Case Report

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Does COVID-19 Cause Hemorrhagic Encephalitis? A Case Report

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Citation Abutorabi Zarchi M, Razavi R, Namiranian N. Does COVID-19 Cause Hemorrhagic Encephalitis? A Case Report. Case Reports in Clinical Practice. 2024; 9(5): 224-228. DOI:10.18502/crcp.v9i5.18456

Running Title Hemorrhagic Encephalitis Due to COVID-19

Article info:
Received: September 10, 2024
Revised: September 25, 2024
Accepted: October 17, 2024

Keywords:
COVID-19; Brain; Encephalitis; SARS-COV-2

ABSTRACT

SARS-CoV-2 causes an inflammatory disease characterized by symptoms such as fever, cough, shortness of breath, and myalgia, along with leukopenia, lymphopenia, elevated serum aspartate aminotransferase levels, and abnormal chest computed tomography findings. It may also lead to respiratory distress, unilateral complications, and secondary infections. COVID-19 infection can result in severe neurological complications, including viral encephalitis, cerebrovascular disorders, acute diffuse encephalomyelitis, and acute necrotizing encephalopathy. Here, we report a case of hemorrhagic encephalitis due to SARS-CoV-2 in a 27-year-old patient with a history of type 1 diabetes.

Introduction

In December 2019, the coronavirus pandemic began in Wuhan, China, and rapidly spread across the globe [1]. The virus causes severe respiratory syndrome, with 36.4% of infected patients presenting with neurological symptoms such as headache, impaired consciousness, and paresthesia. In patients with more severe disease, these neurological symptoms tend to worsen [2].

COVID-19 infection can lead to a range of severe neurological complications, including viral encephalitis, cerebrovascular disorders, acute disseminated encephalomyelitis (ADEM), and acute necrotizing encephalopathy (ANE) [3–5]. ADEM and ANE are not caused by direct viral invasion but result from cytokine storms that stimulate immune-mediated processes [6, 7]. In 2020, the first confirmed case of SARS-CoV-2 encephalitis was reported, with the virus genome detected in cerebrospinal fluid [8]. Here, we present a case of hemorrhagic encephalitis associated with COVID-19, which showed a good prognosis.

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CASE PRESENTION

A 27-year-old patent with a medical history of type 1 diabetes mellitus presented with fever, lethargy, and a decreased level of consciousness. The patent had experienced frequent lethargy and vomitng in the few days before admission. She had been referred to the emergency room due to deterioratng symptoms and a decreased level of consciousness. The patent had a low level of consciousness at the tme of admission (GCS = 7) and was in respiratory distress. The patient also had metabolic acidosis.

The initial laboratory tests were as follows: White Blood Cells (WBC): 54,000; C-Reactive Protein (CRP): 1+; Erythrocyte Sedimentation Rate (ESR): 35; blood glucose: 600 mg/dL. Due to fever, COVID-19 testing was performed. A chest computed tomography (CT) scan revealed ground-glass opacity (GGO) (Figure 1), but the nasopharyngeal polymerase chain reaction (PCR) test was negative.

Due to the decreased level of consciousness, a brain CT scan was performed, which showed no abnormalities on initial examination. Treatment for diabetic ketoacidosis (DKA), empirical antibiotic therapy, and Remdesivir (initiated based on CT findings suggestive of COVID-19) were administered.

While the patient's level of consciousness initially showed relative improvement, they subsequently experienced recurrent decreased consciousness and seizures. A follow-up CT scan demonstrated multiple small-to-medium sized hemorrhages in the bilateral frontal and occipital lobes with associated vasogenic edema, but no midline shift. Brain magnetic resonance imaging (MRI) revealed T1 and T2 hyperintense lesions along with findings consistent with posterior reversible encephalopathy syndrome (PRES) in the bilateral occipital regions (Figure 2).

To investigate the cause of hemorrhagic lesions in the brain, echocardiography was performed, showing an EF of 55%. There were no valve disorders or vegetations. Two negative blood cultures ruled out endocarditis. There was no evidence of vascular malformation or aneurysm in the brain, as determined by Magnetic Resonance Angiography (MRA). Brain Magnetic Resonance Venography (MRV) was performed to evaluate CVT, which was found to be normal (Figure 3). The results of vasculitis and rheumatological tests, including ANA, anti-DNA antibodies, antiphospholipid antibody, lupus anticoagulant, cardiolipin antibody, PANCA, CANCA, DNA, C3, C4, and CH50, were negative.

