



GUILLAIN-BARRÉ AND SARS-COV₂

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SUMMARY

Guillain-Barré is one of the most common syndromes causing acute flaccid paralysis worldwide, usually starting with a motor component and spreading upwards; the most common organism causing this pathology is *Campylobacter Jejuni*. However, due to the pandemic, the presence of this neurological pathology has been reported in patients with SARS-CoV₂. The process by which this disease is produced is due to the interaction between the immunological processes produced by the activation of autoantibodies that triggers an affection at the level of the peripheral nerves(1)(2)(3).

In this literature review, we intend to mention the scientific evidence related to the presence of the coronavirus (or COVID-19 vaccines) and its relationship with Guillain-Barre disease.

KEYWORDS: Guillain-Barre, SARS-CoV₂, Central Nervous System

RECENT STUDIES ON GUILLAIN-BARRÉ DISEASE AND SARS-COV₂

In a study conducted in 2021 in Taiwan, the presence of Guillain-Barré symptoms was found to occur within 11.4 days after vaccination against SAR-CoV₂ virus, with the presence of symptoms such as myalgias, parentheses, facial paralysis and paraparesis. In addition to this, dysautonomias

were also present, which led to these patients being hospitalised for monitoring. Out of a total of 39 patients who underwent lumbar puncture, 30 of these patients were found to have albuminocytologic dissociation. The clinical features of these patients included an inflammatory demyelinating polyneuropathy, followed by motor and sensory neuropathy. All these patients received intravenous immunoglobulins and



only 2 received plasmapheresis. One patient died and nine required mechanical ventilation (4).

Two systematic reviews conducted in 2020 and 2021, mention that the most frequent clinical manifestations are: areflexia, lower limb weakness, facial paralysis, dysphasia, paraparesis, quadraplegia, along with SARS-CoV2 related symptoms such as: fever, diarrhoea, respiratory failure, anosmia and ageusia. All these symptoms manifested 10 to 21 days after diagnosis of SARS-CoV2. These patients were also treated with immunoglobulins, as well as antiretroviral therapy and hydroxychloroquine. Ultimately, two patients died from these studies (5)(6).

In addition, a 2020 study reported that 30% of patients with Guillain-Barré without SARS-CoV2 infection developed respiratory failure and the need for mechanical ventilation. One of the factors associated with respiratory failure is respiratory muscle weakness, with autonomic nerve involvement and progressive bulbar palsy. Patients requiring mechanical ventilation are those with progressive motor deficits and ineffective cough. In these patients, mechanical ventilation is used to prevent aspiration pneumonia and for emergency intubation in cases of life-threatening complications. Early tracheostomy results in improved feeding, oral hygiene and mobilisation of the patient (7).

A study conducted in Tasmania in 2021 showed four clinical cases related to this association of SARS-CoV2 and Guillain-Barré. One case involved a 51-year-old patient who, 2 weeks after receiving the first dose of aztrazenecca vaccine, presented with diplopia, bifacial weakness, diplopia, areflexia, areflexia, quadriparesis, progressing to respiratory failure, and was admitted to the intensive care unit. With evidence of albuminocytological dissociation, the presence of Guillain-Barré was determined, and the patient was managed with immunoglobulins and plasmapheresis. Another case we found was of a 65-year-old patient who, 1 week after his first dose of aztrazenecca vaccine, developed weakness of both lower limbs, which spread to the upper limbs in 1 week. In addition, he presented with diplopia, loss of distal sensation, hypotonia and areflexia, more pronounced in the upper limbs, and respiratory distress requiring intubation. The diagnosis of Guillain-Barré was made by electrophysiology which showed a demyelinating polyneuropathy. After administration of immunoglobulins, a remarkable improvement was evidenced. A third case reported a 72 year old patient who developed a picture of lower limb weakness and loss of sensibility at distal level 3 weeks after administration of the first dose of Aztrazenecca vaccine. The picture evolved with upper limb weakness, quadriparesis with loss of vibration and proprioception, together with sensation of paraesthesia. After demonstrating the presence of albuminocytological dissociation, corresponding to Guillain-Barré, immunoglobulins were administered with considerable improvement. The last case was a 66-year-old patient who developed back pain and bilateral distal paresthesia 1 week after administration of the first Aztrazenecca vaccine. The paraesthesias ascended to the upper limbs, together with right infranuclear facial paralysis, with subsequent development of areflexia and right facial motor weakness. After performing a

lumbar puncture and demonstrating the presence of albuminocytological dissociation, the presence of Guillain-Barré was determined. This patient was administered immunoglobulins, which led to an improvement (8).

