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Case Report

COVID-19 Associated leukoencephalopathy in a term neonate: imaging findings and clinical presentation [☆]

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ARTICLE INFO

Article history:

Received 16 January 2022

Revised 24 January 2022

Accepted 25 January 2022

Keywords:

COVID-19

Coronavirus

Leukoencephalopathy

Neonate

MRI

ABSTRACT

A 5-day old neonate presented with several episodes of seizure-like activity associated with hypoxia. The episodes were responsive to anti-epileptic medications and the infant was given empiric antibiotics and antiviral coverage. Cerebrospinal fluid polymerase chain reaction (PCR), culture, and gram stain were negative for viral or bacterial etiology. However, a nasopharyngeal PCR of the infant was positive for SARS-COV-2. While head computed tomography (CT) was negative, magnetic resonance imaging (MRI) showed evidence of white matter injury in the subcortical and periventricular regions and corpus callosum. With supportive therapies, the infant made a full neurologic recovery and was discharged following a 5-day admission. This case highlights the growing evidence of SARS-COV-2 associated leukoencephalopathy in neonates, and physicians should consider this diagnosis in neonates with similar presentation.

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Introduction

As the COVID-19 pandemic continues, our understanding of the severe acute respiratory syndrome coronavirus-2 (SARS-COV-2) and its effects beyond the respiratory system continues to grow. Neurologic sequelae of coronavirus disease 2019 (COVID-19) extend far beyond ageusia and anosmia to include stroke, hemorrhage, meningoencephalitis,

and demyelinating processes [1]. While initially thought to be associated with mild illness in the pediatric population, growing evidence suggests that neurologic sequelae of COVID-19 can be profound, acting via infectious and parainfectious mechanisms [2]. Few case reports exist documenting CNS findings in neonatal COVID-19 infection [3,4]. We report a case of COVID-19 infection in a term neonate associated with seizures and imaging findings of leukoencephalopathy.

[☆] Competing Interests: All authors certify that they have no affiliations with or involvement in any organization or entity with any financial interest or non-financial interest in the subject matter or materials discussed in this manuscript.

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<https://doi.org/10.1016/j.radcr.2022.01.072>

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Case report

A 5-day old presented to the Emergency Department (ED) following several episodes of seizure-like activity. A witnessed episode was associated with hypoxia and responded to lorazepam and levetiracetam with supplemental oxygen. The patient was admitted to the neonatal intensive care unit (NICU) for further support due to hypothermia and concern for sepsis and seizures.

The infant received routine, uncomplicated prenatal care. Maternal prenatal and perinatal testing was negative for human immunodeficiency virus (HIV), Hepatitis B, Group B streptococcus, syphilis, Chlamydia trachomatis, and Neisseria gonorrhoeae. Mother's SARS-COV-2 test was negative just prior to delivery. Birth was via C-section at 39 weeks, and APGARs were 9 and 9 at 1 and 5 minutes respectively. A positive Combs test was noted at birth; however, serum bilirubin remained within normal limits and the patient was discharged home on day 2 of life.

Physical exam on admission demonstrated hypothermia, with temperature of 33.1°C. Exam was otherwise unremarkable, with normal muscle bulk and tone, normal reflexes, and no clonus. Lumbar puncture on admission revealed clear cerebrospinal fluid (CSF), red blood cells 1/mm³, total nucleated cells 1/mm³, normal protein (92mg/dL), and normal glucose (47mg/dL) [5]. Meningitis/encephalitis panel (BioFire FilmArray), testing for Hemophilus influenzae, K1 strain of Escherichia coli, Listeria monocytogenes, Neisseria meningitidis, Streptococcus agalactiae, Streptococcus pneumoniae, Cytomegalovirus, Enterovirus, Herpes simplex viruses 1,2, and 6, Human parvovirus, Varicella zoster virus, and Cryptococcus neoformans and gattii, was negative. Gram stain and culture on blood agar and chocolate media was also negative. Electroencephalogram (EEG) demonstrated background slowing indicative of mild encephalopathy without epileptiform discharges. In the ED, the patient's mother reported several days of voice hoarseness and sore throat. SARS-COV2 testing of the mother returned positive. A rapid test of the infant was also positive, later confirmed with nasopharyngeal polymerase chain reaction (PCR) testing.

