Fatal necrotizing encephalitis associated with COVID-19: A case report

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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 thalami, temporal lobes and/or cerebellum
Introduction

SARS-CoV-2 is an emerging virus responsible for 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 male was found unconscious at home on April 14th, 2020 in Mayotte, a French island in the Indian Ocean. His past 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.

Upon 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 mmHg, glycemia 1.1 g/L, SpO2 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.

Upon arrival in the intensive care unit, arterial blood gases showed PaO2/FiO2 497 and PaCO2 35 mmHg under PEEP 5 cmH2O and FiO2 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 mmHg. 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 8.9 g/dL, leucocytes 7.1 G/L, CRP 92 mg/L, procalcitonin 81 ng/mL, Fibrinogen 5.9 g/L, D-dimers 66μg/mL (N<0.5), ASAT 658 UI/L, ALAT 169 U/L, TP 39%, Factor V 46%, lactate 4.4 mmol/L, troponin 0.289 μg/L (N<0.019).
creatinine 169 µg/L (80 six months before), potassium 2.5 mmol/L, natrema 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 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 FLAIR and diffusion sequences there was a hypersignal of both thalami (Figure e-1,http://links.lww.com/CPJ/A187), brainstem and cerebellum with some hemorrhagic component on T2* sequences (Supplement e-1,http://links.lww.com/CPJ/A189). T1 weighted sequences with gadolinium injection showed well delimited necrotic areas (Figure e-2,http://links.lww.com/CPJ/A188).

External ventricular derivation was urgently performed in the operation room after coagulation was optimized. Cerebrospinal fluid (CSF) analysis showed a slightly tainted fluid with albuminocytological dissociation (0 leucocytes, proteinorachia 7.9 g/L) and normoglycorachia 4.5 mmol/L. Direct exam and culture were negative. SARS-CoV-2, HSV 1/2, VZV and CMV RT PCR were also negative.
Eighteen hours after admission, despite neuroprotection and external ventricular derivation, patient presented bilateral areactive 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 patient died thirty-six 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 thalami, temporal lobes and/or cerebellum (1–3). Positivity of SARS-CoV-2 RT PCR in CSF has been described although it was negative in our patient (3–5). Direct identification of viral particles in brain tissue would be the ultimate way to confirm diagnosis. Mechanisms of penetration into the CNS could be through olfactory nerve invasion, cellular invasion, transynaptic peripheral nerves transmission or blood brain barrier invasion (6). We can only conclude to ANE due to SARS-CoV-2 by 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 (7). This case is unique because of its rapidly fatal outcome.

Conclusion

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.
Figures legends:

Figure e-1: T2 FLAIR sequence showing hyperintensity within both thalami

Figure e-2: T1 weighted sequences with gadolinium injection showing hypointense signal in thalami and cerebellum with rim enhancement.
Supplement e-1: T1 weighted sequences with gadolinium injection showing hypointense signal in cerebellum and brainstem with rim enhancement.

References


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