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SCIENTIFIC LETTER

Guillain-Barré syndrome associated with SARS-CoV-2 infection☆

Síndrome de Guillain-Barré asociado a infección por COVID-19

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Sir,

Guillain-Barré syndrome is the most common cause of flaccid paralysis in developed countries. This acute, mixed demyelinating and axonal polyneuropathy can manifest at any age, though it is most often observed in childhood. The underlying etiopathogenesis is not fully clear, though immunological phenomena causing destruction of the myelin component of the peripheral nerves are known to be involved.

The anomalous inflammatory events that characterize the syndrome can be triggered by infectious, toxic or biochemical agents, or may manifest in the context of neoplastic disease.[1]

The appearance of the new SARS-CoV-2 pandemic has become a threat for the world population, and has taxed healthcare systems to the limit. This viral infection is particularly virulent in patients with chronic diseases and in immune depressed individuals. Although respiratory problems are the main manifestation of COVID-19 disease, some studies have already described the secondary neurological impact of the infection, affecting at least 36% of all patients, and which reflects the neurotrophic potential of the virus.[2] From the neurological perspective, anosmia is the most frequent finding. The nervous system manifestations have been significantly more common in patients with severe infection than in non-severe cases.[3]

We present the first reported case of Guillain-Barré syndrome in Spain in the context of SARS-CoV-2 infection in a woman admitted to the Intensive Care Unit (ICU) of Miguel Servet Hospital in Zaragoza (Spain). The first published case corresponded to the city of Jinzhou, in the province of Hubei (China),[4] and the first case series (5 patients) was recorded in Italy.[5]

A 55-year-old woman with a history of dyslipidemia and active smoking reported to the emergency room on 6 April 2020 due to fever, dry cough and exertional dyspnea for the previous 15 days. In the last 24 h she had experienced paresthesias of the hands and feet, together with weakness of the legs. She was living with patients diagnosed with SARS-CoV-2 infection.

At initial exploration the patient was conscious and oriented, with a blood pressure of 155/102 mmHg, heart rate 103 bpm, temperature 36.6 °C, and basal $SatO_2$ 93%. She presented eupnea with a respiratory frequency of 20 rpm, and bibasal crepitants were identified at pulmonary auscultation. Strength and sensitivity were preserved in all four

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extremities. The rest of the physical examination revealed no significant alterations.

The chest X-ray study evidenced left lower lobe condensation, while the laboratory blood tests showed leukocytes 7400/mm^3, lymphocytes 2400/mm^3, hemoglobin 14 g/dl, platelets 408.000/mm^3. The liver and kidney function and coagulation parameters were normal. D-dimer 556 ng/mL. Ferritin 544 ng/mL. C-reactive protein 2.04 mg/dl. Fibrinogen 6.8 g/dl. Arterial blood gases: P_{O2} 85 mmHg, P_{CO2} 30 mmHg.

Nasopharyngeal swab polymerase chain reaction (PCR) testing for SARS-CoV-2 proved negative, though this was interpreted as a false negative result, and treatment was started with hydroxychloroquine, ceftriaxone and azithromycin.

On 9 April the patient reported intense lumbar pain irradiating to both legs, with progressive weakness of all four extremities, associated to dysphagia.

Magnetic resonance imaging revealed slightly enhanced leptomeningeal uptake at brainstem and cervical spinal cord level. Lumbar puncture showed clear and transparent cerebrospinal fluid (CSF) with albumin-cytological dissociation, three leukocytes per mm^3 and protein elevation (0.86 g/l; reference $\leq$0.45 g/l). Cerebrospinal fluid culture revealed no bacterial or viral infection.

With a diagnosis of Guillain-Barré syndrome, treatment was prescribed in the form of immunoglobulins at a dose of 0.4 mg/kg/day for 5 days.

After 48 h, the neurological condition worsened, with areflexic tetraparesis (grade 2/5 of the left arm, grade 3/5 of the right arm, and grade 4/5 of both legs) associated to liquid swallowing difficulties, bilateral facial diplegia, eyelid closing weakness and tongue and perioral paresthesias. There were no meningeal signs. Ventilation and $SatO_2$ were adequate, with no need for ventilatory support. In this context, transfer to intensive care was decided. Repeat PCR testing for COVID-19 proved positive.

During her stay in the ICU, the patient showed no progression of the radiological infiltrate or worsening of her respiratory symptoms. She experienced apnea-hypopnea episodes with a transient decrease in $SatO_2$ that subsided, with progressive improvement of the neurological condition.

After 5 days of ICU stay, the patient was moved to the Neurology ward due to clinical improvement, with motor balance 5/5 of the right arm, 3/5 of the left arm and 4/5 of both legs – with persistence of her paresthesias.

The electrodiagnostic study made 8 days after onset of the neurological manifestations reported prolonged distal motor latencies in both the upper and the lower limbs, as well as potentials with a certain time dispersion. There were no F waves in either the posterior tibial or cubital nerves. The left and right facial nerves both showed very prolonged distal motor latencies, with potential time dispersion. Potential desynchronization of the sensory nerve trunks of the arms was recorded, with somewhat reduced velocities, in contrast to the lower extremities, which showed no sensory alterations. The findings were consistent with sensory-motor polyneuropathy of a predominantly demyelinating nature.

On the basis of this clinical case, we support the hypothesis of an association between Guillain-Barré syndrome and SARS-CoV-2 infection, as already documented by other authors.[4,5]

Interpretation of the initial negative PCR test must be made with caution, particularly in the presence of an unusual clinical condition, though with strongly suspicious clinical and epidemiological data. Inadequate sampling, delays in transport, preanalytical error in labeling the sample in the course of the process, or scant elimination of the virus by the patient due to the stage of the disease, are possible causes of false-negative readings that need to be considered.

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Conflicts of interest

The authors declare that they have no conflicts of interest.

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