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Case Report

A case report of newborn infant with severe COVID-19 in Mexico: Detection of SARS-CoV-2 in human breast milk and stool

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ABSTRACT

Although COVID-19 in pregnant women and their neonates has been demonstrated, there is not enough evidence about how this vertical transmission occurs. This report describes a SARS-CoV-2 infection in a 21-year-old mother-daughter duo at the time of birth, focusing on the viral RNA detection in the stool of both and the human breast milk.

Introduction

The coronavirus disease 2019 (COVID-19) caused by the Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) is a global public health threat (Wang et al., 2020). The dynamics of SARS-CoV-2 transmission occurs from human-to-human through respiratory droplets (Li et al., 2020); however, other routes of transmission have not been fully characterized.

The high-risk populations for COVID-19 include elderly individuals and people with severe comorbidities (Jordan et al., 2020); as well, this novel coronavirus causes severe complications in pregnant women, which increases the risk of maternal morbidity (Schwartz and Graham, 2020). Proper documentation of the source and potential for mother-to-infant vertical transmission of SARS-CoV-2 is required to prevent cases of severe COVID-19 in newborn infants. We described the case of a mother with confirmed COVID-19 and her neonate that was positive for SARS-CoV-2 at the time of birth. Since the neonate had central cyanosis, dyspnea, and an oxygen saturation of 87%, she was defined as a severe case of COVID-19.

The infant's stool was positive for SARS-CoV-2 on the fifth day but not on the thirteenth day after birth, nor the nasopharyngeal and oropharyngeal swabs re-collected on the same day. Additionally, viral RNA was detected in the stool and milk of the infected mother who was actively breastfeeding the neonate. This report provides evidence of the risk of intrauterine infection and breastfeeding as mechanisms for vertical transmission of SARS-CoV-2.

Case report

At 38 weeks of gestation, a twenty-one-year-old female (gravida 1, para 1) with fever (39.5 °C) for the last two days was admitted to the Gynecology and Obstetrics Hospital, the Mother-Child Institute from the State of Mexico, Mexico on May 21st, 2020. The woman had had contact with COVID-19 patients and developed symptoms such as coughing, odynophagia, headache,

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diarrhea, and rhinorrhea. Her sore throat, fever, and symptoms started on May 19th, 2020. The chest radiograph showed patchy consolidation in the upper left lobe, and the patient was classified as a suspected case of COVID-19. The nasopharyngeal and oropharyngeal swabs taken on May 21st, 2020, were positive for SARS-CoV-2 by Real-Time Reverse Transcriptase-Polymerase Chain Reaction (real-time RT-PCR).

Also, the acute hypoxemic respiratory failure and atypical pneumonia were consistent with COVID-19. On day 1 at the hospital, she had painful and irregular contractions. Therefore, an emergency caesarian section was performed, and she delivered a female infant. The newborn weighed 3,075 g, the Apgar score was 8/9, and required only routine resuscitation. The infant's body temperature was 36.5 °C, and her heart rate was 140 beats per minute, with a respiratory rate of 52 breaths per minute. The newborn was separated from her mother immediately after birth without skin-to-skin contact. Nasopharyngeal and oropharyngeal swabs samples were taken from the neonate during delivery and tested by real-time RT-PCR, confirming the clinical diagnosis of SARS-CoV-2 infection with a low cycle threshold value (Orf1ab gene, 23), suggesting high viral load.

Moreover, the neonate had newborn jaundice, tachypnea, hyponatremia, central cyanosis, dyspnea, and oxygen saturation of less than 92% (87%). Consequently, this was defined as a severe case of COVID-19 (Dong et al., 2020c). The neonate was kept in the intensive care unit with oxygen therapy, which was withdrawn when the oxygen saturation level was greater than 90%. The infant's clinical laboratory results (Table 1) revealed that basophils, hemoglobin, hematocrit, total bilirubin, indirect bilirubin, and lactate dehydrogenase were above the normal range during the first six days after birth. In contrast, prothrombin time, platelets, and urea were below the normal range.

Regarding the mother, she had severe respiratory depression and episodes of oxygen desaturation between 40–60% in the immediate postoperative period. Therefore, she received rapid sequence intubation and intensive care. After 24 h, the extubation was performed when the mother showed adequate ventilation parameters. The mother was well and afebrile (37.3 °C) during the immediate post-extubation period with vital signs stable, respiratory rate of 22 breaths per minute, blood pressure of 107/87 mm Hg, and blood oxygen saturation >90%. She was treated with anticoagulant therapy using Enoxaparin 40 mg/day via subcutaneous injection and antiviral therapy with Ivermectin 12 mg/single-dose oral administration. The mother's clinical laboratory results (Table 1) indicated that the lymphocytes ratio, hemoglobin, hematocrit, total protein, urea, and calcium were below the normal range. At the same time, triglycerides were still above the normal range as on first-day hospital admission. Even though the lymphocyte ratio was below the normal range, the absolute lymphocyte count was found to be within the reference interval, as previously reported (Dong et al., 2020a).

