Intraventricular Hemorrhage in Children with COVID-19 Confirmed

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ABSTRACT

Background. The most common symptom of Coronavirus disease 2019 (COVID-19) caused by SARS-CoV-2 is respiratory symptoms. However, neurological symptoms in adult patients are increasingly being reported. In children, neurological symptoms of COVID-19 are still underreported. This case report was aimed to describe intraventricular hemorrhage in a child with Covid-19 infection. Case presentation: We report a case of a 15-year-old girl with intraventricular bleeding, which is one of the COVID-19 infection symptoms or a possible symptom of a multisystem inflammatory syndrome in children (MIS-C). Laboratory tests on the first day of treatment showed an increase in leukocytes and decreased lymphocytes. On the 6th day of treatment, the patient had worsening symptoms of consciousness and high fever. The results of laboratory examination showed a decrease in kidney function and an increase in D-dimer. Conclusion: Severe clinical manifestations of COVID-19 can be in the form of neurological manifestations, one of which is intraventricular hemorrhage.

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1. Introduction

Cases of COVID-19 infection in children were first reported in Shenzhen in January 2020.¹ Of the serial cases in China, and the most common symptoms were fever (50%) and cough (38%).² Apart from the respiratory tract, SARS-CoV-2 can affect other organ systems such as nerves, vascular, digestive tract, urinary tract, hematological system, and others. The effect of viruses on the nervous system is yet fully understood. The most common neurological symptoms reported are myalgia, headache, sensory disturbances, and hyposmia. COVID-19 also shows symptoms of the central nervous system such as intracerebral hemorrhage, ischemic stroke, encephalomyelitis, peripheral nervous system manifestations such as Guillain Barre Syndrome, and Bell’s palsy and musculoskeletal manifestations such as rhabdomyolysis.³⁴⁵ There are several cases that describe neurological complications in children, including encephalitis, seizures, and cerebral infarction.⁶ Compared to adult patients, only a few neurological complications of COVID-19 were reported in pediatric patients.

2. Case Presentation

A girl, DA, aged 15 years 11 months, had decreased consciousness and severe headache accompanied by vomiting. She also had disorganized speech and fever. There was no history of coughs, colds, shortness of breath, or throat pain. There was no history of seizures or head trauma. There was no history of limb weakness
or blurred vision. There was no history of bleeding or weight loss. History of contact with patients with long-duration coughs / TB patients was denied. History of contact with patients with suspected or confirmed COVID-19 was denied. There was no history of high blood pressure or frequent headaches. Her appetite was normal. Her micturition and defecation were normal. The patient could still control her micturition and defecation before the loss of consciousness. There was no history of similar illness, high blood pressure, or chronic headaches. None of her family members suffer from high blood pressure. Her family did not suffer nor being suspected of COVID-19. The general condition of the patient appeared to be very ill, GCS E3M5V4 = 12. She did not look pale or icteric. She had no edema and did not appear to have cyanosis. Her heart rate was 80 times/minute, and respiratory rate was 20 times/minute, a saturation of 99%, blood pressure of 120/60 mmHg. Her pupil was within normal limits, and no signs of meningeal stimulation. Physiological reflexes were increased, and pathological reflexes were present. There was no lateralization nor clonus found.

Laboratory tests on the first day of treatment showed an increase in leukocytes and decreased lymphocytes. In contrast, the liver function, kidney function, electrolytes, PT, and APTT were within normal limits and non-reactive rapid test antibodies. Chest X-ray showed an impression of bronchopneumonia. CT scan of the head without contrast showed intraventricular bleeding with hydrocephalus with cerebral edema. The patient received oxygen therapy, empiric antibiotics, medications for lowering intracranial pressure, and other supportive therapy. The patient was subjected to a SARS-CoV2 RT-PCR nasopharyngeal swab examination, and a positive COVID-19 result was obtained.

On the 6th day of treatment, the patient had worsening symptoms of consciousness and high fever, and the laboratory test was carried out again. The results showed a decrease in kidney function and an increase in D-dimer, whereas PT / APTT were within normal limits.

