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EXTRA-AXIAL HEMORRHAGIC COLLECTION OF CENTRAL NERVOUS SYSTEM IN AN INFANT POST SARS-COV-2 INFECTION: A CASE REPORT

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Abstract: The Sars-CoV-2 virus has been responsible for countless deaths and sequelae around the world. In view of this new virus, complications in several systems were noticed, mainly the involvement of the central nervous system (CNS) by the virus, especially in the pediatric population. In our study, we report a case of an infant who presented an episode of seizure and neurological symptoms after infection with COVID-19. On admission, radiological and laboratory investigations were carried out, which showed the presence of extra-axial blood collection in an inflammatory environment. The infant remained hospitalized and, after stabilization, was discharged. At follow-up, in a control imaging exam, there was complete resorption of the cyst without residual neurological signs. The present report sets precedents for the importance of neurological investigation in patients with Sars-CoV-2, as several studies have demonstrated its tropism for the CNS and still few reports describing its possible complications in children and adolescents.
Keywords: Sars-CoV-2 infection, neurological manifestations, pediatrics, neurogenic inflammation.

INTRODUCTION

On January 30, 2020, the World Health Organization declared public health emergency situation worldwide (CUCINOTTA; VANELLI, 2020) due to COVID-19. Currently, deaths caused by this virus already surpass the two million mark, showing the impact of this disease (WHO, 2021).

The most frequent manifestation of the virus are respiratory. Around 96 hours after contact, the virus genetic material can be found in human respiratory epithelial cells, thus generating serous fluids, exudate, fibrin, and formation of hyaline membrane in the alveoli (MONTALVAN et al., 2020). The most common clinical presentation is fever, cough, sore throat, fatigue, headache, myalgia and shortness of breath (ALZYOOD et al., 2020).

However, manifestations other than respiratory are reported, mainly related to the central nervous system (CNS) and vascular system. The first case of COVID-19 encephalitis was reported in a 24-year-old man in February 2020 in China.

It is believed that approximately one third of patients with COVID-19 will have neurological symptoms, ranging from mild, such as anosmia, to severe, such as encephalitis. The main diagnoses are encephalopathy, stroke, epileptic seizures and neuromuscular disorders, and most of these cases were related to severe cases of the disease (STUDART-NETO et al., 2020).

Due to the growth of cases of virus infection, vascular manifestations have also been reported. Cutaneous vasculitis, arterial thromboembolism and cryptogenic stroke were largely associated with COVID-19. Characteristics of these vascular diseases possibly caused by COVID-19 remain unclear, as they do not follow conventional patterns (MCGONAGLE et al., 2021).

Neurological manifestations, especially cerebrovascular ones, are characteristically more prevalent in COVID-19 infections compared to other viruses that cause respiratory syndrome, such as Influenza (MERKLER et al., 2020). Thus, the differential diagnosis with SARS-CoV-2 was advocated in all CNS involvement, in cases where it is possible to establish a clinical correlation (MAO et al., 2020), as will be described in the present case.

CASE DESCRIPTION

On December 3, 2020, N.M., an infant aged 1 year and 5 months, was presented to the emergency with flu-like symptoms, fever, dry cough and irritability. Nasopharyngeal

RT-PCR was performed for SARS-CoV-2, which confirmed the presence of the virus.

Eight days later, he had a gait change followed by recurrent focal epileptic seizures and was referred to a tertiary hospital for investigation.

On admission, he did not present fever, oxygen saturation was normal and the neurological examination showed clonus in the lower limbs without other focal changes.

Laboratory tests did not show any particularities, except for a C-Reactive protein dosage of 10.3 mg/dl. Skull magnetic resonance imaging showed an image of cystic aspect with extra-axial characteristics, with hemorrhagic content, in the upper right frontoparietal convexity, measuring approximately 5.1 x 5.2 x 0.9 cm, without other alterations.

The patient remained asymptomatic during the hospital stay and after 45 days a control cranial magnetic resonance was performed, with reabsorption of the extra-axial blood collection, maintaining only adjacent meningeal enhancement and thickening.