A lumbar puncture (LP) was performed, revealing lymphocytosis and a negative PCR for COVID-19 at the initial examination. The smear and cerebrospinal fluid (CSF) culture were negative. A second LP was performed after 48 hours due to the lack of improvement in consciousness. This time, lymphocytosis and a positive COVID-19 PCR test were documented. Consequently, after ruling out other causes of cerebral hemorrhage and considering the positive PCR result, the patient was treated for COVID-19 encephalitis. In addition to Remdesivir, the patient underwent five sessions of plasmapheresis. Due to a high level of interleukin, the patient was also administered Actemra. Seizures were controlled with antiepileptic therapy.

Gradually, the patient's level of consciousness improved, and they were extubated. The patient was discharged after 45 days without focal neurological symptoms and with a normal level of consciousness. At the three-month follow-up, the patient displayed no focal neurological symptoms or cognitive impairments.

DISCUSSION

Although the primary target of the SARS-CoV-2 virus

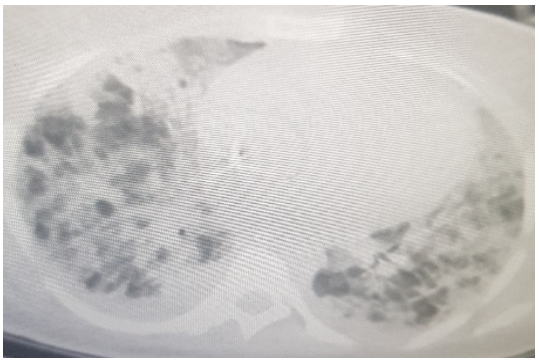

Fig. 1. Lung high-resolution computed tomography show bilateral areas of ground-glass opacities in a peripheral distribution.

