

# Guillain Barre Syndrome and Posterior Reversible Encephalopathy Syndrome as Complications of Coronavirus Disease-2019

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**Abstract** Guillain-Barre syndrome (GBS) is a rare inflammatory disorder that most commonly occurs as a response to a preceding infection. Although GBS is most commonly associated with *Campylobacter jejuni* infection, several reports have indicated a relationship between the novel coronavirus disease-2019 (COVID-19) and GBS. Here, we present a case of a 72-year-old female diagnosed with COVID-19 who developed progressive lower and upper extremity weakness one month following her COVID-19 diagnosis. Magnetic resonance imaging (MRI) of the spine confirmed the diagnosis of GBS and her hospital course was further complicated by posterior reversible encephalopathy syndrome (PRES). She responded well to intravenous immunoglobulin (IVIG) and subacute inpatient rehabilitation.

**Keywords:** Guillain Barre syndrome, posterior reversible encephalopathy syndrome, coronavirus disease-2019

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## 1. Introduction

COVID-19 is a novel respiratory infection that may lead to devastating neurological sequelae that are not entirely understood. Ongoing research on this virus has determined a relationship between COVID-19 and GBS, however, the exact nature of the relationship and mechanism is yet to be determined. [1] Although encephalopathy is a common finding in COVID-19 patients, the exact cause is usually idiopathic. Here, we identify that PRES can be one of the many causes of encephalopathy in these patients and has a favorable prognosis. We also present the rare sequence of a COVID-19 patient developing both GBS and PRES, a constellation of findings that has yet to be reported.

More research is needed to fully understand the neurological sequelae of COVID-19, however, it is important for health care providers to consider PRES as a possible cause of altered mental status. With early and aggressive treatment, PRES can have a favorable prognosis. Further research is also needed to determine the relationship between GBS and PRES.

## 2. Case Presentation

A 72 year-old female with past medical history of asthma and hypertension presented to the emergency department

with dyspnea, generalized weakness and numbness of her feet two weeks after being diagnosed with COVID-19. She was found to have near complete opacification of her lungs and was started on dexamethasone and remdesivir. Throughout the course of her hospitalization, she developed progressive lower extremity weakness and eventually was unable to move her lower and upper extremities. She also reported visual hallucinations and was very lethargic. She soon developed severe respiratory distress and was minimally responsive, requiring intubation.

On exam, she was afebrile but persistently hypertensive throughout her stay. She was also areflexic with decreased tone in all extremities. It was difficult to assess whether her sensation was intact as the patient was somnolent however she seemed to withdraw to pain at times. On electroencephalogram (EEG), the patient demonstrated slowing and generalized suppressions suggestive of severe encephalopathy. She did have one seizure episode witnessed by staff associated with twitching of the eyelids, face, and the left hand. After acutely treating the seizure with benzodiazepine, she was started on levetiracetam thereafter.

Computer tomography (CT) of the head did not show acute abnormality, however MRI of the spine was notable for intramedullary T2 signal representative of demyelination. In addition, longitudinal plaque-like enhancements of the lumbar nerve rootlets were visualized, raising concern for an infectious or inflammatory demyelination. MRI of the brain demonstrated subtle hyperintensity in the occipital lobes. This finding likely

explained her altered mental status and was consistent with a diagnosis of PRES.

On admission, the patient underwent extensive lab work to determine the etiology of her neurological symptoms. Cerebrospinal fluid (CSF) analysis demonstrated albuminocytologic dissociation with an elevated protein of 219 (normal range: 18-58 mg per dL) and a normal white blood cell count, consistent with GBS. CSF glucose was elevated at 155 (normal range: 50-80 mg per dL); lactate dehydrogenase (LDH) was also elevated at 473 (normal range <40 units per L). Blood cultures and viral meningitis panels were negative.

The patient was started on 0.4 g/kg IVIG for a duration of five days. Beginning on day 4 of treatment, the patient slowly regained function of all four limbs. At that time she also regained some cognition and was able to follow simple commands. MRI of the brain was repeated and the occipital hyperintensity resolved.

### 3. Discussion

GBS is a relatively rare disorder that has an incidence of 1 per 100,000 per year. The risk of acquiring the syndrome increases linearly with age and is also slightly increased in males vs females. The disease progresses over approximately two weeks. [2]

GBS is believed to be an autoimmune attack on the peripheral nervous system due to the phenomenon known as molecular mimicry. Although GBS has been studied extensively, the specific myelin antigen that is targeted in the immune response has yet to be determined. In most cases, the immune response is directed towards either the myelin or axon of the peripheral nerve and involves both the cellular and humoral immune response. During the immune response, the nerves are demyelinated via macrophages with resultant complement and immunoglobulin deposition.

