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SARS-CoV-2 associated viral encephalitis with mortality outcome

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ABSTRACT

Background: Severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) appeared in Wuhan, China, in December 2019; apart from common conditions such as cough, fever, and severe respiratory complications, difficulty in breathing, including tachypnea, new studies on neurological manifestations have gained public interest.

Case report: An 89-year-old man was admitted to the neurocritical care department in a specialized hospital with headache, dizziness, hyperpyrexia, myalgia, rash, and tremors. MRI showed viral encephalitis near to basal ganglia and thalami.

Discussion: Coronaviruses interfere with target cells by membrane-bound spike proteins. Angiotensin-converting enzyme 2 was identified as an input receptor for SARS-CoV-2. Due to its wide pattern of expression, COVID-19 was shown to affect several organs, including the central nervous system, where the receptor is mainly expressed as neurons.

Conclusions: In the current pandemic, there is a rising number of global infections, the aim of our case to increase the awareness about SARS-CoV-2 possible complications, even if there are possible further mutations for the virus, especially in the central nervous system.

1. Introduction

Severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) appeared in Wuhan, China, in December 2019, causing an outbreak of severe respiratory complications. The subsequent outbreak was referred to as coronavirus disease in 2019 (COVID-19) and was recognized as a pandemic in March 2020. Apart from common conditions such as cough, fever, and severe respiratory complications such as difficulty breathing, including tachypnea, new studies on neurological manifestations have gained public interest; this involved encephalopathy and encephalitis presumably caused by SARS-CoV-2 [1,2]. The role of the central nervous system (CNS) was seen in the 2002 epidemic of severe acute respiratory syndrome coronavirus (SARS-CoV) [3]. Here, we discuss a case that has been admitted to the neurosurgery department in a specialized hospital with SARS-CoV-2 related viral encephalitis, and this is the first case confirming the mortality of viral encephalitis linked to SARS-CoV-2 infection, to the best of our knowledge.

2. Case report

An 89-year-old man was admitted to the neurocritical care department in a specialized hospital with headache, dizziness, hyperpyrexia, myalgia, rash, and tremors. Dystonia and dyskinesia were present on physical examination. Magnetic resonance imaging (MRI) showed a hyper-intense signal near the basal ganglia and thalami in T2 fluid-attenuated inversion recovery (FLAIR) imaging (Fig. 1). Despite attempts of combined anti-epileptic medication, seizure control was not satisfactory. Based on clinical and radiologic findings, surgical intervention was not possible due to the patient's health status. Intensive care unit (ICU) admission was necessary, anti-viral and anti-inflammatory drugs were prescribed including, acyclovir (zovirax) 400 mg every 12 h and acetaminophen (paracetamol) 500 mg 3 times per day both on daily basis. On the same day of admission, the patients' daughter presented to the emergency department with severe respiratory complications and tested positive for SARS-CoV-2. Our case tested positive for SARS-CoV-2 using an antibody test. The patient was referred to the infectious disease department and was followed-up until SARS-CoV-2

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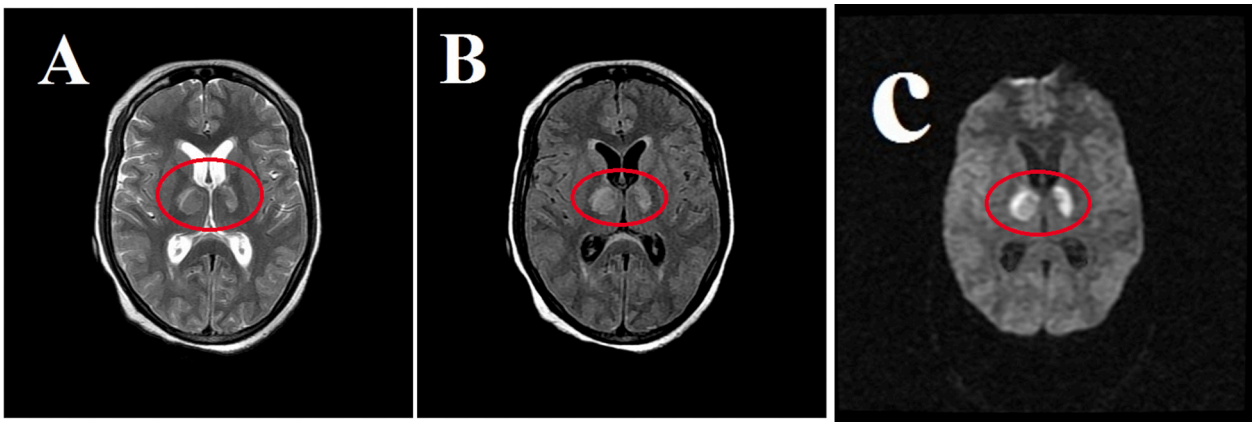

Fig. 1. MRI showing encephalitis (red circle). A: showing axial FLAIR, B: showing axial T2 hyper-intense, and C: showing axial DW. FLAIR: Fluid-attenuated inversion recovery. DW: Diffusion-weighted. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

