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CASE REPORT

# Severe rapidly progressive Guillain-Barré syndrome in the setting of acute COVID-19 disease

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## Abstract

There is concern that the global burden of coronavirus disease of 2019 (COVID-19) due to severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) infection might yield an increased occurrence of Guillain-Barré syndrome (GBS). It is currently unknown whether concomitant SARS-CoV-2 infection and GBS are pathophysiologically related, what biomarkers are useful for diagnosis, and what is the optimal treatment given the medical comorbidities, complications, and simultaneous infection. We report a patient who developed severe GBS following SARS-CoV-2 infection at the peak of the initial COVID-19 surge (April 2020) in New York City and discuss diagnostic and management issues and complications that may warrant special consideration in similar patients.

**Keywords** Coronavirus-19 · SARS-CoV-2 · Neuromuscular disorders · Guillain-Barré syndrome · Polyneuropathy

## Introduction

There is concern that the global burden of coronavirus disease of 2019 (COVID-19) due to severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) infection might yield an increased occurrence of Guillain-Barré syndrome (GBS) (Guidon and Amato 2020). It is currently unknown whether concomitant SARS-CoV-2 infection and GBS are pathophysiologically related (Zhao et al. 2020), what biomarkers are useful for diagnosis, and what is the optimal treatment given the medical comorbidities, complications, and simultaneous infection.

We report a patient who developed severe GBS following SARS-CoV-2 infection at the peak of the initial COVID-19 surge (April 2020) in New York City and discuss management dilemmas that may warrant special attention in similar patients.

## Case report

A 67-year-old female presented with rapidly progressive quadriparesis, low back pain, paresthesias, and urinary retention. Her medical history included breast cancer treated a decade prior with lumpectomy and chemotherapy with paclitaxel, docetaxel, and trastuzumab. Despite the use of neurotoxic chemotherapy (Fehrenbacher 2015), there was no prior complaint of neuropathy. Ten days prior to presentation, she developed nonproductive cough, nausea, and diminished appetite. Five days later, she presented to the emergency department with progressive low back pain radiating down both lower extremities without weakness at the time and was discharged with pain medication. A nasopharyngeal SARS-CoV-2 RT-PCR test drawn at that time subsequently returned as positive. Over the next several days, she developed lower extremity weakness that progressed to also involve the upper

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extremities. She then returned to the emergency department upon being unable to walk.

On initial examination, she was afebrile, intermittently tachycardic, and hypertensive, with normal mental status and cranial nerve examinations. Motor examination revealed symmetric generalized limb weakness with Medical Research Council (MRC) strength of 3/5 deltoid, biceps, triceps, and grip in the upper extremities and 3/5 hip flexion, knee extension, knee flexion, and ankle dorsiflexion and 4/5 ankle plantar flexion in the lower extremities. Pinprick sensation was diminished below the knees. Deep tendon reflexes were diffusely absent, and plantar responses were flexor.

Laboratory studies were notable for hyponatremia (115 mEq/L), leukocytosis ($12.4 \times 10^9$/L), elevated D-dimer (1.41 μg/mL), CRP (107 mg/L), serum IgM (400 mg/dL), and CPK (275 U/L). Mycoplasma IgG antibodies were markedly elevated (2379 U/mL) with normal IgM titers. Ganglioside, acetylcholine receptor, lyme, and HIV antibodies were negative, and TSH, HbA1c, and vitamin B12 were normal. A head CT and non-contrast brain and spine MRIs were unremarkable. A chest x-ray revealed mild bibasilar patchy pulmonary opacifications. CSF studies were notable for elevated protein to 222 mg/dL, 0 WBCs, 10 RBCs, and glucose of 61 mg/dL. Oligoclonal bands, CSF immunofixation, and IgG index and synthesis rate were normal. SARS-CoV-2 RT-PCR in the CSF was negative using three different testing platforms, Cobas® SARS-CoV-2 (Roche), ePLEX® SARS-CoV-2 (GenMarkDx), and Xpert® Xpress SARS-CoV-2 (Cepheid). Hyponatremia was corrected with intravenous hypertonic saline until ≥ 120 mEq/L at which point 5 sessions of alternate day therapeutic plasmapheresis (PLEX) were initiated using one plasma volume exchange with 5% albumin and citrate anticoagulation. She was prophylactically anticoagulated with enoxaparin 1 mg/kg twice daily per institutional COVID-19 protocols.

