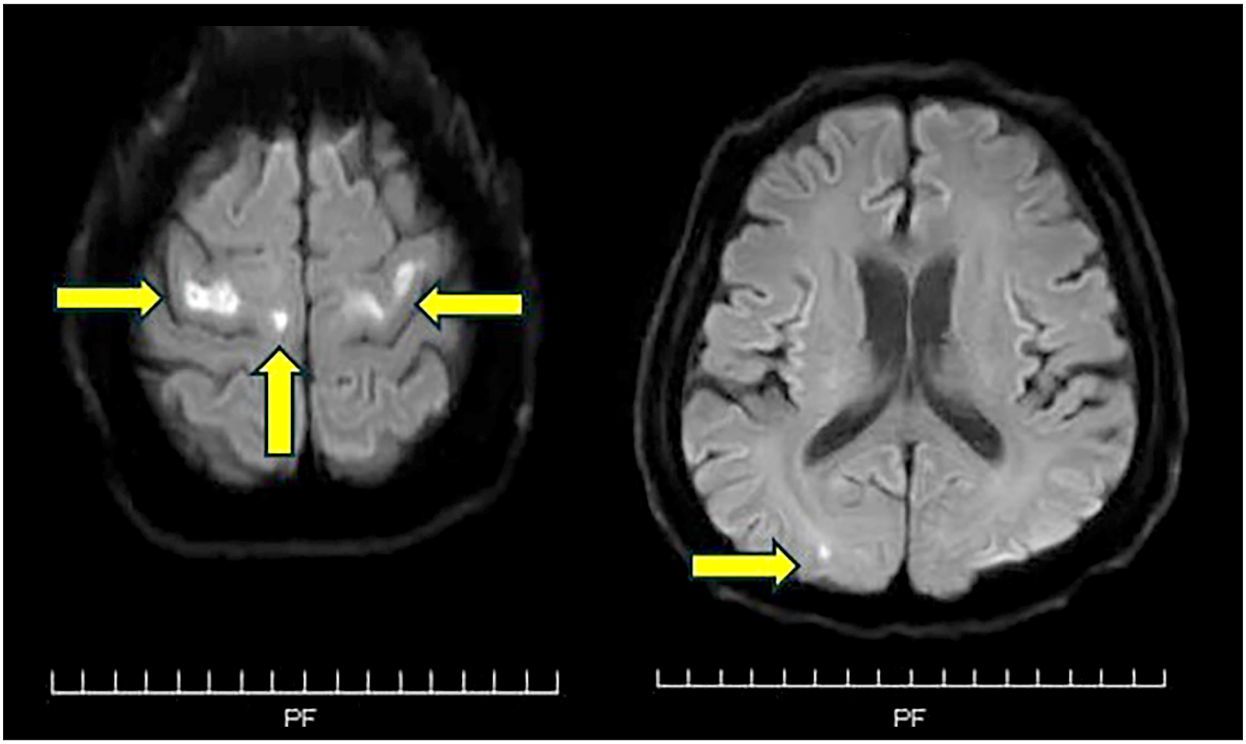

Figure 2. MRI with diffusion-weighted imaging (DWI) showed bilateral scattered cerebral infarction. A small high-intensity area was found on bilateral precentral gyrus, right superior frontal gyrus, and right occipital lobe. The areas indicated by the yellow arrows are small high-intensity areas.

