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Report of a Confirmed SARS-CoV-2 Positive Newborn after Delivery Despite Negative SARS-CoV-2 Testing on Both Parents

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Abstract

We present a case of a term infant born to an asymptomatic mother at a community hospital who required transfer to a local neonatal intensive care unit (NICU) immediately after birth for respiratory distress. The infant was tested for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) at 24 hours of life by reverse transcription polymerase chain reaction (RT-PCR) testing due to the absence of prenatal maternal COVID-19 testing and was found to be positive for SARS-CoV-2 at that time. A second RT-PCR test was obtained on the infant on day of life (DOL) 4 and was also positive, confirming an accurate diagnosis of COVID-19 disease in the infant. Both the mother and father remained asymptomatic and concomitantly tested negative for SARS-CoV-2 on two separate occasions. The infant subsequently clinically improved and was discharged without any complications. This case raises the potential concern for two unreported newborn issues related to COVID-19. First, the potential unreliability of negative maternal COVID-19 testing surrounding the time of delivery as it relates to routine newborn testing and isolation needs, and second, if the negative material testing was accurate, this raises the concern for a potential case of nosocomial COVID-19 infection within the first 24 hours of life.

Keywords
- SARS-CoV-2
- COVID-19
- newborn
- asymptomatic
- congenital
- infection
- nosocomial

The medical community's understanding of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) transmission and infection has been constantly evolving over the course of 2020. In particular, the risk of congenital neonatal infection from SARS-CoV-2 positive mothers has been a topic of great discussion and concern among the general pediatric and neonatology communities. Early in the pandemic, reports from China and other countries raised suspicion for vertical transmission, although the reports were not conclusive or able to provide a reliable estimate of the overall risk due to their limited numbers.[1–4] Since then, there have been several cohort and systematic reviews which discuss vertical transmission of COVID-19.[5–9] At present, most neonatal COVID-19 infections seem to be related to postnatal environmental exposures, although even these rates appear to be lower overall than previously suspected.[10] However, a recent case report has been able to demonstrate a proven instance of definitive transplacental SARS-CoV-2 infection consistent with a true congenital infection.[11] Currently, the majority of reported early onset neonatal infections have been related to active perinatal maternal SARS-CoV-2 infection, whether the mother is clinically symptomatic or remains asymptomatic. Despite a significant number of mothers being asymptomatic at the time of presentation for delivery, there are currently no California

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county or state policies mandating universal SARS-CoV-2 testing, and it is currently left to local hospitals to develop their own testing priorities based on their facilities' testing capacity and local disease prevalence.

There have been reports of SARS-CoV-2 infections without the mother being documented as being SARS-CoV-2 positive, but that does not necessarily mean the mother was actually tested for SARS-CoV-2 and found to be negative.[12] Consequently, there have not been any documented newborn COVID-19 infections in the medical literature when born to mothers who are documented SARS-CoV-2 negative at the time of delivery or directly thereafter, outside of a media report in June 2020 from a possible case in Mexico.[13] There have also been reports of newborn nosocomial SARS-CoV-2 infections after delivery, although the majority of those infections occurred after 7 days of life.[12,14] Therefore, this case raises the concern for one of two potential novel occurrences having taken place; either a congenital infection from an asymptomatic mother, who subsequently tested negative for SARS-CoV-2 infection after delivery, or a potential early nosocomial SARS-CoV-2 infection in the immediate newborn period which would seem less likely.

Results

A 30-year-old Caucasian woman (gravida 2 para 1) presented at $34^{2/7}$ weeks of gestation to the emergency room of a community hospital with onset of preterm labor. She reported no significant past medical or surgical history except for postpartum depression following her previous delivery. She denied recent international travel and her last history of any travel was 2 months prior to delivery (within the United States). She denied any illnesses in the 3 months prior to delivery. No sick contacts were noted in the last month prior to delivery. She also noted no known positive COVID-19 contacts during this time. She denied any recent fever, respiratory symptoms, fatigue, myalgia, anosmia, or cough during or prior to delivery. She received adequate prenatal care with no maternal or fetal concerns during the pregnancy. Prenatal tests were unremarkable except for group B *Streptococcus* (GBS) status that was unknown. SARS-CoV-2 testing was not done at the referring community hospital.

The mother had a precipitous vaginal delivery within 10 minutes of arrival to the hospital with spontaneous rupture of membranes shortly before delivery. She did not have any respiratory symptoms before, during or after delivery. There were no concerns for chorioamnionitis, and placental pathology assessment was not done.

