Probable Vertical Transmission of SARS-CoV-2 Infection

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Background: To date, although neonatal infections with severe acute respiratory syndrome coronovirus 2 (SARS-CoV-2) have been described, none of these have been proven to be the result of vertical transmission of SARS-CoV-2.

Methods: We describe the probable vertical transmission of SARS-CoV-2 in a neonate born to a mother with coronavirus disease 2019 (COVID-19).

Results: Following cesarean section, the neonate was kept in strict isolation. Molecular tests for SARS-CoV-2 on respiratory samples, blood, and meconium were initially negative, but positive on a nasopharyngeal aspirate on the third day of life. On day 5, the neonate developed fever and coryza, which spontaneously resolved. Viral genomic analysis from the mother and neonate showed identical sequences except for 1 nucleotide.

Conclusion: This report has important implications for infection control and clinical management of pregnant women with COVID-19 and their newborns.

Key Words: COVID-19, SARS-CoV-2, neonatal, vertical transmission, pregnancy

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Despite the total number of confirmed coronavirus disease 2019 (COVID-19) cases now exceeding 8 million globally, existing data on COVID-19 in pregnancy, and its impact on neonates, remain limited.[1–4] Previous studies on other coronaviruses suggest that vertical transmission of those particular viruses is possible.[5] However, small case series of pregnant patients with severe acute respiratory syndrome (SARS) or Middle East respiratory syndrome, did not observe any vertical transmission.[6–8]

This report summarizes the clinical course and laboratory findings in a neonate born during the early phase of the COVID-19 outbreak in the United Kingdom in whom infection with severe acute respiratory syndrome coronovirus 2 (SARS-CoV-2) likely occurred via vertical transmission, either antenatally or intrapartum.

CASE SUMMARY

A 34-year-old woman (gravida 3, para 2) was admitted at 38 + 5 weeks' gestation with fever and respiratory symptoms. She had a body mass index of 35.9 kg/m^2. At this early stage in the United Kingdom outbreak, she did not meet the criteria for SARS-CoV-2 testing, which required a history of travel or known exposure to COVID-19; consequently, SARS-CoV-2 testing was not performed at her admission.

Over the course of 5 days, her clinical condition deteriorated, with increasing dyspnea. Interval chest radiograms demonstrated progressive bilateral multifocal consolidation. Blood cultures showed no growth, and polymerase chain reaction (PCR) testing for other respiratory viruses (influenza virus A&B, parainfluenza type 1–4, respiratory syncytial virus, metapneumovirus, adenovirus, rhinovirus, and endemic coronaviruses) on respiratory secretions were negative.

Subsequently, Public Health England responded to the changing global epidemiology by implementing surveillance initiatives and given the compatible clinical picture, respiratory samples were tested for SARS-CoV-2 on day 6 of admission.

Her condition worsened over the following 24 hours, with signs of acute respiratory distress syndrome. On day 7 of admission, acute hypoxemic deterioration led to the decision to proceed with tracheal intubation and delivery of the fetus by urgent cesarean section. A positive SARS-CoV-2 result from sputum was received early on day 8. Later that day, pulmonary gas exchange deteriorated further and venovenous extracorporeal membrane oxygenation (ECMO) was initiated, followed by transfer to a quaternary severe respiratory failure center.

The cesarean section was performed in a large operating room (dimensions 7 × 7.5 m; not laminar air flow) and all healthcare staff involved wore personal protective equipment (PPE) in line with airborne and contact precautions: filtering facepiece-3 respirators (equivalent to N100), visors, long-sleeved gowns, and gloves. The patient was brought in from one end of the room, with the neonatal radiant warmer and resuscitation unit located at the opposite end (distance between operating table and neonatal radiant warmer and resuscitation unit: 4 m). The neonatal team donned PPE outside the operating theatre and entered the room from the side where the and resuscitation unit was located and remained in close proximity to the resuscitation unit throughout. The abdomen of the patient was cleaned with a chlorhexidine solution and draped. A drape barrier was set up between her head and the operating field, before any airway manipulation was performed. She was successfully intubated at the first attempt following rapid sequence induction and direct laryngoscopy. Two minutes later, the skin incision was performed, followed by an uncomplicated lower segment cesarean section. There were no difficulties in delivering the neonate 4 minutes after the skin incision, who was then placed in a transport cot lined with a sterile drape and transferred to the neonatal radiant warmer and resuscitation unit.

The neonate was born at 39 + 5 week gestation, weighing 4.17 kg. The Apgar scores were 5, 9, and 9 at 1, 5, and 10 minutes of life. The neonate underwent oropharyngeal suctioning and support via positive end-expiratory pressure for irregular respiratory effort during the first 3 minutes and was transferred into an incubator at 10 minutes of life.