membrane oxygenation (V-V ECMO) in conjunction with ARDS. Rocuronium was temporarily resumed during the procedure. On HD 20, he exhibited progression of metabolic acidosis, and continuous hemodiafiltration (CHDF) was initiated. His respiratory status subsequently improved, and on HD 22, tracheostomy was performed. On HD 23, V-V ECMO was successfully discontinued. The doses of sedative agents were gradually decreased, and sedatives were then discontinued on HD 24 (**Figure 1**). On HD 44, he was able to follow commands with visual pursuit and nodding but was unable to move his extremities. The patient regained consciousness and was able to communicate by sticking out his tongue. He was noted to be completely quadriplegic. Magnetic resonance imaging (MRI) showed bilateral scattered cerebral infarctions (small high-intensity areas in the left and right precentral gyri, right superior frontal gyrus, and right occipital lobe) on HD 76 (**Figure 2**). We confirmed the absence of intracardiac thrombi on echocardiography and conducted a bubble study, which also confirmed the absence of a patent foramen ovale. The heparin therapy for PE, which had been discontinued on HD 64 due to anemia, was resumed. However, this did not explain the patient's quadriplegia. Neurological examination revealed amyotrophy of all limbs, total paralysis of the extremities and the bulbar and facial muscles, and external ophthalmoplegia. Deep-tendon reflexes were absent in all limbs. Babinski reflex was absent. These findings were symmetrical. Cranial nerve involvement, specifically bilateral facial nerve weakness, was noted. A nerve conduction study showed delayed peripheral nerve conduction velocity, disappearance of the F wave, and decreased amplitude in the left median nerve. These findings were indicative of severe axonal neuropathy. Cerebrospinal fluid showed albuminocytologic dissociation, no white blood cells (0/mm^3), and elevated protein levels (124 mg/dL). Blood serum testing showed strong positivity for IgG antibodies to the ganglioside GD1a. Antibodies to the gangliosides GQ1b and GM1 were not detected. These findings were consistent with the diagnosis of GBS. He received intravenous immunoglobulin (IVIG) (0.4 g/kg) for 5 days, starting on HD 89. His neurological symptoms slightly improved after therapy, and he was able to move both shoulders and his right hand (manual muscle testing, 2/5). On HD 95, the patient developed interstitial nephritis, presumably due to mesalazine.

Discussion

In this case, it was difficult to determine the onset of GBS because the neurological findings were difficult to evaluate in an isolated intensive care setting. Early detection of neurological complications is imperative to providing immediate intervention and achieving a better prognosis, but it is difficult to detect the initial symptoms of COVID-19-associated GBS. The

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Table 1. Clinical characteristics, tests, treatment, and outcome of reported Guillain-Barré syndrome associated with SARS-CoV-2 infection with mechanical ventilation.

No.	Country	Age	Sex	PMH	Severity of COVID-19 Mild: 0 Severe: 1 Critical: 2	V-V ECMO	Hughes Functional Grade of GBS	Diagnostic method of GBS	Time from COVID-19 symptom onset to GBS symptom onset (d)	Time from neurological illness onset to nadir (d)
1 (7)	Italy	55	M	NA	Critical	–	5 – requiring assisted ventilation (for any part of the day or night)	Neurological findings, albuminocytologic dissociation, EDX	10	2
2 (7)	Italy	61	M	NA	Critical	–	5 – requiring assisted ventilation (for any part of the day or night)	Neurological findings, albuminocytologic dissociation, EDX	7	4
3 (7)	UK	42	M	NA	mild	–	2 – able to walk 5m (across an open space) but incapable of manual work/ running	Neurological findings, albuminocytologic dissociation, EDX	13	NA
4 (7)	UK	60	M	NA	Critical	–	5 – requiring assisted ventilation (for any part of the day or night)	Neurological findings, albuminocytologic dissociation, EDX	-1	NA
5 (7)	Italy	70	F	NA	Critical	–	5 – requiring assisted ventilation (for any part of the day or night)	Neurological findings, albuminocytologic dissociation, EDX	23	5
6 (7)	USA	54	M	NA	Critical	–	5 – requiring assisted ventilation (for any part of the day or night)	Neurological findings	8	2
7 (7)	Italy	71	M	HTN, AAA, lung cancer	Critical	–	6 – dead	Neurological findings, albuminocytologic dissociation, EDX	A few days	4
8 (7)	France	64	M	NA	Critical	–	5 – requiring assisted ventilation (for any part of the day or night)	Neurological findings, albuminocytologic dissociation, EDX	11	3
9 (7)	Italy	66	F	HTN	Critical	–	5 – requiring assisted ventilation (for any part of the day or night)	Neurological findings, albuminocytologic dissociation, EDX	10	3
10 (8)	JAPAN	69	M	DM	Critical	–	5 – requiring assisted ventilation (for any part of the day or night)	Neurological findings, albuminocytologic dissociation	24	4
11 (9)	Chile	31	F	NA	Critical	–	5 – requiring assisted ventilation (for any part of the day or night)	Neurological findings, EDX	10	1
12 (10)	USA	36	M	HTN, reanal trans-plants	Critical	v	5 – requiring assisted ventilation (for any part of the day or night)	Neurological findings, albuminocytologic dissociation	22	2
13 (11)	USA	62	F	NA	mild	–	5 – requiring assisted ventilation (for any part of the day or night)	Neurological findings, albuminocytologic dissociation	A few days	1
14 (12)	USA	69	M	Chronic myelo-genous leukemia, HTN, coronary, artery disease	Critical	–	5 – requiring assisted ventilation (for any part of the day or night)	Neurological findings, albuminocytologic dissociation, EDX	35	2

