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CASE REPORT

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Can COVID-19 accelerate neurodegeneration?

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Abstract

COVID-19 may accelerate neurodegeneration in patients with neurodegenerative disease.

KEYWORDS

COVID-19, neurodegeneration, parkinsonism

Coronavirus disease-19 (COVID-19) was primarily recognized in Wuhan, China, in early December 2019. Preclinical studies have been shown that SARS-CoV through the olfactory bulb can spread to brain, and resulting in substantial neuronal infection in SARS-CoV receptor transgenic mice. Current researches correspondingly revealed that SARS-CoV-2 is more contagious than SARS-CoV. Therefore, the high similarity between SARS-CoV-2 and the aforementioned generations of SARS and MERS coronaviruses advocates that SARS-CoV-2 can attack the nervous system.[1] SARS-CoV-2 infection can trigger extreme inflammation and immune responses which may accelerate the evolution of inflammatory neurodegeneration in the brain among the elderly.[2]

Herein, we report a case with rapidly progressive parkinsonism during the COVID-19 pandemic.

A 67-year-old right-handed man was referred to our movement disorders centers 4 months after the COVID-19 pandemic get started in Iran. In March 2020, he had had several episodes of falls after changing position from sitting to standing, dry mouth and skin, tachycardia, and constipation, then bradykinesia was added to his symptoms and he received levodopa/carbidopa 600/150mg which caused hallucination and the patient did not take it anymore. At that time, systemic evaluation, chest CT, and SARS-CoV-2 PCR were negative. His neurological examination showed intact cognition, eye movements were normal, he had mild bilateral action tremor on his hands, severe rigidity on limbs, severe generalized bradykinesia, and pizza sign, and he could not walk without support, and while walking his gait was wide-based. Sensory and motor examination was unremarkable; he did not have appendicular ataxia. Besides, he had orthostatic hypotension, and his systolic pressure dropped (systolic blood pressure 30 mmHg and diastolic 20 mmHg) after changing position from lying to sitting, he could not stand for three minutes to check blood pressure. Brain MRI including DWI sequence did not show any abnormalities, and routine laboratory tests came back negative. The electroencephalogram was normal. EMG-NCS did not show any abnormal findings, and paraspinal muscle needle EMG did not reveal continuous muscle activity. CSF RT-QuIc for sporadic Creutzfeldt-Jakob (SCJ) and 14.3.3 proteins were negative. An autoimmune panels including Glutamate Receptors, DPPX, AMPA1/2 (GluR1/GluR2), LGI1, CASPR2, GABA RB1/2, Amphiphysin, Recoverin, PNMA2 (Ma2/Ta), AGNA (Sox1), Anti CRMP5 (CV2), titin, Ri/ ANNA-2, Zic4, Yo/PCA-1, GAD65, Hu/ANNA-1, and PCA-Tr (DNER) were checked on CSF and blood, and all were negative. Work-ups for malignancy including whole-body scan, chest and abdominal CT scan did not

show any pathology. SARS-CoV-2 PCR has been checked several times during the last four months but was negative. He received Levodopa/benserazide 150/37.5 mg and gradually increased to 300/75 mg and lead to mark improvement, and he could walk with a cane afterward, but urge incontinence was added to his symptoms. Brain MRI was done again and did not show any change from the previous one. After four months due to malaise, SARS-CoV-2 PCR has been checked and was positive; therefore, the patient took conservative management at home and recovered. He did not experience anosmia or respiratory symptoms. But his parkinsonism got worsened subsequently, and he could not walk independently. In addition, he suffered from hallucination and cognitive decline. Laboratory workups including inflammatory markers (CRP, ESR, blood count, etc) did not show any abnormalities. Unfortunately, after two months in January 2021, he had a cardiac arrest and died.

Though we know more about the acute presentation of the ongoing COVID-19 pandemic, the long-term consequence of this virus is yet to be understood.[3]

A case of Creutzfeldt-Jakob disease has been reported whose first manifestations arose in tandem with the symptomatic onset of COVID-19.[4] Also, we reported a case of parkinsonism which had a rapidly progressive course after getting COVID-19 infection. So, it can be hypothesized that COVID-19 can accelerate neurodegeneration.

Neurodegeneration might be the consequence of neuroinflammation accompanying COVID-19. Receptors of ACE2 are expressed in astrocytes among brain stem and cerebellum and may attack by SARS-CoV-2 infection. An axonal protein called neurofilament light chain (NfL) is released as a consequence of axonal damage and axonal neurodegeneration, whereas neurofilament light chain (GFAP) is stated in astrocytes and it is noticeably upregulated during CNS inflammation. Severe infection with COVID-19 meaningfully increases the plasma concentrations of GFAP and NfL, and GFAP was also amplified in modest COVID-19 infection. It was suggested that astrocytosis (astrocytes activation) possibly will be a distinctive feature of infection with COVID-19.[2] Autoimmune response against α-synuclein is another mechanism, which by assumed to cause long-term neuronal changes.[3] Even though the etiology of PD is still unclear, neuroinflammation in dopaminergic neurons can be a possible cause.[5] A study was done during COVID-19 pandemic showed that anxiety is more prevalent among patient with PD in this era[6]; therefore, increased psychological stress may have a role to accelerate neurodegeneration.

Although the correlation between viral infections and PD is yet to be known, a relation between the "Spanish flu" (1918–1920) and the lethargic encephalitis epidemic of 1916 to 1926 has been shown in history.[7]

We are facing a new pandemic in which its long-term neurological outcome is still unclear, and follow-up studies need to disclose this association.

AUTHOR CONTRIBUTIONS

MS: Conception, Organization, Execution, Writing the first draft. ME: Execution, Review and critique.

ETHICAL STATEMENT

The study was approved by ethical committee of Shahid Beheshti University of Medical Science, and informed consent form was taken from patient's family.

DATA AVAILABILITY STATEMENT

Data are available on request.

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