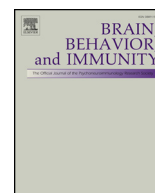




Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Elsevier hereby grants permission to make all its COVID-19-related research that is available on the COVID-19 resource centre - including this research content - immediately available in PubMed Central and other publicly funded repositories, such as the WHO COVID database with rights for unrestricted research re-use and analyses in any form or by any means with acknowledgement of the original source. These permissions are granted for free by Elsevier for as long as the COVID-19 resource centre remains active.



Letter to the Editor

The neuroinvasive potential of severe acute respiratory syndrome coronavirus 2

To the Editor:

Recently, we read with greatest interest the article by Wu et al (Wu et al., 2020), who reviewed the neurological manifestations of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection and the possible mechanisms. We sincerely appreciate the immense achievement they make, however, some aspects of the neuroinvasive potential of SARS-CoV-2 still need to be discussed.

Like it was described for other human coronavirus, SARS-CoV-2 mainly invaded respiratory tract, which had already been demonstrated by previous clinical practice and pathological findings (Xu et al., 2020). Although there is widely accepted that human coronavirus, including SARS-CoV-1 that emerged in China in the late 2002, have neuroinvasive capacities based on both animal models and human studies, the properties of SARS-CoV-2 to invade and infect CNS remains controversial.

In general, virus with neuroinvasive potential could invade CNS cell through transneuronal route, or hematogenous route, or both, as a result of viral encephalitis and various neurological disorders, and the infection of CNS is finally confirmed by laboratory examinations (Desforges et al., 2014). In the early March 2020, medical workers from Beijing Didan Hospital reported the first case of coronavirus disease 2019 (COVID-19) with encephalitis whose cerebrospinal fluid (CSF) tested positive for SARS-CoV-2, raising the concern that SARS-CoV-2 might spread from respiratory tract to CNS. Since then, increasing number of attention are given to the neuroinvasive potential of SARS-CoV-2. However, to the best of our knowledge, it is currently the only case of SARS-CoV-2 infection with positive findings in CSF. A retrospective consecutive case series indicated 78 of 214 patients presented neurological symptoms, including central nervous system (CNS) symptoms (e. g. headache, dizziness), peripheral nervous system (PNS) impairments (e. g. taste impairment, smell impairment), and skeletal muscular injury (Mao et al., 2020).

It is difficult to draw strong conclusions since the CSF findings of 214 patients were not available, and it is unclear that whether these specific and nonspecific symptoms (e. g. headache) were a systemic inflammatory response or neurological disorders itself. Apart from symptoms, the evidence of neurological sign, particularly meningeal irritation sign, is equally essential regarding the neurological manifestations of COVID-19, which was lack to date based on the reported studies. In this light, previous studies do not provide a valid evidence

for the neuroinvasive potential of SARS-CoV-2, and much is left to be learned with thorough neurologic testing in large series with COVID-19 or animal models.

Despite of the controversy, we completely agree that the authors suggest caution when one patient with COVID-19 presents neurological symptoms and signs.

Funding

The current work has no funding.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.bbi.2020.05.079>.

References

- Desforges, M., Le Coupanec, A., Stodola, J.K., Meessen-Pinard, M., Talbot, P.J., 2014. Human coronaviruses: viral and cellular factors involved in neuroinvasiveness and neuropathogenesis. *Virus Res.* 194, 145–158.
- Mao, L., Jin, H., Wang, M., Hu, Y., Chen, S., He, Q., Chang, J., Hong, C., Zhou, Y., Wang, D., Miao, X., Li, Y., Hu, B., 2020. Neurologic Manifestations of Hospitalized Patients With Coronavirus Disease 2019 in Wuhan, China. *JAMA Neurology*.
- Wu, Y., Xu, X., Chen, Z., Duan, J., Hashimoto, K., Yang, L., Liu, C., Yang, C., 2020. Nervous system involvement after infection with COVID-19 and other coronaviruses. *Brain and Immunity Behavior*.
- Xu, Z., Shi, L., Wang, Y., Zhang, J., Huang, L., Zhang, C., Liu, S., Zhao, P., Liu, H., Zhu, L., Tai, Y., Bai, C., Gao, T., Song, J., Xia, P., Dong, J., Zhao, J., Wang, F.-S., 2020. Pathological findings of COVID-19 associated with acute respiratory distress syndrome. *Lancet Respir. Med.* 8, 420–422.

Tong Sun, Junwen Guan, Chao You
 Department of Neurosurgery, West China Hospital, Sichuan University,
 Chengdu, Sichuan, PR China
 E-mail address: guanjunwen_scu@outlook.com (J. Guan).