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CASE REPORT

A thromboembolic event in an infant born from a mother with COVID-19

Mariana Gaspar Mendonça[1], Anelise Steglich Souto[2], Mônica Akemi de Souza dos Reis[3,4]

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Abstract

Introduction: Premature birth is one of the main perinatal complications of maternal SARS-CoV-2 infection. **Case report:** Premature newborn, the daughter of a mother with a severe condition of COVID-19, who presented a thromboembolic event on the first day of life and evolved with hypoxic-ischemic encephalopathy. **Discussion:** Investigation was carried out on the cause of the framework, management with enoxaparin and curative with collagenase, even though it was not possible to avoid the loss of the auricular region. Immunohistochemical evidence of Spike-19 protein was found in the fetal placental part. RT-PCR tests for SARS-CoV-2 without oropharyngeal swab were negative. A maternal coronavirus infection should be included in any differential diagnosis as a cause of a thromboembolic event in the neonatal period.

[1] Joana de Gusmão Chidren's Hospital, Pediatrician, Neonatal Intensive Care Unit - Florianópolis - Santa Catarina - Brazil.
[2] Federal University of Santa Catarina, Adjunct Professor at the Pediatrics Department - Florianópolis - Santa Catarina - Brazil.
[3] Hospital of the Federal University of Santa Catarina, Neonatologist, Neonatal Intensive Care Unit - Florianópolis - Santa Catarina - Brazil.
[4] Joana de Gusmão Children's Hospital, Neonatologist, Neonatal Intensive Care Unit - Florianópolis - Santa Catarina - Brazil.

Endereço para correspondência:
Mariana Gaspar Mendonça.
Hospital Infantil Joana de Gusmão. Rua Rui Barbosa, 152 - Agronômica, Florianópolis - SC, Brazil. CEP: 88025-301. E-mail: marig_mendonca@hotmail.com

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INTRODUCTION

The pandemic caused by the novel coronavirus (SARS--CoV-2) has become a serious public health problem worldwide with serious impacts in all areas of medicine, including Neonatology. Knowledge of the maternal and neonatal repercussions of COVID-19 during pregnancy is still limited[1]. The possibility of vertical transmission has become a significant concern in symptomatic pregnant women with high levels of viremia from the onset of symptoms[2].

One of the most relevant concerns is hypercoagulability and the potential ensuing thromboembolic complications[3,4]. Neonatal thromboembolic events can be multifactorial and are often caused by exposure of the newborn to risk factors, such as preterm birth, perinatal asphyxia, sepsis, heart disease, maternal diabetes, and presence of a vascular catheter[5,6].

All things considered, it is important to investigate whether newborns born from women with COVID-19 may be at risk for thromboembolic events and related complications. This article describes the case of a female infant born from a woman with COVID-19. The newborn developed severe hypoxic-ischemic encephalopathy and an area of necrosis in the ear one day after birth. The Ethics Committee of the Federal University of Santa Catarina approved this report (certificate no.: 5.019.518).

CASE REPORT

The patient described in this report is a female infant born from a cesarean section at 35 weeks and 5 days of gestation, weighing 2,620g. Her mother was diabetic, obese, and did not have a history of coagulopathies or other prenatal complications. She presented with severe symptoms and was referred to intensive care for coronavirus infection. The infant had bradycardia, apnea with generalized hypotonia, and central cyanosis at birth. Resuscitation maneuvers were required, and she was intubated and placed on positive pressure ventilation; other procedures included cardiac massage, placement of an umbilical line, and infusion of intravenous adrenaline. She was taken to the neonatal intensive care unit (NICU). Her 1-, 3-, and 5-minute Apgar scores were 1, 3 and 3, respectively, establishing the diagnosis of perinatal anoxia. There was no birth injury.

Two hours after birth, she presented with a right hand and a swollen left ear, in the parietal region, with ecchymosis (Figure 1A). Prothrombin time (PT) and activated partial thromboplastin time (APTT) were increased, and she was treated with plasma and vitamin K. Antibiotic therapy with ampicillin and gentamicin was started due to increased C-reactive protein and leukocytosis. Since blood cultures were negative, antibiotic therapy was discontinued 72 hours after birth. Dopamine was administered 24 hours after birth and maintained for seven days due to hypotension and significant deterioration of perfusion. An echocardiogram performed three days after birth showed significant septal hypertrophy, probably associated with maternal diabetes.

