

Cerebral White Matter Injury in a Newborn Infant With COVID-19

A Case Report

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Abstract

Because the COVID-19 pandemic evolves, reports of neurologic manifestations and neuroimaging associated with SARS-CoV-2 have been reported in children and in neonates, although very few when compared with adults.

Objectives

To describe a 3-day-old neonate presenting afebrile seizures with a persistent positive nasopharyngeal swab for SARS-CoV-2 and neuroimaging demonstrating extensive cerebral white matter injury.

Methods

Consent was obtained to report this case. SARS-CoV-2 was tested using real-time reverse transcriptase-polymerase chain reaction amplification of virus acid from a nasopharyngeal swab. MRI of the brain was performed using axial T1, T2, fluid-attenuated inversion recovery, diffusion-weighted imaging, and T1 postcontrast sequences.

Results

Brain MRI showed restricted diffusion in the periventricular white matter, subcortical white matter, and splenium of the corpus callosum.

Discussion

Neurologic presentation of SARS-CoV-2 in newborns seems to be rare and is not fully known. SARS-CoV-2 infection should be considered in newborns with seizures and white matter abnormalities.

Case Presentation

A 3-day-old boy was born at 36.5 weeks' gestation by vaginal delivery without complications. He presented with seizures characterized by clonic movements of the upper limbs and persistent bradypnea. Vital signs, temperature, heart rate, and blood pressure were normal. Phenobarbital was administered and repeated for persistence of seizures. Antibiotic therapy was initiated empirically, and orotracheal intubation was performed because of the recurrent apnea associated with epileptic seizures. His mother had fever and cough for 3 days before admission and tested positive in a nasopharyngeal swab for SARS-CoV-2 using real-time reverse transcriptase-PCR (rRT-PCR). CSF presented a normal cell count and protein and glucose levels. Serology for herpes virus, cytomegalovirus in the CSF, and blood and urine cultures were negative; therefore, the antibiotic treatment was stopped. The cranial CT

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(64-section scanner, Brilliance CT Philips Medical Systems, The Netherlands) showed periventricular hypodensity, involving white matter and corpus callosum. A nasopharyngeal swab was performed and tested for SARS-CoV-2 using rRT-PCR and returned positive on the 2nd, 6th, 9th, and 12th days of life.

A cranial magnetic resonance imaging (1.5T system, Intera 1.5T Philips Medical Systems, The Netherlands) was performed on the 20th day of life, which revealed symmetrical restricted diffusion in the periventricular white matter, subcortical white matter, and corpus callosum (Figure). Metabolic screening for inborn errors of metabolism (chromatography of amino acids, organic acids urine, and acylcarnitine profile), SARS-CoV-2 antibodies IgG and IgM, and SARS-CoV-2 in CSF were negative. On the 16th day of life, a nasopharyngeal swab for SARS-CoV-2 PCR was negative. Throughout his hospital stay, he did not present more seizures or any respiratory symptoms. The patient was discharged on the 22nd day of life alert, breastfeeding, and without any neurologic deficit. He was seen in a medical consultation again at 2 and 6 months of age and had normal neurologic development.

Discussion

Since the first reports of respiratory symptoms caused by SARS-CoV-2 in December 2019, a growing number of case series have reported COVID-19-associated neurologic manifestations mostly in adults.¹ Some studies in adults found mainly the following abnormalities: meningitis, acute disseminated encephalomyelitis, and venous thrombosis.²

