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Pediatric Acute Hydrocephalus Developing after COVID-19 Infection: A Case Report Study

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Abstract

Introduction: Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2 virus) is a pandemic viral disease led to many morbidities worldwide, one area of symptoms are neurological manifestations such as sudden onset of hydrocephalus in pediatrics.

Case presentation: We represent two cases of acute neurological symptoms following Covid-19 infection, first an 8-year-old girl with fever, nausea, vomiting, headache and 5 episodes of seizure before admission to the hospital. At the moment of admission, the child had asymmetrical movement of extremities and she was not able to localize painful stimulants. Brain CT-scan revealed ventriculomegaly with cytotoxic edema suggesting acute hydrocephalus; An External Ventricular Drains (EVD) shunt was placed and the patients were followed.

Second case was a one year and four months old girl admitted to the hospital with generalized tonic colonic seizure and 4 days history of fever and nausea vomiting under control with over-the-counter medications; Brain CT-scan revealed generalized hydrocephalus in all ventricles, an EVD shunt was placed and the toddler was followed.

Conclusion: Our case reports could suggest the possible effect of SARS-CoV-2 infection on severe clinical neurological manifestations and acute Hydrocephalus.

Keywords: Covid-19; Acute hydrocephalus; Neuroimaging; Pediatric neurosurgery; Post-infectious inflammation

Introduction

SARS-CoV-2 is a pandemic viral infection reported in Wuhan, China, in 2019 at the beginning and was responsible for many morbidities and mortalities worldwide [1].

Corona virus is a large, enveloped, positive-sense RNA virus primarily involving respiratory system including both upper and lower airways, yet many systemic displays have been reported; the pathogen has manifested neuro invasive abilities leading to a wide range of neurologic complications during and post infection [2-4].

The possible mechanism for neural invasion of the virus is the interaction of viral spike proteins with the cells Angiotensin Converting Enzyme 2 (ACE2) receptors which are widely distributed in human tissues [5]. Recent researches express that these receptors are largely expressed in the olfactory tract, basal ganglia and choroid plexus of lateral ventricles [6].

Acute hydrocephalus is described as sudden onset of symptomatic accumulation of cerebrospinal fluid inside the cerebral ventricles [7] which can lead to a wide range of sign and symptoms such as headache, vision impairment, vomiting, sluggishness (lethargy), Irritability, poor eating and seizures [8]. Herein, we report two pediatric cases of acute hydrocephalus occur shortly after covid-19 infection which may manifest an unknown association between them.

Case Presentation

Case Number One

An 8-year-old girl with a history of nondocumented fever, vomiting, diarrhea, headache and sore throat one week prior to her admission to the hospital, she has used Deltafen syrup (Acetaminophen, ibuprofen and caffein) as an OTC medication; three days prior to her hospital admission she had an episode of Generalized Tonic Colonic (GTC) episode with post ictal phase, two days prior to her admission she had another episode of seizure and the day of admission she had three episodes of GTC seizure five minutes each with upward gaze and foaming at her

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mouth and inability to talk or walk afterwards, dysphagia and drooling.

The patient had no past medical history or any remarkable family history and her developmental milestones were normal.

General examination was unremarkable and neurological examination revealed +3 Deep Tendon Reflux (DTR) in the right side and +2 in the left, the patient couldn't localize painful stimulants.

Her fever got under control by intravenous acetaminophen and seizure under control with phenytoin, phenobarbital and levetiracetam.

In laboratory examination at the first day of admission, White Blood Cell (WBC) count was 11.400/mm^3 (84% neutrophils and 8.5% lymphocytes), hemoglobin level was 13.2 g/dL, platelet count was 287.000/mm^3, ESR level was 45 mm/hr and C-reactive protein was 19 mg/dL (normal value <1mg/dL) and the D-dimer was 695; her liver and kidney examination was normal. Her Cerebrospinal Fluid (CSF) examination revealed glucose level of 60 mg/dl, protein level was 55 mg/dl, LDH level was 128 IU/L, WBC count was 60 (20 neutrophils and 40 lymphocytes) and RBC count was 5 suggesting viral meningitis and her urine toxicology was negative.

On second day of admission, her fever was controlled by intravenous acetaminophen and her nasopharyngeal Covid-19 Polymerase Chain Reaction (PCR) was positive while the CSF Covid-19 PCR was negative and her Purified Protein Derivation (PPD) test was also negative.

On the third day of admission, Brain MRI revealed 4 ventriculomegaly with CSF seepage and communicating hydrocephalus with periventricular diffusion restrictions suggesting acute infarction (Figure 1); EVD shunting was performed by pediatric neurosurgery.

From the fourth to the 15th day of admission her CSF examination revealed glucose level of 76 mg/dl, protein level was 23 mg/dl, LDH level was 49 IU/L, WBC count was 5 and RBC count was 5 suggesting no sign of viral infection. Her spiral brain CT-scan revealed the right sphenoidal sinus opacification, the tip of the EVD shunt could be seen in the right ventricle and left 3rd and 4th ventriculomegaly was seen.