A study in 2020 showed that a total of 31 patients were found to have Guillain-Barré after 11.92 days of infection with COVID-19. Symptoms manifested themselves between 3 and 24 days. The mean age was 57.26 years, the most common symptoms were paresthesia in the hands and feet, symmetrical lower limb weakness, facial paralysis, tetraparesis and pain in all 4 limbs. The most frequent variant in these patients was acute inflammatory demyelinating demyelinating polyneuropathy. All patients were given intravenous immunoglobulins (9).

A 2021 study in Israel showed that five patients out of 40 who were previously vaccinated with one dose of BNT162b2 vaccine for COVID-19 developed paraesthesias, tremor and seizures. One of the patients had a history of Guillain-Barré and was managed with plasmapheresis without neurological sequelae. This patient was admitted to hospital after his second dose of COVID-19 vaccine for increasing lower limb weakness and paraesthesias. Plasmapheresis was administered and his improvement was remarkable, although he retained some minimal proximal weakness (10).

A 2020 study in the journal *Clinical Neurology and Neurosurgery* mentions the case of a 60-year-old patient with a history of migraine, who presented with fever, non-productive cough, myalgia and dysgeusia of 10 days' duration. A PCR-RT study was performed with a positive result. She was treated with oxygen, azithromycin and hydroxychloroquine. 22 days after the aforementioned clinical picture, the patient suddenly presented lumbar pain, numbness of the lower limbs and weakness of the same; the picture progressed 48 hours later with increasing weakness of the upper and lower limbs, requiring her to be bedridden in the hospital. The condition progressed with respiratory distress, requiring 8 litres of oxygen per minute. The neurological clinical picture showed grade 2/5 weakness and areflexia in the upper and lower muscle groups. A study of cerebrospinal fluid showed albuminocyte dissociation. Treatment was started with intravenous immunoglobulins at a dose of 0.4 g/kg/day for 5 days together with 30 mg enoxaparin every 12 hours. One week later, the patient's clinical picture improved. Two months later, during clinical follow-up, neurological sequelae, such as persistent neuropathic pain in the lower extremities, became evident (11).

It is important to mention that the interaction between the microorganisms and the host indicates an immune response, which leads to autoreactivity. The undesirable part is the fact that no autoimmunity develops, so it is thought that there are environmental and genetic factors that produce susceptibility in the individual. When it was discovered that there is a link to Guillain-Barré syndrome, it was decided to investigate this factor. However, the pathogenesis remains unknown (12).

In a review that analysed articles up to December 2020, it was determined that the presence of Guillain-Barré in patients with COVID-19 was due to a secondary immune



reaction, as no evidence of the virus was found in cerebrospinal fluid when tested for the presence of SARS-CoV2 virus (13).

A 2021 study found that few cases of this syndrome have been demonstrated following administration of the first dose of COVID-19 vaccines. One of the theories by which it can be concluded that Guillain-Barré syndrome may occur is due to antibody cross-reactivity at the time of immunisation to SARS-CoV2. However, it is estimated that a total of 1 to 2 cases per 100,000 people per year of Guillain-Barré can be found for each dose of COVID-19 vaccine. However, it should be remembered that cases can be caused by other factors independent of vaccination (14)(15).

One review mentions a clinical case of a 76-year-old patient presenting with a 9-day presentation characterised by progressive weakness of all 4 limbs. Two weeks prior to admission, he had received the second dose of CoronaVac vaccine. Physical examination revealed motor weakness of 3/5 in the lower limbs and 4/5 in the upper limbs, accompanied by areflexia. An electromyographic study showed a reduction in the amplitude of the motor and sensory nerves. After treatment with immunoglobulins, the clinical picture evolved favourably (16).

There is another clinical case report of a 12-year-old female patient who presented to the emergency department with weakness in all 4 limbs and a feeling of paraesthesia 2 weeks after receiving the Pfizer COVID vaccine. On physical examination the only complaint was 4/5 muscle weakness in the hip flexors. A PCR test for COVID-19 was performed with negative result. In the cerebrospinal fluid, albuminocytological dissociation was found. Therefore, a diagnosis of Guillain-Barré was made and immunoglobulins were administered intravenously (17).

CONCLUSIONS

Guillain-Barré syndrome is a pathology characterised by viruses, including *Campylobacter jejuni*. This literature review demonstrates that the presence of Guillain-Barré is associated with COVID-19 vaccines. However, it is necessary to mention that the number of clinical cases presented, either by vaccination against COVID-19 or by the presence of COVID-19, is very low. In one of the studies we have mentioned that the number of cases of patients with Guillain-Barré syndrome related to COVID-19 is 220 in total; this number may represent a minority, but we must remember that there is an association between the presence of Guillain-Barré and COVID-19. Finally, this is an important point to note because the presence of the COVID-19 virus cross-reacts and produces this Guillain-Barré syndrome, as can any other virus.

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