The newborn was fed with synthetic milk formula instead of human milk until she was confirmed with COVID-19, without any adverse effects. On the fourth day after delivery (May 25th), real-time RT-PCR analyses of the mother's milk and stool samples were positive for SARS-CoV-2 RNA, a similar result was obtained for the infant's stool sample. On June 3rd, 13 days after delivery, the infant's nasopharyngeal and oropharyngeal swabs and stool

Table 1
Clinical Laboratory Results of Mother and Newborn Infant.

Clinical Laboratory Results						
	Mother		Newborn Infant			
Variable	Reference range	Day 2 after onset of symptoms (Hospital day 1)	Reference range	Day 1 after birth	Day 3 after birth	Day 6 after birth
White blood cell count ($\times 10^9$/L)	4.5–10	11.7	4.5–17	16.46	11.23	12.16
Lymphocyte count ($\times 10^9$/L)	1.1–3.2	1.8	3–8	4.6	5.3	8.5
Lymphocyte ratio (%)	21–48	15.09	21–65	28	47	69.9
Monocyte ratio (%)	–	–	2–12	11	12	10
Basophil ratio (%)	–	–	0–1	0	0	6
Eosinophil ratio (%)	–	–	1–4	2	5	0
Neutrophil ratio (%)	–	–	10–74	59	36	14.9
Hemoglobin (g/dl)	12–16	9.85	12–15	17.1	15.18	18.39
Hematocrit (%)	37–47	29.4	37–40	50.21	44.82	55.17
Prothrombin time (sec)	11–16	11.8	10–14	4.8	–	–
Platelet count (per mm^3)	150,000–450,000	348,000	150,000–450,000	218,000	354,000	126,000
Globulin (g/dl)	–	–	2–3.5	1.9	–	–
Glucose (mg/dl)	74–106	71	45–126	50	92	–
Cholesterol (mg/dl)	≤200	149	–	–	–	–
Triglycerides (mg/dl)	≤150	342	–	–	–	–
Total protein (g/dl)	6.3–8.2	4.7	3.5–5.4	4.8	–	–
Albumin (g/dl)	3–5	4.3	2.5–3.9	2.9	–	–
Total bilirubin (mg/dl)	0.1–1.2	0.5	1.4–8.7	5.5	12.9	13.8
Direct bilirubin (mg/dl)	0–0.3	0.1	0–0.2	0.5	0.4	–
Indirect bilirubin (mg/dl)	0.1–1	0.4	0.2–1.9	5	12.4	–
Lactate dehydrogenase (U/liter)	125–250	221	145–395	646	–	–
Alanine aminotransferase (U/liter)	5–34	15	–	–	–	–
Aspartate aminotransferase (U/liter)	5–34	19	30–150	45	–	–
Creatinine (mg/dl)	0.5–0.9	0.49	0.2–1	0.81	–	0.1
Blood urea nitrogen (mg/dl)	6–20	6	4–19	13	–	4
Urea (mg/dl)	16.6–48.5	12.8	14.9–40	27.8	–	8.6
Uric acid (mg/dl)	2.4–5.7	5.2	1–7	5.5	–	–
Magnesium (mg/dl)	1.6–2.4	1.84	1.6–2.4	2.03	2.71	2.02
Calcium (mg/dl)	8.4–10–2	7.7	9–10.6	7.1	9.1	7.1
Sodium (mmol/liter)	136–145	137	136–145	129	131	134
Potassium (mmol/liter)	3.5–5.1	3.1	3.7–7.2	4.9	5.2	5.4
Chloride (mmol/liter)	98–107	116	98–107	109	103	100

samples were negative for SARS-CoV-2 compared with the maternal samples, which remained positive. The mother and infant were discharged from the hospital when they had a resolution of respiratory symptoms and an uneventful postpartum and neonatal course.

Real-time RT-PCR of clinical specimens

Written informed consent was obtained from the patient, according to the Declaration of Helsinki 2013. Human milk, maternal stool, and infant's stool or nasopharyngeal and oropharyngeal swabs were collected at or after cesarean delivery. The clinical sample collection, processing, and laboratory testing were based on WHO guidelines. Viral nucleic acid extraction from clinical specimens was performed using QIAamp Viral RNA Mini Kit (QIAGEN) according to the manufacturer's instructions. Real-time RT-PCR was performed with the nucleic acid testing kit (Daan, Guangzhou, China) for SARS-CoV-2 detection according to the manufacturer's instructions. The open reading frame 1 ab (ORF1ab) (forward primer 5'-ACC-TTC-TCT-TGC-CAC-TGT-AGC-3′, reverse primer 5'-AGT-ATC-AAC-CAT-ATC-CAA-CCA-TGT-C-3′, and probe FAM 5'-ACG-CAT-CAC-CCA-ACT-AGC-AGG-CAT-AT-BHQ1-3′) and nucleocapsid protein (N) (forward primer 5'-TTC-AAG-AAA-TTC-AAC-TCC-AG-3′, reverse primer 5'-AGC-AGC-AAA-GCA-AGA-GCA-GCA-TC-3′, and probe VIC 5'-TCC-TGC-TAG-AAT-GGC-TGG-CAA-TGG-CG-BHQ1-3′) were designed as the two target genes for the detection of SARS-CoV-2 in clinical samples. The thermal cycling was performed under the following conditions: incubation at 50 °C for 15 min and 95 °C for 15 min, 45 cycles of denaturation at 94 °C for 15 s, and extension and collection of fluorescence signal at 55 °C for 45 s. A cycle threshold value (Ct-value) $\leq$40 was defined as a positive result, whereas a Ct-value >40 was considered a negative test.