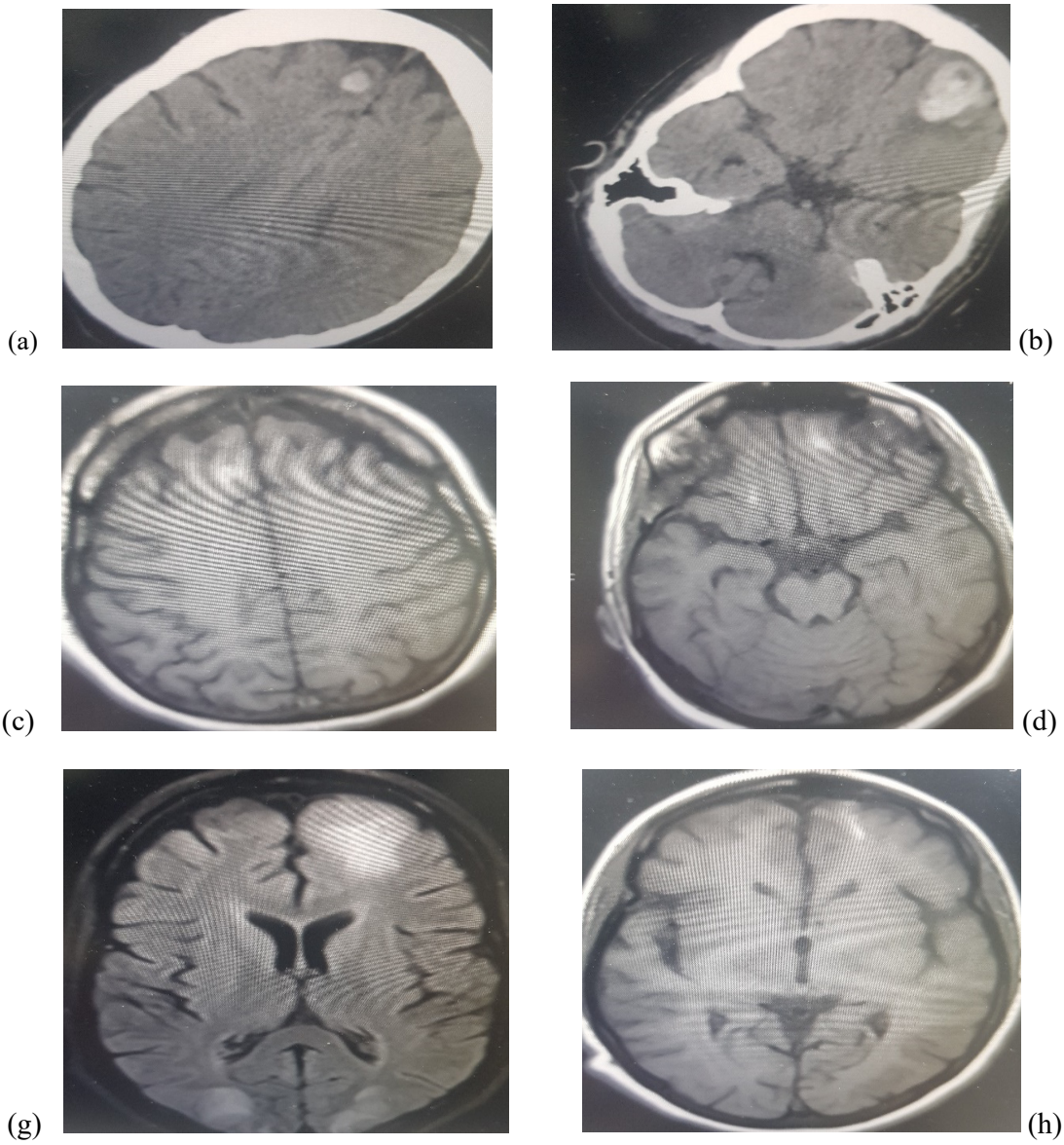

Fig. 2. Brain CT scan show bilateral frontal hemorrhage (a & b) brain MRI (axial T1 weighted) show bilateral frontal hyper intensity according to hemorrhage (c & d) and in FLAIR sequence show bilateral subcortical occipital white matter edema according to posterior reversible encephalopathy syndrome (PRES). Follow up MRI (6 months later) show significant clearance of hemorrhage.

is the respiratory system, it affects many other systems of the body and has numerous manifestations. One of these complications includes neurological symptoms, which involve central nervous system (CNS) involvement such as encephalitis, headache, dizziness, impaired consciousness, ataxia, acute cerebrovascular disease, and epilepsy. The virus can also affect the peripheral nervous system (PNS) and lead to complications such as hypogeusia, hyposmia, hypopsia, and neuralgia, as well as skeletal muscle symptoms [2,3]. Additionally, it can stimulate immune-mediated reactions, leading to Acute Disseminated Encephalomyelitis (ADEM) and Acute Necrotizing Encephalopathy (ANE) [5].

The exact mechanism of COVID-19-induced CNS infection is not fully understood [3]. However, the target receptor for SARS-CoV-2 is the angiotensin-converting enzyme 2 (ACE2) receptor. After attachment and internalization, viral ribonucleic acid (RNA) is released into the cytoplasm, subsequently leading to translation and replication. This receptor is also present on glial cells in the brain and spinal cord, which may explain the involvement of the CNS by this virus [9].

After the virus invades the CNS, it can damage the nervous system in two ways: 1. immune-mediated mechanisms caused by a cytokine storm; 2. pneumonia, which causes severe hypoxia and acute respiratory distress syndrome (ARDS) and damages neurons [10]. Symptoms of viral encephalitis are nonspecific (e.g., seizure encephalopathy); hence, the