Case Number Two

A one year and four months old girl with 4 days history of fever and vomiting has visited a clinic and received hydration

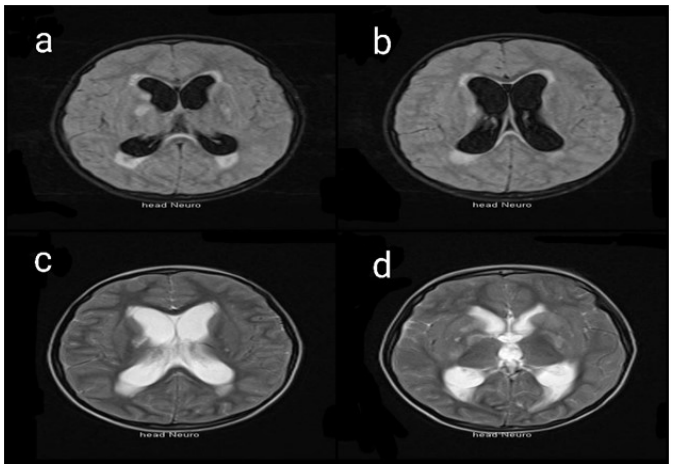

Figure 1: (a,b) Axial TI-weighted image with dilated lateral ventricles. **(c,d)** Axial T2-weighted image with dilated lateral ventricles.

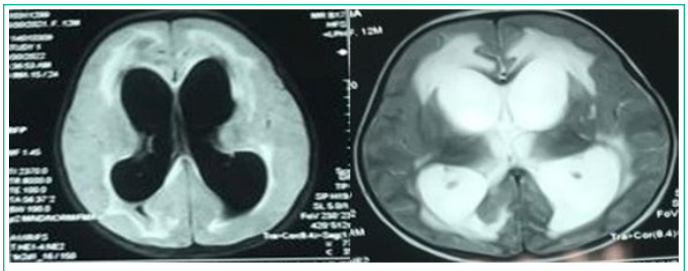

Figure 2: (a) Axial TI-weighted image with dilated lateral ventricles. **(b)** Axial T2-weighted image with dilated lateral ventricles.

therapy, intravenous acetaminophen and ondansetron; following the medication she got lethargic, then had prolonged GTC seizure with upward gaze and was transferred to the hospitals ER. The patient had no past medical history or any remarkable family history and her developmental milestones were normal.

Her fever was brought under control by intravenous acetaminophen, and her seizure was controlled by the use of phenytoin, phenobarbital, and levetiracetam. In laboratory examination at the first day of admission, blood white cell (WBC) count was 4.300/mm^3 (65% neutrophils and 32% lymphocytes), ESR level was 103 mm/hr and the D-dimer was 50566; her liver and kidney examination was normal. Her Cerebrospinal Fluid (CSF) examination revealed glucose level of 102 mg/dl, protein level was 19 mg/dl, LDH level was 58 IU/L.

Spiral chest CT-scan revealed pulmonary opacity and visible airbronchogram in favor of Covid-19 while spiral brain MRI revealed lateral, 3rd and 4th ventriculomegaly; Brain MRI revealed generalized ventriculomegaly with cytotoxic edema (Figure 2); the toddler received an EVD shunt via neurosurgery.

Discussion

Despite hydrocephalus being described as early as fifth century BC [9], the pathophysiology of postinfection cases remains controversial. Several studies have focused on the role of inflammation in the pathogenesis of acute hydrocephalus [10,11]. It has been revealed that the activation of Toll-like receptors and NFKB pathway in the brain's choroid plexus of rats leads to the hypersecretion of CSF [12].

During COVID-19 infection, a multifaceted inflammatory syndrome occurs that may lead to sudden immune system response [13] and the central nervous system is a common target of SARS-CoV-2 due to the high affinity of the virus spike proteins to ACE 2 receptors, which are widely expressed in various parts of the CNS, including the olfactory epithelium, posterior cingulate cortex, temporal gyrus, and especially the choroid plexus [5,14]. When the choroid plexus is infected, its microscopic structure is altered, followed by the loss of integrity of the hemostatic barrier, which may result in the activation of cytokine production pathways [15]; The immense release of inflammatory madiators may result in an important change in the CSF dynamics and result in acute hydrocephalus [16].

Based on these results, we assume that the sudden deterioration of our patients can be explained as a neurological manifestation of SARS-CoV-2 infection; One patient tested positive for nasopharyngeal molecular swab, and the other had chest X-ray involvement, indicating that they were infected by the virus prior to their symptoms; Moreover, the temporal sequentiality of patients symptoms after being infected by the virus and the plausible pathophysiology of inflammation pathways bears in mind the possible correlation between Covid infection and acute hydrocephalus

As far as we know, there are no other pediatric cases reported in the literature of an acute hydrocephalus presenting shortly after the infection of SARS-CoV-2 requiring neurosurgical approaches. None of these patients had other risk factors or past medical histories towards acute hydrocephalus. As for our article, the principal limitation is these reports to be observational and empiric.

Conclusions

In this article we have reported two pediatric cases of acute hydrocephalus following respiratory SARS-CoV-2 infection and on account of this experience, we recommend considering SARS-CoV-2 infection as a possible etiology for a sudden and otherwise unexplainable case of acute hydrocephalus; Furthermore we suggest future studies to concentrate on the molecular interaction between SARS-CoV-2 and choroid plexus resulting in CSF dynamics alteration to support our hypothesis.

Author Statements

Conflict of Interest Statement

The authors have no conflicts of interest to declare

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Author Contributions

Dr. Kachui made the diagnosis, had direct patient contact and contributed in writing the report, Dr, Zare had direct patient contact, monitored the patients in the intensive care unit and contributed in writing the report. Dr. Eghdami had direct patient contact and contributed in writing the report and Dr. Afsharkhas oversaw the patients care and contributed in writing the report.

Data Availability Statement

All the authors confirm that the data supporting the findings of this study are available within the article.

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