Discussion

SARS-CoV-2 is responsible for the epidemic of the COVID-19 worldwide (Li et al., 2020). Previous reports suggest the intrauterine vertical transmission potential of SARS-CoV-2 and its implications on newborn infants (Chen et al., 2020b; Wang et al., 2020; Zhu et al., 2020). Nevertheless, there is not enough evidence about how mother-to-infant vertical transmission occurs. Here, we report the first SARS-CoV-2 infection in a neonate born to a woman with COVID-19 in Mexico. SARS-CoV-2 infection in the newborn infant was characterized as a severe case of COVID-19 because she had central cyanosis, dyspnea, and oxygen saturation of 87% (Dong et al., 2020c). Moreover, the newborn had thrombocytopenia accompanied by high lactate dehydrogenase levels, which suggested abnormal liver function (Chen et al., 2020c; Zhu et al., 2020). Lymphopenia (lymphocyte count of less than 1.5×10^9/L) is an indicator of the severity of COVID-19 in patients (Zhao et al., 2020); however, it was not observed in the mother and newborn as in a previous study (Dong et al., 2020a). Even though the mother was treated with Ivermectin, we do not recommend its use since there are no clinical trials suggesting its efficacy against SARS-CoV-2 infection.

The infant was born by emergency caesarian without the premature rupture of the membrane or placental abruption, and with airborne transmission precautions. Also, we did not observe that the newborn swallowed amniotic fluid. Thus, we rule out these causes of SARS-CoV-2 detection in this newborn. Her nasopharyngeal and oropharyngeal swabs samples taken immediately after birth were positive for SARS-CoV-2, suggesting intrauterine vertical transmission. No umbilical cord or placenta tests were performed, so whether the SARS-CoV-2 infection was acquired by intrauterine transmission cannot be confirmed. A recent report has demonstrated the transplacental transmission of SARS-CoV-2 with clinical manifestation in the neonate (Vivanti et al., 2020) as in this case, which confirms that mother-to-infant transmission is possible. Therefore, SARS-CoV-2 infection could be considered as a TORCH (Toxoplasmosis, Other (syphilis, varicella-zoster, and parvovirus B19), Rubella, Cytomegalovirus, and Herpes simplex virus) infection (Muldoon et al., 2020). The fact that this case is an intrauterine vertical transmission or not remains unconfirmed, but this is not ruled out. Also, we rule out SARS-CoV-2 infection in the newborn infant as nosocomial, since the risk of infection was reduced according to Management Guidelines for Obstetric Patients and Neonates Born to Mothers With Suspected or Probable SARS (Maxwell et al., 2017).

On the other hand, the shedding of SARS-CoV-2 RNA in stool from both patients and breast milk was detected. Thus, human breast milk could be involved in SARS-CoV-2 transmission from mother to newborn infant during breastfeeding but not in this case. It is not yet known how SARS-CoV-2 shedding occurs in breast tissue, and whether this viral RNA represents infectious viral particles. We ruled out that the milk had been contaminated because the self-expression of human milk was performed with hand hygiene and after breast decontamination, and it was expressed directly into a sterile specimen container. Although SARS-CoV-2 RNA was not detected in breast milk thirteen days after delivery, it may have contained a low viral load or even elevated IgM and IgA antibodies against the virus, as has been reported (Chen et al., 2020a; Dong et al., 2020b). Since human breast milk is essential to provide immunity to the infant, monitoring of the human milk banks is required to prevent the risk of infection through breastfeeding. We recommend that whether or not SARS-CoV-2 RNA is detected in breast milk, breastfeeding could be suspended, and instead, pump the milk to avoid mastitis. Nevertheless, human milk's benefits could greatly outweigh the risk of vertical transmission of COVID-19 since it contains IgM and IgA antibodies to SARS-CoV-2 (Dong et al., 2020b), suggesting that breastfeeding might have a protective role in neonates. Further studies will determine whether breastfeeding is appropriate during maternal COVID-19 infection. In summary, this report provided evidence on the risk of SARS-CoV-2 infection during pregnancy and breastfeeding.

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Ethical approval

The informed consent was obtained from the patient for publication of this case report.

Conflict of interest

The authors declare no conflicts of interest.

Contributions

F.B.-G., J. M.R.-R., A.H.-V., J.G.M.-D., D.G.R.-H., and P.Z.-S collaborated equally in writing the manuscript. F.B.-G., J.M.R.-R., A.H.-V., P.V.B.-M.D., L.e.g.-S., J.G.M.-D., M.J.P.-M., E.D.-G., D.G. R.-H., J.G.-M., and P.Z.-S. collaborated in data collection and analysis. F.B.-G. and J. M.R.-R. coordinated and edited the manuscript.

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