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Letter to the Editor

# COVID-19 and stroke: Red flags for secondary movement disorders?

*Dear editor,*

The coronavirus disease 2019 (COVID-19), caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), has sickened more than 23 million people across the globe over the past eight months. Acute cerebrovascular disease is a common complication of COVID-19 infection [1,2]. Previous reports estimated a 0.5-5% risk of stroke among patients with COVID-19 [1]. The presence of SARS-CoV-2 within endothelial cells facilitates diffuse endothelial inflammation, which may disrupt the vascular equilibrium in favor of a procoagulant state [3]. In addition, the exaggerated inflammatory immune response exhibited by patients with COVID-19 may also stimulate the activation of coagulation and clotting processes [4]. These findings suggest that the presence of a hypercoagulable state along with a severe inflammatory response may predispose COVID-19 patients to thromboembolic complications [2,4].

Recently, Rábano-Suárez and colleagues reported 3 patients infected with SARS-CoV-2 who presented with generalized myoclonus. They showed both positive and negative myoclonic jerks, which mostly involved the facial, trapezius, sternocleidomastoid, and upper extremity muscles. These jerking movements occurred spontaneously and worsened with voluntary movement and tactile and auditory stimuli. An excessive startle reaction was also present. Neuroimaging was normal in all patients, and clinical improvement was observed following immunotherapy [5]. Similarly, Méndez-Guerrero et al. reported a patient who presented with generalized myoclonus and an acute hypokinetic-rigid syndrome characterized by parkinsonian symptoms such as resting and postural tremor, rigidity and bradykinesia. The [$^{123}$I]-ioflupane dopamine transporter single-photon emission CT (DaT-SPECT) revealed a decrease of dopamine transporter uptake in both putamina. The patient showed an improvement in the parkinsonian symptoms without treatment [6]. Finally, Cohen and colleagues reported a patient with probable Parkinson's disease, who was diagnosed after SARS-CoV-2 infection. On examination, the patient presented with hypomimia, hypophonic fluent speech, bradykinesia, and cogwheel rigidity. During the period of hospitalization, he started complaining of tremor in both legs and increased urinary frequency. The $^{18}$F-fluorodopa ($^{18}$F-FDOPA) PET scan showed decreased $^{18}$F-FDOPA uptake in both putamina. A suspected mild decreased uptake in the left caudate was also observed [7].

Post-stroke movement disorders develop as residual complications of brain lesions mainly involving the basal ganglia and thalamus. These disorders can either occur immediately after the acute stroke onset or have a progressive, delayed onset. Small vessel disease, primarily impacting deep structures, is the most frequent stroke subtype resulting in movement disorders [8,9]. Stroke may present with hypokinetic or hyperkinetic movements depending on the affected brain structure [8–10]. Given that cerebrovascular diseases account for about 20% of all secondary movement disorders [11], might we expect an increase in the prevalence of movement disorders as a consequence of neurological injuries in COVID-19 patients?

The neurotropism of SARS-CoV-2 has not yet been conclusively demonstrated [2] and, although there is no clear evidence for the association between COVID-19 and movement disorders, a direct consequence of an active SARS-CoV-2 infection on the development of abnormal movements should not be underestimated. A prospective study of 103 patients done by Netravathi and colleagues found that vascular events (22.3%) and infections (20.4%) were the most common causes of secondary movement disorders. They also reported that 65% of the patients with vascular events developed abnormal movements following an arterial stroke, which was related to thrombotic complications in the great majority of the cases (80%). The Japanese encephalitis was the leading cause of movement disorders due to infections, but a wide variety of infectious agents such as HIV, influenza A, herpes simplex virus, Treponema pallidum, and Streptococcus has also been associated with abnormal movements [11].

Together, these findings highlight the importance of carefully evaluating COVID-19 patients with clinical suspicion of acute stroke [12]. Any delay in diagnosis and treatment for patients with stroke may increase the incidence of long-term disability, such as those caused by post-stroke movement disorders [13]. While most cases are transient, movement disorders following stroke may persist and progressively deteriorate as in the case of vascular parkinsonism [10,13]. Therefore, health professionals on the front line of COVID-19 should have a reasonable understanding of the clinical features of acute stroke [12]. They also should be vigilant for signs and symptoms of movement abnormalities since their recognition may be helpful in identifying brain structures affected by stroke lesions [13,14]. Although brain imaging may be challenging in critically ill COVID-19 patients, guidelines to support the management of acute stroke in such patients are currently available [12]. In addition, future studies should consider including detailed neurological examinations and imaging in order to improve our understanding of the interplay between SARS-CoV-2 infection and its neurological manifestations.

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## Declaration of Competing Interest

None.

