COVID-19 Associated With Encephalitis

Case Report and Review of Literature

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Introduction: Neurological problems may be part of severe and early course of coronavirus disease 2019 (COVID-19). COVID-19 associated encephalitis as an evident etiology of altered consciousness has been rarely reported in the literature.

Case Report: A case of 66-year-old female presented with classic COVID-19 symptoms and associated diabetic ketoacidosis. Although diabetic ketoacidosis was managed, the patient had persistent impaired level of consciousness with recurrent attacks of left focal fits because of COVID-19-associated encephalitis. However, the patient has markedly improved after recovering from COVID-19.

Conclusion: Neurologists should be involved in the evaluation and management of COVID-19 patients who present with associated neurological problems.

Key Words: coronavirus, infection, COVID-19, encephalitis, case report

(*The Neurologist* 2021;26:268–270)

Coronavirus disease 2019 (COVID-19) or is a serious pathogen with multisystem alteration, causing > 1.5 million deaths until now. Apart from taste and smell dysfunction, the early typical presentations of COVID-19 disease did not include other central nervous system (CNS) symptoms. In the past few months, neurological manifestations associated with COVID-19 have been increasingly reported.¹ Manifestations such as seizures, stroke, and encephalopathy were reported as an indirect CNS affection from severe systemic viral reactions outside the nervous system. Other rare reports of meningitis, encephalitis, myelitis, and cranial nerve palsy were due to direct central or peripheral nervous system invasion by the virus.^{2,3} Here, we report a rare case of disturbed conscious level due to COVID-19 encephalitis.

CASE SCENARIO

In late August 2020, a case of a 66-year-old female patient presented to our hospital with complaints of fever (38°C), shortness of breath, tachypnea, and 3-day history of delirious state, confusion,

fluctuant conscious level, and disorientation. Of note, the patient is a known case of type-2 diabetes mellitus and hypertension, with a history of chronic bronchitis and ischemic heart disease. Upon initial evaluation, diabetic ketoacidosis (DKA) was confirmed through his high random blood sugar (385 mg/dL), urinary ketone bodies, and evident metabolic acidosis (pH 7.2, with HCO_3^- 14) in her arterial blood gases. In addition, COVID-19 was suspected; thus, a polymerase chain reaction (PCR) nasopharyngeal swab was arranged and the patient was isolated under the endocrinology unit for DKA management. A chest x-ray showed bilateral infiltration with obliteration of the right costophrenic angle. In the meantime, the COVID-19 swab came positive. Four days at admission, blood sugar and acidemia were well-controlled; however, the patient was still confused and developed recurrent attacks of left focal fits with secondary generalization. Upon further examination, the patient showed that she is confused (postictal state) and feverish, with left facial nerve affection of upper motor neuron character. Also, left side lateralized weakness and bilateral extensor plantar response were observed, but there were no neck rigidity or signs of meningeal irritation. Computed tomography (CT) scan of her chest showed bilateral pleural effusion with subsequent relaxation collapse of the underlying lower lung lobes, pneumonic changes with pleural thickening (Fig. 1). Along with COVID-19 pneumonia treatment, antiepileptic medication (phenytoin loading dose), and treatment of suspected CNS infection including vancomycin, meropenem, levofloxacin, favipiravir, and acyclovir were administered. An urgent CT brain showed right temporal hypo-dense area.

The patient was then shifted to the intensive care unit with highly suspected CNS infection for further magnetic resonance imaging (MRI) brain, lumbar puncture for cerebrospinal fluid (CSF) analysis, routine laboratory measures, and septic screening. The complete blood count revealed an elevated white blood cell count (10.66×1000) with normal septic screening. The MRI brain results showed an ill-defined area of faint low signal intensity lesion in T1, hyperintense in T2. Fluid attenuated inversion recovery images showed partial restriction in diffusion-weighted images with no significant enhancement post-IV gadolinium contrast injection, involving the right cerebral hemisphere, mainly at the temporal area, suggesting an inflammatory process/encephalitis (Fig. 2). The patient continued to develop recurrent attacks

FIGURE 1. Computed tomography scan of patient's chest.

