

# COVID-19—White matter and globus pallidum lesions

## Demyelination or small-vessel vasculitis?

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Since December 2019, a novel coronavirus, also called severe acute respiratory syndrome CoV-2 (SARS-CoV-2), emerged in Wuhan, China, and caused a pandemic disease (COVID-19). Respiratory impairment is the most common symptom in patients with confirmed COVID-19; however, neurologic symptoms were documented in approximately 36%, including headache, disturbed consciousness, and paresthesia.<sup>1</sup> The virus can take different pathways to involve the CNS: in one way through hematogenous or lymphatic route and in another way via the cribriform plate close to the olfactory bulb. Very few studies have shown CNS abnormalities related to COVID-19 on MRI. Herein, we report a case of SARS-CoV-2 brain lesions suggesting an acute demyelination.

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## Case

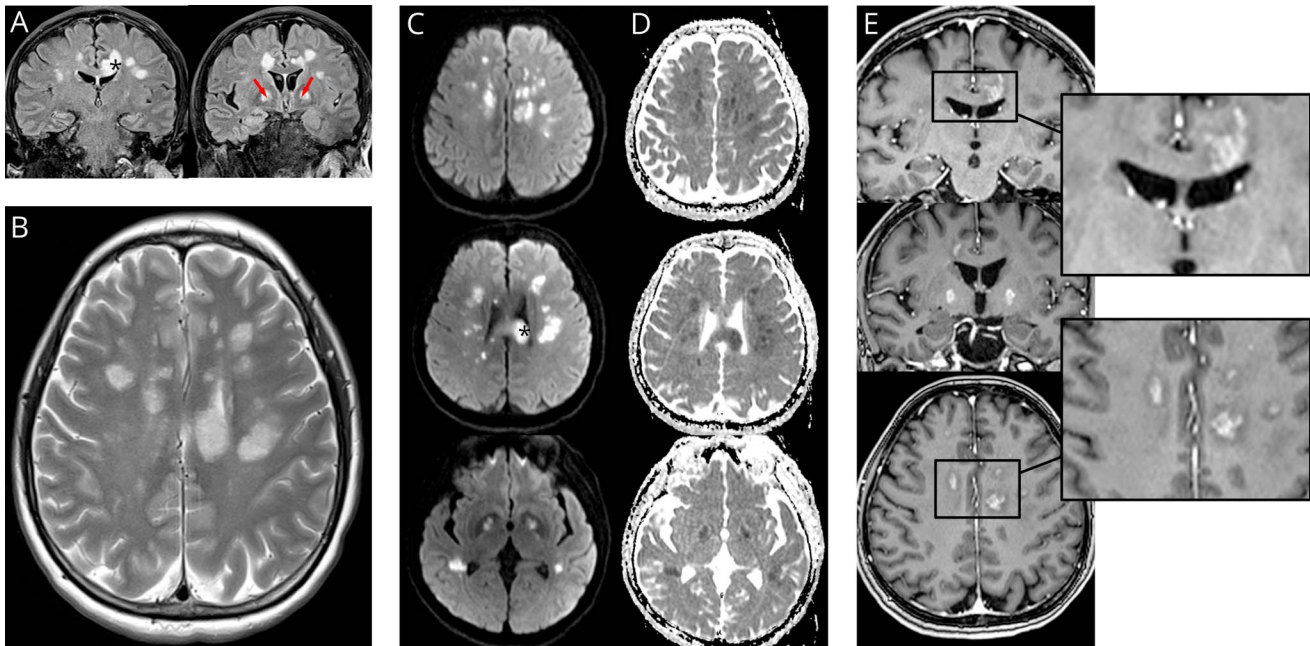
A 54-year-old woman was admitted in the emergency department for a respiratory distress. She had an unremarkable medical history except for a treated mild arterial hypertension. No history of toxic substances was found. She presented with an 8-day history of fever, asthenia, and respiratory symptoms. On admission, her respiratory rate was 35–40 with an oxygen saturation of 75%. The patient's Glasgow Coma Scale score was 14 with altered mental status but without focal neurologic deficit. Blood investigation showed an increased C-reactive protein (346 mg/L), hyperferritinemia, and elevated liver enzymes. A reverse transcriptase polymerase chain reaction (RT-PCR) test for SARS-CoV-2 was positive in nasopharyngeal swab. Her CSF was hemorrhagic because of a traumatic lumbar puncture but without any other abnormality. RT-PCR screening for neurotropic agents was negative. A CT of the lungs demonstrated pathologic findings compatible with a severe COVID infection. Endotracheal intubation with mechanical ventilation in prone position led to a rapid improvement of the respiratory distress. Hydroxychloroquine in combination with azithromycin and amoxicillin/clavulanic acid treatment was initiated. After stopping sedation at day 2, the patient presented with wake-up delay and her GSC score was 6. A CT scan of the brain demonstrated hypodense lesions involving supratentorial white matter and pallidum bilaterally. Initially, an embolic cause was suspected but cardiac ultrasound and ECG were normal. EEG showed a slowed background activity. At day 7, a brain MRI revealed lesions with restricted diffusion without any hemorrhage or enhancement after gadolinium injection (figure). The thalamus, the striatum, and the posterior fossa were spared. The intracranial vessels were without abnormalities on time-of-flight and postcontrast 3D T1-weighted black-blood images. No sinovenous thrombosis was noted. At day 9, a second lumbar puncture was performed, and it was shown that no relevant alterations and RT-PCR for SARS-CoV-2 remained negative. Although the consciousness slightly improved, a hemiplegia on the right side was observed at day 10. A follow-up MRI showed no new lesions. However, all lesions had homogenous contrast enhancement without any sign of hemorrhage. A spinal cord MRI was