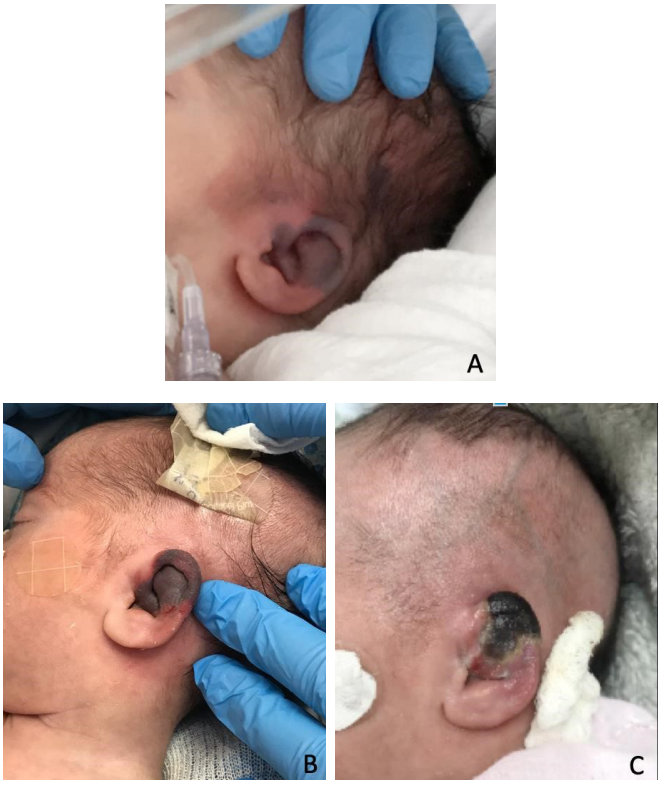

Figure 1. Progression of the lesion in the left ear. (A) Two hours after birth. (B) 48 hours after birth. (C) 20 days after birth.

A necrotic area appeared in the patient's left ear 48 hours after birth (Figure 1B), and coagulation tests were ordered. A D-dimer of 12,059 two days after birth indicated a tendency towards thrombotic events. After discussing the case with the Pediatric Hematology team, prophylactic enoxaparin (1.5 mg/kg/day) was prescribed. Nasopharyngeal RT--PCR swab tests for COVID swabs were performed 24 and 48 hours after birth and the results were negative, as were the IgM and IgG serology tests performed seven days after birth. An IgG antibody test for SARS-CoV-2 repeated 14 days after birth was also negative.

The pathologist described a placenta measuring 14x12cm with a maximum thickness of 5.2 cm and weighing 436g with sizes consistent with a pregnancy in the third trimester with areas of coagulative necrosis in the chorionic villi and signs of chorioamnionitis. The test for spike protein with immunohistochemistry in endotheliocytes and trophoblastic cells was positive with strong focal expression (Figure 2).

The patient presented uncoordinated seizure-like movements 72 hours after birth. A loading dose of intravenous phenobarbital was administered, followed with a maintenance dose. Doppler cranial ultrasound scans evidence of diffuse cerebral edema.

The patient was successfully extubated ten days after birth. MRI scans of the head performed at 12 days showed lesions in the basal ganglia and thalamus,