## References


[1] S. Shahjouei, S. Naderi, J. Li, A. Khan, D. Chaudhary, G. Farahmand, S. Male, C. Griessenauer, M. Sabra, S. Mondello, A. Cernigliaro, F. Khodadadi, A. Dev, N. Goyal, Risk of stroke in hospitalized SARS-CoV-2 infected patients: A multinational study, EBioMedicine. 59 (2020), 102939.

[2] A. Pezzini, A. Padovani, Lifting the mask on neurological manifestations of COVID-19, Nat. Rev. Neurol. 19 (2020), https://doi.org/10.1038/s41582-020-0398-3.

[3] F.A. Klok, M.J.H.A. Kruip, N.J.M. van der Meer, M.S. Arbous, D.A.M.P.J. Gommers, K.M. Kant, F.H.J. Kaptein, J. van Paassen, M.A.M. Stals, M.V. Huisman, H. Endeman, Incidence of thrombotic complications in critically ill ICU patients with COVID-19, Thromb. Res. (2020), https://doi.org/10.1016/j.thromres.2020.04.013.

[4] M. Levi, J. Thachil, T. Iba, J.H. Levy, Coagulation abnormalities and thrombosis in patients with COVID-19, Lancet Haematol. (2020), https://doi.org/10.1016/S2352-3026(20)30145-9.

[5] P. Rábano-Suárez, L. Bermejo-Guerrero, A. Méndez-Guerrero, J. Parra-Serrano, D. Toledo-Alfocea, D. Sánchez-Tejerina, T. Santos-Fernández, M.D. Folgueira-López, J. Gutiérrez-Gutiérrez, B. Ayuso-García, J. González de la Aleja, J. Benito-León, Generalized myoclonus in COVID-19, Neurology. (2020), https://doi.org/10.1212/wnl.0000000000009829.

[6] A. Méndez-Guerrero, M.I. Laespada-García, A. Gómez-Grande, M. Ruiz-Ortiz, V.A. Blanco-Palmero, F.J. Azcarate-Diaz, P. Rábano-Suárez, E. Álvarez-Torres, C.P. de Fuenmayor-Fernández de la Hoz, D.V. Pérez, R. Rodríguez-Montalbán, A. Pérez-Rivilla, J.S. Catalán, A.R.- González, J. González de la Aleja, Acute hypokinetic-rigid syndrome following SARS-CoV-2 infection., Neurology. (2020). doi:https://doi.org/10.1212/WNL.0000000000010282.

[7] M.E. Cohen, R. Eichel, B. Steiner-Birmanns, A. Janah, M. Ioshpa, R. Bar-Shalom, J.J. Paul, H. Gaber, V. Skrahina, N.M. Bornstein, G. Yahalom, A case of probable Parkinson's disease after SARS-CoV-2 infection, Lancet Neurol. (2020), https://doi.org/10.1016/S1474-4422(20)30305-7.

[8] N. Gupta, S. Pandey, Post-Thalamic Stroke Movement Disorders: A Systematic Review, Eur. Neurol. (2018), https://doi.org/10.1159/000490070.

[9] R. Mehanna, J. Jankovic, Movement disorders in cerebrovascular disease, Lancet Neurol. (2013), https://doi.org/10.1016/S1474-4422(13)70057-7.

[10] F. Alarcón, J.C.M. Zijlmans, G. Dueñas, N. Cevallos, Post-stroke movement disorders: Report of 56 patients, J. Neurol. Neurosurg. Psychiatry. (2004), https://doi.org/10.1136/jnnp.2003.011874.

[11] M. Netravathi, P.K. Pal, B. Indira Devi, A clinical profile of 103 patients with secondary movement disorders: Correlation of etiology with phenomenology, Eur. J. Neurol. (2012), https://doi.org/10.1111/j.1468-1331.2011.03469.x.

[12] A.I. Qureshi, F. Abd-Allah, F. Al-Senani, E. Aytac, A. Borhani-Haghighi, A. Ciccone, C.R. Gomez, E. Gurkas, C.Y. Hsu, V. Jani, L. Jiao, A. Kobayashi, J. Lee, J. Liaqat, M. Mazighi, R. Parthasarathy, T. Steiner, M.F.K. Suri, K. Toyoda, M. Ribo, F. Gongora-Rivera, J. Oliveira-Filho, G. Uzun, Y. Wang, Management of acute ischemic stroke in patients with COVID-19 infection: Report of an international panel, Int. J. Stroke. (2020), https://doi.org/10.1177/1747493020923234.

[13] D.-Y. Kwon, Movement Disorders Following Cerebrovascular Lesions: Etiology, Treatment Options and Prognosis, J. Mov. Disord. (2016), https://doi.org/10.14802/jmd.16008.

[14] S. Bansil, N. Prakash, J. Kaye, S. Wrigley, C. Manata, C. Stevens-Haas, R. Kurlan, Movement Disorders after Stroke in Adults: A Review, Tremor and Other Hyperkinetic Movements. (2012), https://doi.org/10.5334/tohm.110.



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