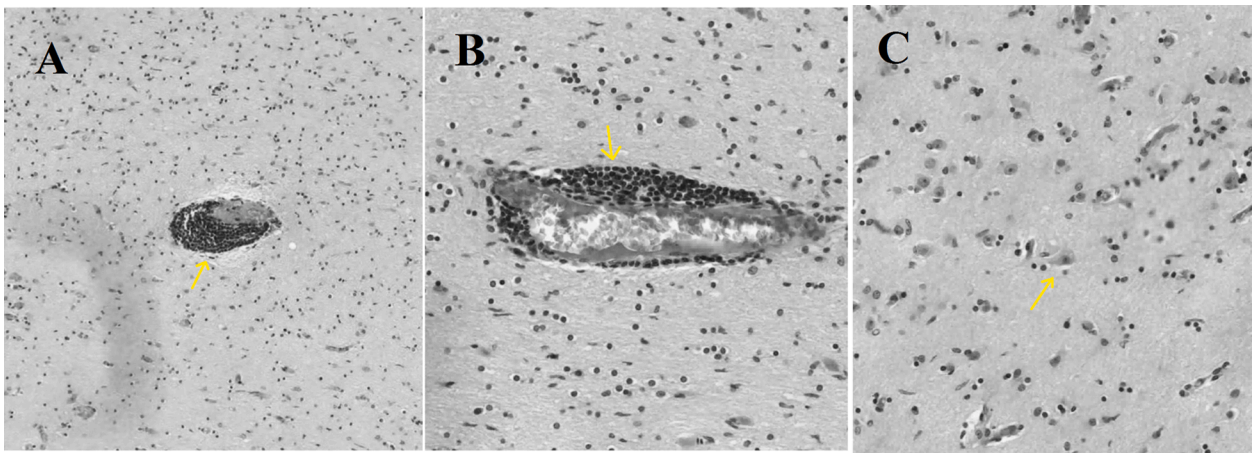

Fig. 2. Post-mortem brain biopsy showing viral encephalitis microglial nodules (yellow arrow). (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

negative testing. On a retrospective basis, he stated that he had a flu-like illness ten days before the onset of neurological symptoms. By a week, the patient died in the ICU from severe seizures and respiratory failure, and his corpse was referred to a medico-legal specialist; examinations found that the cause of death was viral encephalitis infection (Fig. 2).

3. Discussion

Coronaviruses interfere with target cells by membrane-bound spike proteins. Angiotensin-converting enzyme 2 was identified as an input receptor for SARS-CoV-2. Due to its broad expression, COVID-19 can affect several organs, including the CNS, where the receptor is mainly expressed as neurons. SARS-CoV-2 is believed to have entered the CNS through two main routes. After infecting the nasal mucosa, coronaviruses may enter the brain via the cribriform plate, passing along the olfactory nerve.

Additionally, coronaviruses can enter the capillaries through the bloodstream and interact with angiotensin-converting enzyme 2 to infiltrate and replicate the endothelium. Viral budding induces disruption to the endothelial liner, allowing for increased viral entry to the neural environment [1]. Previously, neuro-invasion in SARS-CoV and Middle East respiratory syndrome coronavirus (MERS-CoV) was detected. Of the 70 patients with MERS-CoV, 25% had changed mental state, and 10% had seizures [5]. SARS-CoV responsible for the 2002–2004 outbreak has been reported to cause polyneuropathy, ischemic stroke, and encephalitis [2]. Autopsy findings of SARS patients revealed ischemic neuronal disruption and demyelination. Viral RNA has been detected in brain tissue, particularly in and around the hippocampus [3]. In SARS, neurological symptoms have been reported to develop, on average, three weeks after respiratory symptoms have occurred [2].

Similarly, mild to moderate, flu-like symptoms emerged two weeks before the onset of neurological symptoms, probably indicating a concurrent illness path. However, it remains unproven if the infection caused the flu-like effects with SARS-CoV-2. The high genetic correlation between SARS-CoV and the novel SARS-CoV-2 highlights related and potentially life-threatening CNS manifestations in COVID-19. As in our situation, previous studies on SARS-CoV-2 associated encephalopathy have indicated a predominant involvement of the temporal lobe. Poyiadji et al. [4] identified the suspected case of acute necrotizing encephalopathy in a female COVID-19 patient. Hypertensive lesions in the thalamus and medial temporal lobes were detected in T2 FLAIR. Another male patient displayed T2 FLAIR hyper-tensity in the right temporal lobe and hippocampus, indicating encephalitis [5]. Moreover, there were some common symptoms, as in our case, including headache and dizziness, but no mortality events occurred.

4. Conclusions

To the best of our current knowledge of SARS-CoV-2 associated viral encephalitis with mortality outcome, we have reported the first case. In

the current pandemic, there is a rising number of global infections, our case's aim to increase the awareness about SARS-CoV-2 possible complications, even if there are possible further mutations for the virus, especially in the CNS. For prompt diagnosis and prevention of transmission as best as possible, physicians should recognize SARS-CoV-2 infection in patients with similar symptoms of our case as early as possible to avoid poor prognosis.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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