

Neurological Manifestations of COVID-19: A Brief Update on the Cuban Context

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ABSTRACT

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Introduction

Despite of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is considered a respiratory virus, several neurologic manifestations can appear during acute COVID-19 [1]. At present, the increasing number of patients hospitalized with coronavirus disease involving the nervous system has attracted extensive attention, because of the short and long-term impact that it could represent on population health worldwide [2]. But certainly, it is too early to know accurately how to identify and manage appropriately these manifestations. Precise and targeted documentation of the neurological symptoms and signs of the cases and autopsies of the victims, may clarify the roles played by this pathogen in causing nervous system compromise [3]. Wide spectrums of neurological troubles related to COVID-19 are recently reported [4]. Clinical experience with this ill in different countries has shown some initial neurological abnormalities such as: headache, dizziness, convulsions, pathological wakefulness after sedation, confusion, alteration of consciousness, gustatory/olfactory disorders, spatial disorientation, neuromuscular disturbances, agitation and cognition impairment [5]. It has been suggested that SARS-CoV-2

neuroinvasion, neuroinflammation and impairment of the Blood Brain Barrier (BBB) are responsible for the neurological symptoms in humans [6].

These new properties exhibited by the virus are due to the occurrence of pathophysiological mechanisms that are not well understood yet. This picture is actually known in most of studies like Neuro-COVID and it can be divided in early and late clinically. It depends on variables associated with the timely medical attention, the virus strain and also with the hosts features like age, genetic background, comorbidities, sex and geographical location [6]. The most common neurological complications fell into three categories [7]

- a) Central Nervous System (mostly inflammation-mediated): headache, delirium, seizures, infectious toxic encephalopathy, acute encephalitis, meningitis, cerebrovascular accidents and dysexecutive syndrome.
- b) Peripheral Nervous System (mostly immune-mediated): dysosmia/anosmia, dysgousia/agousia, acute myelitis,

Guillain-Barre syndrome, Miller Fisher syndrome, Polyneuritis cranialis; and

c) Musculoskeletal (direct injury): atonia y paresis.

A considerable number of investigations have reported the presence of SARS-CoV-2 in the CSF (Cerebrospinal Fluid) and postmortem brain tissue of COVID-19 patients with encephalitis. However, there are contradictory findings that may indicate that the neurological complications are due to severe systemic inflammation and not the direct invasion of the brain. It has been suggested that pathogen could invade the CNS (Central Nervous System) via hematogenous route through the binding to its receptors on BBB endothelial cells, passing across them (which do not involve any viral replication) by transcytosis and finally reaching the brain. The other proposed mechanism involves infecting immune cells that express ACE2, such as monocytes, granulocytes, and lymphocytes (Trojan horse" mechanism) [8]. The infected immune cells may then carry SARS-CoV-2 to the CNS, where it can infect the brain; however, viral replication in this kind of cells needs to be confirmed. Another mechanism consists in passing through disrupted endothelial cells' tight junctions (paracellular route). The virions may also reach the CNS via peripheral nerves, more specifically the olfactory sensory neurons. The high expression of ACE2 and the priming protease Transmembrane Serine Protease 2 (TMPRSS2) in sustentacular cells and stem cells of the olfactory epithelium and olfactory bulb, may allow for retrograde or antegrade transport into the CNS [8]. There is an urgent need to understand the pathophysiology of these disorders and develop disease-modifying therapies [1].

Early in the COVID-19 pandemic, patients have described lingering syndromes following acute infection, now called Long Covid. These syndromes often include predominant neurologic and psychiatric symptoms, like difficulty with memory, concentration and ability to accomplish everyday tasks, frequent headaches, alterations in skin sensation, autonomic dysfunction, intractable fatigue, delusions and paranoia in severe cases. This has raised the possibility that infection may accelerate or trigger future development of neurodegenerative diseases such as Alzheimer's or Parkinson's maladies. It is emphasizing that many people who experience Long Covid are less than 50 years old and were healthy and active prior to infection [1]. No information is yet available regarding neurodevelopmental trajectories in children, who usually experience mild COVID-19 and manifest few neurologic or psychiatric symptoms during or after acute illness. During the last two years, the Institute of Neurology and Neurosurgery of Cuba carried out studies on the neurological manifestations in convalescents from COVID-19 in Havana [9]. The objective was to evaluate the percentage of patients who suffered from this type of clinical picture, its intensity and possible persistence. Investigations

of the effects were made through a retrospective survey in a mobile application designed by the Cybernetics Department of the Neuroscience Center of the country. In addition, brain electrical activity was explored through electroencephalography and some questionnaires were applied to determine the psychiatric alterations associated with COVID-19.

The inquiries were made in a language understandable to the patients in order to specify the alterations of the nervous system. Participants with neurological evidence prior to infection with SARS-CoV-2 were excluded from the study. The analyses showed a high frequency of symptoms such as headaches and loss of taste/smell and chronic fatigue, diarrhea and cardiac arrhythmias were declared as occasional. In 2020, a high incidence of visual damage was found, since 20% of the individuals testified a decrease in visual acuity and 30% had dizziness related to the infection [9]. It should be noted that in both years, a high number of these alterations were notified in individuals who suffered from mild symptoms, even completely asymptomatic. Regarding to the residual manifestations, the persistence time is still not clearly known. Another study took place at the Pedro Kourí Institute of Tropical Medicine to measure the impact of SARS-CoV-2 infection; this time, it was demonstrated that neurological sequelae were the most frequent in the convalescent's egresses from the institution. After recovery, the patients exhibited sleep and adjustment disorders, nervousness, anxiety, depression and chronic fatigue [10].

Based on the follow-up of the cases that manifested severe and critical stages, the persistence of neurological complications was confirmed up to six months after the onset of the disease (Long Covid). The results of the project also made possible to characterize the immunological behavior and to find evidence regarding to the future of Cuban anti-COVID-19 vaccines. In the case of the pediatric population in Cuba, some usual neurological alterations have been described, such as: encephalitis, excitability and lack of concentration. In January 2021, around 93% of all convalescents in the country had been fully evaluated [11]. The consultations with the highest attendance were pneumology and physiotherapy, which covered 50% of the cases respect to those of nephrology, cardiology, psychology and psychiatry. Currently the care protocol in these cases covers fourteen specialties.

Final Considerations

The unpredictable nature of the convalescence stage can be declared with complete certainty, since COVID-19 is a disease about which we still do not know more than we do. This occurs because the first cases recovered have just a few months, which is a little time to have a comprehensive vision and make an effective description of the stage. In this sense, the health system in Cuba,

in addition to the multidisciplinary care and treatment of patients in acute periods of the disease, focuses on identifying and treating sequelae that persist during convalescence. In relation to early and late neurological manifestations, there is evidence of an increase in diagnoses worldwide. Taking into account the negative impact of these complications, a call for self-care and social responsibility is made in order to stop the spread of the pandemic.

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Competing Interests

The authors do not declare competing interest.

Author's Contribution

All authors have actively participated in the writing and critical review of the final version of this scientific paper.

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