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Multiple supratentorial punctiform and tumefactive lesions involving the white matter bilaterally and showing hypersignal on coronal fluid attenuation and inversion recovery (FLAIR; A), axial T2-weighted images (B), and diffusion-weighted imaging (C) with low apparent diffusion coefficient (ADC; D). Some lesions are periventricular or involve the corpus callosum with a mass effect on the left lateral ventricle (\*). Note the restricted diffusion with hyperintensity on FLAIR images within the globus pallidum bilaterally (black arrows). On a follow-up brain MRI, the lesions demonstrate avid enhancement on postgadolinium coronal and axial T1-weighted images (E).

without abnormalities. Steroid treatment was initiated after negative nasopharyngeal PCR on day 12.

## Discussion

The first radiologic description of neurologic complications due to SARS-CoV-2 infection was described by Poyiadji et al.<sup>2</sup> with a case of acute necrotizing encephalopathy (ANE), probably related to virus-induced cytokine storm. The most characteristic finding in ANE is the bilateral and symmetrical thalamus involvement with possible restricted diffusion or hemorrhage. Then, meningitis and encephalitis associated with SARS-CoV-2 were also described<sup>3</sup> with leptomeningeal enhancement, perfusion abnormalities, and ischemic stroke. Several mechanisms are supposed to lead to CNS involvement such as toxic encephalopathy, inflammatory, and autoimmune or hypoxia injuries.<sup>4</sup> In our case, the distribution of bilateral but asymmetrical lesions with periventricular and deep white matter involvement is rather suggestive of an acute demyelination. In a murine model, the mouse hepatitis coronavirus can cause an acute demyelination<sup>5</sup> with probable implication of astrocytes, microglia, and endothelial cells. In 2004, Ann Yeh et al.<sup>6</sup> described the first case of pediatric acute disseminated encephalomyelitis (ADEM) associated with a coronavirus. However, some findings such as sparing the infratentorial white matter, the restricted diffusion, and the prominent involvement of the pallidum are unusual for ADEM. Besides demyelination, the associated punctiform lesions might

be consistent with ischemic lesions because of small-vessel vasculitis. SARS-CoV-2 infects the host using the angiotensin-converting enzyme 2 receptor that is expressed in several organs, especially in endothelial cells. Recently, Varga et al.<sup>7</sup> have showed direct viral infection of the endothelial cell and diffuse endothelial inflammation. This endothelial dysfunction can lead to vasoconstriction and break of the blood-brain barrier with cerebral ischemia and inflammation. Although mechanisms remain obscure, our case shows the importance of the MRI in the exploration of neurologic symptoms in COVID-19. Demyelination or small-vessel CNS vasculitis might be a rare but silent complication of sedated patients with COVID-19.

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Name	Location	Contribution
<b>Gilles Brun</b>	APHM	Data acquisition, drafting/ revising the manuscript, study concept or design, and analysis or interpretation of the data
<b>Jean-Francois Hak</b>	APHM	Drafting/ revising the manuscript and study supervision
<b>Stéphanie Coze</b>	APHM	Drafting/ revising the manuscript and study supervision
<b>Elsa Kaphan</b>	APHM	Analysis or interpretation of the data
<b>Julien Carvelli</b>	APHM	Drafting/ revising the manuscript, data acquisition, analysis or interpretation of the data, and study supervision
<b>Nadine Girard</b>	APHM	Data acquisition, analysis or interpretation of the data, and study supervision

## Appendix (continued)

Name	Location	Contribution
<b>Jan-Patrick Stellmann</b>	APHM	Drafting/ revising the manuscript and analysis or interpretation of data

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