



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.

In Response to the Letter to the Editor Regarding “Acute Hemorrhage After Intra-cerebral Biopsy in COVID-19 Patients: A Report of 3 Cases”



We appreciate the interest of, and valuable suggestions from, Munakomi et al.¹ regarding our recently reported study “Acute Hemorrhage After Intracerebral Biopsy in COVID-19 Patients: A Report of 3 Cases.”

In their letter, Munakomi et al.¹ rightly emphasized the necessity for preoperative screening of patients with coronavirus disease 2019 (COVID-19) to identify those patients prone to hemorrhagic complications after neurosurgical interventions. They discussed the 3 stages of NeuroCOVID, described by Fotuhi et al.² NeuroCOVID stage I, in which the binding of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is limited to the angiotensin-converting enzyme II receptors in the nasal and gustatory cells, can lead to impairment of smell or taste, without a significant cytokine storm.² Fotuhi et al.² referred to stage II as the phase in which an immune response is activated that subsequently leads to increased cytokines and hypercoagulation cascades. During NeuroCOVID stage III, the blood–brain barrier will become damaged, resulting in edema and brain injury and potentially leading to encephalopathy. At stage III, the risk of intracranial hemorrhage is at its highest.²

The findings from postmortem brain magnetic resonance imaging analyses and autopsies, recently conducted at our center, have supported this theory. Analyses of postmortem brain magnetic resonance imaging studies have demonstrated macro- and micro-subcortical bleeding, asymmetric olfactory bulbs, and posterior reversible encephalopathy syndrome–related brain lesions in patients who had died of COVID-19.³ No specific brainstem abnormalities were found. In addition, 11 brain autopsy reports revealed cerebral hemorrhage in 8 patients, focal ischemic necrosis in 3 patients, edema in 5 patients, and diffuse or focal spongiosis in 10 patients.⁴ No evidence of viral encephalitis was found. Real-time reverse-transcription polymerase chain reaction tests showed the presence of SARS-CoV-2 in 9 of the 11 cerebral samples.⁴

Munakomi et al.¹ proposed the assessment of anosmia and ageusia and the examination of the viral load of SARS-CoV-2 in the cerebrospinal fluid (CSF) to screen for high-risk patients. However, we believe that careful interpretation is needed when assessing these data.

We do agree with the importance of a preoperative check for symptoms such as fever, cough, shortness of breath, anosmia, ageusia, and other neurological symptoms. The presence of alterations in olfactory and taste function is, however, not limited to NeuroCOVID stage I. It is crucial to realize that patients with COVID-19 can present with a variety of immune-mediated neurological symptoms but that other underlying etiologies could still be present and have resulted in their neurological conditions.²

Second, SARS-CoV-2 CSF analysis has been proposed by Munakomi et al.¹ Several cases of SARS-CoV-2–triggered immune-

mediated encephalopathy or meningitis have been reported. Three cases were found with a positive PCR test from a SARS-CoV-2 CSF analysis.^{5,6} Nonetheless, such analyses were negative for 9 reported cases of COVID-19 associated with encephalopathy and meningitis.^{7–9} Al Saiegh et al.¹⁰ described 1 case of a subarachnoid hemorrhage due to a ruptured aneurysm and a second case of an ischemic stroke with massive hemorrhagic conversion. However, the SARS-CoV-2 CSF analysis was negative for both cases.

From the currently available reported data, we have concluded that the value of SARS-CoV-2 CSF analysis should be limited to screening for neurotropism among patients with COVID-19 requiring neurosurgical intervention. Whether the presence of SARS-CoV-2 in the CSF is related to an advanced NeuroCOVID stage should be subjected to further examination to obtain a comprehensive understanding regarding the role of SARS-CoV-2 CSF analysis in screening patients with COVID-19 requiring neurosurgical intervention. Until then, high degree of vigilance is recommended.

Aurélie Degeneffe, Olivier De Witte, Alphonse Lubansu

Department of Neurosurgery, Erasmus Hospital, Brussels, Belgium

To whom correspondence should be addressed: Aurélie Degeneffe, M.D.

[E-mail: aurelie.degeneffe@erasme.ulb.ac.be]

Conflict of interest statement: The authors declare that the article content was composed in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

<https://doi.org/10.1016/j.wneu.2020.07.045>

REFERENCES

- Munakomi S, Bharati K. Letter to the editor regarding “acute hemorrhage after intracerebral biopsy in COVID-19 patients: a report of 3 cases”. *World Neurosurg.* 2020;141:558.
- Fotuhi M, Mian A, Meysami S, Raji CA. Neurobiology of COVID-19. *J Alzheimer Dis.* 2020;76:3-19.
- Coolen T, Lolli V, Sadeghi N, et al. Early postmortem brain MRI findings in COVID-19 non-survivors [e-pub ahead of print]. *Neurology* <https://doi.org/10.1212/WNL.0000000000010116>, accessed June 25, 2020.
- Remmelink M, De Mendoca R, D’Haene N, et al. Unspecific post-mortem findings despite multiorgan 1 viral spread in COVID-19 patients [e-pub ahead of print]. *medRxiv* <https://doi.org/10.1101/2020.05.27.20114363>, accessed June 25, 2020.
- Moriguchi T, Harii N, Goto J, et al. A first case of meningitis/encephalitis associated with SARS-Coronavirus-2. *Int J Infect Dis.* 2020;94:55-58.
- Li YC, Bai WZ, Hashikawa T. Response to commentary on “the neuroinvasive potential of SARS-CoV-2 may play a role in the respiratory failure of COVID-19 patients”. *J Med Virol.* 2020;92:707-709.
- Ye M, Ren Y, Lv T. Encephalitis as a clinical manifestation of COVID-19. *Brain Behav Immun.* 2018;74:28-42.
- Yin R, Feng W, Wang T, et al. Concomitant neurological symptoms observed in a patient diagnosed with coronavirus disease 2019 [e-pub ahead of print]. *J Med Virol* <https://doi.org/10.1002/jmv.25888>, accessed June 25, 2020.
- Helms J, Kremer S, Merdji H, et al. Neurologic features in severe SARS-CoV-2 infection. *N Engl J Med.* 2020;382:2267-2268.
- Al Saiegh F, Ghosh R, Leibold A, et al. Status of SARS-CoV-2 in cerebrospinal fluid of patients with COVID-19 and stroke. *J Neurol Neurosurg Psychiatry.* 2020;91:846-848.