Invited Editorial

Being aware of the neurological manifestations of COVID-19 infection

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The novel coronavirus disease-2019 (COVID-19) was first reported from China, but is unfortunately no longer restricted and has spread over all geographic areas.[1] The main symptoms of COVID-19 infection are respiratory tract related. Infected patients usually have symptoms such as fever, sore throat, and fatigue, and they may have atypical symptoms like headache, seizures, anosmia, stroke, and even impaired consciousness.[2,3] Although most patients with COVID-19 have a mild or moderate illness, up to 5-10% have a life-threatening disease course, with a mortality rate of about 2%.[4] Strong evidence of an association between COVID-19 infection and neurological manifestations has been reported.[5] Besides, the neurologic manifestations may be the initial presentation of COVID-19 infection.[6]

Although it is now accepted that neurological involvement and complications may accompany, studies on this topic are being added to the literature every day. One of the most extensive systematic reviews about neurological manifestations of COVID-19 infection involved 6335 patients from 49 studies. Acute ischemic and hemorrhagic strokes or cerebral sinus venous thrombosis were the most common neurological complications, whereas headache, dizziness, nausea, vomiting, and confusion were the most common neurological symptoms. Encephalopathy, encephalitis, oculomotor nerve palsy, anosmia, and Guillain-Barré syndrome were the other COVID-19 relevant neurological disorders.[5]

While there have been attempts to explain the increased stroke rates in COVID-19 patients by hypercoagulopathy that may have been induced by inflammation, this issue remains open to research.[7] Other neurological findings can be explained by the passage of infected leukocytes through the blood-brain barrier or the direct olfactory pathway of the neurotropic virus.[8] Once the body is in contact with the virus, a cytokine storm can be triggered by a dysregulated immune host response. This cytokine storm may lead to neurological diseases such as encephalitis or acute necrotizing encephalopathy.[9] With disseminated intravascular coagulation arterial and venous thromboembolic phenomena in the severely ill COVID-19 patients have been reported.[10] Also isolated sudden onset of anosmia has been reported as an early symptom of COVID-19 infection. The interesting point is that COVID-19 patients can have anosmia without signs of nasal obstruction and rhinorrhea. Whether this is caused by damage to epithelial tissue or by retrograde transmission to the central nervous system is not clear yet.[11]

Despite extensive data on typical respiratory signs of COVID-19 infection, radiological data on neurological signs that may accompany or may be an initial finding are still lacking. In addition, many patients have not been evaluated by imaging and some have normal imaging findings. It is also difficult to obtain imaging, especially for patients in intensive care units.

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The fact that patients with neurological findings or with worsening conditions during follow-up have been reported increasingly, awareness of complications such as stroke, encephalitis, and seizures, which are of vital importance, raises the importance of brain imaging and the role of the radiologist in terms of not only the detection of pulmonary infection findings but also brain involvement.

At the beginning of the pandemic, people were asked not to visit hospitals, unless it was required, in our country as in the whole world, according to the restrictions and recommendations of the Health Ministry and social media to avoid COVID-19 transmission and preserve hospital capacity. As a consequence, we observed a decrease in both the number of hospital admissions and imaging. This situation, which we initially observed in non-COVID hospital admissions, has gained a different dimension in this dynamic period where varied data are constantly flowing. With the increasing cases of COVID-19 infection, a significant rise in the number of inpatients and intensive care patients was observed. In our practice, one of Turkey's largest university hospitals, we also observed stroke, spontaneous intracerebral hemorrhage, meningitis, encephalitis, and signal intensity changes among imaging modalities. We experienced that the most common neurological complication was stroke and that both hemorrhagic and ischemic strokes could be seen. Considering that minimal or transient neurological findings such as transient ischemic attack (TIA) can be neglected by patients and overlooked by clinicians, it is expected that we have seen more frequent stroke complications caused by large vessel occlusions. Also, patients referred to the radiology department with a prediagnosis of headache, anosmia, tremor, movement disorders, and seizures were evaluated for any abnormality on computed tomography (CT) or magnetic resonance (MR) imaging. Nevertheless, most of the patients with these symptoms did not show abnormal findings on imaging.

Although the justification of neurovirulent potential seems to be speculative, the referring clinicians and radiologists should consider the possibility of central nervous system transmission and its possible sequelae in COVID-19 patients with neurological symptoms. Although the reasons for the tendency to thromboembolism and stroke, and also to the neurological manifestations are still not obvious, both the clinicians and radiologists should be aware of this possibility. The necessity of imaging of the brain is essential for an exact diagnosis. Regardless of any direct or indirect neurological manifestations, the COVID-19 pandemic has a huge impact on the management of neurological patients. Using a global network with standardized protocols and common data elements is critical to facilitate further studies to understand COVID-19 neurological manifestations.

REFERENCES

1. Zhu N, Zhang D, Wang W, et al. A novel coronavirus from patients with pneumonia in China, 2019. N Engl J Med 2020;382:727-33. doi: 10.1056/NEJMoa2001017.
2. Guan WJ, Ni ZY, Hu Y, et al. on behalf of the China Medical Treatment Expert Group for Covid-19. Clinical characteristics of coronavirus disease 2019 in China. N Engl J Med 2020;382:1708-20. doi: 10.1056/NEJMoa2002032.
3. Jiang F, Deng L, Zhang L, Cai Y, Cheung CW, Xia Z. Review of the clinical characteristics of coronavirus disease 2019 (COVID-19). J Gen Intern Med 2020;35:1545-9. doi: 10.1007/s11606-020-05762-w.
4. Gavriatopoulou M, Ntanasis-Stathopoulos I, Korompoki E, et al. Emerging treatment strategies for COVID-19 infection. Clin Exp Med 2021;21:167-79. doi: 10.1007/s10238-020-00671-y.
5. Collantes MEV, Espiritu AI, Sy MCC, Anlacan VMM, Jamora RDG. Neurological manifestations in COVID-19 infection: a systematic review and meta-analysis. Can J Neurol Sci 2021;48:66-76. doi: 10.1017/cjn.2020.146.
6. Singhania N, Bansal S, Singhania G. An atypical presentation of novel coronavirus disease 2019 (COVID-19). Am J Med 2020;133:e365-e6. doi: 10.1016/j.amjmed.2020.03.026.
7. Katal S, Balakrishnan S, Gholamrezanezhad A. Neuroimaging and neurologic findings in COVID-

19 and other coronavirus infections: a systematic review in 116 patients. J Neuroradiol 2021;48:43-50. doi: 10.1016/j.neurad.2020.06.007.

8. Mankad K, Perry MD, Mirsky DM, Rossi A. COVID-19: a primer for neuroradiologists. Neuroradiology 2020;62:647-8. doi: 10.1007/s00234-020-02437-5.
9. Mehta P, McAuley DF, Brown M, et al. on behalf of the HLH Across Speciality Collaboration, UK. COVID-19: consider cytokine storm syndromes and immunosuppression. Lancet 2020;395:1033-4. doi: 10.1016/S0140-6736(20)30628-0.
10. Ma J, Xia P, Zhou Y, et al. Potential effect of blood purification therapy in reducing cytokine storm as a late complication of critically ill COVID-19. Clin Immunol 2020 ;214:108408. doi: 10.1016/j.clim.2020.108408.
11. Aghagoli G, Gallo Marin B, Katchur NJ, Chaves-Sell F, Asaad WF, Murphy SA. Neurological involvement in COVID-19 and potential mechanisms: a review. Neurocrit Care 2020:1-10. doi: 10.1007/s12028-020-01049-4.