

Arterial Thrombosis and Gangrene in a Neonate with COVID-19: A Case Report

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ABSTRACT

Background: Coronavirus disease 2019 (COVID-19) in neonates is an emerging challenge to pediatricians. The majority of the neonates with COVID-19 reported so far are suspected to be infected due to postnatal transmission. Vertical transmission has already been reported in two case-cohort studies.

Case report: A 32-week preemie with a birth weight of 2 kg was admitted to the neonatal intensive care unit due to respiratory distress. The case was born to a primigravida mother with a history of preterm premature rupture of membranes. The neonate developed arterial thrombosis on the first day of life and subsequent gangrene of the right foot and tested positive for serology and reverse transcription polymerase chain reaction (RT-PCR) of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) with elevated inflammatory markers (C-reactive protein, D-dimer, serum ferritin, lactate dehydrogenase). Since the mother was asymptomatic, she was not tested for SARS-CoV-2 antenatally. After the confirmation in the neonate, the mother was also tested for SARS-CoV-2 and tested positive by RT-PCR as well as serology.

Conclusion: This rare presentation calls for further research in transmission patterns either antenatally or vertical transmission. This report emphasized the possibility of vertical transmission of COVID-19 in neonates from asymptomatic mothers, with significant, early-onset neonatal infection in the form of thrombosis.

Keywords: COVID-19, Horizontal transmission, Neonate, Vertical transmission, Thrombosis

Introduction

Vertical transmission of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in neonates is suspected if the mother is positive for SARS-CoV-2 between 14 days before the birth and 2 days after the birth. The virus is detected through the swab of the neonatal respiratory tract in the first 24 h of life, amniotic fluid, umbilical cord blood, or neonatal blood sample in the first 24 h of life (1). Neonatal SARS-CoV-2 infection can be asymptomatic in the majority of cases and presents with fever in a few patients. This case study was performed on a preterm neonate who developed arterial thrombosis on the first day of life and subsequent gangrene of the right foot. The case tested positive for serology and reverse transcription polymerase chain reaction (RT-PCR) of SARS-CoV-2.

Case report

Preterm at 32 weeks gestation, weighing 2.0 kg, delivered by cesarean section, presented respiratory distress at 1 h of life. Preemie delivered to primigravida with an uneventful antenatal period with a history of preterm premature rupture of membranes who had received antenatal steroids. Neonate cried at birth with Apgar scores of 8 and 9 at 1 and 5 minutes, respectively. The mother had no history of fever or any other significant respiratory and medical complaints during the antenatal and intrapartum period.

At admission, the neonate had tachypnea and grunting with a Silverman Anderson score of 3/10. Chest X-ray was indicative of features of Respiratory Distress Syndrome. The neonate was subjected to continuous positive airway pressure, maintenance intravenous fluids, and first-line

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Figure 1. Discoloration of right lower limb on day 1

antibiotics as per unit protocol. After 3 h, the neonate was noticed to have cyanosis of the right lower limb with diminished pulses (Figure 1). Initial sepsis screen revealed leukocytosis with neutrophil predominance and negative C-reactive protein. However, over the next 24 h, the respiratory distress aggravated with the need for increased oxygen, and the neonate was subjected to conventional ventilation. The right lower limb continued to reveal cyanosis with diminished pulses. The results of the color Doppler test showed diffuse arterial wall thickening with echogenic content inside the lumen of right common femoral, superficial femoral, and popliteal arteries suggestive of thrombosis. It also revealed trickle flow in anterior tibial and dorsalis pedis arteries possibly because of collaterals. Low molecular weight heparin (Enoxaparin injection) was started by subcutaneous route. Both prothrombin time and activated partial thromboplastin time were prolonged with elevated inflammatory markers (CRP, ferritin and, lactate dehydrogenase) with elevated d-dimer (Table 1). The researchers continued enoxaparin along with vitamin K and transfused one aliquot of fresh frozen plasma.

