

# Fatal Necrotizing Encephalitis Associated With COVID-19

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Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is an emerging virus responsible for the coronavirus disease 2019 (COVID-19) disease, which manifests as flu-like and respiratory symptoms but can also have severe neurologic manifestations. We present a case of necrotizing encephalitis.

## Case

A 56-year-old man was found unconscious at home on April 14, 2020, in Mayotte, a French island in the Indian Ocean. His medical history was relevant for malnutrition, renal lithiasis with left renal abscess, and *Mycobacterium abscessus* pulmonary infection. There was no recent history of fever or respiratory symptoms.

On emergency medical services' arrival, his Glasgow Coma Scale score was 6 (E4V1M1). His vitals were temperature 40°C, heart rate 140 bpm, BP 63/23 mm Hg, glycemia 1.1 g/L, and SpO<sub>2</sub> 88% on room air. Endotracheal intubation was performed, and he presented a short cardiocirculatory arrest (low flow <1 min). Hemodynamic stabilization was obtained with 3L of crystalloid filling and norepinephrine infusion for transfer to Mayotte hospital.

On arrival in the intensive care unit, arterial blood gases showed PaO<sub>2</sub>/FiO<sub>2</sub> 497 and PaCO<sub>2</sub> 35 mm Hg under PEEP 5 cmH<sub>2</sub>O and FiO<sub>2</sub> 30%. Sedation was managed with midazolam and sufentanyl. Pupils were symmetrical miotic and weakly reactive. Norepinephrine was running 1 µg/kg/min to maintain a mean arterial pressure of 65 mm Hg. Transcranial Dopplers were symmetrical with PI < 1.2 but diastolic velocities <20 cm/s. Transthoracic echocardiography was normal. Brain CT scan was normal. Chest CT scan did not show signs of COVID-19 pneumopathy but aspiration pneumonia.

Laboratory findings showed hemoglobin of 8.9 g/dL, leucocytes of 7.1 G/L, C reactive protein of 92 mg/L, procalcitonin of 81 ng/mL, fibrinogen of 5.9 g/L, D-dimers of 66 µg/mL (N < 0.5), aspartate transaminase of 658 U/L, alanine transaminase of 169 U/L, TP 39%, factor V 46%, lactate 4.4 mmol/L, troponin of 0.289 µg/L (N < 0.019), creatinine of 169 µg/L (80 6 months before), potassium of 2.5 mmol/L, and natremia of 138 mmol/L. Nasopharyngeal swab and protected distal airway sample were positive for SARS-CoV-2 RT-PCR. HIV serology was negative.

Piperacillin-tazobactam and amikacin were started after blood cultures; urinalysis and pulmonary specimen were taken (which came back negative later), along with hydrocortisone.

Eight hours after admission, right anisocoria appeared. Hypertonic saline 7.5% was injected for osmotherapy. Another brain CT scan was urgently performed, which showed acute hydrocephalus with diffuse cerebral edema, spontaneous bilateral thalamic hyperdensities with discrete contrast enhancement, and spontaneous hyperdensity in subarachnoidal spaces. Brain

## PRACTICAL IMPLICATIONS

- SARS-CoV-2 should be kept in mind by physicians as a possible cause of encephalitis even in the absence of respiratory symptoms.
- SARS-CoV-2 encephalitis can be fatal.
- MRI findings are hyperintensities in the thalami, temporal lobes, and/or cerebellum.

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MRI showed compression of the 3rd ventricle by both thalami, causing hydrocephalus; compression of the 4th ventricle by the cerebellum; diffuse signs of intracranial hypertension; and a starting tonsillar engagement. In fluid-attenuated inversion recovery and diffusion sequences, there was a hyper-signal of both thalami (figure e-1, [links.lww.com/CPJ/A187](https://links.lww.com/CPJ/A187)), brainstem, and cerebellum with some hemorrhagic component on T2\* sequences (Supplement e-1, [links.lww.com/CPJ/A189](https://links.lww.com/CPJ/A189)). T1-weighted sequences with gadolinium injection showed well-delimited necrotic areas (figure e-2, [links.lww.com/CPJ/A188](https://links.lww.com/CPJ/A188)).

External ventricular derivation was urgently performed in the operation room after coagulation was optimized. CSF analysis showed a slightly tainted fluid with albuminocytological dissociation (0 leucocytes, proteinorachia 7.9 g/L) and normoglycorachia 4.5 mmol/L. Direct examination and culture were negative. SARS-CoV-2, herpes simplex virus 1/2, varicella zoster virus, and cytomegalovirus RT-PCR were also negative.

Eighteen hours after admission, despite neuroprotection and external ventricular derivation, the patient presented bilateral reactive mydriasis. Transcranial Dopplers showed signs of intracranial hypertension with increased pulsatility indexes (1.4) and very low diastolic velocities (<20 cm/s). Mannitol infusion did not improve cerebral blood flow. Multiorgan failure developed, and the patient died 36 hours after his admission.

## Discussion

Acute necrotizing encephalitis (ANE) is a rare complication of viral infections. Cases of encephalitis with COVID-19 have been published with MRI showing hyperintensities in the thalami, temporal lobes, and/or cerebellum.<sup>1-3</sup> Positivity of SARS-CoV-2 RT-PCR in CSF has been described, although it was negative in our patient.<sup>3-5</sup> Direct identification of viral particles in the brain tissue would be the ultimate way to confirm diagnosis. Mechanisms of penetration into the CNS could be through olfactory nerve invasion, cellular invasion, transsynaptic peripheral nerves transmission, or blood-brain barrier invasion.<sup>6</sup> We can only conclude to ANE because of SARS-CoV-2 by the exclusion of other investigated causes. In this malnourished patient, encephalitis could be due to another

rare microorganism with SARS-CoV-2 being a serendipitous finding. Thalamic edema could also be a consequence of low flow (although it was short) or vascular (arterial or venous) thrombosis, but MRI did not find any. Lack of vascular territory is in favor of ANE. COVID-19 itself causes thrombosis, as largely described in the literature.<sup>7</sup> This case is unique because of its rapidly fatal outcome.

Encephalitis is a life-threatening complication of COVID-19. SARS-CoV-2 should always be kept in mind by physicians as a possible cause of encephalitis even in the absence of respiratory symptoms.

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All authors have been involved in writing the manuscript at all stages and has read and approved the final version.

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