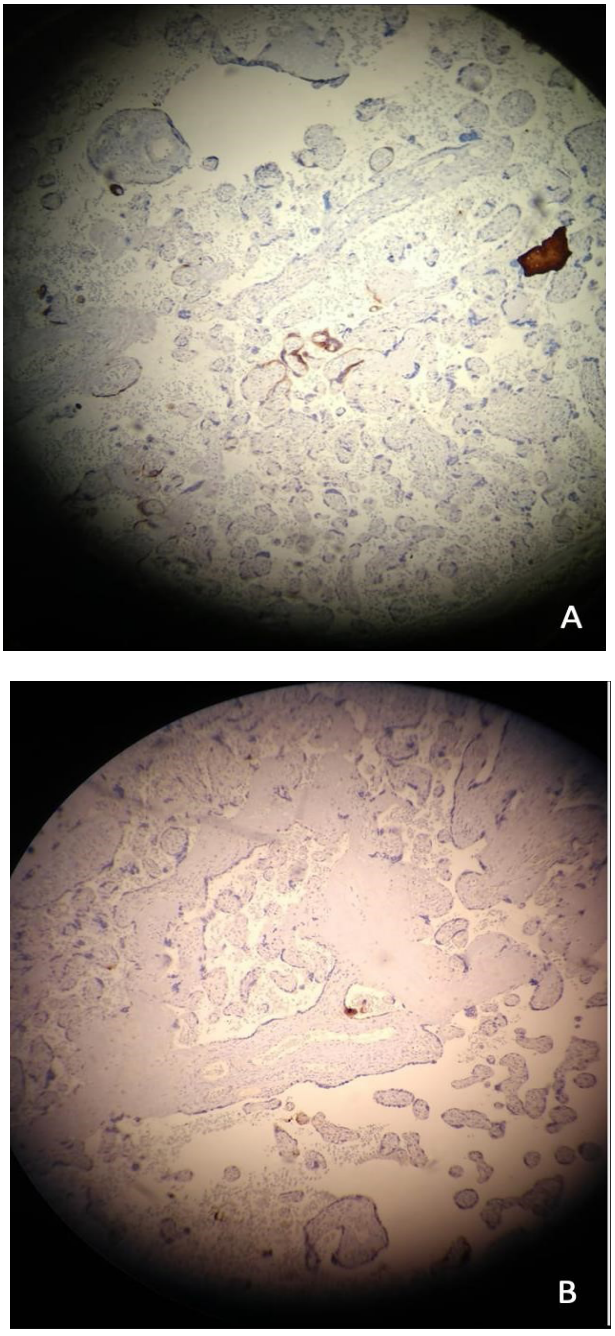

Figure 2. Positive immunohistochemistry test for spike protein in fetal placenta. (A) Chorionic villi. (B) Endotheliocytes.

confirming severe hypoxia and a poor prognosis. Despite the administration of enoxaparin, necrosis progressed and caused the patient to lose the upper part of her left ear (Figure 1C). She was discharged from the NICU 25 days after birth. She remained under the care of the pediatric team for another month, and was discharged from the hospital with a nasogastric tube, weekly sessions of motor physical therapy, and multidisciplinary home care.

DISCUSSION

The thromboembolic event affecting the infant born from a mother with COVID-19 has not been fully elucidated, despite evidence from immunohistochemistry tests of spike protein in fetal placenta. Her family did not have a history of coagulopathy.

Neonatal thromboembolism is a rare, multifactorial condition, potentially associated with prenatal events such as maternal thrombophilia and diabetes mellitus, early rupture of membranes, preeclampsia, fetal placental thrombosis, and postnatal events including preterm birth, very low birth weight, severe growth restriction, perinatal asphyxia, meconium aspiration, sepsis, and central venous catheter malpositioning. Maternal coagulation proteins do not cross the placenta, and the levels of several procoagulant proteins in the newborn, particularly the ones related to vitamin K, are reduced[7]. Management of thromboembolism and use of anticoagulants has not been clearly described. Anticoagulants may vary in terms of risk versus benefit. Low molecular weight heparin is the preferred medication[8].

An increase in the number of reports of preterm birth, newborns with hypoxic-ischemic encephalopathy, and small for gestational age (SGA) newborns was observed during the COVID-19 pandemic. This increase has been attributed to a decrease in the number of prenatal visits resulting from social distancing measures and fear of contagion[9]. A systematic review[10] found that maternal COVID-19 infection in the third trimester appears to be associated with low rates of vertical transmission (approximately 3.2%), although the possibility exists due to the presence of COVID-19 viral RNA in fetal and neonatal sources[3]. Histology examinations of the placenta showed poor fetal vascular perfusion and vascular thrombi. A report from the United States described a case of clear SARS-CoV-2 invasion in the placenta, suggesting a relationship between COVID-19 and coagulopathy with possible transplacental impacts on the fetus[11,12,13].

Two cases of neonatal gangrene related to coagulopathy caused by COVID-19 have been described[14,15]. The first was a leg gangrene due to spontaneous aortic thrombosis in a patient with fetal inflammatory response syndrome (FIRS) after intrauterine SARS-CoV-2 infection. The RT-CPR test for COVID was negative, but the antibody tests (IgG and IgM) were positive. The newborn was treated with steroids, heparin infusion, and recombinant tissue plasminogen activator, and required surgical embolectomy followed by amputation of the leg. The other case involved a preterm newborn with congenital gangrene in an arm associated with a history of maternal coronavirus infection in 2019. The etiology of the lesion was difficult to clarify despite extensive investigation for hypercoagulability and biopsy of the lesion. Amputation of the affected area was required.

CONCLUSION

A clear relationship between intrauterine thromboembolic events and maternal coronavirus infection has not been established, although intrauterine infection may trigger systemic inflammatory response in some fetuses, causing thromboinflammation. Maternal coronavirus infection should be considered in the differential diagnosis of thromboembolic events in the neonatal period.

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