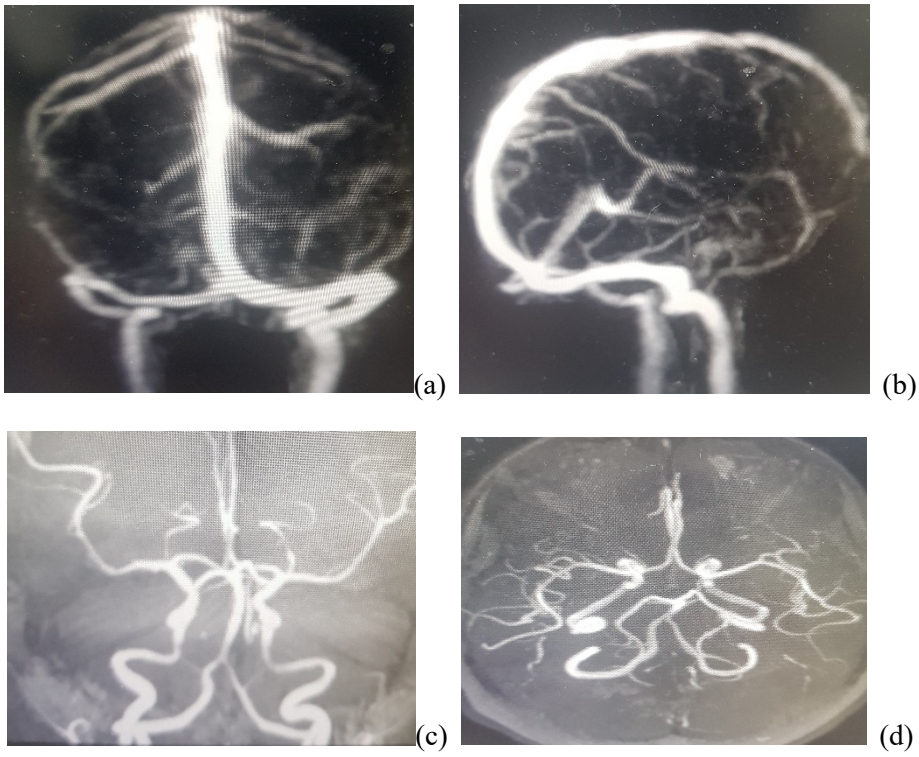

Fig. 3. Normal brain magnetic resonance venography (a&b) and normal brain magnetic resonance angiography (c &d).

definitive diagnosis of this disease is the presence of the virus genome in CSF [11].

Cases of COVID-19-induced hemorrhagic encephalitis have been reported in some studies [12,13]. It is believed to be a post-infectious process and is considered a severe form of disseminated encephalomyelitis. Similar cases have also been observed with other viruses, such as the H1N1 flu [14].

The patient's PCR test was negative; however, the results of this test can be falsely negative in some cases, and a CT scan can be used to diagnose COVID-19 [15]. Due to lung involvement, COVID-19 treatment was initiated. After the patient's condition deteriorated further, a CT scan of the brain was performed. Findings from the CT scan revealed cerebral hemorrhage. The MRVI of the brain showed no evidence of CVT. Brain MRA was normal and showed no evidence of aneurysm, vascular malformations, or vasculitis. Tests for vasculitis were also conducted to diagnose systemic vasculitis, but the results were normal. Therefore, due to the exclusion of secondary causes of cerebral hemorrhage and the detection of a positive PCR result in CSF samples, the patient was diagnosed with COVID-19 hemorrhagic encephalitis.

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The patient's PCR test was negative; however, the results of this test can occasionally yield false-negative results. In such cases, a CT scan can be utilized to diagnose COVID-19 [15]. Due to lung involvement, COVID-19 treatment was initiated. Following further deterioration of the patient's condition, a CT scan of the brain was performed. The CT findings revealed cerebral hemorrhage. The MRVI of the brain showed no evidence of CVT, while the brain MRA was normal, with no indications of aneurysm, vascular malformations, or vasculitis. Vasculitis tests were also conducted to assess systemic vasculitis, but the results were normal. Consequently, with secondary causes of cerebral hemorrhage ruled out and a positive PCR result detected in CSF samples, the patient was diagnosed with COVID-19 hemorrhagic encephalitis. The treatment of Covid encephalitis is supportive and includes various treatments such as High-dose IV steroids, IV immunoglobulin, and immunomodulators (e.g., rituximab) are given in different cases. The results showed that these treatments had limited consequences [16].

For the patient, supportive and symptomatic treatment, 5 sessions of plasmapheresis and injection of Actemra were performed. Fortunately, the patient's level of consciousness gradually improved and the patient was discharged with a level of consciousness of 15 and no lateralized symptoms, with continued anticonvulsant therapy and rehabilitation. However, neurological symptoms may persist in many cases but in our patient [17], CNS involvement had a relatively good outcome.

Conclusions

Hemorrhagic encephalitis should be considered in COVID-19 patients presenting with altered mental status or seizures, even if initial PCR test results are negative. Maintaining a high index of suspicion, along with repeated testing and advanced imaging techniques such as MRI, is essential for accurate diagnosis.

Ethical Considerations

Compliance with ethical guidelines

There were no ethical considerations to be considered in this article.

Funding

No funding was received to assist with the preparation of this manuscript.

Conflict of Interests

The authors have no conflict of interest to declare.

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