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.

Letter to the Editor Regarding "Battle-Tested Guidelines and Operational Protocols for Neurosurgical Practice in Times of a Pandemic: Lessons Learned from COVID-19"

Letter:

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is increasingly associated with multiorgan disease, including the potential involvement of the central nervous system.[1] We read with great interest the article by Al Saiegh et al.[2] recently published in **WORLD NEUROSURGERY** on the need to have strict protocols to provide safe and efficient neurosurgical care in the 2019 novel coronavirus disease (COVID-19) pandemic era. The prothrombotic state caused by SARS-CoV-2–induced inflammation of the vascular epithelium would seem to be responsible for the ischemic strokes in COVID-19, especially in young adults and affecting the great vessels.[3] As many young adults with COVID-19 who have experienced stroke had other cardiovascular risk factors, such as diabetes and hypertension, it is essential to emphasize the role of comorbidities, especially in the case of rare diseases such as moyamoya disease.

Stroke related to moyamoya has been anecdotally reported in association with new SARS-CoV-2 infection. Ghosh et al.[4] reported a 19-year-old woman with SARS-CoV-2 infection who presented with thalamic hemorrhage and acute cognitive impairment, unmasking moyamoya angiopathy. Children and adolescents with moyamoya disease have a fragile hemodynamic balance, and many conditions can worsen their symptoms, such as dehydration, systemic hypotension, infection, emotional outburst, increased body temperature, and crying.

SARS-CoV-2 infection is associated with hemodynamic stress, emotional disruption, and multisystem inflammatory syndrome in children.[5] These conditions could act as powerful ischemic stroke triggers in children and young adults with moyamoya. Moreover, adults with moyamoya angiopathy usually present with intracerebral hemorrhage because of the development of microaneurysms as a result of long-standing hemodynamic stress on the fragile moyamoya collaterals.

In the era of the COVID-19 pandemic, as pediatric neurosurgeons involved in the care of moyamoya patients, many questions arise regarding what to do in the case of patients, especially children and young adults, with moyamoya and SARS-CoV-2 infection, as follows:

- What is the real risk of stroke in this subpopulation of patients in case of infection?
- Is there a need to change therapy (aspirin vs. heparin) or to add heparin in symptomatic patients with moyamoya in whom SARS-CoV-2 is diagnosed? Does the age of the patients play a role in the therapeutic protocol?
- Should there be distinct therapeutic protocols for patients who have undergone revascularization and for patients awaiting revascularization? Is there a difference in patients with moyamoya-associated aneurysms?
- Is there a difference between patients with a primary diagnosis of moyamoya disease and patients with moyamoya secondary to other pathologies (neurofibromatosis type 1, Down syndrome, post-radiotherapy)?
- Should surveillance be increased in patients with moyamoya?
- In the case of SARS-CoV-2 infection, nonspecific symptoms such as headache and dizziness could be signs of increased hypoperfusion; is it correct to define these patients as paucisymptomatic?
- In the case of SARS-CoV-2 infection in patients with moyamoya, what could be the long-term consequences of disease progression? Could we see an acceleration in the process?

Practical guidelines and protocols for the care of COVID-19–positive patients with moyamoya need to be developed. Given the current high prevalence of SARS-CoV-2, dedicated triage protocols must be implemented to allow rapid access to patients with rare diseases such as moyamoya who have an increased risk of neurological complications in case of neurological signs and symptoms. Owing to the rarity of moyamoya disease, especially in Western countries, a global registry of patients with COVID-19 neurological manifestations such as Global Consortium Studies of Neurological Dysfunction in COVID-19 (GCS-NeuroCOVID)[6] is essential, and its importance must be emphasized. A global registry has both clinical and basic research implications. It enables us to increase our knowledge of rare diseases, and it could provide useful information about the etiopathology of moyamoya, such as the role of the inflammatory response in the progression of the disease.

CRediT AUTHORSHIP CONTRIBUTION STATEMENT

Giuseppe Mirone: Conceptualization, Writing - original draft, Writing - review & editing. **Giuseppe Cinalli:** Conceptualization, Writing - original draft, Writing - review & editing.

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REFERENCES

1. Ellul MA, Benjamin L, Singh B, et al. Neurological associations of COVID-19. *Lancet Neurol*. 2020;19:767-783.
2. Al Saiegh F, Mouchtouris N, Khanna O, et al. Battle-tested guidelines and operational protocols for neurosurgical practice in times of a pandemic: lessons learned from COVID-19. *World Neurosurg*. 2020;146:20-25.
3. Oxley TJ, Mocco J, Majidi S, et al. Large-vessel stroke as a presenting feature of COVID-19 in the young. *N Engl J Med*. 2020;382:e60.
4. Ghosh R, Dubey S, Kanti Ray B, Chatterjee S, Benito-León J. COVID-19 presenting with thalamic hemorrhage unmasking moyamoya angiopathy. *Can J Neurol Sci*. 2020;47:849-851.
5. Whittaker E, Bamford A, Kenny J, et al. Clinical characteristics of 58 children with a pediatric inflammatory multisystem syndrome temporally associated with SARS-CoV-2. *JAMA*. 2020;324:259.
6. Helbok R, Chou SH, Beghi E, et al. NeuroCOVID: it's time to join forces globally. *Lancet Neurol*. 2020;19:805-806.