



Unlikely SARS-CoV-2 vertical transmission from mother to child: A case report

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ABSTRACT

As the 2019 novel coronavirus disease (COVID-19) rapidly spread across China and to more than 70 countries, an increasing number of pregnant women were affected. The vertical transmission potential of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is of great concern to the obstetrics, neonatologists, and public health agencies. Though some studies indicated the risk of vertical transmission is low, few cases have been reported with comprehensive serial tests from multiple specimens. In this case, a female preterm infant was born to a mother with confirmed COVID-19. She presented with mild respiratory distress and received general management and a short period of nasal continuous positive airway pressure support. During her stay at the hospital, a series of SARS-CoV-2 nucleic acid test from her throat and anal swab, serum, bronchoalveolar lavage fluid, and urine were negative. The nucleic acid test from the mother's amniotic fluid, vaginal secretions, cord blood, placenta, serum, anal swab, and breast milk were also negative. The most comprehensively tested case reported to date confirmed that the vertical transmission of COVID is unlikely, but still, more evidence is needed.

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Introduction

Since the end of 2019, an unexplained pneumonia, later named 2019 novel coronavirus disease (COVID-19), was originated in Wuhan and has rapidly spread throughout the whole country and to more than 70 countries. As of Mar 5, 2020, more than 80,000 laboratory-confirmed cases were reported in China, while around 16,000 cases outside, of which the youngest was 30 h. All general people are vulnerable to COVID-19, particularly the population with relatively weaker immunity, including the minor, elderly, and pregnant women. Existing evidence demonstrated the person-to-person transmission, mostly at a family or a cluster [1,2].

Respiratory droplets and close physical contact are thought to be the main transmission route, although the aerosols transmission is highly suspected recently. The possibility of mother-to-child transmission is of great concern to the obstetrics and neonatologist. However, due to the shortage of reagent for virus detection, a vast majority of patients only underwent oropharyngeal swab testing, which is not sufficient to prove or rule out the presence of mother-to-child transmission.

Case presentation

A female neonate was born at 35⁺³ weeks' gestation by cesarean section to a 25-year old G1P1 mother because of fetal intrauterine distress. The birth weight was 2.6 kg, and the Apgar score was 9 in 1 min and 10 in 5 min. The amniotic fluid was clear, and the grossing of the placenta was unremarkable. During the third trimester of pregnancy, the pregnant woman was admitted to the hospital because of the symptoms of fever, fatigue, shortness of breath. Her chest CT scan showed multiple patchy nodular opacities bilaterally, intermingled with ground-glass opacity in both sub-pleural

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Table 1
Results of SARS-CoV-2 nucleic acid testing in mother.

	Amniotic fluid	Vaginal secretion	Cord blood	Placenta	Serum	Anal swab	Breast milk	Throat swab
Prepartum	/	/	/	/	/	/	/	(22.69, 22.37)
Day 1 of delivery	(-)	(-)	(-)	(-)	(-)	(-)	/	(23.38, 24.55)
Day 2	/	/	/	/	(-)	(-)	(-)	(25.29, 25.97)
Day 3	/	/	/	/	(-)	(-)	(-)	(24.95, 25.82)
Day 4	/	/	/	/	(-)	(-)	(-)	(26.52, 27.31)
Day 5	/	/	/	/	(-)	(-)	(-)	(27.63, 27.98)
Day 6	/	/	/	/	(-)	(-)	(-)	(28.27, 28.58)
Day 7	/	/	/	/	(-)	(-)	(-)	(28.68, 29.42)
Day 10	/	/	/	/	(-)	(-)	(-)	(-)
Day 14	/	/	/	/	(-)	(-)	(-)	(-)

Note: The number in the bracket indicates cycle threshold value of ORF1ab gene (left) and N gene (right) on real-time fluorescent polymerase chain reaction, with a cutoff value of 30 in this study.

Table 2
Results of SARS-CoV-2 nucleic acid testing in newborn.

	Throat swab	Anal swab	Serum	Sputum	Urine
2 h after birth	(-)	(-)	(-)	/	(-)
Day 1	(-)	(-)	(-)	(-)	(-)
Day 2	(-)	(-)	(-)	/	(-)
Day 3	(-)	(-)	(-)	/	(-)
Day 7	(-)	(-)	(-)	(-)	(-)
Day 14	(-)	(-)	(-)	/	(-)

spaces. On 6d of symptom onset, her throat swab was positive for severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2), which is considered the causative agent of COVID-19, by means of the real-time fluorescent polymerase chain reaction with primers and probes targeting the ORF1ab and N gene. The mother was isolated in the hospital and received interferon nebulization, oral lopinavir, intravenous antibiotics, and oxygen supplement. Besides, she was given one single course of dexamethasone to promote fetal lung development, for the possibility of preterm delivery. The mother was not affected by hypertension, diabetes, or other pregnancy-associated complications throughout the pregnancy. She received the cesarean section on 7d of symptom onset. The entire procedure was done in a negative pressure operation room. The droplet, contact, and airborne precautions were implemented throughout the operation, including all medical staff wearing the N95 mask, goggles, gown, and gloves, and mother wearing an N95 mask and not in contact with her child. After delivery, the nucleic acid test from the mother's amniotic fluid, vaginal secretions, placenta, cord blood, serum, and breast milk were all negative (Table 1).