On day 2 of life, to further evaluate the cause for thrombosis in the right foot, the neonate was sent for the serology for Covid-19 in light of the ongoing pandemic of COVID-19, which resulted in positive immunoglobulin M and immunoglobulin G for Covid-19.

The nasopharyngeal swab was sent for SARS-CoV-2 polymerase chain reaction (PCR) testing which was detected positive. The neonate was transferred to a negative pressure room with enhanced infection control precautions. The mother's nasopharyngeal swab was sent for SARS-

Table 1. Baseline characteristics of the studied neonate's obtained by observations

Neonate Characteristics	Observations
Gestational age	32 weeks
Age at presentation	1 hour of life
Gender	Male
Mode of delivery	Caesarean delivery
Resuscitation at delivery	Cried at birth
Apgar scores (1 and 5 min)	8, 9
Vital signs on admission	
Temperature (rectal)	35°C
Heart rate	160/min
Respiratory rate	76/min
Blood pressure	72/38 mmHg (mean 46 mmHg)
Oxygen saturation	91% (preductal)
Presentation	Thrombosis of right lower limb
Laboratory values	
Complete blood count	
Hemoglobin (g/dL)	16.3
Hematocrit	49
White blood cells (μL)	16,350
Neutrophils (%)	72
Lymphocytes (%)	21
Platelets (μL)	2,98,000
C Reactive Protein (mg/dL)	Negative followed by positive
Blood Culture	Negative
Urine analysis Urine culture	Negative
Serum ferritin(ng/ml)	Negative 890
D-dimer (mg/L)	1.9
Lactate dehydrogenase	625
PT/INR	30/1.8
APTT	78
Chest radiography	Features of RDS
Echocardiogram	NAD
IgM and IgG for SARS-CoV-2	Positive
RT-PCR for SARS-CoV-2	Positive
Probable mode of transmission	Vertical?
Outcome	Improved

PT: prothrombin time, INR: international normalized ratio, APTT: activated partial thromboplastin time, RDS: respiratory distress syndrome, IgM: immunoglobulin M, IgG: immunoglobulin G, RT-PCR: reverse transcription polymerase chain reaction, SARS-CoV-2: severe acute respiratory syndrome coronavirus 2

CoV-2 PCR testing after discussion with the obstetrician which was detected positive. Her serology was also positive for Covid-19 antibodies.

C-reactive protein was elevated on day 4 of life; therefore, neonate's antibiotics were graded up to second-line antibiotics as per unit protocol. It was also decided to add intravenous immunoglobulins due to the clinical illness with elevated inflammatory markers. The result of two-dimensional echocardiography was normal. After 48 h of starting enoxaparin, the color of the right lower limb improved and appeared pink except the forefoot and toes which stayed blackish (i.e. proceeding to gangrene) (Figure 2). The neonate



Figure 2. Distal gangrene involving right foot on day 5

was hemodynamically stable on conventional ventilation and was extubated to heated humidified high flow nasal cannula and then to room air. Trophic feeding was initiated on day 3 of hospitalization and was gradually stepped up to reach the full feeding amount. The antibiotics administration was discontinued 7 days later when the bacterial cultures did not show any growth. The neonate was discharged after 10 days of hospitalization with advice on infection control at home when taking care of this neonate, including hand hygiene and respiratory hygiene. To prevent community transmission of COVID-19, the family was advised to self-quarantine.

Discussion

Severe acute respiratory syndrome coronavirus 2 is a single-stranded ribonucleic acid virus belonging to the *Betacoronavirus* genus which is transmitted across humans, primarily through respiratory droplets and contact. The research investigating vertical transmission of SARS-CoV-2 is sparse, while the majority of studies indicated the horizontal transmission. In the present case, early-onset COVID-19 disease in the neonate was most probably acquired by vertical transmission. The transmission could have occurred either via the transplacental route antenatally close to delivery or intrapartum.