Prior to the initiation of PLEX, the patient developed left facial and bulbar weakness. After the second PLEX session, the weakness led to an aspiration event which caused brief cardiac arrest that was treated with intubation, mechanical ventilation, and therapeutic cooling. Fortunately, despite this medical decompensation, the patient neurologically improved with further PLEX sessions. Tracheostomy was required given prolonged neuromuscular weakness. Her hospitalization was subsequently complicated by streptococcal bacteremia requiring a 14-day course of antibiotics and heparin-induced thrombocytopenia for which she was treated with argatroban followed by apixaban. Repeat SARS-CoV-2 nasopharyngeal PCR was serially negative following hospital day 21. The patient was discharged to acute rehab on hospital day 30. At time of discharge, she had normal mental status and cranial nerve exams. Motor exam revealed MRC 4/5 biceps; 3/5 triceps; 4/5 grip; 0/5 hip flexion, knee extension, and knee flexion; and 4/5 ankle dorsiflexion and plantar flexion strength. Sensation to light touch had subjectively improved, and reflexes remained absent.

## Discussion

This is among the earliest reported cases of COVID-19 disease associated with GBS (Zhao et al. 2020; Toscano et al. 2020; Padroni et al. 2020; Sedaghat and Karimi 2020; Gutierrez-Ortiz et al. 2020). A clinical diagnosis of GBS was made based on the acute pattern of weakness, sensory dysfunction, areflexia, dysautonomia, and albuminocytologic dissociation (Wijdicks and Klein 2017). The diagnosis of GBS represents a level 2 of diagnostic certainty (Fokke et al. 2014). A limitation in this case was that nerve conduction studies and electromyography were not performed given logistical challenges related to the COVID-19 surge. Given the rapidly progressive weakness, it was necessary to initiate treatment without delay for further electrodiagnostic testing.

CSF SARS-CoV-2 RT-PCR was assessed by three different commercially available assays, suggestive that this does not appear to be a useful diagnostic marker in acute GBS and that direct viral infection was not the pathophysiologic mechanism of GBS. The elevated serum IgM, mycoplasma IgG, and CSF protein and negative ganglioside antibodies may be suggestive of a yet unidentified parainfectious antibody that causes peripheral nerve injury via molecular mimicry (Guidon and Amato 2020; Wijdicks and Klein 2017). The marked elevation of IgG antibodies raises the possibility that the patient's GBS may be attributable to mycoplasma exposure even in the absence of IgM antibodies (Meyer Sauteur et al. 2016).

The hyponatremia was attributed to preceding poor oral intake and SIADH which may co-occur with or precede GBS (James and Jose 2017). Intravenous immunoglobulin (IVIg) and PLEX are equally effective for GBS (Wijdicks and Klein 2017), but IVIg was withheld given concern that fluid translocation from increased serum protein and dextrose diluent might trigger catastrophic hyponatremia (Steinberger et al. 2003). Additionally, IVIg is associated with prothrombotic states through increased circulating protein content, serum hyperviscosity, and the potential production of platelet-fibrin IgG complexes (Abrams and Elder 2018). This risk was thought to compound the hypercoagulable effects from SARS-CoV-2 infection that at the time were only first being recognized (Bikdeli et al. 2020; Terpos et al. 2020). There was only a single report available at the time documenting the seemingly safe use of IVIg in these cases adding to the tenuous decision of choice of treatment. PLEX was performed safely in this case, and despite medical decompensation, PLEX seemed neurologically beneficial. To our knowledge, this is the first report of SARS-CoV-2-associated GBS treated with PLEX as the initial therapeutic intervention, demonstrating both safety and efficacy for this

disease entity. Antiviral therapy was deferred given the medical complexity and lack of efficacy or safety data at the time. Convalescent plasma therapy was also deferred given the possibility of exacerbating the GBS should the donor plasma contains parainfectious antibodies that may attack peripheral nerves (Zhao and He 2020).

This case highlights several neurological and medical complications from COVID-19-provoked GBS including neuromuscular respiratory failure, hyponatremia, and coagulopathy. The presence of electrolyte derangements or systemic signs of hypercoagulability should factor into decision-making regarding the standard of care GBS treatments. The optimal medical management of this entity remains to be determined.

## Compliance with ethical standards

**Conflict of interest** The authors declare that they have no conflict of interest.

**Abbreviations** COVID-19, Coronavirus disease of 2019; GBS, Guillain-Barré syndrome; HIV, Human immunodeficiency virus; IVIg, Intravenous immunoglobulin; MRC, Medical Research Council; PLEX, Therapeutic plasmapheresis; RT-PCR, Reverse transcriptase polymerase chain reaction; SARS-CoV-2, Severe acute respiratory syndrome coronavirus-2

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