Following transfer to the neonatal unit, the neonate was kept under airborne and contact isolation precautions in a single room, did not have contact with any family members, and was fed exclusively with infant formula. Initial laboratory tests revealed elevated liver function tests, prompting initiation of empiric antibiotics for possible neonatal sepsis. SARS-CoV-2 was not detected by reverse transcriptase (RT) PCR performed on samples from respiratory secretions, meconium, blood, and cerebrospinal fluid obtained within the first 24 hours of life.[9] A chest radiogram taken on day 1 of life was unremarkable. However, SARS-CoV-2 was detected by RT-PCR performed on a nasopharyngeal aspirate taken on day 3 (stool and blood samples obtained the same day remained negative).

The neonate remained well until day 5 of life, when she developed fever (38.0°C), coryza, and mild tachypnea, prompting transfer to a tertiary unit for further management. However, she did not require any respiratory support, and all symptoms resolved within 48 hours. The results of PCR testing of blood, respiratory, and stool samples are shown in Figure 1. She regained her birth weight at 12 days of life and was discharged on day 18.

The mother was mechanically ventilated for 17 days, during which time she required a 12-day venovenous ECMO run. She was discharged from hospital 31 days after the cesarean section in good condition. Retrospective testing of her blood detected low-level SARS-CoV-2 viremia: 1 of 2 samples tested using 2 different PCR targets (RDRP and Orf) on the date of the cesarean section indicated a low-viral load (Cycle threshold [Ct] value: 34.87); a sample taken 2 days later was also positive (Ct value: 39.37).

SARS-CoV-2 virus isolated from samples from the mother's and the neonate's respiratory tract secretions were sequenced based on Joshua Quick's protocol (https://www.protocols.io/view/ncov-2019-sequencing-protocol-bbmuik6w). The genetic sequences were identical across the entire genome apart from a single-nucleotide difference between the baby and mother's genomes. The maternal sequence at that position showed a mixed base population, only one of which was represented in the neonate (GISAID deposition number for the mother EPI_ISL_417262, EPI_ISL_417305; neonate EPI_ISL_417314, EPI_ISL_417315).

DISCUSSION

This report describes a case of probable vertical transmission of SARS-CoV-2, either via the transplacental route antenatally or intrapartum via contact with maternal blood, considering that maternal viremia was present on the day of delivery.

Although a few reports have described SARS-CoV-2 infection in neonates, most likely acquired the infection postnatally. Publications in the first 2 months of the outbreak described no or negative SARS-CoV-2 molecular testing from multiple sites in infants born to mothers with COVID-19 pneumonia in late pregnancy: in 9 well infants[1]; in 10 infants with varying clinical outcomes[10]; in 2 infants with radiologic evidence of lower respiratory tract infection and good clinical outcome[3]; in 6 asymptomatic infants, including 2 with elevated IgM antibodies (in serologic assays prone to false-positive results and cross-reactivity) against SARS-CoV-2[11]; and in an asymptomatic infant with elevated but rapidly declining IgM antibodies against SARS-CoV-2.[12] In a case series of 33 neonates born to mothers with COVID-19, the clinical symptoms were mild and outcomes were favorable in most patients.[13] Three of the neonates developed confirmed COVID-19, including 1 with critical illness likely unrelated to SARS-CoV-2. Postnatal transmission also seemed the most plausible mechanism in other reports of positive SARS-CoV-2 PCR testing in a 36-hour-old with lymphopenia and mildly abnormal liver function; in a 17-day-old neonate with mild fever, sneezing, intermittent vomiting, and diarrhea[14,15]; and in a 27-day-old neonate who only developed mild symptoms.[16]

In contrast, postnatal transmission appears unlikely in our case. The mother underwent intubation (an aerosol-generating procedure) a few minutes before delivery, but had no subsequent contact with the baby. While this sequence of events and the distance between the mother and the neonatal radiant warmer and resuscitation unit make droplet transmission of SARS-CoV-2 from the mother very unlikely, aerosol transmission by particles dispersed through the room and not cleared prior to extraction of the neonate cannot be ruled out with certainty. Other possible, but unlikely, routes are contact transmission via contaminated hands or operating room environment, and droplet transmission from an infected healthcare worker. However, all staff in theatre were asymptomatic for 2 weeks following the delivery and all staff in contact with the neonate during the admission were wearing filtering facepiece-3 masks and using contact precautions, making droplet transmission unlikely. The baby did not receive any breast milk, ruling out this potential route of transmission. Furthermore, the sequencing data provide supportive evidence that the virus originated from the neonate's mother, although homology among worldwide SARS-CoV-2 strains has generally been high to date.[17] Given these circumstances, vertical transmission must be considered the most likely cause. We are only aware of one other case where vertical transmission appears more likely than postnatal transmission; however, the report contained insufficient details regarding the delivery and subsequent isolation of the neonate, leaving the possibility of transmission via droplet or contact route.[18]

While this case provides strong evidence for vertical transmission of SARS-CoV-2, this mode of transmission is likely to be a rare event and may reflect the severity of the disease in this mother, who in contrast to other reports of pregnant women with mild or moderate illness required ECMO support. Viremia has been shown to be uncommon in adults with COVID-19.[19] Although the pathophysiology that resulted in vertical transmission remains uncertain, we hypothesize that the high pulmonary viral load combined with extensive inflammation of lung tissue resulted in secondary viremia, thereby facilitating transmission via the hematogenous route.

