Case Report

Acute necrotic hemorrhagic leukoencephalitis related to COVID-19: a report of 2 cases

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ABSTRACT

Acute necrotic hemorrhagic leukoencephalitis (ANHLE) is a subform of acute disseminating leukoencephalitis which is a post viral or vaccination uncommon disease with poor prognosis. Radiological findings include multiple or diffuse lesions involving the white matter and sparing the cortex with or without rim enhancement. In addition to areas of hemorrhages with possible involvement of basal ganglia and thalami. We describe the imaging findings for 2 cases of ANHLE: a 59-years-old male and a 47-years-old female. Both of them were tested positive of SARS-COVID2 with presentation of consciousness loss and respiratory failure. CT and MRI brain show global white matter changes associated with acute hemorrhagic necrosis, although uncommon, are compatible with postviral acute necrotic hemorrhagic leukoencephalitis with end point of death for the first patient and coma for the second patient.

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Introduction

During the global pandemic of COVID-19 started in December 2019 in Wuhan, China, many scientific articles reported neurological involvement related to the coronavirus. It involves the central and peripheral nervous system with various clinical and imaging findings [1-11]. In regards to neuroimaging findings related to COVID-19 which were reported in different patterns collected in the systemic review done by Katal S, et al [12], the majority of findings were normal on CT and MRI. In addition, the first case which was suspected with imaging findings related to COVID-19 was representing meningitis and encephalitis [13].

Abbreviations: CT, computed tomography; DM, diabetes mellitus; DNR, do not resuscitation; EEG, electroencephalogram; ESRD, end stage renal disease; GCS, Glasgow Coma Score; HTN, hypertension; ICU, intensive care unit; MRI, magnetic resonance imaging; SARS-COVID2, COVID-19; VAP, ventilator associated pneumonia.

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However, here we are reporting a different pattern of brain CT and MRI findings in 2 patients who tested positive for COVID-19 that had not been amply reported in the literature, mainly involving the global white matter and sparing the gray matter and the deep cortex of basal ganglia with possible areas of necrosis and microhemorrhages.

Case report (1)

A 59-years-old male known case of diabetes, hypertension, and end stage renal disease on dialysis tested positive for SARS-COVID2. The patient was referred to our institution to treat COVID-19 related pneumonia. Upon admission, he was assessed to have hypoxic respiratory failure, complicated by cardiac arrest. The patient was resuscitated for 5 minutes and subsequently revived. The patient consequently experienced a low level of consciousness with high oxygen demand. Then, he was intubated and shifted to ICU with an absence of some brainstem reflexes. He was put on mechanical ventilation with parameters of (FiO$_2$ of 45, PEEP of 8, and TV of 6 mL/kg). CT scan was done showing extensive bilateral hemispheric white matter hypoattenuation (Fig. 1). The differential diagnosis included encephalitis or white matter disease. A follow-up MRI brain with contrast was subsequently done revealing extensive brain abnormality predominantly involving the deep white matter with scattered patchy areas of ischemia/infarcts as well as possible necrosis and extensive scattered blooming artifacts likely related to microhemorrhages (Fig. 2).

The patient received treatment per Saudi Ministry of Health guidelines [14]. A few days later, the patient continued to worsen. The consensus of ICU-COVID team was a gener-
Case report (2)

A 47-years-old female medically free was referred to the hospital with confirmed positive SARS-COVID2 as well as fever, shortness of breath, blurred vision, and abnormal movement of the right upper limb and left lower limb. The patient was intubated and shifted to ICU-COVID ward as a case of acute hypoxic respiratory failure related to COVID-19 and altered mental status.

Neurological assessment was made on daily basis initially revealing no eye-opening, no response to painful stimuli, plantars mute bilaterally with multiple maintained off sedative and narcotics in attempt to evaluate the mental status and GCS, without much change in GCS of 3-4 during hospitalization. Initial MRI brain shows diffuse petechial hemorrhages especially in the basal ganglia that is compatible with diffuse necrotizing leukoencephalitis (Fig. 3). In addition, as recommended an EEG study was performed and reported abnormal III (comatose) due to continuous generalized slow activity. That is clinically interpreted as evidence of severe diffuse nonspecific cerebral dysfunction without epileptiform discharges or seizure activity.