GBS is most commonly associated with *Campylobacter jejuni* infection, however, other organisms such as Cytomegalovirus, Epstein-Barr virus, Zika virus, and Human Immunodeficiency Virus (HIV). In addition to infective agents, other triggering events have also been noted in the literature. For instance, immunization, trauma, surgery, and some organ transplants have been demonstrated to be the cause of GBS. Other reports also suggest that GBS may be linked to systemic diseases such as sarcoidosis, systemic lupus erythematosus, and Hodgkin lymphoma. [3] According to a meta-analysis of several adverse event monitoring systems, the 2009 H1N1 influenza A vaccine was associated with a minor increased risk of GBS. [4] Some studies have also suggested that the quadrivalent meningococcal conjugate vaccine has a minor association with GBS, however, larger studies failed to provide evidence of such a relationship. [5]

Clinically, GBS most commonly presents as progressive, symmetric muscle weakness that begins in the lower extremities and ascends rapidly. Symptoms may range from mild to severe; some patients report mild difficulty walking while others may experience complete paralysis. GBS may also be associated with decreased deep tendon reflexes and up to 30% of patients may experience respiratory muscle weakness requiring ventilation. [6]

The typical lab findings associated with GBS include an elevated CSF protein count on lumbar puncture but a normal white blood cell count. This finding is known as albuminocytologic dissociation and is present in the majority of patients with GBS. In addition, nerve conduction studies commonly demonstrate acute polyneuropathy with either demyelinating features or axonal features depending on the subtype of GBS. [2] It is helpful to perform serial electrodiagnostic studies over time since findings may be normal in early disease. Spinal MRI may also show enhancement of intrathecal spinal nerve roots and the cauda equina. [7]

Treatment of GBS primarily focuses on supportive care. It is imperative to closely monitor respiratory status and protect the airway since neuromuscular respiratory failure can progress quickly. Additionally, patients may develop severe autonomic dysfunction and require intensive care unit (ICU) monitoring. Pain is also a common feature of the disease progression and is most commonly treated with gabapentin or carbamazepine. Acute-phase rehabilitation is also often necessary once the patient is medically stabilized.

Although reserved for patients with moderate to severe symptoms, disease modifying treatment may also be implemented. The most common intervention is plasmapheresis or administration of IVIG; both have been shown to be equally effective and combination of the two treatments have not been proven to be beneficial. [8] Plasmapheresis modifies the course of GBS by removing circulating antibodies and complement, effectively blunting the immune response. [8] The mechanism of action of IVIG is still not completely understood.

PRES is also a rare disorder characterized by altered mental status, visual disturbances, seizures, and headache. Our patient demonstrated several of these symptoms in addition to MRI brain findings suggestive of this diagnosis. While the exact incidence of the syndrome is unknown, it has been noted that it is moderately more common in females. The pathogenesis of this syndrome is ambiguous. One theory suggests that a pathological activation of the immune system results in endotheliopathy of the occipital vasculature. It has been noted that hypertension is a common finding in the majority of PRES cases.

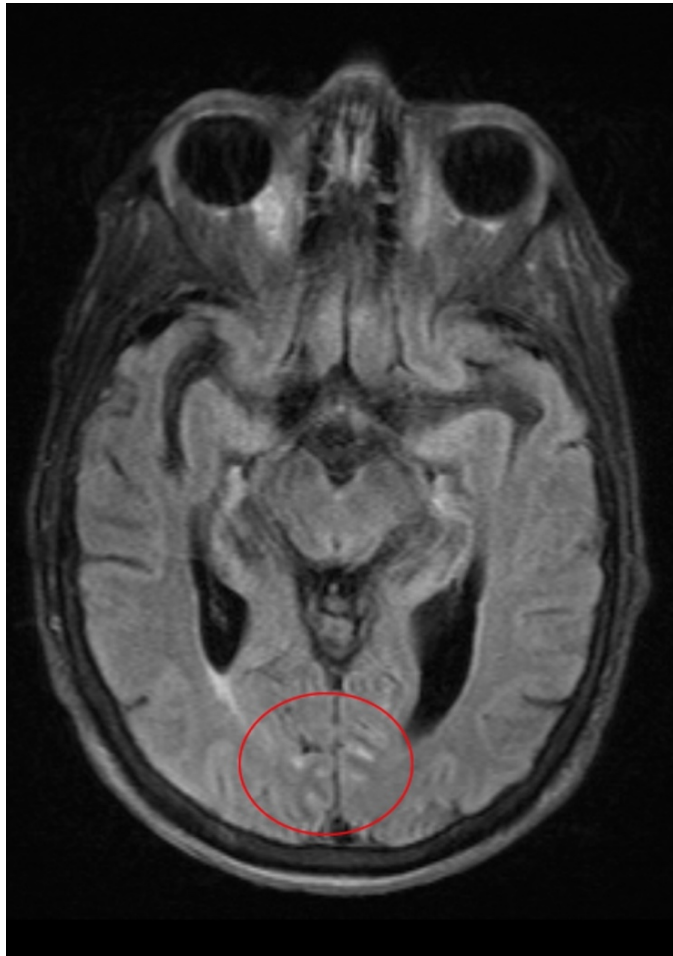
Diagnosis is based on clinical suspicion and MRI. MRI brain typically demonstrates increased T2 signaling in the occipital and parietal lobes due to subcortical vasogenic edema. These image findings often resolve in several days. EEG is also a helpful tool to monitor the presence of seizure activity.