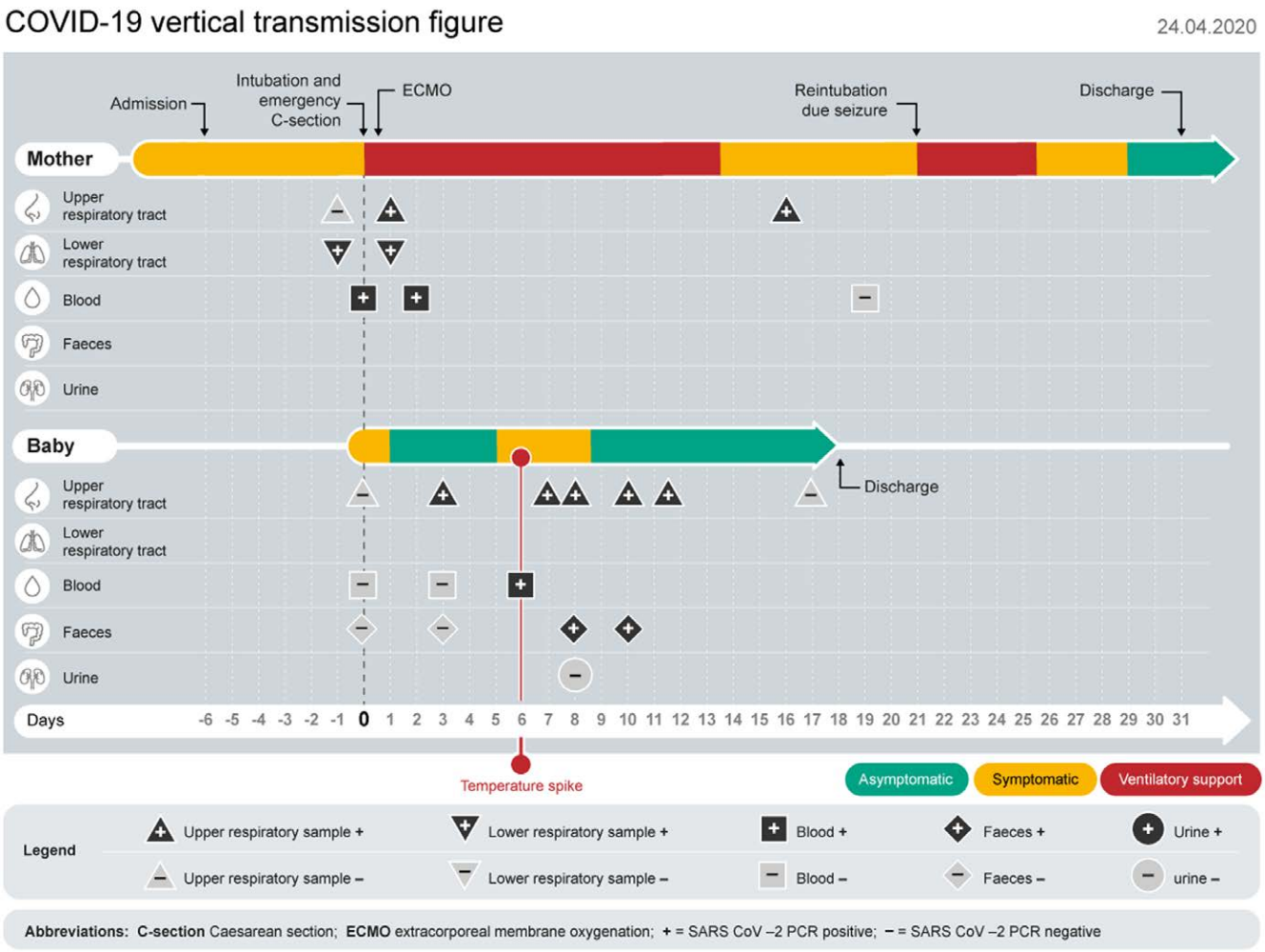

FIGURE 1. Timeline of clinic progression and PCR results in the described neonate and mother with COVID-19.

The potential for vertical transmission of SARS-CoV-2 has significant implications for the management of neonates born to women with COVID-19, particularly as previous guidance in the United Kingdom and United States assumed that antenatal transmission does not occur.[20,21] Future guidelines should reflect that vertical transmission can potentially occur and recommend that appropriate infection prevention and control measures are put into place, especially at the time of delivery and postnatally. Nationwide surveillance through the UK Obstetric Surveillance System and the British Paediatric Surveillance Unit to identify further neonatal cases has already been initiated, and the resulting data will help to further inform future guidelines.

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