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Table 1 continued. Clinical characteristics, tests, treatment, and outcome of reported Guillain-Barré syndrome associated with SARS-CoV-2 infection with mechanical ventilation.

No.	Country	Age	Sex	PMH	Severity of COVID-19 Mild: 0 Severe: 1 Critical: 2	V-V ECMO	Hughes Functional Grade of GBS	Diagnostic method of GBS	Time from COVID-19 symptom onset to GBS symptom onset (d)	Time from neurological illness onset to nadir (d)
15 (13)	France	53	M	BPPV, asthma	Mild	–	5 – requiring assisted ventilation (for any part of the day or night)	Neurological findings, albuminocytologic dissociation, EDX	22	3
16 (13)	France	68	F	Localized sclero-derma	Critical	–	5 – requiring assisted ventilation (for any part of the day or night)	Neurological findings, EDX	32	22
17 (13)	France	78	F	Af, hypothy-roidism, depre-ssive disorder, herniated disk	Critical	–	5 – requiring assisted ventilation (for any part of the day or night)	Neurological findings, albuminocytologic dissociation, EDX	24	18
18 (14)	Syria	55	M	NA	Critical	–	5 – requiring assisted ventilation (for any part of the day or night)	Neurological findings, albuminocytologic dissociation, EDX	4	3
19 (15)	USA	59	F	HTN, hyperli-pidemia, cerebral vascular accident, DM	Critical	–	6 – dead	Neurological findings, albuminocytologic dissociation	20	2
20 (16)	Iran	38	M	NA	critical	–	5 – requiring assisted ventilation (for any part of the day or night)	Neurological findings, EDX	11	3
20 (16)	UK	57	M	HTN, psoriasis			5 – requiring assisted ventilation (for any part of the day or night)	Neurological findings, albuminocytologic dissociation	6	2
21	JAPAN	55	M	UC, DLP, HTN	Critical	+	5 – requiring assisted ventilation (for any part of the day or night)	Neurological findings, albuminocytologic dissociation, EDX	57	2

No.	MRC	GBS clinical subtype	Cranial nerve involvement	Facial palsy (unilateral or bilateral)	Brighton criteria level	Initial neurological symptoms	Key neurological signs	Protein in CSF (mg/dL)	Cell in CSF (/mm^3)
1 (7)	NA	Typical	Facial weakness evolving to areflexia/diplegia	Positive	1	Paresthesia in the four limbs and lower limb weakness	Flaccid tetraparesis and facial weakness evolving to areflexia and respiratory failure	193	0
2 (7)	NA	Typical	Facial weakness and dysphagia	Positive	1	Asthenia	Facial weakness, flaccid areflexic paraplegia, and respiratory failure	40	3
3 (7)	NA	Typical	Dysphagia	Negative	2	Distal limb numbness and weakness; dysphagia	Quadriparesis; areflexia; sensory loss	50	3
4 (7)	NA	Typical	Facial and bulbar weakness	Negative	2	Distal limb numbness and weakness	Quadriparesis; are- flexia; sensory loss; dysautonomia; facial and bulbar weakness	60	2
5 (7)	4/5 UL and LL	Typical	Negative	Negative	1	Asthenia, hands and feet paresthesia and gait difficulties	Polyradiculoneuropathy with predominant demyelination of both motor and sensory fibers, sural sparing pattern	48	1