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All the methods were performed in accordance with the relevant approved guidelines, regulations, and declaration of Helsinki. Written informed consent was obtained from the patient to have her details and accompanying images published.

The authors declare no conflict of interest.

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ISSN: 2331-2637/21/2606-0268

DOI: 10.1097/NRL.0000000000000347

FIGURE 2. Magnetic resonance imaging of the patient's brain.

of left focal fits. The CSF results showed low cellular count (2 cells) with normal protein and glucose levels, with no bacterial growth nor staining for both gram bacteria and acid-fast bacilli. Also, the PCR result for the herpes virus was negative. Also, another COVID-19 swab was taken and the result was still positive. Therefore, the diagnosis of COVID-19 and encephalitis was the most probable scenario. On day 8 of intensive care unit admission, the patient's symptoms were finally controlled on both levetiracetam and carbamazepine. Also, a third COVID-19 swab was arranged and came negative. Thus, the patient was discharged home, fully conscious with no neurological deficits.

DISCUSSION

Impaired consciousness level in the course of severe COVID-19 infection has been increasingly reported in the literature.³ However, underlying encephalitis as an evident etiology confirmed by MRI has not been frequently reported in the course of COVID-19 disease.⁴⁻⁶ This report describes a case of a COVID-19 patient who presented with classic features of coronavirus disease associated with encephalitis. Neurological complications including vomiting,

headache, seizures, decreased level of consciousness, and Guillain-Barré syndrome have been reported as early features of COVID-19.^{3,7-9} Neurological problems in the COVID-19 course may indicate severe disease; however, a report of COVID-19 associated encephalitis has shown that neurological features of the virus are not a reflection of disease severity.^{3,4}

While the identical diagnosis of virus encephalitis mainly relies on virus isolation, this seems challenging for COVID-19 as its dissemination is transient and the CSF titer may be considerably low.⁶ Thus, physical assessment of neurological features is substantial to establish a hypothetical diagnosis. A major limitation in the present report is that the CSF was not examined for COVID-19 ribonucleic acid due to refusal of the patient's relative for a second CSF sampling. However, the brain imaging and clinical observations were consistent with COVID-19 encephalitis. In a previous report of COVID-19-associated limbic encephalitis, the authors have not isolated the SARS-CoV-2 from CSF sample although the CSF samples were checked for COVID-19 in 2 laboratories.⁵ The authors

proposed that the presence of the virus in CSF may be provisional or that the pathogenesis is COVID-19-induced immune response.⁵ This is consistent with the presumption of Iadecola et al¹⁰ that COVID-19 alters nervous system through systemic inflammation and the hyperactive innate immunity of cytokine production.

The exact pathogenesis of COVID-19-associated encephalitis is not yet clearly explored. Experimental studies showed that COVID-19 enters host cells via the angiotensin-converting enzyme 2 receptors, which are expressed in several organs including CNS. Consistent with the Wu et al¹¹ report, we hypothesized that COVID-19-induced immune response may lead to inflammatory damage and edematous changes, hence, causing an altered level of consciousness. It has been reported that COVID-19-associated encephalitis is self-limiting. Upon purifying of the virus and mannitol administration, the CSF pressure gradually decreases and the levels of consciousness gradually recover.⁶ This is consistent with our report where the patient did not show any clinical improvement of conscious level except after a negative nasopharyngeal swab for COVID-19 RNA.

CONCLUSION

Neurological complications should be considered in patients presenting with features of COVID-19. Given the mounting prevalence of COVID-19 and lack of reliable PCR testing of CSF, further reports would clarify if associated encephalitis is not simply coincidental. Henceforth, neurologists should be involved in the evaluation and management of COVID-19 patients who present with associated neurological problems.

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