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COVID-19-induced hepatic encephalopathy: A case report

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Abstract

By the end of December 2019, a single stranded ribonucleic acid (RNA) virus, Coronavirus, was said to be responsible for an outbreak of respiratory infections of unknown origin in Wuhan, China. Globally, this virus has caused over 160,000 deaths and is expected to increase as the pandemic continues. The majority of patients with the coronavirus disease 2019 (COVID-19) infection present symptomatically with fever, shortness of breath, or cough; however, given that the Coronavirus targets the angiotensin converting enzyme 2 receptors (ACE2), it has been suspected that the virus also exhibits neuroinvasive effects. We present a case of a 32-year-old man with a one-week history of progressive shortness of breath, myalgias, arthralgias, fever peaks, who tested positive for COVID-19 and developed acute hepatic encephalopathy with altered mental status.

Key words: Coronavirus disease 2019, COVID-19**,** SARS-CoV-2, encephalopathy, central nervous system, hepatic encephalopathy.

Introduction

Ever since its emergence back in December 2019, the novel coronavirus, better known as COVID-19, has been a threat to international health, with enough impact to be declared a pandemic by the World Health Organization (WHO). (1,2) The common symptoms of this virus include fever, cough, dyspnea, fatigue, and sputum production. (3,4) That said, the clinical presentation does not limit itself within the respiratory frame, as it could go as broad as septic shock, to as specific as acute fulminant myocarditis. (5) As we will see in this case, the neurological system, being non-spared by this virus, has been reported to be a target in a few cases. (6) The first neurological case was reported through the genome sequencing of the presence of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in cerebrospinal fluid in Beijing Ditan Hospital. (7) We present a case of COVID-19-induced hepatic encephalopathy, that should remind us that any patient with the infection should be evaluated for neurological symptoms in a timely manner.

Case presentation

A 32-year-old African American male presented to our medical facility for continuity of care, after reverse transcription polymerase chain reaction (RT-PCR) test came back positive for COVID-19 in another hospital. The patient complained of a 7-day history of progressive shortness of breath, generalized weakness, and multiple non quantified fever peaks. The patient has a past medical history of non-insulin dependent diabetes mellitus and seizures, treated with glyburide and levetiracetam respectively.

On admission he was febrile, tachycardic, and tachypneic. Initial laboratory workup was negative for influenza, negative toxicology screening; with the diagnosis of COVID-19 made by RT-PCR and confirmed at our facility with qualitative IgM, computerized tomography (CT) of the chest and

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clinical presentation. In addition, he had increased interleukin 6, C-reactive protein, ferritin, and d-Dimer at the time of admission.

On hospital day 4 the patient started to develop behavioral and cognition changes; his Glasgow Coma Scale (GCS) was 13/15. The brain CT without contrast demonstrated cerebral edema, symmetric hypoattenuation within the medial thalami and bilateral ventricular calcifications, with no signs of intracerebral hemorrhage (**Figure 1**). Complete blood work was ordered revealing acute transaminitis, lymphopenia, and high levels of serum ammonia (74.2 umol/l). No other major electrolytes or glucose disturbances were found; blood and urine cultures showed no growth.

Based on the radiological findings and laboratory data, hepatic encephalopathy as a consequence of COVID-19 was suspected, demonstrating a grade 3 West Haven Criteria. Immediate treatment with lactulose was initiated. On day 6, after 2 days of nonabsorbable disaccharide (lactulose) therapy, the patient exhibited a significant improvement with a GCS of 15/15 and plasma ammonia (NH3) of 52.6umol/l. On day 7 the patient GCS was 15/15, showing no trace of the neurological impairment.

Discussion

Our case depicts neurological deterioration in the setting of liver affection in a patient diagnosed with a COVID-19. It is clear that coronaviruses can affect the nervous system, either directly or indirectly through different pathways. This unique virus can gain direct access to the nervous system either via blood circulation, neuronal pathways or direct extension through the olfactory bulb. (7) More importantly, indirect pathways of central nervous system (CNS) affection can occur in the setting of hypoxemia, immune-mediated insults or, as highlighted by this case, through multiple organ affection with potential of CNS consequences. In the setting of infection, the liver is the second most common organ to be affected after the lungs, which is what we were able to see in this case. Another mechanism that could explain specific organ affinity is the one related to the angiotensin converting enzyme 2 (ACE2) receptors. There is evidence of ACE2 receptors in the brain specifically on glial cells and neurons, and also in the liver, meaning that there is high binding affinity between the coronavirus and these receptors that make infection, and thus injury, very feasible. (7,8) SARS-CoV-2 has also been detected in the cerebro spinal fluid (CSF) of neurologically symptomatic patients of other cases, which affirms its neuroinvasive nature. (9,10) This doesn't come at us as a surprise, as SARS-1 CoV, which portrays a 79.5% genomic similarity with the SARS-CoV-2, has also been causing nervous system involvement in the past, and has been found in the CSF or on postmortem brain autopsy. (11,12)

The neurologic manifestations of COVID-19 include headaches, seizures, nausea, vomiting, and altered mental status, either as a primary or secondary inflammation after blood-brain barrier disruption. (7) Encephalopathy could be a presenting symptom, yet also an in-hospital complication. (13) Our case was unique in the sense that it showed secondary neuronal damage as a consequence of direct liver injury caused by a SARS-CoV-2 infection. The patients declining liver function eventually resulted in a buildup of ammonia levels and as result affected the CNS. Consequently, we believe that not only did the cytokine storm affect the liver, it also caused a hyperinflammatory state that altered the permeability of the blood-brain barrier, possibly explaining the neuroinflammatory process that we saw with this case. (14)