The newborn was noted to be vigorous at birth with 1- and 5-minute Apgar scores of 8 and 9, respectively. He received routine skin-to-skin care with the mother for 10 minutes immediately after the delivery. However, he subsequently developed mild respiratory distress (grunting) and was taken to a radiant warmer for assessment, followed by transfer to the newborn nursery for further management.

While in the newborn nursery, the infant received noninvasive respiratory support with Vapotherm (Exeter, NH) at 4 liters per minute. Capillary blood gas was obtained and was unremarkable. Chest X-ray revealed hazy lung fields with no clear infiltrates or effusions. Complete blood count (CBC) with differential was normal. Due to the infant's prematurity, continued need for respiratory support and lack of neonatal intensive care services at the referral hospital, the infant was transferred to a level III NICU at 5 hours of life for further management. Due to worsening hypercarbia noted on a repeat blood gas, his respiratory support was escalated to continuous positive airway pressure followed by noninvasive positive pressure ventilation with 21% FiO_2 by the NICU transport team, with subsequent improvement.

Due to a lack of prenatal maternal COVID-19 testing, the infant was tested for SARS-CoV-2 by RT-PCR (Thermo Fisher Scientific, Waltham, MA) via nasal pharyngeal swab at 24 hours of life per hospital protocol while in the NICU (see appendix for specific hospital testing details). Due to the local in-house testing capabilities, the test result was found to be positive approximately 48 hours later (DOL 4). To attempt to confirm the neonatal diagnosis, repeat testing for SARS-CoV-2 by RT-PCR was repeated on DOL 4 and again resulted positive 48 hours later on DOL 6 (►**Fig. 1**).

The parents were afebrile and asymptomatic at the time and hence were allowed at the bedside for skin to skin per the hospital policy, while the initial SARS-CoV-2 test was in process. Breastfeeding was not done due to respiratory distress, but the infant was fed expressed breast milk. Once the infant was found to be COVID-19 positive on DOL 4, parental visitation was restricted pending further testing on the parents and the infant was monitored under advanced droplet and contact precautions.

After the first test on the infant resulted positive (DOL 4), the parents were both voluntarily tested as outpatients with Sofia SARS Antigen Fluorescent Immunoassay testing (Quidel, San Diego, CA) and were found to be negative at that time for SARS-CoV-2. However, due to concerns about the reliability of antigen testing, they also subsequently both obtained SARS-CoV-2 testing by RT-PCR (unknown type) on the following day (DOL 5) and both tested negative again. The parents did not report any new symptoms suggestive of COVID-19 during this time or for the following 2 weeks. After the negative results of both sets of parental testing, they were subsequently allowed back at the bedside with adequate counseling and isolation precautions.

Respiratory support on the infant was weaned off without issues within 24 hours of admission. The infant was treated with empiric antibiotics (ampicillin and gentamicin) for 48 hours; however, these were discontinued after his initial sepsis evaluation (blood culture, CBC, and C-reactive protein) appeared unremarkable. Feedings were initially provided via gavage support, but the infant was able to be discharged home at 9 days of life in good condition while taking full oral feeds. The baby's hospital course was otherwise only remarkable for indirect hyperbilirubinemia requiring brief phototherapy and a positive newborn screen for possible congenital adrenal hyperplasia, which was subsequently ruled out after further testing.

The referring hospital and the NICU transport team were notified of the positive COVID-19 status of the infant. No