The results of a study carried out by Vivanti et al. reported vertical transmission acquired transplacentally in a preterm neonate (2). Earlier studies have failed to reveal the maternal-fetal transmission of SARS-CoV-2, including negative testing in amniotic fluid, umbilical cord blood, vaginal swabs, and breast milk. In other studies, two neonates were tested positive for reverse transcription (RT)-PCR for SARS-CoV-2 within 30 h of life. This finding is in line with that of the

present research; however, the mentioned cases lacked satisfactory precise information regarding isolation methods and perinatal transmission could not be ruled out (3, 4).

The researchers of this study found 11 published cases of neonatal COVID-19 detected by SARS-CoV-2 PCR (5-8). Among these studies, 6 of the reported cases presented within 3 days of life, whereas the remaining subjects presented between day 5 and 28 of life. Fever was the presenting complaint in 7 out of the 11 neonates. In the majority of the neonates, fever is the main presenting symptom of COVID-19 as described in the literature so far (66%) with favorable prognosis (9-12). In our case report, the neonate presented at 1 h of life and was tested positive by 30 h of life. The searchers suspected COVID-19 in light of the ongoing pandemic, although the presenting complaint was thrombosis in the right lower limb due to coagulation abnormalities which have never been reported to date in neonates. There are reports of thrombotic complications contributing to mortality and morbidity in adult COVID-19 patients (13).

Among the 11 published cases of neonatal COVID 19, 8 cases were born to mothers who tested positive for COVID-19 as quoted by Dumpa V et al¹⁴. Nevertheless, in our study, the mother was retrospectively assessed after the neonate's report and found to be positive for RT-PCR and serology.

The frequent laboratory abnormalities observed in cases of COVID-19 include lymphocytopenia, thrombocytopenia, leukopenia, and elevated inflammatory markers (15). Laboratory abnormalities of neonatal COVID-19 in our case report were suggestive of leucocytosis followed by leukopenia with elevated CRP, serum ferritin, D-dimer, and lactate dehydrogenase.

Dumpa et al. (14) postulated that neonatal infection can be an early-onset neonatal infection (first 3 days of life) or late-onset neonatal infection (4-28 days of life). Our case fitted into the early-onset category probably due to the vertical transmission. The postnatal transmission was extremely unlikely in our case since the neonate was separated from mother post-delivery. Though the 'gold standard' test for SARS-CoV-2 is RT-PCR, some articles reported false-negative rates of between 2% and 29% (equating to the sensitivity of 71-98%) (16). Since the studied neonate became symptomatic of COVID-19 infection with raised inflammatory markers on day 2 of life, the researchers of the present research believed that there was a high possibility of vertical

transmission. To the best of our knowledge, there is no evidence suggesting that this infection can be transmitted through breast milk. The majority of the cases were reported to be infected due to horizontal spread, as is previously revealed by Chen et al. (17), except in few cohort studies.

Conclusion

Currently, data suggesting the possibility of vertical transmission of SARS-CoV-2 is unclear except for few case reports, including our study. The most common mode of neonatal transmission of COVID-19 seems to be horizontal, while the vertical transmission is likely in early-onset infections. The literature on serological testing from larger cohorts will give more information into the transmission patterns, including both antenatal and vertical transmissions. Thrombosis of peripheral arteries involving digits should raise suspicion of neonatal COVID-19.

There are case reports of chilblains among children and young adults associated with SARS-CoV-2¹⁸. Therefore, this might be the first study investigating such a case among neonates. An international registry for emergent pathogens and pregnancy has been conceptualized. Such a strong surveillance registry will facilitate the identification of more cases of antenatal and vertical transmission of COVID-19, and thereby, contribute to better management of neonatal COVID-19 in the future. Our case emphasized the need for further research into the mechanisms of transmission of SARS-CoV-2 from mother to baby.

Conflicts of interest

The authors declare that there is no conflict of interest.

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