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Table 1 continued. Clinical characteristics, tests, treatment, and outcome of reported Guillain-Barré syndrome associated with SARS-CoV-2 infection with mechanical ventilation.

No.	MRC	GBS clinical subtype	Cranial nerve involvement	Facial palsy (unilateral or bilateral)	Brighton criteria level	Initial neurological symptoms	Key neurological signs	Protein in CSF (mg/dL)	Cell in CSF (/mm³)
6 (7)	2/5 UL and LL	Typical	Negative	Negative	3	Numbness and weakness of his lower extremities	Absent lower extremity deep tendon reflexes along with decreased lower extremity strength compared to upper extremities.	Not performed	Not performed
7 (7)	3/5 UL, 2/5 LL	Typical	Negative	Negative	1	Paresthesia at limb extremities	Paresthesia at limb extremities	54	9
8 (7)	2/5 arms, 3/5 forearms, 4/5 hands, 2/5 LL	Typical	Swallowing disturbance	Negative	1	Paresthesia in feet and hands	Paresthesia in feet and hands and swallowing disturbance	166	0
9 (7)	4/5 distal muscle, UL	Typical	Positive	Unilateral	1	Weakness in LL	Proximal weakness in all limbs, dysesthesia, and unilateral facial palsy	108	0
10 (8)	Mild muscle weakness	Typical	A loss of cough reflex	Negative	1	A loss of cough reflex	Diminished tendon reflexes, mild muscle weakness	202	1
11 (9)	1/1 UL, 1/1 LL	Typical	Facial diplegia, tongue paresis	Positive	1	Paresthesia at all limb extremities	Paresthesia at limb extremities	1,8	5
12 (10)	4/5 UL, 3/5 LL	Typical	Negative	Negative	1	Numbness tingling over his fingers,toes,and perioral region	Paresthesia in feet	117	1
13 (11)	4/4 UL, 4/4 LL	Typical	Positive	Positive	1	Progressive weakness and numbness in bilateral lower extremities	Flaccid tetraparesis and facial weakness evolving to areflexia and respiratory failure	587	4
14 (12)	1/1 UL, 1/1 LL	Typical	Negative	Negative	1	Paresthesia at all limb extremities	Flaccid tetraparesis and respiratory failure	92,8	9
15 (13)	1/1 UL, 1/1 LL	Typical	Negative	Negative	1	Painful tetraparesis, sensory impairment	Areflexia in lower limbs, Hyporeflexia in upper limbs	1,7	2
16 (13)	1/1 UL, 1/1 LL	Typical	Positive	Positive	1	Flaccid tetraplegia	Flaccid tetraplegia and external ophthalmoplegia	0,23	2
17 (13)	1/1 UL, 1/1 LL	Typical	Positive	Positive	1	Flaccid tetraplegia	Flaccid tetraplegia and facial diplegia	3,31	2
18 (14)	2/5 UL, 2/5 LL	Typical	Negarive	Negative	1	lower extremities weakness	Flaccid tetraplegia and facial diplegia	325	0
19 (15)	1/1 UL, 1/1 LL	Typical	Negative	Negative	1	Flaccid tetraplegia	Flaccid tetraplegia	50	1
20 (16)	4/5 UL, 2/5 LL	Typical	Positive	Positive	1	Parethesia of his hands and feet	Facial weakness, flaccid areflexic paraplegia, and respiratory failure	Not performed	Not performed
20 (16)	4/5 UL, 4/5 LL	Typical	positive	positive	1	Difficulty standing unaided and noticed some tingling sensation in his feet	Flaccid tetraplegia	0,51	1
21	0/5 UL and LL	Typical	positive	bilateral	1	Complete quatriplegia	Bilaretal facial palsy quadplasia	124	0

