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Isolated Chronic Aseptic Meningitis Due to SARS-COV-2 Unresponsive to Ordinary Treatments

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Abstract

Serious, and sometimes, deadly complications of coronavirus disease 2019 (COVID-19) caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) are devastating. Whereas most manifestations of COVID-19 are respiratory (fever, dry cough, fatigue, pneumonia), it is getting to be progressively recognized that numerous organ functions can be affected by this disease, and the nervous system is one of them as neurological complications can affect up to 36% of adult patients. However, the prevalence and pathophysiology of these complications have yet to be fully elucidated in children. Here, we discuss an infant with neurological symptoms manifested as chronic isolated aseptic meningitis associated with COVID-19, which was unresponsive to ordinary treatments and dramatically responsive to dexamethasone. Immune-mediated reactions may have had a major pathophysiologic role in this case.

Keywords: Children, Neuro-COVID, Aseptic Meningitis

1. Introduction

The rapidly evolving coronavirus disease 2019 (COVID-19) pandemic is caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). In COVID-19-affected patients, neurological manifestations such as impaired consciousness, stroke, seizure, headache, delirium, GBS, acute transverse myelitis, and acute encephalitis have been reported, with a higher incidence in those with a more severe course of COVID-19 (**?**). However, the occurrence of these manifestations does not necessarily require the direct infection of the peripheral nervous system (PNS) or the central nervous system (CNS) but could also be secondary to a systemic reaction in response to a viral infection outside the nervous system (**?**). Therefore, indirect neurotoxicity may arise secondary to immune-mediated pathogenesis and end to some complications in the nervous system such as meningitis and encephalitis.

2. Case Presentation

The present case was a four-month-old boy born prematurely with a normal APGAR score at 33 weeks of gestation through a caesarian section because of PROM. In his neonatal period, he was admitted to the neonatal intensive care unit due to intrauterine growth retardation, respiratory distress, and jaundice but discharged on the 40th day of age. One month later, he was readmitted with an episode of fever, poor feeding, and suspected seizure and discharged again with phenobarbital. Phenobarbital continued, and after routine vaccination at four months of age, he was again admitted because of one episode of seizure with tonic colonic movements lasting for seven minutes with a typical postictal period of 15 minutes. He experienced two more episodes on admission with a longer duration. Then, he was transferred to our hospital.

At first, the parents did not permit performing LP for him, and antibiotic therapy with ceftriaxone and vancomycin began due to suspected meningitis. At this time, the COVID-19 PCR was positive, but he did not receive antiviral agents. Because of sustained fever, LP was performed, which revealed an increased WBC count with neutrophil dominancy with low glucose and high protein (glucose: 54, protein: 150, WBC: 50 with PMN: 80%). The CSF culture was negative, which seemed to be due to partially treated meningitis and preceding antibiotic usage.

Antibiotics continued, and anticonvulsive drugs (phenobarbital and levetiracetam) began to prevent more convulsions. Brain ultrasonography showed mild ventriculomegaly and brain CT indicated some evidence of brain atrophy without any remarkable mass effect, as well as dilated ventricle bilaterally. The brain CT with contrast also showed hydrocephalus ex vacuo with some abnormal hypo-density in the right frontal lobe. However, EEG and echocardiography were normal. Without performing another LP, he was discharged after three weeks of antibiotic therapy, with good condition, fever resolution, and negative COVID-19 PCR on anticonvulsive drugs.

Unfortunately, after one week, he came back with an episode of status epilepticus accompanying by fever, suspected of meningitis complications such as subdural effusion, partial treatment of bacterial meningitis, or other etiologies of fever. At this time, he did not have any symptoms and signs or lab evidence of MIS-C. Again, LP was performed, and CSF analysis was compatible with high WBC and protein and low glucose (glucose: 26, protein: 112, WBC: 20 with PMN 60%). Again, the COVID-19 PCR was checked on the nasopharyngeal specimen and CSF; also, other viral markers (EBV, VZV, HIV, JC, and CMV) were checked in the CSF. Unbelievably, the only positive viral biomarker was COVID-19 PCR in the nasopharyngeal sample. Thus, favipiravir began and continued for seven days together with ceftriaxone and vancomycin. A brain CT showed the same findings as before without any evidence of empyema, abscess, or subdural effusion. After two weeks, a second LP showed glucose: 26, protein: 80, and WBC: 30 (PMN: 55%), and the patient was febrile. Concurrently, COVID-19 antibodies were positive [IgG: 5.07 (negative < 0.9), IgM: 0.83 (negative < 0.9)]. Thus, it was considered that the last positive PCR should be the remnants of the preceding viral infection, not the live virus. Since the fever persisted and all bacterial and viral investigations were negative, concerning a suspicious immune-mediated inflammatory pathophysiology, it was decided to stop antivirals and administer dexamethasone to subside brain inflammation and meninges. After three days of dexamethasone administration, another lumbar puncture was performed that showed a dramatic therapeutic response, with normalization of all CSF indices (glucose: 42, protein: 46, WBC: 0). The patient had no other episodes of seizure or fever and was discharged after five days of dexamethasone treatment, with negative COVID-19 PCR and drug dose tapering plan over two weeks. On the follow-up visit after two weeks, he could have regained developmental millstones; ABR was normal, and the parents reported no fever or neurologic symptoms. A brain MRI was suggested six months later.

3. Discussion

From the beginning of the pandemic to date, about 2 - 5% of COVID-19 cases were reported in the age group of pediatrics who appear to be less seriously affected than adults, primarily presenting with pneumonic symptoms (**?**). While the number of affected neonates and children remains low, pediatric specialists must be aware of the potential complications of COVID-19 infection, including neurologic ones. Neurologic manifestations of COVID-19 in children seem, by all accounts, to be scant yet might be underestimated (**?**). By somehow, some reports of cerebral edema, altered mental status, and aseptic meningitis have been reported in this age group (**?**).

On the last admission, our patient primarily was investigated for etiologies of aseptic meningitis such as bacterial infections, viral infections, fungal infections, and mitochondrial diseases, which all were negative, except for positive nasopharyngeal COVID-19 PCR. Thus, an antiviral drug, favipiravir, was prescribed that ended in no improvement. Meanwhile, regarding positive COVID-19 antibodies, without any symptoms in favor of MIS-C, it was considered that an immune-mediated inflammatory process could be the basic pathophysiologic phenomenon, so the antiviral agent discontinued, and dexamethasone was administered, which ended in the dramatic resolution of symptoms and CSF indices. It is suggested that similar cases of COVID-19-infected infants presenting with fever and aseptic meningitis unresponsive to routine treatments be treated with dexamethasone.

3.1. Conclusions

Since the epidemiology, presentations, pathophysiology, and ideal treatment of neurological complications of COVID-19, especially in children, remain unknown, sharing any experience would be worthy, and our case may add to the growing literature on this topic. We believe that this is the first report of a pediatric patient with COVID-19 and aseptic meningitis that was successfully treated with dexamethasone, which can be suggested for similar cases.

Footnotes

Authors' Contribution: Abdollah Karimi: Review and editing; Sedigheh Rafiei Tabatabaei: Review and editing; Ghazal Shariatpanahi: Data gathering, writing, review, and editing; Mohsen Javadzadeh: Review and editing; Shahnaz Armin: Review and editing; Zahra Yeganeh: Data gathering and review.

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