Initial non-contrast computer tomography (CT) imaging was normal, without evidence of hydrocephalus or mass effect. Magnetic resonance imaging (MRI) performed on day 2 of admission demonstrated decreased diffusion involving the splenium and genu of the corpus callosum, as well as patchy areas of decreased diffusion in the peri atrial and frontal subcortical white matter (Fig. 1). These regions demonstrated intrinsic T1 shortening (Fig. 2). There was no evidence of intracranial hemorrhage on susceptibility weighted imaging or abnormal enhancement, and myelination pattern was normal for patient age.

Initially empiric treatment for meningitis/encephalitis was administered with intravenous acyclovir, ampicillin, and gentamicin. External warming was supplied for hypothermia and supplemental oxygen for hypoxia. For seizure activity, lorazepam and levetiracetam were administered. The above antibiotics were discontinued after a 36-hour course and acyclovir was stopped after herpes simplex virus PCR returned negative.

The patient's hypothermia and hypoxia eventually resolved. He was discharged home on day 5 of admission with normal vital signs and a normal physical examination. There was no concern for further seizure activity and the patient appeared normal at a 5 day follow up visit.

Discussion

This case report describes the presentation and imaging findings of a term neonate, with unremarkable gestation and delivery, presenting with seizure on day 5 of life following exposure to a COVID positive mother. Prior to birth, PCR testing of the mother was negative for SARS-COV-2. She became symptomatic on the infant's second day of life. Vaccination status for the mother and other close household contacts were not documented, and the patient presented at the peak of the delta variant in this geographic location. Of note, variant testing was not performed. This case highlights a growing understanding of the neurologic manifestations of COVID-19 in the pediatric and, more specifically, the neonatal population.

While children were initially thought to be mildly affected in SARS-COV-2 infection [5], evidence gained over the course of the pandemic has shown children susceptible to severe illness, particularly when a post infectious hyperinflammatory response such as multisystem inflammatory syndrome in children (MIS-C) develops [6]. Neurologic manifestations in children appear to act in hyperinflammatory, parainfectious patterns [2]. In adults, suggested mechanisms of neurologic injury involve global hypoxia, parainfectious and hyperinflammatory leukoencephalopathy, as well as microvascular injury from endothelial dysfunction [7,8]. Additionally, adult COVID-19 patients have demonstrated PCR positive CSF suggestive of direct neuroinvasion and encephalitis [1,7], although this is a rare clinical scenario.

This case highlights a growing association of neonatal SARS-COV-2 infection with clinical seizures and imaging findings of leukoencephalopathy. The patient was born at term, with good prenatal care, and an unremarkable gestational course. Infectious evaluation both at birth and time of presentation did not offer an alternative etiology. While the findings on imaging can also be seen with hypoxic ischemic encephalopathy, the clinical history of the patient did not identify any risk factors for this entity.

There are several limitations to this brief case report. First, CSF analysis for SARS-COV-2 was not performed. Future studies may benefit from histopathologic analysis to determine if the associated findings occur via direct infection or indirect, hyperinflammatory responses. Additionally, while a negative SARS-COV-2 test was reported by the mother prior to delivery, it is unknown how long before delivery this test was performed. While we assume that transmission occurred in the first few days of life, it is not possible to confirm route of transmission. Finally, the witnessed seizure in the ED was associated with marked hypoxia. Given that several of these seizures occurred at home, it is possible the patient was temporarily hypoxic for an unknown duration. This may have exacerbated the findings visualized on MRI.

