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Case report

Post COVID-19 Multisystemic Inflammatory Syndrome Revealed by Seizures: A Case Report

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Abstract

The Covid-19 infection disrupts various organs, including the liver, kidney, and nervous system. Common neurological symptoms of the Covid-19 infection include delirium, confusion, headache, and loss of sense of smell and taste. In rare cases it can cause seizure. The virus enters the nervous system either directly through nerve pathways or indirectly through the ACE2 receptor. Understanding the potential mechanisms is necessary to gain better insight into COVID-19 induced seizure pathogenesis and to design the correct treatment strategies to achieve appropriate treatment for seizure and epilepsy.

We report the case of a child with post covid syndrome with multisystemic inflammatory syndrome damage, and we explain the mechanisms of the damage to the nervous system.

Keywords: ***Covid-19, Seizure, Pandemic***

Introduction

Coronavirus or COVID-19 has affected many people around the world and is now a major global health threat. The major symptoms in infected people include fever, dry cough, aches, pain, tiredness, chills, headache, anorexia, and loss of smell or taste. Covid-19 can also cause some organs to fail, such as the respiratory system, kidneys, liver, and heart. Cardiovascular complications may include heart failure, irregular electrical activity in the heart, coagulation disorders, and acute myocardial injury [1]. Moreover, in some people, gastrointestinal symptoms such as anorexia, nausea, vomiting, diarrhea, and abdominal pain are associated with COVID-19 [2]. These symptoms may start before other symptoms such as fever, aches, and cough. People infected with COVID-19, also may experience neurological symptoms [3] which may occur with or without cardiovascular and respiratory symptoms [4,5]. Specific neurological symptoms accompanying the COVID-19 infection include loss of smell and taste, muscle weakness and pain, tingling in the hands and feet, vertigo, delirium, ischemic and hemorrhagic stroke, and seizures [6].

The exact mechanisms leading to seizures are not yet completely understood. However, the suggested mechanisms include a sever increase in neuronal excitability following an imbalance in the ion channel function, either as an increase in excitatory neurotransmitters of glutamate and aspartate or a decrease in the γ-aminobutyric acid (GABA) neurotransmitter [7]. Other causes of seizures include acute metabolic disorders such as hypo or hyperglycemia, electrolyte imbalance, acute neuronal damage following infection and inflammation, stroke, head trauma, mitochondrial dysfunction, hypoxia, and fever. Only a few studies have been so far conducted to investigate the underlying mechanism of neurological complications of COVID-19, especially seizures and epilepsy.

Case Report

The child, G.A., aged 15, with no notable pathological history, with good psychomotor development, and well vaccinated. The patient presented two days before his admission with pain in the throat, vomiting, fever, and headache. The patient on admission was febrile at 39C, had a stiff neck and conjunctival hyperemia, but he had no focal signs. The diagnosis of bacterial meningitis was suspected, and the patient was placed on a meningeal dose of Triaxon. The study of the cerebrospinal fluid and the multiplex polymerase chain reaction of the cerebrospinal fluid were normal, the symptomatology was complicated by the installation of a convulsive status epilepticus with an attitude in gun dog. A cerebral computed tomography with injection of the contrast product was made and showed an

enhancement of the meninges and the falx cerebri (**Figure 1**), a decrease in the enhancement of the posterior longitudinal sinus (**Figure 2**). the biological assessment had shown a reactive protein C =195mh/L, lactate dehydrogenase =1768 U/L, ferritinemia =11079 ng/ml, triglycerides = 1.22, aspartate aminotransferases =172 µi/l, alanine aminotransaminase= 421 µ/l. prothrombin rate = 42%, fibrinogen = 3.7 g/l. the d-dimers = 9060 µg/l, in view of these results, infection with the corona virus-19 was suspected, which led to the performance of a rapid COVID-19 test which was negative, the Polymerase Chain Reaction multiplex SARS-COV-2 was negative, but COVID-19 serology was positive with Ig G positive, Ig M negative. A chest X-ray showed ventilation disorders with cardiomegaly (**Figure 3**). Echocardiography was in favor of myocarditis. The diagnosis of post COVID-19 syndrome with multi-systemic involvement revealed by central nervous system involvement was retained. The patient was transferred to the intensive care unit where he was managed with good progress.