DISCUSSION

Coronavirus belongs to a family predominantly responsible for respiratory infections, first described in 1965. Until now, 6 types of coronavirus are known, with Sars-CoV-2 being described in China in 2019 (LIMA, 2020). It is an RNA virus, with high genetic variability and, therefore, a high mutation rate (ALBUQUERQUE et al., 2020).

The airway epithelium constitutes the first immunological barrier against respiratory viruses, and many infections are restricted to this location and are self-limited. However, Sars-CoV-2 and other opportunistic viruses from the same family manage to overcome these first barriers and present themselves as serious respiratory infections, even spreading to other tissues (ALBUQUERQUE et al., 2020).

Initially, the virus affects respiratory epithelial cells through the binding of viral spike protein S to angiotensin 2 converting enzyme (ACE2) receptors. The type 2 transmembrane serine protease – present in the host cell – interferes with the uptake of viral material by cleavage of ACE2, with activation of the SARS-CoV-2 S protein, mediating the entry of the virus into the host cell. In the human body, vital organs such as kidneys, heart, central nervous system and lungs have ACE2 receptors, which may explain the systemic manifestation of coronavirus infection (HICKMANN et al., 2020). In addition to the deregulation of the renin angiotensin system, the virus provokes an intense immune response from the production of pro-inflammatory cytokines - cytokine storm -, with consequent damage to vital organs (HICKMANN et al., 2020).

SARS-CoV-2 can access the CNS in two ways: via hematogenous or via neural. The intense inflammatory response triggered by the virus can lead to increased permeability of the blood-brain barrier, allowing infected cells, cytokines and even the virus to reach the CNS. Neural access occurs by transporting the virus through the nasal cavity and rhinopharynx through the olfactory and trigeminal nerves, while the lower respiratory tract is accessed by the vagus nerve.

In a case report, the first one correlating COVID-19 infection with meningitis and encephalitis, unlike other cases, the presence of SARS-CoV-2 in the CSF was noted. However, the genetic material of the virus was not identified in the patient's nasopharyngeal swab (MORIGUCHI et al., 2020). In a post-mortem biopsy obtained from a patient with Severe Acute Respiratory Syndrome by COVID-19, the presence of the virus in neural endothelial cells through RT-PCR was observed, but the same was not evidenced in the collection of cerebrospinal fluid (CSF)

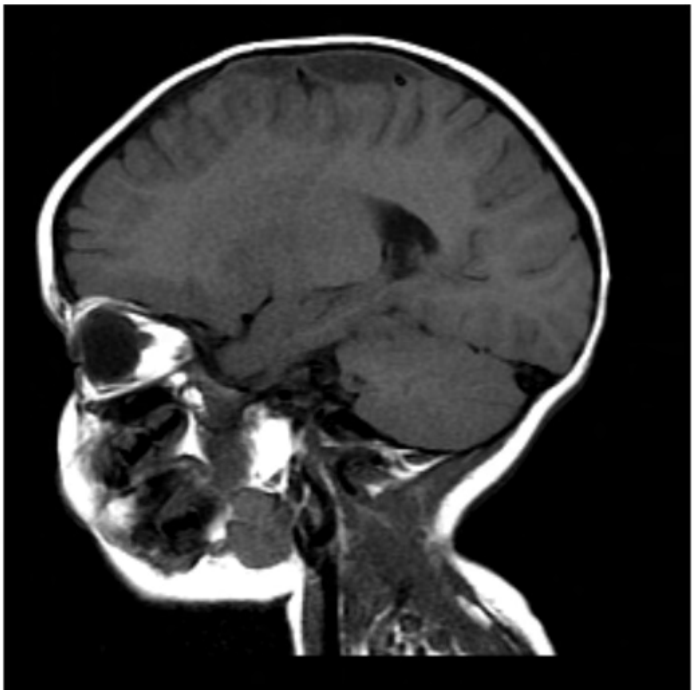

Figure 1: T1-weighted MRI in sagittal view demonstrates extra-axial collection located in the high convexity of the frontoparietal region on the right, with content showign a slightly increased signal in relation to the CSF

