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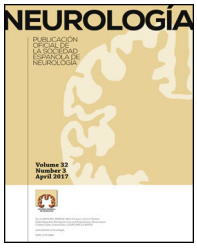

LETTER TO THE EDITOR

Tremor and ataxia in COVID-19☆

Temblor y ataxia en COVID-19

Dear Editor:

In addition to the respiratory syndrome, SARS-CoV-2 infection has also been associated with other manifestations, including neurological symptoms.[1—3] These can be classified into 3 categories:

- Manifestations of central nervous system involvement (dizziness, impaired level of consciousness, headache, acute cerebrovascular disease, ataxia, seizures, etc).
- Manifestations of peripheral nervous system involvement (gustatory and olfactory alterations, vision loss, neuropathic pain, post-infectious polyneuropathy, etc).
- Musculoskeletal symptoms (myalgia, etc).[4]

The literature also includes cases of post-infectious disorders in the context of SARS-CoV-2 infection, including post-infectious acute myelitis, Guillain-Barré syndrome,[5] Miller Fisher syndrome,[6] and acute disseminated encephalomyelitis. In all cases, RT-PCR results were positive for SARS-CoV-2 in nasopharyngeal exudate and negative in CSF. Other authors have reported cases of generalised myoclonus in patients with COVID-19,[7] but no cases of tremor have been reported.

We present the case of a 70-year-old man with personal history of chronic obstructive pulmonary disease. He was evaluated due to fever of 7 days' duration, with no accompanying symptoms. Cardiopulmonary auscultation revealed bibasilar crackles, with no other relevant findings.

Complementary testing showed PO_2 of 49 mm Hg, lymphocytopaenia (0.6×10^9 cells/L), urea 58 mg/dL, fibrinogen 915 mg/dL, D-dimer 716 μg/L, triglycerides 235 mg/dL, and ferritin 1695 ng/mL; chest radiography revealed bilateral pneumonia and PCR testing of nasopharyngeal exudate yielded positive results for SARS-CoV-2. During hospitalisation, the patient was treated with ceftriaxone, azithromycin, hydroxychloroquine, and salbutamol. He also received corticosteroids due to secondary haemophagocytic syndrome.

Seventeen days after symptom onset, the patient progressively developed tremor in the arms and legs, affecting gait; no other focal neurological signs were observed. The examination revealed marked, symmetrical bilateral tremor in all 4 limbs with an orthostatic component, as well as voice tremor; no resting tremor was observed. The patient also displayed gait instability and wide-based stance, probably as a result of the tremor. He did not present truncal ataxia. The Romberg test could not be performed as the patient was unstable while standing due to orthostatic tremor. No other abnormal findings were observed during the examination.

Tremor was initially attributed to corticosteroids and beta-blockers prescribed for COVID-19, but did not improve when these drugs were suspended. Treatment with clonazepam achieved a slight improvement. Brain MRI, serology testing, and a comprehensive laboratory analysis including tests for thyroid hormones, tumour markers, and onconeuronal antibodies all yielded normal results. PCR results from the CSF were negative for SARS-CoV-2, and the CSF analysis detected no alterations.

Respiratory symptoms resolved and ataxia and tremor improved slowly over the first month after discharge.

In the case presented here, tremor started in the context of infection. Our patient had no personal or family history of tremor or gait alterations.

MRI, CSF analysis, and a complete blood test yielded no abnormal findings that may explain his symptoms. Furthermore, symptoms did not improve after withdrawing the medications potentially causing them.

These findings suggest an infectious or parainfectious aetiology. PCR results from the CSF were negative for SARS-CoV-2; however, by the time this test was conducted, the patient had already tested negative in a nasopharyngeal exudate sample.

Parainfectious ataxia is an autoimmune process triggered by a clinical or subclinical infection or vaccination.[8] The immune pathogenic mechanisms are similar to those of such other parainfectious diseases as Guillain-Barré syndrome, Miller Fisher syndrome, and acute disseminated encephalomyelitis, all of which have already been reported in patients with SARS-CoV-2 infection.[5,6]

While the diversity, frequency, and causes of many of the neurological manifestations of SARS-CoV-2 infection are yet to be determined, the available evidence suggests that the virus may even cause parainfectious disorders associated with neurological symptoms.

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We present a patient with ataxia and tremor in the context of COVID-19, an association not previously reported. More data from cases with similar characteristics are needed to establish a causal relationship between SARS-CoV-2 infection and these symptoms. In any case, our report contributes further evidence of the potential role of the virus in the development of neurological symptoms.

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The future of neurorehabilitation after the SARS-CoV-2 pandemic☆

Futuro de la neurorrehabilitación tras la pandemia por el SARS-CoV-2

Dear Editor:

The novel coronavirus SARS-CoV-2, causing coronavirus disease 2019 (COVID-19), emerged in the Chinese province of Hubei in December 2019. The epidemic outbreak in China rapidly spread over a period of months into the current pandemic, which has changed the lives of the world's population.[1]

Like other respiratory viruses, SARS-CoV-2 initially affects the respiratory system. Among other reasons, its high morbidity and mortality rates are explained by the exaggerated inflammatory response triggered in many patients, as it is a novel pathological agent for immune systems.

Little is known about the disease today, but the unprecedented efforts made in scientific research and publishing have enabled us to expand our knowledge of the condition over the past 3 months. However, although it is still too soon to know the long-term consequences, we already know that the disease affects many systems.[1] While the cardiovascular system was one of the first systems to be studied, the neurological system is not one of the least affected.[2]

Considerable prevalence of neurological complications has been reported (45% to 48%, depending on the methods used, in the few studies published to date). Complications affect both the central nervous system (confusional syndromes, stroke, encephalopathies, encephalitis, secondary epilepsy, etc) and the peripheral nervous system (critical illness polyneuropathy, Guillain-Barré syndrome, cranial neuropathies, etc.), with associated muscular disease (critical illness myopathy).[2–5] Neurological sequelae are not limited to the functional level (loss of ventilatory/pulmonary capacity, generalised weakness and postural problems, secondary pain) but also include dysphagia, dysexecutive syndrome, apraxia, cognitive impairment, and such psychiatric disorders as depression, anxiety, and post-traumatic stress disorder, among others.[6]

As with other respiratory viruses, several hypotheses are emerging around the pathway by which it enters the central nervous system. It may enter through a trans-synaptic pathway involving the vagus nerve, which innervates the lower respiratory tracts, through the nasal epithelium and olfactory nerve; and/or through the haematogenous pathway, crossing the blood-brain barrier. Neurological involvement is likely to be caused by 2 mechanisms: hypoxic brain lesions and immune-mediated damage caused by the cytokine storm.[2]

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