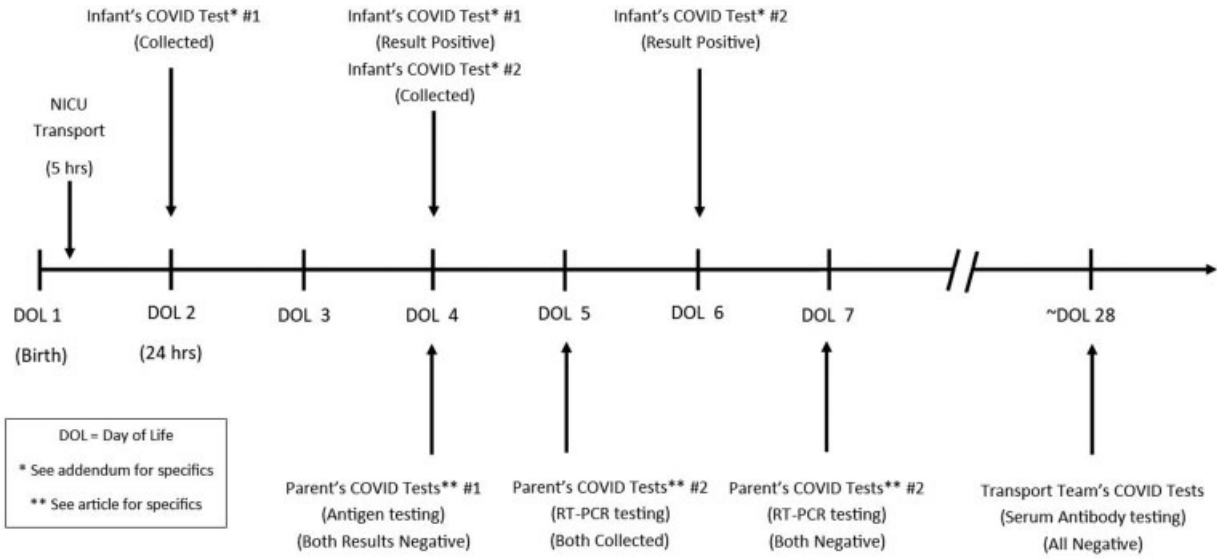

Fig. 1 Timeline of COVID testing for infant, parents and transport team.

known COVID-19 cases were reported among the caretakers of the infant at the referring hospital, receiving hospital or transport team. In the following weeks, the NICU transport team members (nurses and respiratory therapists) who were involved in the patient's initial transport were subsequently voluntarily tested for SARS-CoV-2 antibodies and all tested negative.

Discussion

Cases of neonatal SARS-CoV-2 infection have been reported to mothers who are positive for SARS-CoV-2 infection, although the overall rate appears to be relatively low.[1–4,11] There is also good evidence for the presence of asymptomatic SARS-CoV-2 infection among delivering mothers in the various communities struggling with high rates of SARS-CoV-2 infection.[15] However, there are no reported cases of asymptomatic COVID-19 positive mothers resulting in vertical transmission to their infants. This could be explained by the supposition that higher maternal viral loads would logically correlate with higher degrees of maternal symptoms as well as a higher possibility of vertical transmission. Therefore, asymptomatic mothers would likely have lower viral loads and be less likely to transmit the virus vertically. In addition, there have been no reported cases of mothers contracting SARS-CoV-2 infection during early/mid pregnancy, subsequently clinically resolving the infection, yet still resulting in neonatal congenital infection as can be seen with other congenital viral infections.

We report a case of neonatal SARS-CoV-2 infection, documented at 24 hours of life in the setting of respiratory distress at birth, born to an asymptomatic mother with multiple subsequent negative SARS-CoV-2 tests after delivery. Therefore, there are a few possible scenarios which can explain the findings in this case; each of these scenarios being clinically relevant.

First, this may represent a case of congenital infection prior to the peripartum period, which would explain the mother's lack of any recent symptoms and negative postpartum RT-PCR tests. This would then have implications for the need for heightened maternal prenatal testing to potentially detect prior SARS-CoV-2 infection and the need for increased newborn testing regardless of the presence of maternal symptoms or even recent negative SARS-CoV-2 RT-PCR testing prior to delivery.

Alternatively, this could represent active but asymptomatic maternal SARS-CoV-2 infection at the time of birth that was not detected on postnatal testing due to an undetectable low viral load at the time of testing, yet still enough virus present to result in vertical transmission. This possibility would be clinically relevant and emphasize the need for prompt universal maternal antepartum testing as well as potential universal newborn testing to ensure that asymptomatic mothers or newborns do not pose exposure risks to other patients and healthcare workers.

Lastly, it is possible that the infant may have acquired a postnatal infection from the mother or various health care workers caring for the infant during the first 24 hours of life. This scenario is quite unlikely given the short-time span from birth to testing. Also, due to the relatively immediate respiratory distress, the infant was only held for a few minutes by the mother and did not receive any breastmilk prior to the test at 24 hours of life, making it unlikely for these to be modes of transmission in this case.

While there are limitations in this case regarding the timing and variability of the SARS-CoV-2 testing that was available to the parents, they were both negative on antigen fluorescent immunoassay tests as well as RT-PCR tests within a few days of the neonate's positive test. While the sensitivities of these tests have been placed in question, the fact that all four tests were negative would suggest that they were less likely to be all false negatives. Another significant limitation is the fact that placental pathology and maternal SARS-CoV-2 antibody testing, that could have potentially provided evidence for an asymptomatic SARS-CoV-2 infection earlier in the prenatal period, were unavailable.

Conclusion

We present a case in which a newborn infant seems to have acquired a true SARS-CoV-2 infection based on two positive RT-PCR tests, despite being born to an asymptomatic mother with two subsequent negative SARS-CoV-2 tests. This case highlights the need for increased universal maternal SARS-CoV-2 testing prior to delivery and potentially the need for neonatal SARS-CoV-2 testing, even in the setting of a remote maternal SARS-CoV-2 infection, since the risk of congenital infection, is still unknown.

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Conflict of Interest
None declared.

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