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Table 1 continued. Clinical characteristics, tests, treatment, and outcome of reported Guillain-Barré syndrome associated with SARS-CoV-2 infection with mechanical ventilation.

No.	PCR assay of SARS-CoV-2 on CSF	EDX subtype	Antigan-glioside antibodies	MRI (Head)	MRI (Spine)	IVIG	PEx
1 (7)	Negative	AMAN	Negative	Normal	Enhanced of caudal nerve root	+	–
2 (7)	Negative	AIDP	Negative	NP	normal	+	+
3 (7)	Not performed	AIDP	NP	NP	Not performed	+	–
4 (7)	Not performed	AIDP	NP	normal	Not performed	+	–
5 (7)	Not performed	AIDP	NP	NP	Not performed	+	–
6 (7)	Not performed	NP	NP	NP	Normal	+	–
7 (7)	Negative	AIDP	NP	NP	Not performed	+	–
8 (7)	Not performed	AIDP	Negative	NP	2	+	–
9 (7)	Negative	AIDP	Negative	NP	Not performed	+	–
10 (8)	Not performed	AIDP	Positive	NP	Not performed	+	v
11 (9)	Not performed	AIDP	NP	NP	Not performed	+	–
12 (10)	Not performed	AIDP	NP	normal	Not performed	+	+
13 (11)	Not performed	NP	NP	normal	Not perfomed	+	–
14 (12)	Not performed	AIDP	NP	NP	Not performed	+	–
15 (13)	Not performed	AIDP	Positive	NP	Not performed	+	–
16 (13)	Not performed	Miller Fisher syndrome with involvement of the peripheral nerves	Negtive	NP	Not performed	+	–
17 (13)	Not performed	AIDP	Negative	Leukoen-cephalopathy, cortical/subcortical brain atrophy	Not performed	+	–
18 (14)	Not performed	AMAN	NP	NP	Not perfomed	–	+
19 (15)	Not performed	NP	Negative	NP	Not performed	+	–
20 (16)	Not performed	AIDP	NP	NP	Not performed	-	+
20 (16)	Not performed	AIDP	NP	NP	Not peformed	+	–
21	Negative	AMAN	Positive	Multiple cerebral infarction	Normal	+	–

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Table 1 continued. Clinical characteristics, tests, treatment, and outcome of reported Guillain-Barré syndrome associated with SARS-CoV-2 infection with mechanical ventilation.

