Case Report

A Fatal Case Coronavirus Disease 2019 – Associated Acute Hemorrhagic Necrotizing Encephalopathy

Abdoulahy Diallo, Yacouba Dembele, Mohamadou Niang, Lucas Balloy, François Pousset, Issifou Yaya, Sarah Permal

Departments of Infectious and Tropical Diseases, 1Radiology and 1Intensive Care Unit, Mayotte Hospital, 1IRD, Inserm, Univ Montpellier, TransVIHMI, Montpellier, 3African Public Health Association, Paris, France

Abstract

Coronavirus disease 2019 (COVID-19) has been reported in association with a variety of brain imaging findings such as acute hemorrhagic necrotizing encephalopathy. To the best of our knowledge, we are reporting a second case of acute necrotizing hemorrhagic encephalopathy associated with COVID-19, which was fatal in a few hours in a 56-year-old male without a specific history. We claim that this case is important because this case shows that the unconscious patients are potentially infected by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and might cause the horizontal infection. In order to end the pandemic of SARS-CoV-2 diseases, the diagnosis of the disease must be prompt and not overlook any findings. We think that diffusion magnetic resonance imaging is a promising and useful sequence to evaluate the changes in brain tissue in the acute necrotizing encephalopathy.

Keywords: Acute hemorrhagic necrotizing encephalopathy, COVID-19, death, SARS-CoV-2

INTRODUCTION

Coronavirus disease 2019 (COVID-19) started with an outbreak in Wuhan, China, in December 2019 and quickly became a worldwide public health crisis. A variety of neurological manifestations have been reported and a few reports of brain imaging findings, encompassing Acute hemorrhagic necrotizing encephalopathy (AHNE), ischemic infarct, and hemorrhage are available. AHNE is characterized by bilateral necrotic, hemorrhagic lesions occurring symmetrically in the thalami, dorsal brainstem, and dentate nuclei. While predominantly described in the pediatric population, AHNE is known to occur in adults as well. This communication describes a 56-year-old patient with AHNE associated with COVID-19, with emphasis on the results of computed tomography (CT) at the intake that was normal at the beginning, magnetic resonance imaging (MRI) for diagnosis and death within 24 h of the patient.

CASE REPORT

A 56-year-old male with no previous history admitted to intensive care unit for coma with a Glasgow at 6 associated with respiratory distress with short cardiac arrest at home.

Given the epidemic context of COVID-19, an un.injected body-CT showed no brain lesions or typical COVID-19 lesions or pulmonary embolism but rather early alveolar condensation of the left pulmonary base.

Biology showed leukocytes were 7.1 gigs/L, C-reactive protein were 92 mg/L, hemoglobin were 8g/dl, prothrombin level were 39%, factor V were 46%, fibrinogen were 5.9 g/L, D-Dimer were 66 µg/ml, lactates were 8.6 mmol/l's. He was treated intravenous perfusion with crystalloids associated with vasoactive amines, probabilistic antibiotherapy (ceftriaxone dose and rovamycine dose) and oxygenotherapy. A few hours after his admission, he had a straight anisocoria with episode of tensional lability; a new brain scanner with injection showed bilateral cerebellar lacunar hypodensities and a hyperdense appearance of upper vermis. At the upper level,
a heterogeneous bi-thalamic contrast taking associated with hydrocephalus is objective [Figure 1].

Cerebral MRI performed in the crowd showed bilateral, upper vermin, and bi-thalamic hypersignal beaches b 1000 with signal restriction on ADC mapping, and upper vermin hemorrhagic stigma and bi-thalamic T2* thalamic, with heterogeneous contrast after injection of gadolinium associated with cerebellar amygdala ptosis [Figures 2-4]. He benefitted from urgent external ventricular bypass for drainage, but unfortunately his neurological status worsened after brain surgery with bilateral areactive mydriase, multivisceral failure and then fatal outcome.

Etiologically, the reverse transcription-polymerase chain reaction (PCR) test for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is positive at the nasopharynx and bronchial sampling protected. The results of cerebrospinal fluid on ventricular drainage show a fluid disorder with 0 leukocytes and red blood cells at 1060/mm³, Cerebrospinal fluid sugar at 4.32 mol/l, and cerebrospinal fluid proteins at 7.90 g/l, culture returned negative. SARS-CoV-2 PCR, herpes simplex virus, cytomegalovirus, varicella zoster virus and mycobacteria returned negative in cerebrospinal fluid.

