Reccurent guillain barré syndrome after COVID-19

Svetlana D. Miletic Drakulic, PhD, *Snezana R. Lazarevic,* PhD, *Ivana P. Miloradovic,* MD, *Vladimir S. Jankovic,* MD.

ABSTRACT

من المعروف أن مرض فيروس كورونا 19 (كوفيد19) يظهر في الغالب مع أعراض تنفسية. إلا أن التجارب السابقة مع هذا المرض والعديد من الدراسات العلمية لفتت الانتباه إلى مظاهره العصبية. تمت الإشارة إلى العلاقة بين كوفيد 19 والعديد من الأمراض العصبية، بما في ذلك متلازمة غيلان باريه (GBS). على الرغم من أن GBS يعتبر مرضًا أحادي الطور، إلا أن انتكاساته تحدث في 2–6% من الحالات. نعرض حالة مريضة مصابة بمتلازمة غيلان باريه المتكررة الناجمة عن كوفيد 19. بالنظر إلى أن 2–6% من المرضى يعانون من انتكاسة لمتلازمة غيلان باريه، وأن جائحة كوفيد19 تعتبر محفزًا محتملاً للانتكاس، فإننا نؤكد على أهمية المراقبة العصبية المكثفة للمرضى الذين تم تشخيص إصابتهم بكوفيد19 والذين لديهم تاريخ طبي للإصابة GBS.

Coronavirus disease 19 (COVID-19) is known to manifest itself predominantly with respiratory symptoms. However, previous experiences with this disease and many scientific studies have drawn attention to its neurological manifestations. The link between COVID-19 and many neurological diseases, including Guillain Barré syndrome (GBS), has been pointed out. Although GBS is considered a monophasic disease, its relapses occur in 2–6% of cases. We present the case of a female patient with recurrent GBS caused by COVID-19. Given that 2–6% of patients experience a relapse of GBS, and that the COVID-19 pandemic is recognized as a possible trigger of the relapse, we emphasize the importance of intensive neurological monitoring for patients diagnosed with COVID-19 who have a history of GBS.

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From the Department of Neurology, Faculty of Medical Sciences, University of Kragujevac,Kragujevac, Serbia

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Address correspondence and reprint request to: Dr. Vladimir S. Jankovic, the Department of Neurology, Faculty of Medical Sciences, University of Kragujevac, Kragujevac, Serbia. E-mail: vjankovic118@gmail.com
ORCID ID: https://orcid.org/0000-0002-6758-7606

Coronavirus disease 19 (COVID-19) is known to manifest itself predominantly with respiratory symptoms. However, previous experiences with this disease and many scientific studies have drawn attention to its neurological manifestations.[1] Moreover, the connection between COVID-19 and subsequent occurrence of autoimmune diseases such as immunological thrombocytopenic purpura, Guillain-Barré syndrome (GBS), antiphospholipid syndrome, and Kawasaki disease, has been pointed out.[2] Since the beginning of the pandemic, cases of GBS have been reported in patients who contracted COVID-19.[3,4] Also, two cases of recurrent GBS caused by COVID-19 infection have already been reported.[5,6] This case report describes the case of a female patient who had a relapse of GBS after the COVID-19 infection.

Case Report. *The initial episode of GBS.* Patient information and clinical findings. A 30-year-old female patient was brought to our institution in October 2017 because of leg weakness that had persisted for 7 days (**Figure 2**). During hospitalization, weakness of the upper extremities developed, indicating the ascending course of the disease. The patient had no data on infection or other types of immune stimulation that preceded the onset of present symptoms. A neurological examination revealed facial diplegia, decreased muscle strength with Medical Research Council (MRC) scale of 3/5 in upper extremities and 2/5 in lower extremities, and areflexia in lower extremities.

Diagnostic assessment. The cerebrospinal fluid (CSF) analysis revealed presence of albuminocytological dissociation, with a protein level of 6.82 g/l in the CSF, and a normal cytological finding. The electromyoneurography (EMNG) findings suggested predominantly motor demyelinating polyneuropathy (**Figure 1**).

Therapeutic intervention. The patient was treated with immunoglobulins (IVIg; 0.4 g /kg), which improved her condition and reduced the neurological deficit. During the hospitalization, the physical

Figure 1 - Conduction study of right peroneal nerve.

therapy was started, and after the hospital discharge, the rehabilitation treatment was continued in spa conditions.

Follow-up and outcome. At the time of discharge, 1 month after the admission, the patient showed bilateral facial weakness, with muscle weakness of 3/5 on MRC scale in the lower extremities and 4/5 in the upper extremities. At the follow-up examination in June 2020, the patient still had weakness of the facial muscles on both sides, but this was a significant improvement from the condition at the discharge, with strength of 5/5 on MRC scale in the upper extremities and 4/5 in the lower extremities.

The second episode of GBS. Clinical findings. In April 2021, the patient contracted COVID-19 (the dominant Delta strain in Serbia at the time). The disease passed in the form of a milder clinical picture. Two weeks after the onset of the COVID-19 symptoms, the patient felt muscular pain and weakness in the lower extremities (**Figure 2**). For this reason, she visited a neurologist for an examination and was hospitalized. On admission, the patient had facial diplegia, symmetrical weakness with MRC grade 4/5 in the upper limbs and 3/5 in the lower limbs, with areflexia in both upper and lower limbs.

Diagnostic assessment. The EMNG finding indicated presence of sensorimotor polyneuropathy of the demyelinating type. These findings corresponded to acute inflammatory demyelinating polyneuropathy. The CSF analysis revealed albuminocytological dissociation, with a protein level of 7.13 g/l in the CSF, and a normal cytological finding. Laboratory blood test results showed significantly elevated D-dimer values of 9.39 µg/ml.