No.	Diagnostic SARS-CoV-2 testing	Screening for other infective agents	Another reported treatment	Systemic steroid	Outcome
1 (7)	nasopharyngeal swab was positive for SARS-Cov-2 (not mentioned RT-PCR or other)	NA	Azithromycin	–	Poor outcome, still in ICU owing to neuromuscular respiratory failure and flaccid tetraplegia.
2 (7)	Positive SARS-CoV-2 IgG	*Campylobacter jejuni*, EBV, CMV, HSV, VZV, influenza, HIV (all were negative)	NA	–	Mechanical ventilation through tracheostomy.
3 (7)	Positive nasal-pharyngeal throat SARS-CoV-2 PCR test	no	NA	–	NA
4 (7)	Positive nasal-pharyngeal throat SARS-CoV-2 PCR test	no	NA	–	NA
5 (7)	Positive for SARS-CoV-2-RNA on RT-PCR with a nasopharyngeal swab	*Mycoplasma pneumoniae* and Cytomegalovirus (CMV) serology (IgM and IgG), *Legionella pneumophila* and *Streptococcus pneumoniae* CSF: herpes simplex virus, varicella zoster virus, Epstein-Bar virus, CMV, HIV-1, *Borrelia burgdorferi* IgM and IgG)	NA	–	NA
6 (7)	Specimen; SARS-CoV-2 test (not clearly mentioned the detail)	Espiratory viral panel testing (nasopharyngeal PCR): Rhinovirus (+)	Hydroxychloroquine	–	Clinical course showed improvement in his respiratory status with liberation from mechanical ventilation on day 4 of IVIG therapy
7 (7)	Nasopharyngeal swab was positive for SARS-Cov-2 (not mentioned RT-PCR or other)	NA	Hydroxychloroquine	–	Died because of progressive respiratory failure
8 (7)	Positive for SARS-CoV-2 on RT-PCR with nasopharyngeal swab	*Campylobacter jejuni*, *Mycoplasma pneumoniae*, *Salmonella enterica*, CMV, EBV, HSV1 & 2, VZV, Influenza virus A & B, VIH, and hepatitis E (all were negative)	NA	–	NA
9 (7)	Positive for SARS-CoV-2 on RT-PCR with nasopharyngeal swab	NA	Hydroxychloroquine	–	IVIg was ineffective
10 (8)	Positive for SARS-CoV-2-RNA on RT-PCR with sputum sample	NA	Hydroxychloroquine	–	Clinical course showed improvement in his respiratory status with liberation from mechanical ventilation on day 5 of IVIG therapy
11 (9)	Positive for SARS-CoV-2 on RT-PCR with nasopharyngeal swab	NA	NA	–	Clinical course showed improvement on day 5 of IVIG therapy
12 (10)	Positive for SARS-CoV-2 on RT-PCR with nasopharyngeal swab	NA	NA	+	Clinical course showed improvement in his respiratory status with liberation from mechanical ventilation
13 (11)	Positive for SARS-CoV-2 on RT-PCR with nasopharyngeal swab	NA	NA	+	Clinical course showed improvement in his respiratory status with liberation from mechanical ventilation
14 (12)	Positive for SARS-CoV-2 on RT-PCR with nasopharyngeal swab	NA	NA	+	Clinical course showed improvement in his respiratory status with liberation from mechanical ventilation

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Table 1 continued. Clinical characteristics, tests, treatment, and outcome of reported Guillain-Barré syndrome associated with SARS-CoV-2 infection with mechanical ventilation.

No.	Diagnostic SARS-CoV-2 testing	Screening for other infective agents	Another reported treatment	Systemic steroid	Outcome
15 (13)	Positive for SARS-CoV-2 on RT-PCR with nasopharyngeal swab	*Campylobacter jejuni*, EBV, HBV, HCV, HEV, HIV (all were negative), CMV IgG positive, IgM positive	NA	–	Sensory impairment of sole, balance disorder
16 (13)	Positive for SARS-CoV-2 on RT-PCR with nasopharyngeal swab	NA	Hydroxychloroquine, azithromycin, Atazanavir/ ritonavvir	–	Complete recovery
17 (13)	Positive for SARS-CoV-2 on RT-PCR with nasopharyngeal swab	EBV, HBV, HCV, HEV, HIV, M pneumoniae(all negative)	Dexamethasone	+	Weakness in lower limbs, balance disorder
18 (14)	serum COVID-19 antibodies	NA	NA	–	Clinical course showed improvement in his respiratory status with liberation from mechanical ventilation and improvement in his muscles weakness
19 (15)	Positive for SARS-CoV-2 on RT-PCR with nasopharyngeal swab	NA	Dexamethasone	+	Died
20 (16)	Negative	NA	Dexamethasone	+	Complete recovery
20 (16)	Negative	NA	NA	–	Clinical course showed improvement in his respiratory status with liberation from mechanical ventilation
21	Positive nasal-pharyngeal throat SARS-CoV-2 PCR test	*Campylobacter jejuni*, *Legionella pneumophila* and *Streptococcus pneumoniae*,HIV, EBV, Syphilis, Tuberculosis CSF: bacteria, Cryptococcus, CVM (all negative)	Ciclesonide, Favipiravir and methylprednisolone	+	Mechanical ventilation through tracheostomy