Although neurological manifestations have been previously shown to occur more commonly in patients with severe illness, our patient demonstrated these findings as a result of a deteriorating liver. As we witnessed, the SARS-CoV-2 was able to extend to other organs, in this case, the liver and as a secondary response, the brain was also affected. The reason we were able to see improvement after starting the lactulose treatment was because of its efficacy in reducing ammonia levels in the blood. In the colon, lactulose is able to use its gut flora by increasing its acidity through conversion of short chain fatty acids that favors the formation of ammonia into ammonium ions and thus reducing the levels of ammonia in the plasma. (15) With a decrease in ammonia levels, the patients symptoms were able to be reversed, as there was a reduce amount of toxic buildup in their system.

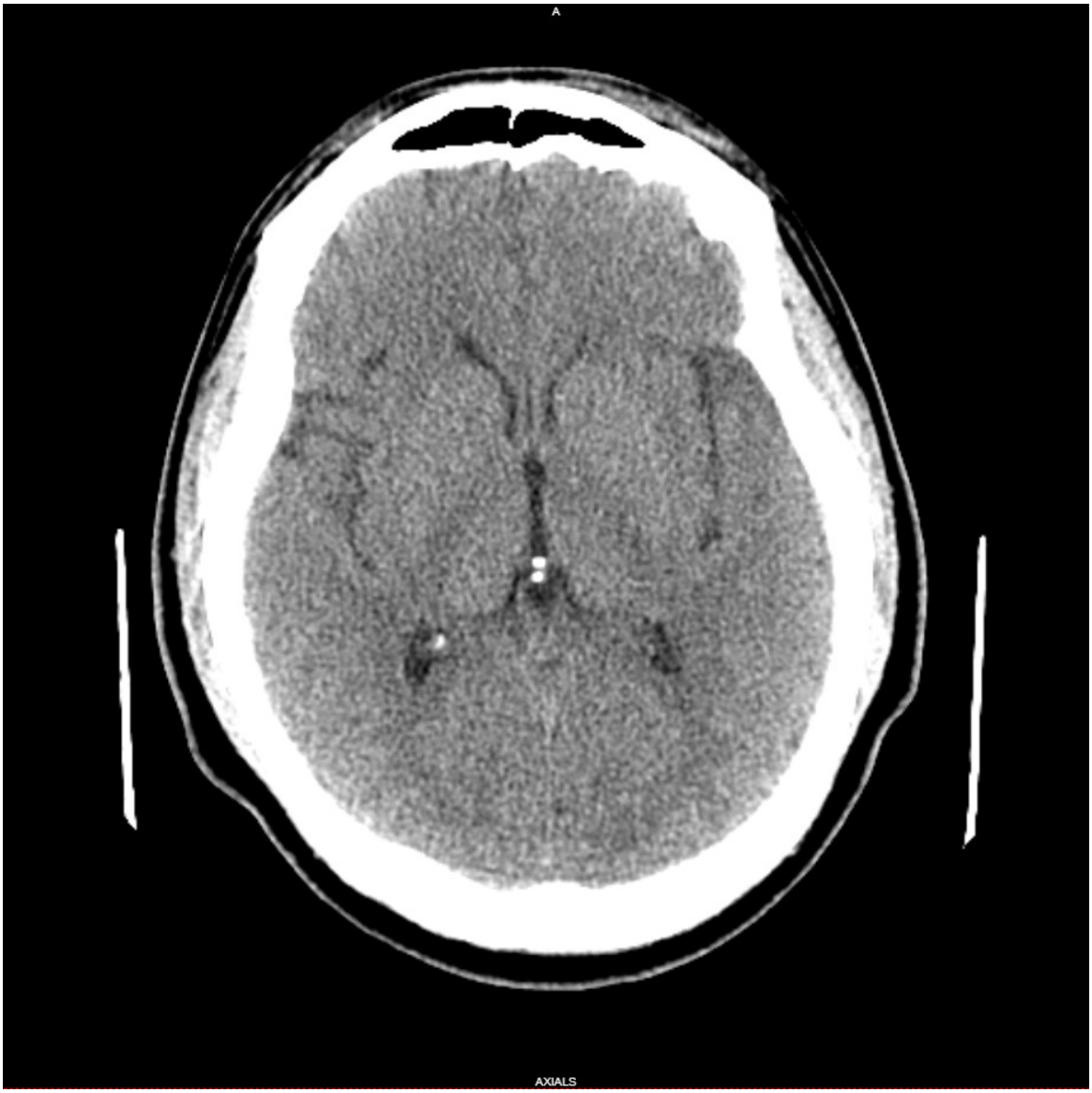
Conclusion

The novel Coronavirus, primarily thought to be a respiratory virus, can impact several systems. We recommend healthcare workers taking care of COVID-19 positive patients to consider the different presentations, symptoms and/or complications, including neurologic ones; especially in the presence of suggestive symptoms, as the spectrum is wide and they can have devastating outcomes.

Disclosure

The authors declare no conflicts of interest in the writing of this manuscript.

Figure 1. Non contrast brain computerized tomography scan depicting symmetric hypoattenuation within the medial thalami and bilateral ventricular calcifications. No signs of intracerebral hemorrhage were noted



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