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## Cerebral White Matter Injury in a Newborn Infant With COVID-19: A Case Report

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Lucas Alves: Drafting/revision of the manuscript for content, including medical writing for content;

Major role in the acquisition of data; Study concept or design; Analysis or interpretation of data

Thaís Alcântara: Drafting/revision of the manuscript for content, including medical writing for content

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**Practical Implications:** *Consider SARS-CoV-2 infection of the central nervous system in the differential diagnosis of 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.*

## **Abstract**

As the Covid pandemic evolves, reports of neurological manifestations and neuroimaging associated with SARS-CoV-2 have been reported in children and in neonates, although very few when compared to adults. Objective: 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 via real time reverse transcriptase-polymerase chain reaction (rRT-PCR) amplification of virus acid from a nasopharyngeal swab. Magnetic resonance imaging (MRI) of the brain was performed using axial T1, T2, FLAIR and diffusion-weighted imaging (DWI) and T1 post contrast sequences. Results: Brain MRI showed restricted diffusion in the periventricular white matter, subcortical white matter and splenium of corpus callosum. Discussion: Neurological presentation of SARS-CoV-2 in newborns appears 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 were 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 virus via real time reverse transcriptase-polymerase chain reaction (rRT-PCR). Cerebrospinal fluid (CSF) presented a normal cell count, protein and glucose. Serology for herpes virus, cytomegalovirus in the CSF, blood and urine cultures were negative, therefore the antibiotic treatment was stopped. The cranial computed tomography (64-section scanner, Brilliance CT Philips, Medical Systems, The Netherlands) showed periventricular hypo density, involving white matter and corpus callosum. A nasopharyngeal swab was performed and tested for the SARS-CoV-2 virus via rRT-PCR and returned positive on the 2th, 6th, 9th and 12th day of life.

A cranial magnetic resonance imaging (1.5 - T system, Intera 1.5T Philips, Medical Systems, The Netherlands) was performed at the 20th day of life, revealed symmetrical restricted diffusion in the periventricular white matter, subcortical white matter and corpus callosum (Figure). Metabolical screening for inborn errors of metabolism (chromatography of amino acids, organic acids urine, 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 neurological 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. Some studies in adults found mainly the following abnormalities, meningitis, acute disseminated encephalomyelitis and venous thrombosis<sup>2</sup>.

There are very few reports of important neurologic complications of SARS-CoV-2 in children and especially in neonates<sup>3, 4</sup>. It remains unclear if the neurological 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<sup>5, 6</sup>. 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.

To the best of our knowledge, 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 described by Martin and al, a 9-day-old newborn with seizures and showing the same neuroimaging as this case<sup>7</sup>.

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 as well as metabolic causes. Given the persistence positive rRT-PCR for SARS-CoV-2 virus with the clinical presentation of seizures along with the neuroimaging, we believe that this infant presented an acute encephalitis with white matter injury secondary to SARS-CoV-2 infection, probably due to post-natal transmission from his SARS-CoV-2 positive mother.

## **Conclusion**

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. Neurological presentation of SARS-CoV-2 in newborns appears 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

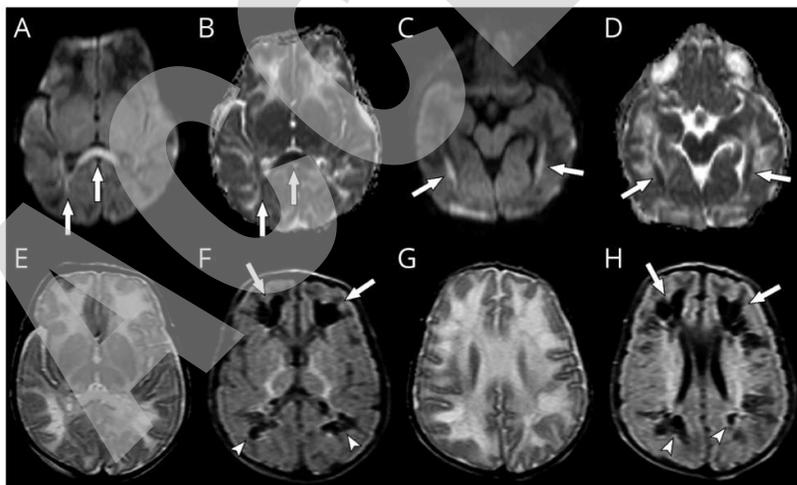
COVID-19 pandemic, SARS-CoV-2 infection of the central nervous system should be part of the differential diagnosis of newborns with seizures for no apparent reason. In these cases, white matter abnormalities should be investigated through neuroimaging tests.

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## 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 peritrial 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, that can be seen at this age, although there are some areas that are more hyperintense than normally expected for nonmyelinated white matter. Axial FLAIR images (**F and H**) depict these areas as portions of rarefaction or cystic degeneration of the white matter, since FLAIR signal is similar to cerebrospinal fluid; some of these areas have linear shape in the peritrial 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.



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