AAA – abdominal aortic aneurysm; AIDP – acute inflammatory demyelinating polyneuropathy; AMAN – acute motor axonal neuropathy; COVID-19 – coronavirus disease 2019; d – days; DLP – dyslipidemia; DM – diabetes mellitus; EDX – electrophysiological; F – female; GBS – Guillain-Barré syndrome; HTN – hypertension; ICU – Intensive Care Unit; IVIg – intravenous immunoglobulin; LL – lower limbs; M – male; MRC – Medical Research Council scale; MRI – magnetic resonance imaging; NA – not applicable; NP – not performed; PEx – plasma exchange; PMH – past medical history; UC – ulcerative colitis; UL – upper limbs; V-V ECMO – veno-venous extracorporeal membrane oxygenation.

initial symptoms included flaccid paralysis and facial diplegia, occurring 5-10 days after the onset of acute respiratory symptoms [2]. The initial symptoms of neurological complications in severe COVID-19 are challenging to diagnose because the patients are isolated, making neurological evaluation difficult, especially for intubated patients.

It was also difficult to diagnose the neurological complications of COVID-19, including GBS and stroke, because MRI and neurophysiological tests, including electroencephalography and nerve conduction studies, are difficult to perform in an intensive care setting. Moreover, safe nursing and adequate infection control need to be practiced.

Furthermore, it was difficult to differentiate GBS from other neurological diseases. Our patient was receiving V-V ECMO and was sedated with several drugs, including a muscle relaxant. General weakness was challenging to differentiate from ICU-acquired weakness (ICU-AW) and other neurological diseases. Muscle injury and myalgia are commonly reported neurological findings in COVID-19 (19.2%, 95% CI 15.4-23.2%) [3]. The weakness attributed to cerebral infarction on MRI was considered in the differential diagnosis. However, both pyramidal signs, including absent tendon reflexes and absent Babinski reflex, were noted, leading us to suspect a peripheral rather than central origin. Critical illness polyneuropathy (CIP) was one of the essential differential diagnoses in this patient. However, in CIP, peripheral facial paralysis is uncommon, and antiganglioside antibodies are not detected [4]. To differentiate GBS from other neurological diseases, antiganglioside antibody testing was useful in confirming the diagnosis of GBS, especially for an isolated intensive care setting because antiganglioside

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antibodies can be collected without moving, and are strongly associated with certain forms of GBS [5].

In our case, COVID-19 was complicated by GBS, cerebral infarction, and PE. These complications can be associated with cytokines. SARS-CoV-2 can induce an excessive immune reaction with increases production of cytokines, such as IL-6, by activated leukocytes. These stimulate the inflammatory cascade, leading to extensive tissue damage [6]. In this case, the patient developed respiratory failure, requiring V-V ECMO. In this state, a hyperinflammatory cytokine profile, often termed a "cytokine storm," can be fatal. Cytokine storm is one of the clinical complications of SARS-CoV-2 infection [6]. In patients with GBS with mechanical ventilation, our patient required V-V ECMO (**Table 1**) [7-17]. In this case, the patient`s respiratory condition deteriorated to the point that V-V ECMO was required due to pulmonary embolism complicating ARDS caused by COVID-19. It is conceivable that this PE, similar to GBS and cerebral infarction, could have originated from a cytokine storm induced by COVID-19.

Cytokine storm was also associated with increased IL-6 levels, resulting in hyperviscosity and increased risk of stroke [6]. Hypercoagulability was also a possible cause of PE. In our case, the patient had COVID-19 complicated by stroke and PE. This case emphasized that multiple coagulation complications can occur sequentially in COVID-19.