Figure 1. Chest X-ray (AP view)
3. Discussion

Intraventricular hemorrhage (IVH) is bleeding that occurs in the ventricular system of the brain and has a high mortality rate, which is about 30% to 80%. IVH without cerebral parenchymal bleeding or subarachnoid hemorrhage is referred to as primary intraventricular hemorrhage (PIVH), which is a rare type of hemorrhagic stroke. The reported incidence of PIVH accounts for 2-4% of all intracranial hemorrhages. Most studies mention ruptured arteriovenous malformations (AVMs) as the main cause of primary intraventricular hemorrhage (PIVH), which accounts for 55%. Other possible causes include aneurysms (39%), dural arteriovenous fistulas, and Moyamoya disease. Whereas 21–46.5% of cases have unknown causes. Computed tomography (CT) scan, computed tomography angiography (CTA), and digital subtraction angiography (DSA) are used to establish the etiology of IVH.

Hydrocephalus is the most common complication of IVH, which can increase the risk of death. The underlying mechanism of hydrocephalus is the presence of blockage caused by blood clots in the circulating cerebrospinal fluid. In IVH patients who have obstruction of the cerebrospinal circulation, the high risk for herniation is 25.7%. The management of IVH includes conservative, lumbar drainage, extraventricular drainage (EVD), hematoma evacuation, and endovascular embolization. To date, the management of IVH caused by AVM is still controversial and without guidelines. In a study by Ye et al., early nidus resection and EVD had better results.

In this case, hydrocephalus is the most common complication of IVH. The management was conservative, which was therapy to reduce intracranial pressure. On the 4th day of hospitalization, the patient began to show a decrease in consciousness. However, both CT scans of the head and surgery procedures could not be done because of the limited facilities and resources. The etiology of IVH in this patient was suspected of rupture of the AVM, but supporting investigations such as computed tomography angiography (CTA) and digital subtraction angiography (DSA) could not be performed on the patient. It is possible that IVH, in this case, is a neurological manifestation of SARS-CoV-2 infection. However, the neurological manifestations in children with confirmed COVID-19 remain unclear.

It is confirmed that the patient was infected with COVID-19 from history, in which she had complaints of fever, not high but intermittent, but other respiratory complaints such as coughs and colds were denied. Physical examination showed an increase in body
temperature during treatment. The results of blood tests showed a decrease in the number of lymphocytes, where the Neutrophil Lymphocyte Ratio (NLR) was in the danger category. There was an increase in D-dimer. Chest X-ray examination showed an impression of pneumonia. The COVID-19 RT-PCR nasopharyngeal swab showed positive for COVID-19 on the first swab, but the second swab was negative. The result of the COVID-19 Rapid test was found to be non-reactive.

Patients with COVID-19 infection show a decrease in the number of leukocytes, lymphocytes, and platelets. Lymphopenia is a cardinal sign of COVID-19. On the other hand, an increase in lactate dehydrogenase (LDH), an increase in liver enzymes, muscle enzymes, and C-reactive protein (CRP) are also common in patients with COVID-19, and one-third of COVID-19 patients were reported to have an increase in D-Dimer. Procalcitonin testing was reported to be normal in several cohort studies of COVID-19. The rapid test has the advantage of low cost and high specificity. However, it has a high false-negative result due to low sensitivity. SARS-CoV-2 nucleic acid detection using real-time reverse transcriptase-polymerase chain reaction (RT-PCR) is the standard for diagnosing COVID-19. Viruses can be detected from upper and lower respiratory tract secretions (nasopharyngeal swab or tracheal aspiration if intubated, sputum, and bronchoalveolar lavage), blood, urine, and feces. In this case, there was an increase in leukocytes, a decrease in the number of lymphocytes, whereas liver enzymes were within normal limits, and there was an increase in D-Dimer level, as well as a positive SARS-CoV-2 RT-PCR nasopharyngeal swab. Increased D-dimers in COVID-19 infection may indicate an inflammatory response and may also represent acute thrombosis. Monitoring of D-dimer, fibrinogen, and fibrin levels may be useful in preventing complications of thrombosis in COVID-19 patients.