Treatment of PRES depends on removal of the underlying cause. Lowering of blood pressure is essential in addition to seizure prophylaxis. Prognosis is generally favorable with early and aggressive treatment, however cerebral hemorrhage, ischemia, and death has been reported. [9]

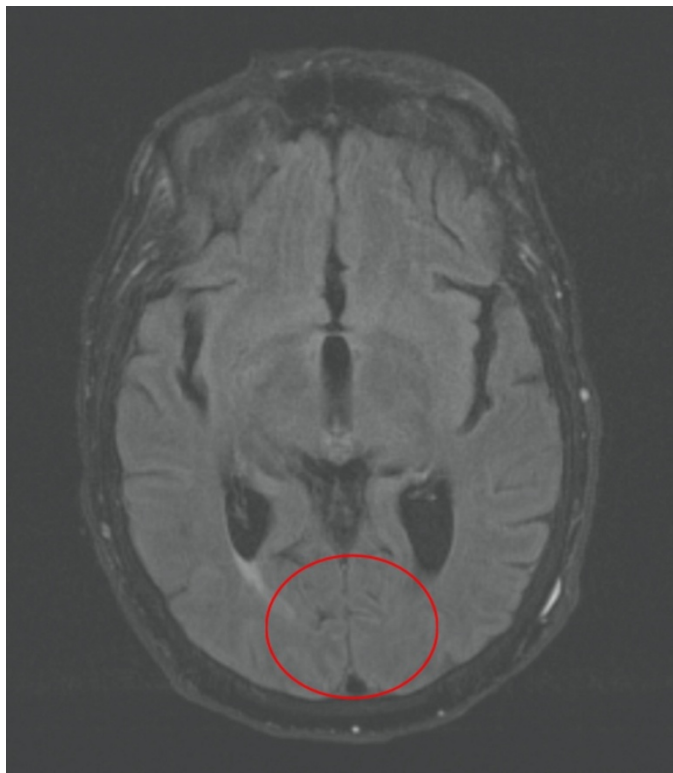
In our patient, it is unclear whether the COVID-19 infection or GBS triggered PRES. It is important to note that the patient's underlying hypertension may also have contributed to the precipitation of these findings.

In conclusion, PRES is an important complication of COVID-19 infection and should not be overlooked as a cause of encephalopathy. COVID-19 infection may

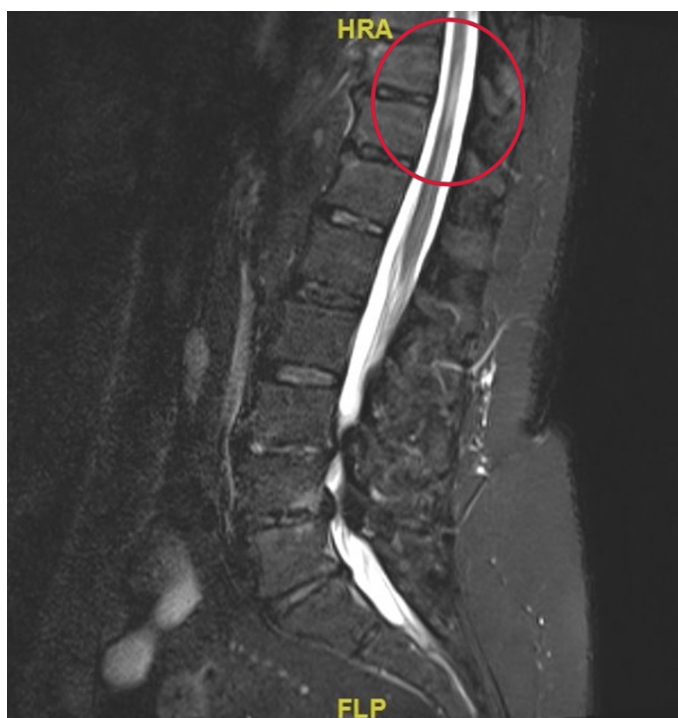
precipitate GBS; early warning signs should be monitored closely. The rare sequence of COVID-19 infection followed by both GBS and PRES requires more research in order to understand the underlying pathophysiology.



**Figure 1.** Initial MRI of the brain demonstrates hyperintensity of the occipital region, confirming the diagnosis of PRES.



**Figure 2.** MRI of the brain was repeated after 4 days of treatment, demonstrating resolution of the occipital lesions



**Figure 3.** Initial MRI of the thoracic spine shows intramedullary T2 signaling, suggestive of demyelination

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