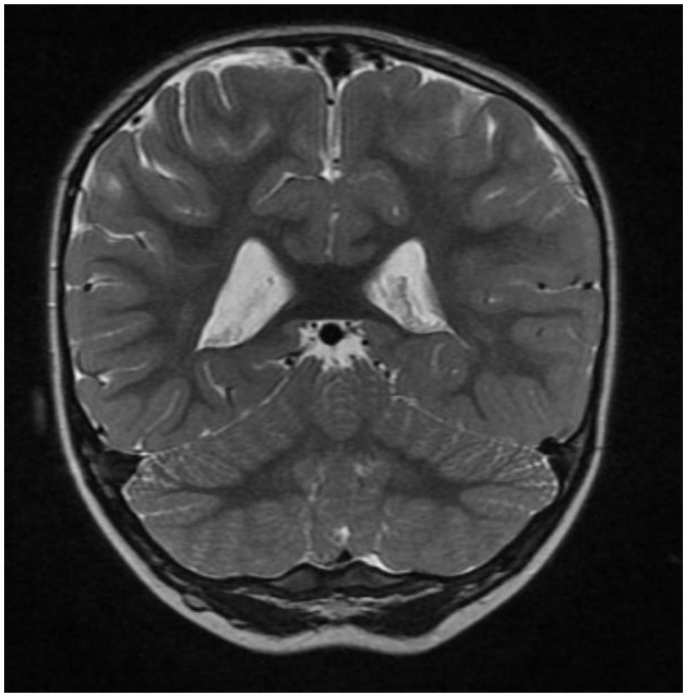

Figure 2: Coronal T2-weighted MRI scan showing almost complete reabsorption of the extra-axial collection in the high convexity of the frontoparietal region on the right, with a small cystic lesion with high signal remaining, similar to that of the cerebrospinal fluid. It is still possible to observe bone remodeling adjacent to the lesion.

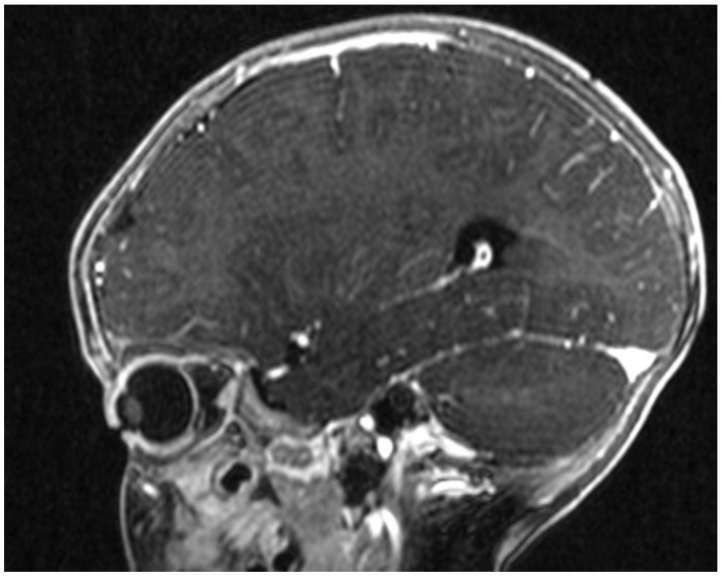

Figure 3: T1-weighted MRI after the administration of paramagnetic contrast in a sagittal view demonstrates enhacement and thickening of the pachymeningeal lining adjacent to the colletion site