On the chest X-ray examination, the impression of bilateral pneumonia was found in 80% of cases after 10 days of symptoms of COVID-19. Fang et al. reported that CT scan sensitivity reached 98% and RT-PCR sensitivity was 71% in diagnosing COVID-19. In this case, chest CT-Scan was not performed due to limited facilities.

On March 4th, 2020, there was the first reported case of encephalitis caused by COVID-19 that affected the central nervous system. Researchers found SARS-CoV-2 in CSF using genome sequencing. This suggests that COVID-19 has the potential to damage the nervous system. Cerebrovascular manifestations were reported in 13 patients (6%) of 221 COVID-19 patients in a retrospective study in Wuhan: 11 (5%) patients had an ischemic stroke, 1 (<1%) patients had an intracerebral hemorrhage, and 1 (<1%) patients had cerebral venous thrombosis. In Milan, Italy, 9 (2%) patients out of 388 confirmed COVID-19 had a stroke. According to Ellul et al., the incidence of cerebrovascular disease in confirmed COVID-19 patients, ranged from 1% to 6%. Savuc et al. described a previously healthy 13-year-old girl who experienced a decrease in consciousness without any specific symptoms of COVID-19. The child had a pseudoaneurysm rupture in the left cerebral artery, and the SARS-CoV-2 RT-PCR nasopharyngeal swab was positive. In this case report, the patient also did not have respiratory symptoms/acute URI but had neurological manifestations and intraventricular bleeding.

The pathophysiology of cerebrovascular disease in COVID-19 patients is yet fully understood. There is a possibility of direct brain invasion, endothelial dysfunction, hypercoagulation, embolism, cytokine storms, and hypoxia. The novel coronavirus uses Angiotensin-Converting Enzyme (ACE) II receptors to enter host cells. ACE II is found in the epithelial cells of the lung and the digestive system. Angiotensin II receptors are also present in cerebrovascular endothelial cells, which have functions of hormone regulation and sympathoadrenal system, water and sodium regulation, vascular autoregulation, and cerebral blood flow. Angiotensin II is a vasoconstrictor and has a pro-inflammatory effect. This is what underlies the hypothesis that ACE II in the brain can be infected with COVID-19 and interfere with autoregulation and increase blood pressure and cause rupture of blood vessels which can increase the risk of
intracranial hemorrhage. An early indicator of cerebrovascular disease in COVID-19 is the possibility of coagulopathy. SARS-CoV-2 can cause endothelial damage, activating the inflammatory system and clotting pathways. Recent studies have reported that ACE2 receptors in the nasal epithelium are age-dependent, which is found at least in younger children. This may have caused the pediatric population to be less exposed to neurological manifestations of COVID-19 infection. In this case, the patient died on the 6th day of care, presumably due to herniation and compression of the brainstem and leading to death.

There were neurological manifestations in this case, in which we can also suspect the Multisystem Inflammatory Syndrome in children (MIS-C), a potentially life-threatening manifestation in children associated with SARS-CoV-2 infection. On May 14th, 2020, the Centers for Diseases Control and Prevention (CDC) announced MIS-C is a disease, which occurs in patients aged 21 years and under with fever (> 38°C in ≥ 24 hours), inflammation on blood tests (increased CRP, ESR, fibrinogen, procalcitonin, ferritin, LDH, or interleukin-6, increased neutrophils, decreased lymphocytes, and low albumin), serious illness requiring hospitalization, affecting two or more organ systems (heart, kidney, lung, hematological system, gastrointestinal tract, skin, or nervous system), with a positive SARS-CoV-2 test result, and no other possible cause.

4. Conclusion
Severe clinical manifestations of COVID-19 can be in the form of neurological manifestations, one of which is intraventricular hemorrhage.

5. References