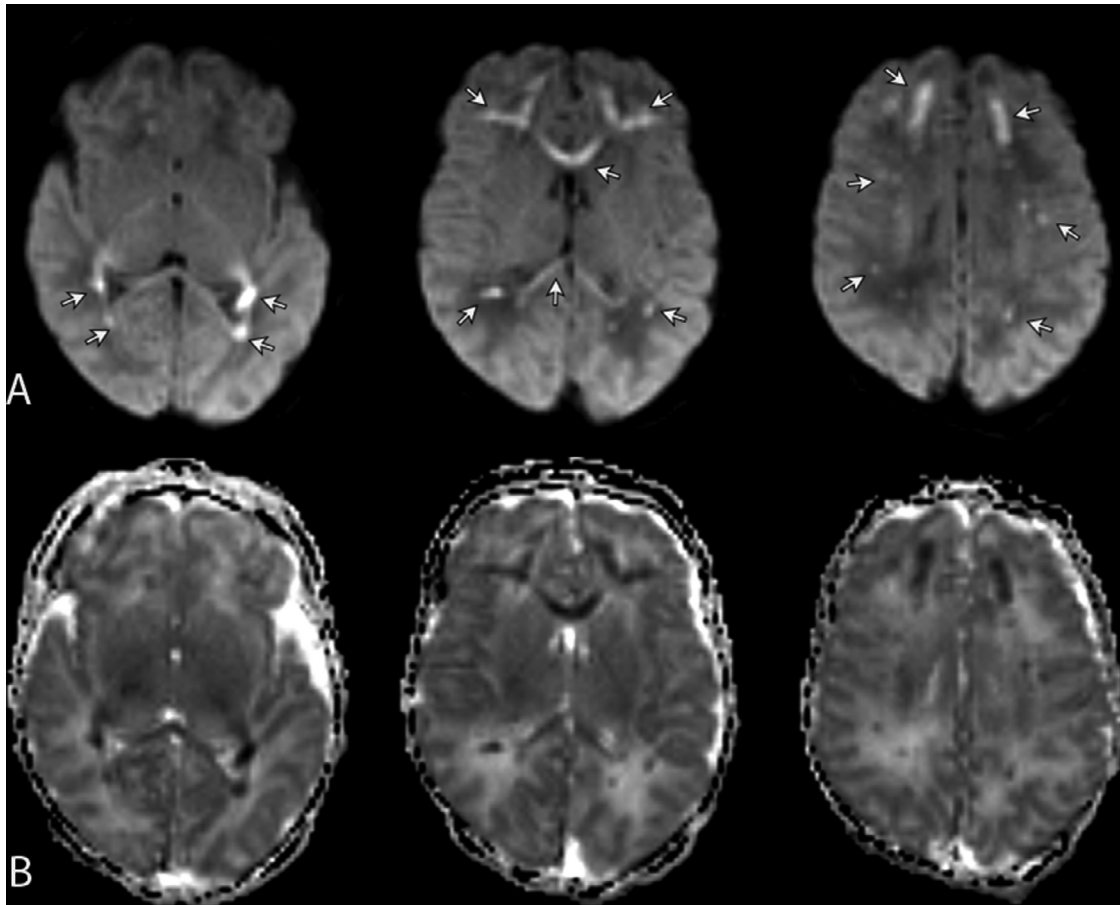


Fig. 1 – Axial B=1000 diffusion weighted images (A) demonstrating multiple bilateral lesions of increased signal in the periventricular and subcortical white matter, also involving the corpus callosum (arrows). (B) Corresponding apparent diffusion coefficient maps showing decreased diffusion.