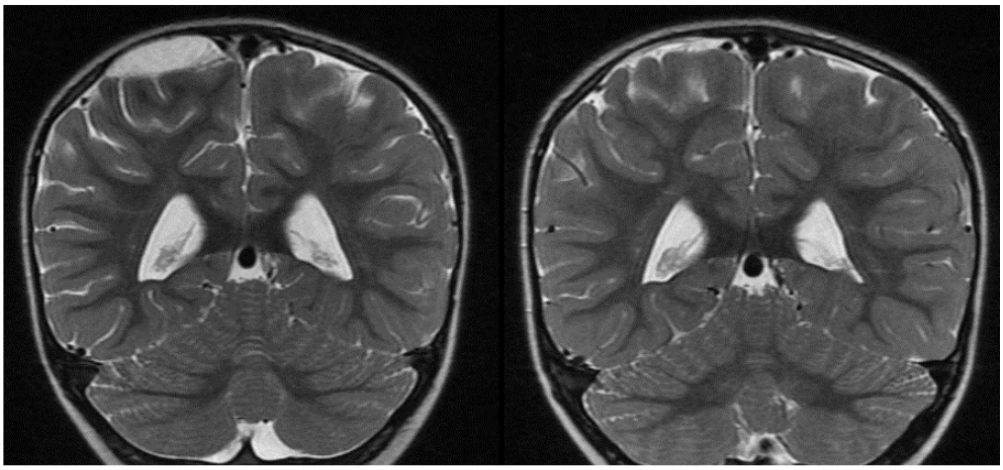

Figure 4: MRI with contrast in coronal section showing comparatively the evolution of complete resorprion of the extra-axial hemorrhagic collection over 45 days.

(PANIZ-MONDOLFI et al., 2020). In this sense, the clinical correlation of patients with positivity in RT-PCR exams is the one that most corroborates the confirmation of SARS-CoV-2 infection in the CNS. although not always correlated with CSF positivity, and vice versa.

This report describes a case of extra-axial hemorrhagic CNS collection in a pediatric patient after SARS-CoV-2, with cystic hemorrhagic appearance on magnetic resonance imaging 8 days after confirmation of SARS-CoV-2 infection by nasopharyngeal RT-PCR and resolution spontaneous in 45 days.

Subdural collection in children is a rare event from one year of age onwards, with its highest incidence peak around 6 months of age. The etiology is possibly related to rupture of the bridge veins, which communicate with the sagittal sinus, leading to hemorrhages into the subdural space. Most of the events are asymptomatic and self-limited, but a small portion has convulsive crises, focal symptoms as presented by the infant in the case reported (GUSMÃO et al., 1997).

Most of them are events resulting from traumatic brain injury, however, in the case described, there were no previous associated traumatic events, corroborating a possibly infectious cause. SARS-CoV-2 infection triggers an excessive inflammatory response mediated by cytokines that can directly affect the endothelial tissue of blood vessels, making them more vulnerable to rupture, as in the case of bridging veins. It is believed that this could possibly be one of the causes of CNS bleeding associated with COVID-19 (MAHALAKSHMI et al., 2021).

Vasculitis associated with COVID-19 has also been studied. Some correlations of vasculitis mimicked by SARS-CoV-2 infection were observed. It is believed that the disease is probably a mimic of vasculitis, as observed in patients who presented a typical picture of Kawasaki disease after SARS-CoV-2 infection. Elevation of vascular inflammatory mediators and D-dimer is evident in some patients. McGonagle et al., suggest that systemic microembolization of small thrombi may possibly be associated with the pattern of vasculitis after COVID-19. Possibly, this can be another cause of hemorrhage, not only in the CNS, but also in other parts, such as lungs, skin (MCGONAGLE et al., 2021).

There have been no other similar cases reported in the extra-axial collection literature related to COVID-19 to date. There are still few studies describing the possible clinical manifestations and problems of SARS-CoV-2 in children due to the possible lower virulence in these patients (MONTALVAN et al., 2020).

Another hypothesis to be put forward is that the cellular and humoral immune system of children is even less developed and the ACE2 receptors are still immature (PALMEIRA et al., 2020).

CONCLUSION

Although recognition of the manifestations of COVID-19 infection has been advancing rapidly (ALZYOOD et al., 2020), the literature still lacks studies that detail the mechanism of action of this virus in different systems. Furthermore, certain clinical findings still need to be explained. Case reports, such as the present one, set precedents for further investigations into the clinical profile of this infection, covering different organs and age groups. The case described demonstrates the need to include SARS-CoV-2 infection as a differential diagnosis in complaints involving the central nervous system in infants, which is rarely reported in the literature.

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