**Discussion**

We report a second case of COVID-19-associated acute necrotizing hemorrhagic encephalopathy that was fatal to the patient. The first reported case of COVID-19-associated acute necrotizing hemorrhagic encephalopathy was described by Neo Poyiadji in March 2020.

COVID-19 was diagnosed by detection of SARS-CoV-2 viral nucleic acid in a nasopharyngeal swab sample used in Mayotte. Testing for the presence of SARS-CoV-2 in the CSF was negative. The imageries were also identical.¹
Acute necrotizing encephalopathy (ANE) is a rare complication of influenza and other viral infections and has been related to intracranial cytokine storms, which result in blood–brain barrier breakdown but without direct viral invasion or parainfectious demyelination.⁶⁶ Accumulating evidence suggests that a subgroup of patients with severe COVID-19 might have a cytokine storm syndrome.⁷⁷

Acute necrotizing encephalopathy is characterized by bilateral necrotic, hemorrhagic lesions which occur symmetrically in the thalami, dorsal brainstem, and dentate nuclei. The development of an extensive breakdown of the blood–brain barrier in the prominent lesions of acute necrotizing encephalopathy was demonstrated in a 7-month-old boy with the disorder, within 14 h after hospitalization by an initially negative postcontrast CT scan, and subsequently positive postcontrast T1-weighted MRI. Diffusion MRI demonstrated concomitant cytotoxic and vasogenic edema in the lesions.⁸⁸

We observed the same development in our patient with a normal brain scan on admission and then positive on cerebral MRI.

To end the pandemic of SARS-CoV-2 diseases, the diagnosis of the disease must be prompt and not overlook any findings. Finding the suspected patient is the first step of a preventive measure against the pandemic. It should be kept in mind that the symptoms of the encephalitis may be the first indication, as well as respiratory symptoms, to find the hidden SARS-CoV-2 patients. Diffusion MRI is a promising and useful sequence to evaluate the changes in brain tissue in the AHNE. In addition, diffusion MRI can provide data on different histopathologic stages of the AHNE.

Research quality and ethics statement
We declare that the EQUATOR Network guidelines, notably the CARE guidelines were followed during the conduct of this report.

Declaration of patient consent
We certify that we have obtained all appropriate patient consent forms. In the form, the patient has given his consent for his clinical information to be reported in the journal. The patient understands that his name and initials will not be published and due efforts will be made to conceal his identity, but anonymity cannot be guaranteed.

Financial support and sponsorship
Nil.

Conflicts of interest
There are no conflicts of interest.

REFERENCES
1. Mao L, Jin H, Wang M, Hu Y, Chen S, He Q, et al. Neurologic manifestations of hospitalized patients with coronavirus disease 2019 in Wuhan, China. JAMA Neurol 2020;77:683-90.
2. Radmanesh A, Raz E, Zan E, Derman A, Kaminetzky M. Brain imaging use and findings in COVID-19: A single academic center experience in the epicenter of disease in the United States. AJNR Am J Neuroradiol 2020;41:1179-83.
3. Poyiadji N, Shahin G, Noujaim D, Stone M, Patel S, Griffith B. COVID-19-associated acute hemorrhagic necrotizing encephalopathy: Imaging features. Radiology 2020;296:E119-20.
4. Yagishita A, Nakano I, Ushioda T, Otsuki N, Hasegawa A. Acute encephalopathy with bilateral thalamotegmental involvement in infants and children: Imaging and pathology findings. AJNR Am J Neuroradiol 1995;16:439-47.
5. Porto L, Lanferman H, Möller-Hartmann W, Jacobi G, Zanella F. Acute necrotising encephalopathy of childhood after exanthema subitum outside Japan or Taiwan. Neuroradiology 1999;41:132-4.
6. Rossi A. Imaging of acute disseminated encephalomyelitis. Neuroimaging Clin N Am 2008;18:149-61.
7. Mehta P, McAuley DF, Brown M, Sanchez E, Tattersall RS, Manson JJ, et al. COVID-19: Consider cytokine storm syndromes and immunosuppression. Lancet 2020;395:1033-4.
8. Nuri Sener R, Atalar MH. Acute necrotizing encephalopathy in an infant: Observations by CT, contrast-enhanced MRI and diffusion MRI. A case report. Neuroradiol J 2008;21:538-42.