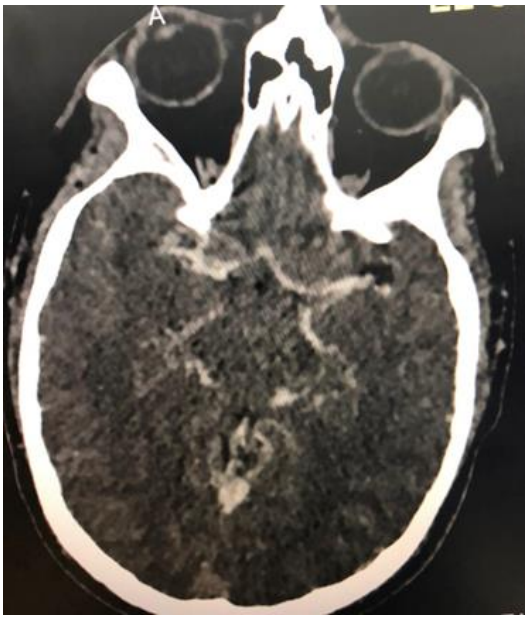

Figure 1: Enhancement of the meninges and falx cerebri

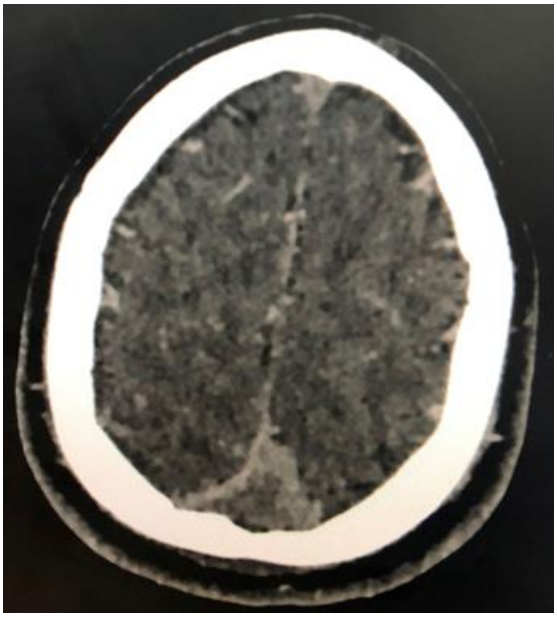

Figure 2: Decreased enhancement of the posterior longitudinal sinus

Discussion

COVID-19 has the ability to enter the nervous system and cause neurological symptoms. The receptor for angiotensin-converting enzyme 2 (ACE2) [8], found mainly in the brainstem, is the entry route for the coronavirus into the central nervous system which leads to the release of cytokines pro -inflammatory (TNF-α, IL-6, IL-1B), nitric oxide, prostaglandin E2 and free radicals, which cause inflammation and neural hyper-excitability, convulsions and death [9,10]. Pro-inflammatory cytokines play a key role in seizure pathogenesis. They also cause epilepsy by increasing glutamate and decreasing GABA in the cerebral cortex and hippocampus. These cytokines increase the entry of calcium into neurons through AMPA and NMDA receptors, thereby increasing neuronal hyperexcitability and death [11,12]. IL-Iβ, which is expressed in microglia and astrocytes, produces the highest concentration of glutamate at synapses, increasing glutamate release from astrocytes or reducing glutamate reuptake can lead to neuronal hyperexcitability [13]. TNF-α increases the release of glutamate from the glia and regulates AMPA receptors [14]. Overactive AMPA receptors absorb a lot of calcium ions and cause neuronal toxicity. Through the mechanism of endocytosis, TNF-α not only increases the number of glutamate receptors but also decreases the number of GABA receptors, which increases neuronal excitability [15,16]. Studies have revealed that IL-6, pro-inflammatory cytokine, reduces long term potentiation (LTP) and neurogenesis of the hippocampus, thereby helping to initiate and increase the severity of epilepsy [17].

COVID-19 infection breaks the integrity of the blood-brain barrier (BBB), which severely impairs brain homeostasis and leads to neuronal apoptosis. On the other hand, the degradation of the BBB causes the migration of blood cells and proteins, such as albumin, which disturbs the osmotic balance in the central nervous system (CNS) and causes seizures [12,18]. BBB degradation is the other pathway for peripheral cytokines to enter the brain. The other cause of BBB disruption and induction of seizures by COVID-19 is fever and hyperthermia.

Patients infected with COVID-19 showed coagulation abnormalities characterized by prolonged prothrombin time, increased D-dimer levels and diffuse intravascular coagulation, as is the case of our patient [19,20]. Certain cytokines, including IL-6, activate the coagulation cascade and suppress the fibrinolytic system. Endothelial damage to the pulmonary and peripheral arteries due to direct viral attack may be an equally important factor in increased blood clotting. In addition, the appearance of antiphospholipid antibodies can also alter blood coagulation [21,22,23].

Studies have reported various electrolyte abnormalities in patients infected with coronavirus [24,25]. COVID-19 infection is associated with decreased serum concentrations of sodium, potassium, magnesium, and calcium, resulting in hypokalemia, hypocalcemia, and hypomagnesemia hyponatremia (as in our patient). These disorders, in particular hypokalaemia, can have serious clinical consequences for infected persons. Hypokalemia leads to exacerbation of ARDS and acute heart damage [9,26,27]. SARS-CoV-2 binds to its host ACE2 receptor, eventually reducing ACE2 expression, thereby increasing angiotensin II, which can increase renal potassium excretion, and eventually lead to hypokalemia. Seizures are the most important clinical symptoms of electrolyte disturbances and are more common in patients with hyponatremia, hypocalcemia, and hypomagnesemia. In these individuals, successful seizure treatment begins with an accurate diagnosis of the underlying electrolyte disturbances [28,29]. Early detection and correction of these disorders are key to controlling seizures and preventing permanent brain damage. If the electrolyte disturbance persists, antiepileptic drugs (AEDs) alone are

ineffective and inadequate to control seizures. Treatment of seizures induced by electrolyte imbalance is determined by the underlying cause and in most cases, AED administration is not required until the disturbance is corrected [30,31,32].

Conclusion

A better understanding of the Covid-19 mechanism leading to organs failure would help to identify strategies and/or therapeutically treatment options for the infection. The virus can cause complicated disorders in the nervous system, such as seizures and epilepsy. The destructive effects of Covid-19 in the central nervous system are mainly caused by a cytokine storm produced by either the entry of pro-inflammatory cytokines from the periphery into the CNS or the production of these cytokines by activated microglia. Secondary seizures may be initiated after strokes, electrolyte imbalance, increased oxidative stress, a mitochondrial dysfunction in Covid-19 patients. More research is needed to prove the exact mechanism of seizures in Covid-19 patients.

Ethics approval and consent to participate

Not applicable

Data availability

Not applicable

Conflicts of interest

The authors declare that there is no conflict of interest regarding the publication of this paper.

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Authors' Contributions

This work was carried out in collaboration among all authors. NM and AAM designed the study, performed the statistical analysis, wrote the protocol, wrote the first draft of the manuscript, and managed the analyses of the study. NM and AAM managed the literature searches. All authors read and approved the final manuscript.

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