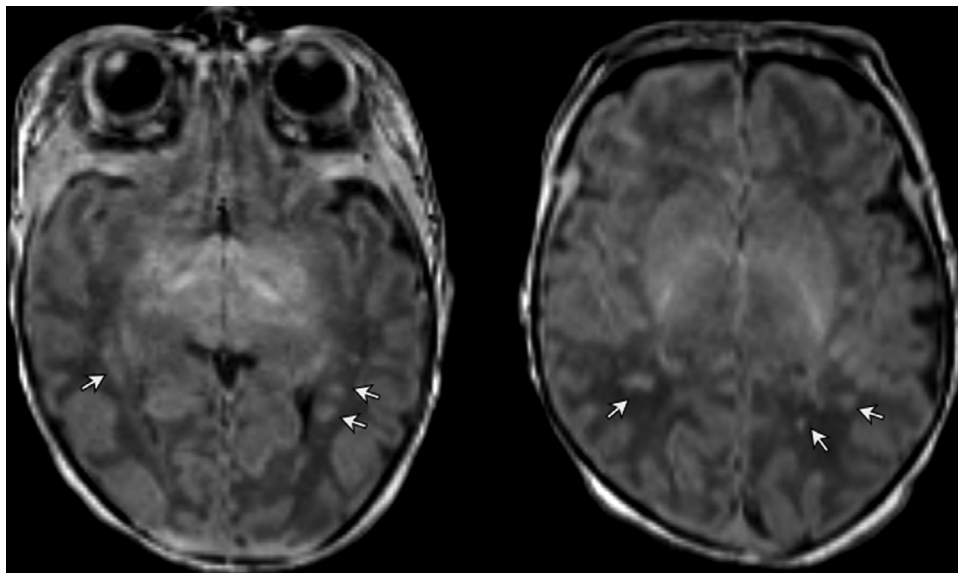


Fig. 2 – Axial T1 weighted images showing T1 shortening of the white matter lesions (arrows).

In conclusion, we describe a SARS-COV-2 positive neonate presenting with clinical seizures, with multifocal white matter insults. This presentation and the imaging findings are not specific to SARS-COV-2. However, this case highlights growing evidence of COVID associated leukoencephalopathy in neonates, and physicians should consider this diagnosis in newborns presenting with similar signs or symptoms.

Ethical standards attestation

Waiver from the institutional review board was granted for this retrospective report which follow HIPAA guidelines.

Patient consent

Informed consent has been obtained for the publication of this case report.

REFERENCES

- [1] Huth SF, Cho SM, Robba C, Highton D, Battaglini D, Bellapart J, et al. Neurological manifestations of coronavirus disease 2019: a comprehensive review and meta-analysis of the first 6 months of pandemic reporting. *Front neurol* 2021;12:664599.
- [2] Lindan CE, Mankad K, Dipak R, Kociolek L, Silvera VM, Boddaert N, et al. Neuroimaging manifestations in children with SARS-CoV-2 infection: a multinational, multicentre collaborative study. *Lancet Child Adolesc Health* 2021;5(3):167–77.
- [3] Martin PJ, Felker M, Radhakrishnan R. MR Imaging findings in a neonate with COVID -19-associated encephalitis. *Pediatr Neurol* 2021;119:48–9.
- [4] Fragoso DC, Marx C, Dutra BG, da Silva CJ, da Silva PM, Maia Jr ACM, et al. COVID-19 as a cause of acute neonatal encephalitis and cerebral cytotoxic edema. *Pediatr Infect Dis J* 2021;40(7):e270–1.
- [5] Dong Y, Mo X, Hu Y, Qi X, Jiang F, Jiang Z, et al. Epidemiology of COVID-19 among children in China. *Pediatrics* 2020;145(6):e20200702.
- [6] Chiotos K, Bassiri H, Behrens E, Blatz A, Chang J, Diorio C, et al. Multisystem inflammatory syndrome in children during the coronavirus 2019 pandemic: a case series. *J Pediatric Infect Dis Soc* 2020;9(3):393–8.
- [7] Marsiglia M, Chwalisz BK, Maher M. Neuroradiologic imaging of neurologic and neuro-ophthalmic complications of coronavirus-19 infection. *J Neuroophthalmol* 2021;41(4):452–60.
- [8] Huang H, Eichelberger H, Chan M, Valdes E, Kister I, Krupp L, et al. Pearls & Oy-sters: leukoencephalopathy in critically ill patients with COVID-19. *Neurology* 2020;95(16):753–7.