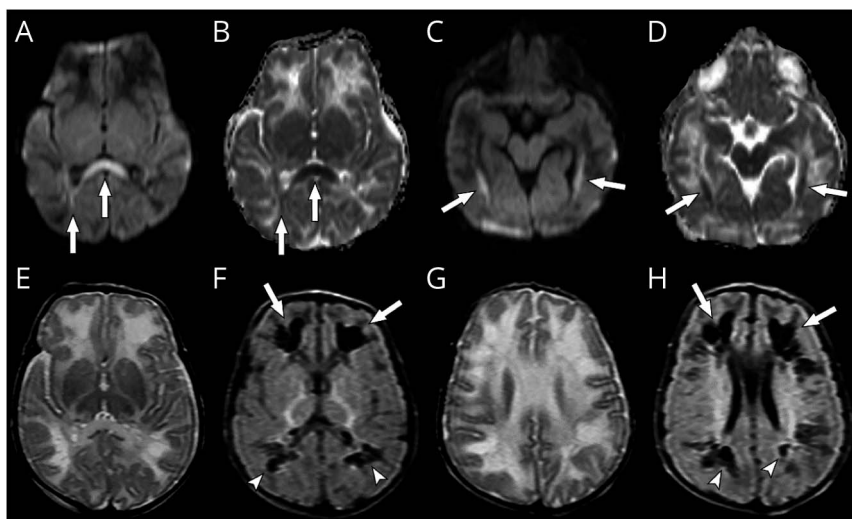
There are very few reports of important neurologic complications of SARS-CoV-2 in children, especially in neonates.^{3,4} It remains unclear whether the neurologic symptoms and neuroimaging abnormalities due to SARS-CoV-2 are caused by neuroinvasion of the virus, thromboembolic or immune-mediated phenomenon associated with the virus.^{5,6} We believe that in this case it was probably the latter, an intense inflammatory response against the virus due to cytokine release, resulting in diffuse brain dysfunction.

This is the second case documenting symmetric and diffuse restricted diffusion involving the cerebral white matter and corpus callosum associated with SARS-CoV-2 in a newborn infant with afebrile seizure, similar to a case describing a 9-day-old newborn with seizures and showing the same neuroimaging as this case.^{4,7}

The newborn was initially in good clinical conditions and did not have a history of any antenatal complications. We were able to discard many other more frequent causes of neonatal seizures, such as acute brain injury, systemic infections, and metabolic causes. Given the persistent positive rRT-PCR for SARS-CoV-2 with the clinical presentation of seizures along with the neuroimaging, we believe that this infant presented acute encephalitis with white matter injury secondary to SARS-CoV-2 infection, probably because of postnatal transmission from his SARS-CoV-2-positive mother.

We describe a newborn with SARS-CoV-2 infection with a severe neurologic presentation and neuroimaging of an extensive symmetrical restricted diffusion in the periventricular white matter. Neurologic presentation of SARS-CoV-2 in

Figure Axial Diffusion-Weighted (DWI) Images (A and C) and Corresponding Apparent Diffusion Coefficients (ADC) Maps (B and D) Demonstrate Restricted Diffusion in the Splenium of the Corpus Callosum and Adjacent Periventricular White Matter (Arrows in A-D), Characterized by Hyperintensity in DWI and Hypointensity in ADC Maps



Notice that in the right periatlial white matter, the areas of restricted diffusion have linear morphology (corresponding arrows in A and B). Axial T2-weighted (E and G) images show diffuse hyperintensity in the cerebral white matter, which can be seen at this age, although there are some areas that are more hyperintense than normally expected for nonmyelinated white matter. Axial fluid-attenuated inversion recovery (FLAIR) images (F and H) depict these areas as portions of rarefaction or cystic degeneration of the white matter because FLAIR signal is similar to CSF; some of these areas have linear shape in the periatlial white matter bilaterally (arrowheads in F and H) while, especially in the frontal lobes, one can appreciate some confluence of the lesions (arrows in F and H). Taken together, MR images demonstrate an active process going on in the splenium and adjacent white matter, while in other areas a chronic phase of the disease seems to be already established.

PRACTICAL IMPLICATIONS

Consider SARS-CoV-2 infection of the CNS in the differential diagnosis of a newborn with epileptic seizures for no apparent reason, and a brain magnetic resonance imaging may be helpful in distinguishing white matter abnormalities in these children.

newborns seems to be rare and is not fully known. SARS-CoV-2 infection should be considered in newborns with seizures and white matter abnormalities. In times of the COVID-19 pandemic, SARS-CoV-2 infection of the CNS should be part of the differential diagnosis of newborns with seizures for no apparent reason. In these cases, white matter abnormalities should be investigated through neuroimaging tests.

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Lucas Alves, MD, MSc, PhD	Department of Neuropediatric, Instituto de Medicina Integral Prof. Fernando Figueira (IMIP)	Drafting/revision of the manuscript for content, including medical writing for content; major role in the acquisition of data; study concept or design; and analysis or interpretation of data

Appendix (continued)

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