A follow-up CT scan of brain was done later shows extensive bilateral supratentorial subcortical white matter hypodensities with no evidence of hemorrhagic transformation (Fig. 4). That was confirmed in the follow-up MRI showing interval worsening in the extensive bilateral white matter changes (Fig. 5).

Unfortunately, after a long stay in ICU for about 2 months patient GCS was still 3 to 4, she did not interact or respond to surroundings despite being off sedation, she is found to be hemodynamically stable, difficult to wean from mechanical ventilation, requiring pressure control, and did not tolerate pressure support mode. She finished courses of antibiotics for

ally poor prognosis and flagged for do not resuscitation (DNR) status. He was on high-dose vasopressors and suffered severe shock and hyperlactatemia, leading to an increase in oxygen requirements. The patient, unfortunately, passed away a few hours later. The autopsy was not performed.
VAP and ventilator settings are better on PEEP 10 and FiO₂ 40%. Given the fact of severe brain damage with follow-up Imaging studies and the latest CT brain reveals no changes (Fig. 6), she was put into a do not resuscitation state. She is not going to wake up and she will remain in a vegetative state and nothing more could be offered to improve or change the disease trajectory.

Discussion

The common neurological symptoms manifested with novel coronavirus include headache, dizziness [15], sudden onset of anosmia [16], ageusia [17]. Less commonly, significant neurological deficits which are detailed in the review article studied the neurological complications of COVID-19 [18].

The exact mechanism of transmission of coronavirus to the brain is still debatable. Many hypotheses suggest direct hematogenous spread, trans-neural, immune response to the cytokine storm [4]. The first case in literature describes the findings of brain changes related to COVID-19 in MRI was reported by Moriguchi et al [13] confirming ventriculitis and encephalitis associated with pan-paranasal sinusitis that could indicate the source of infection.

The radiological findings varying depending on the severity of neurological involvement. The most reported were normal. Features of ischemic changes [19-21], parenchymal hem-
or hemorrhage [22], and sinus thrombosis [23–24] were reported as well. Moreover, different patterns of MRI findings associated with severe COVID-19 include unilateral FLAIR and diffusion hyperintensities, multifocal white matter changes and extensive white matter microhemorrhages, extensive white matter FLAIR hyperintensity, Multifocal white matter lesions with variable enhancement, and acute necrotizing encephalopathy [25]. As we believe the presenting cases are showing patterns of acute necrotic hemorrhagic leukoencephalitis. Unlike the 3 similar cases described by Kandemirli [26] that show cortical high signal intensity in FLAIR weighted images. In addition, the reported case by Poyiadji that revealed the involvement of medial thalami and medial temporal lobes [27]. Similarly, cases disclosed by Virhammar et al [28] and Elkady et al [29]. The total cases of Acute Necrotizing Encephalopathy reported in the literature were summarized up to August 2020 [30].

Acute hemorrhagic necrotic leukoencephalitis is a hyperacute form of acute disseminated leukoencephalitis (ADEM) with a poor prognosis. It's an immune-mediated inflammatory disorder of the CNS, which is commonly preceded by an infection, and predominantly affects the white matter of the brain [31]. The reported MRI findings are multiple focal lesions involving the white matter and sparing the cortex with or without rim enhancement. It is associated with hemorrhages, extensive mass effect and edema with possible involvement of ganglia and thalami [32–33].

The unique characterization of our aforementioned cases is the involvement of global white matter and basal ganglia sparing the cortical gray matter without any enhancing lesion associated with multiple regions of necrosis and foci of microhemorrhages resulting in severe damage in form of leukoencephalitis with hemorrhagic necrosis that is clinically end-point of coma or death.

**Conclusion**

Diffuse global white matter changes sparing the cortical gray matter associated with necrotic changes and hemorrhagic foci are uncommon findings in CT and MRI that are believed to be related to COVID-19 in terms of acute necrotic hemorrhagic leukoencephalitis. The reporting radiologist should be aware of various COVID-19 brain imaging findings as aforementioned.

**Patient consent statement**

A formal consent is not required for the use of entirely anonymized images from which the individual cannot be identified- for example, CT and MRI images provided do not contain any identifying marks and are not accompanied by text that might identify the individual concerned.

**Declaration of Competing Interest**

The authors declare that they have no conflict of interests.

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