Conclusions

Neurological complications of severe COVID-19 ARDS are challenging to diagnose because patients are deeply sedated, and neurological symptoms need to be distinguished from ICU-AW. Neurologic examinations in COVID-19 patients are also limited by isolation guidelines. Early detection and treatment of neurological complications are essential to achieve a good prognosis. This case emphasizes that neurological complications are not uncommon and are prone to delays in detection. When evaluating patients with COVID-19, neurological complications, including GBS and stroke, should be strongly suspected.

Declaration of Figures' Authenticity

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References:

1. Mao L, Jin H, Wang M, et al. Neurologic manifestations of hospitalized patients with coronavirus disease 2019 in Wuhan, China. JAMA Neurology. 2020;77(6):683-90
2. Toscano G, Palmerini F, Ravaglia S, et al. Guillain-Barré syndrome associated with SARS-CoV-2. N Engl J Med. 2020;382(26):2574-76
3. Pinzon RT, Wijaya VO, Buana RB, et al. Neurologic characteristics in coronavirus disease 2019 (COVID-19): A systematic review and meta-analysis. Front Neurol. 2020;11:565
4. Zhou C, Wu L, Ni F, et al. Critical illness polyneuropathy and myopathy: A systematic review. Neural Regen Res. 2014;9(1):101-10
5. Gregson NA, Koblar S, Hughes RA. Antibodies to gangliosides in Guillain-Barré syndrome: Specificity and relationship to clinical features. Q J Med. 1993;86(2):111-17
6. Chen G, Wu D, Guo W, et al. Clinical and immunological features of severe and moderate coronavirus disease 2019. J Clin Invest. 2020;130(5):2620-29
7. De Sanctis P, Doneddu PE, Viganò L, et al. Guillain-Barré syndrome associated with SARS-CoV-2 infection. A systematic review. Eur J Neurol. 2020;27(11):2361-70
8. Wada S, Nagasaki Y, Arimizu Y, et al. Neurological disorders identified during treatment of a SARS-CoV-2 infection. Intern Med. 2020;59(17):2187-89
9. Cea G, Romero C, Aguilar S, Salinas R. Guillain-Barré syndrome in patients with SARS-CoV-2 infection. Report of three cases. Rev Med Chile. 2021;149(12):1812-16
10. Rajdev K, Victor N, Buckholtz ES, et al. A case of Guillain-Barré syndrome associated with COVID-19. J Investig Med High Impact Case Rep. 2020;8:2324709620961198
11. Rane RP, Jain A, Hussain KM, et al. A rare case of Guillain-Barré syndrome associated with SARS-CoV-2 infection requiring mechanical ventilation. Cureus. 2022;14(6):e25810
12. Yiu AC, Hussain A, Okonkwo UA, et al. Guillain-Barré syndrome associated with COVID-19 pneumonia – the first documented case in a U.S. Military Intensive Care Unit. Military Medicine. 2023;188(3-4):e852-e56
13. Diaz P, Leveque M, Hautecloque G, et al. The challenge of diagnosing Guillain-Barré syndrome in patients with COVID-19 in the intensive care unit. J Neuroimmunol. 2022;366:577842
14. Labbad I, Shammas I, Abbas A, et al. Guillan-Barré syndrome during COVID-19 pandemic: A case series from Syria. Ann Med Surgery (Lond). 2023;85(6):3166-70
15. Sidhom F, Sandhu H. Guillain-Barré syndrome in a patient with COVID-19 infection. Cureus. 2021;13(8):e17052
16. Okhovat AA, Ansari B, Hemasian H, et al. Guillain-Barré syndrome in patients with coronavirus disease-2019: Report of six cases and review of literature. Curr J Neurol. 2020;19(3):122-30
17. Webb S, Wallace VC, Martin-Lopez D, Yogarajah M. Guillain-Barré syndrome following COVID-19: A newly emerging post-infectious complication. BMJ Case Rep. 2020;13(6):e236182

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