This baby presented with tachypnea, moaning, and periodic breath immediately after birth, then she was transported to the neonatal intensive care unit using a closed isolette. Nasal continuous positive airway pressure was initialized soon, and pulmonary surfactant was administered at 6 h due to the bilateral lung volume reduction demonstrated by chest X-ray. Gentamycin and ampicillin were also empirically prescribed because of the significant elevation of white blood cells and procalcitonin, which was discontinued at 48 h due to negative blood and sputum cultures. This baby was successfully weaned from the nasal continuous positive airway pressure on 5d. During her hospital stay, the baby's throat swab, anal swab, serum, and urine samples were sent for the SARS-CoV-2 nucleic acid test at 2 h, 1d, 2d, 3d, 7d, and 14d, and the sputum was tested at 1d and 7d. All reports were negative (Table 2). This baby was discharged home 14 days after birth.

Discussion

A novel coronavirus was isolated from COVID-19 patients, which was initially named novel coronavirus-2019 and subsequently SARS-CoV-2. SARS-CoV-2 is the 7th coronavirus that could pro-

duce human infection, with the previous six species including 229E, NL63, OC43, HKU1, Middle East respiratory syndrome-related coronavirus and severe acute respiratory syndrome-related coronavirus (SARS-CoV) [3]. A recently published article showed that SARS-CoV-2 has a 79.5% identity with SARS-CoV and 96% with a bat coronavirus [1]. The clinical manifestations of COVID-19 are very similar to SARS [2], ranging from mild flu-like symptoms to severe pneumonia. Vertical transmission is a common transmission routine for some contagious disease, by which the pathogens passed from mother to the child across the placenta, through direct contact during delivery, or in the breast milk. Some coronavirus, such as 229E, OC43, NL63, and HKU1, are common respiratory viruses, which have proven to be characteristic of vertical transmission [4]. However, based on the limited evidence, the vertical transmission of SARS-CoV and middle east respiratory syndrome-related coronavirus is still not confirmed [5–8]. On Feb 5, 2020, a neonatal patient with COVID-19, born to a mother with laboratory-confirmed COVID-19, was diagnosed based on a positive nucleic acid test from the oropharyngeal swab 30 h after birth. It raises concerns among obstetricians, neonatologists, and public health agencies about the possibility of mother-to-child transmission of this novel coronavirus. Medical experts said it could be a case where the infection was contracted in utero, but it is also possible the baby was infected after birth from having close contact with the mother [9].

One study recruited ten neonates born to mothers with COVID-19. The nucleic acid test was performed on pharyngeal swab samples collected from 9 neonates from 1 to 9 days after birth, and all tests were negative [10]. The similar results were presented on another subsequent study, which sent the amniotic fluid, cord blood, neonatal throat swab, and breastmilk samples from 6 pregnant women with COVID-19 for nucleic acid test and all samples tested negative for SARS-CoV-2 [11]. In our case, amniotic fluid, vaginal secretions, placenta, cord blood, breast milk, venous blood from mother, and the throat and anal swab, sputum, venous blood, urine samples from the newborn were all tested negative for SARS-CoV-2, which is consistent with the published studies. These existing pieces of evidence are predictive of low risk of mother-to-child transmission for SARS-CoV-2. To our knowledge, this is by far the most comprehensive tested case in the world, providing the most convincing evidence to the question of whether there is a mother-to-child vertical transmission of this novel coronavirus. However, the possibility of viral load influencing the transmission risk should be of concern. Published studies have demonstrated a positive relationship between the viral load of some viruses and their ability to spread from mother to child [12,13]; it is still unclear whether SARS-CoV-2 has similar characteristics. In this case, we cannot estimate the mother's highest viral load before delivery, because she received the initial test on 6d of symptom onset, already after viral load reached the peak at 3 to 5d [14–16]. Therefore, at this time point, although the risk is minimal, it still cannot

exclude the possibility that a much higher viral load might lead to vertical transmission.

Several weeks ago, Zheng et al. found the angiotensin-converting enzyme 2 (ACE2), the receptor that SARS-CoV-2 enters the cell, has deficient expression in the different cell types of early maternal-fetal interface, which could partially explain why the risk of intrauterine mother-to-child transmission for SARS-CoV-2 is low [17]. However, until now, few basic studies have been involved in vertical transmission through birth canal contact and breast milk.

Conclusion

Conclusively, it should still be cautious about concluding that the vertical transmission is unlikely, as the biological characteristics and pathogenesis of SARS-CoV-2 remains unclear. Further evidence from epidemiological surveillance and experiment studies is still necessary to clarify this issue.

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Competing interests

None declared.

Ethics approval

Not required.

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