Therapeutic intervention. IVIg therapy (0.4 g/kg) was prescribed.

Follow-up and outcome. At the discharge (10 days after the admission), facial diplegia was still present, with strength of 4/5 on MRC scale in both upper and lower extremities.

Discussion. Since the beginning of the COVID-19 pandemic, the link between COVID-19 and many neurological diseases, including Guillain Barré syndrome,[1] has been pointed out. The pathogenetic mechanism that would explain how COVID-19 leads to GBS has not been fully established yet, but one assumption is that the cause is a strong stimulation of the humoral and cellular immune responses due to COVID-19, during which the formation of antibodies and proinflammatory cytokines can lead to cytokine storm.[7] Under these conditions, a cross-reaction occurs between the formed antibodies and neural antigens, causing a damage to myelin and axons in the peripheral nervous system.[2,8] This is supported by the fact that patients with GBS caused by COVID-19 respond well to the therapeutic use of immunoglobulin or therapeutic plasma changes.[3]

Although GBS is considered a monophasic disease, its relapses occur in 2–6% of cases.[6] Recurrent GBS is defined as 2 or more episodes of GBS with either ≥4 months between the episodes without complete recovery or ≥2 months between the episodes if the patient achieves complete or near-complete recovery. Two cases of recurrent GBS caused by the COVID-19 infection have already been reported.[5,6] Our patient met the diagnostic criteria for recurrent GBS in accordance with the current recommendations, considering that 2.5 years had passed since the first episode of GBS until the recurrence. In addition, the patient showed the features that supported the diagnosis, such as progressive bilateral leg weakness that persisted for up to 4 weeks, extinguished muscle reflexes on the affected extremities, symmetry of symptoms and signs, cranial nerve involvement, albuminocytological dissociation in the CSF, and electrophysiological confirmation, without the features that reduced probability of the diagnosis.[9] There was evidence of a previous COVID-19 infection based on a positive polymerase chain reaction test result 2 weeks prior to neurological symptoms, which corresponded to the infection that can trigger the onset of GBS. Moreover, the patient responded favorably to the administration of immunoglobulin. Chronic inflammatory demyelinating polyneuropathy with the acute onset (A-CIDP) was considered in the differential diagnosis. However, patients with A-CIDP rarely have cranial nerve involvement and are less severely disabled being able to walk independently.[10] Also, the common

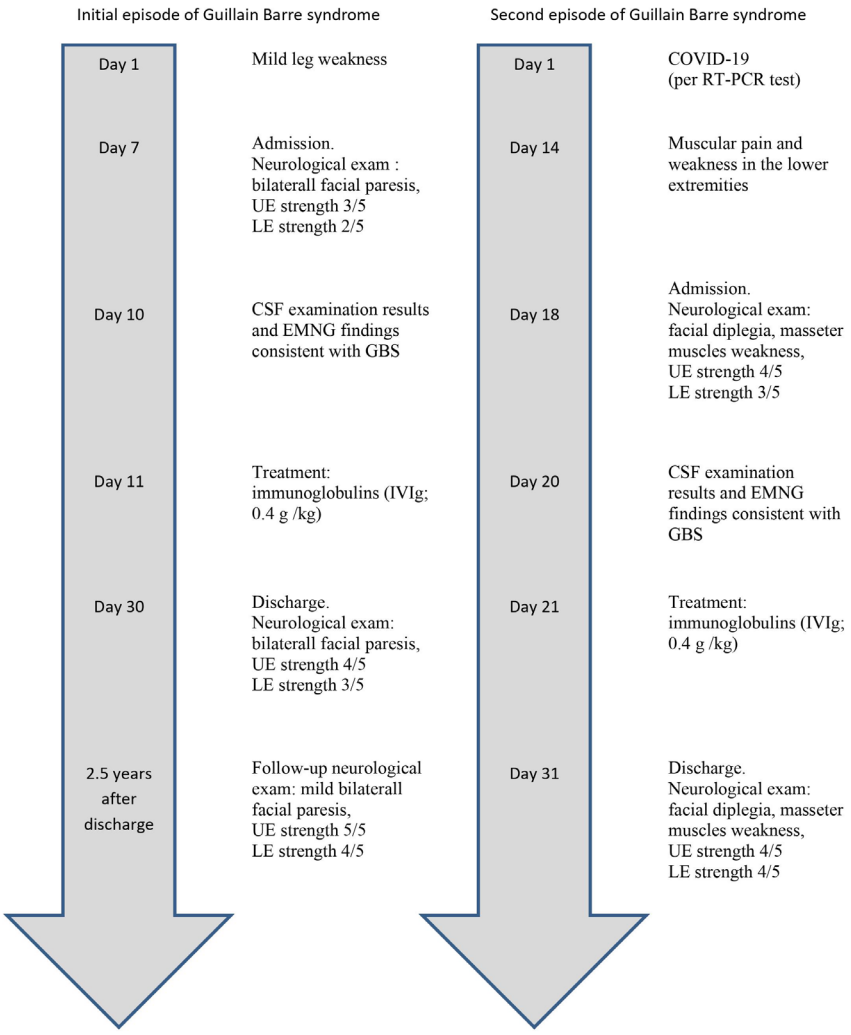

Figure 2 - Timeline of clinical course and outcome for each of Guillain Barre syndrome (GBS) episode. UE - upper extremities, LE- lower extremities EMNG -electromyoneurography

symptoms of A-CIDP are sensory signs and ataxia. Our patient did not show the features that supported the diagnosis of A-CIDP.

In conclusion, given that 2–6% of patients experience a relapse of GBS, and that the COVID-19 pandemic is recognized as a possible trigger of the relapse, we emphasize the importance of intensive neurological monitoring for patients diagnosed with COVID-19 who have a history of GBS.

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