Severe Acute Respiratory Syndrome Coronavirus-2 Pneumonia in a Newborn Treated With Remdesivir and Coronavirus Disease 2019 Convalescent Plasma

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Severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) is a novel pandemic virus. Mounting evidence supports the possibility of vertical transmission, which at the present time appears to be rare [1–3]. We report a newborn with vertically acquired SARS-CoV-2 who developed acute respiratory failure and received remdesivir and coronavirus disease 2019 (COVID-19) convalescent plasma.

Key words. coronavirus; COVID-19; newborn; remdesivir; SARS-CoV-2; treatment; vertical transmission.

Severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) is a novel pandemic virus. Mounting evidence supports the possibility of vertical transmission, which at the present time appears to be rare [1–3]. We report a newborn with vertically acquired SARS-CoV-2 who developed acute respiratory failure and received remdesivir and coronavirus disease 2019 (COVID-19) convalescent plasma.

CASE PRESENTATION

A 15-year-old primigravida woman presented at 40 weeks of gestation with contractions and amniotic fluid leakage. Maternal routine prenatal labs were negative, including human immunodeficiency virus and syphilis. At our institution, all pregnant women are tested for SARS-CoV-2 upon admission to labor and delivery. Her nasopharyngeal (NP) swab tested positive for SARS-CoV-2 by isothermal amplification (Abbott ID NOW, Abbott Park, IL). She was diagnosed with asymptomatic COVID-19; however, 5 days later, she developed anosmia. Rupture of membranes occurred 29 hours prior to delivery and fever 3 hours prior to delivery. She did not receive intrapartum antibiotics.

A female infant was delivered vaginally with a birth weight of 3936 g; the delivery was uncomplicated. Apgar scores were 8 and 9 at 1 and 5 minutes of life, respectively. The infant did not contact the parents in the delivery room and was immediately bathed. She was well appearing and the remainder of vital signs were normal. A blood culture was obtained and vital signs were closely monitored. The infant roomed in with the mother with the open bassinet situated 6 feet apart except when feeding. The mother attempted breastfeeding during the first day. When breastfeeding, mothers are instructed to wash their hands and breasts prior to each feed and wear a level 3 mask. The mother wore a level 3 American Society for Testing and Materials (ASTM) surgical mask at all times during the hospital stay. Both patients were under strict contact and enhanced droplet isolation per hospital protocol.

SARS-CoV-2 testing was obtained on the infant per hospital protocol at 24 hours of life. The infant’s NP swab tested positive for SARS-CoV-2 at 24 hours of life by isothermal amplification (Abbott ID NOW, Abbott Park, IL). She was diagnosed with asymptomatic COVID-19; however, 5 days later, she developed anosmia. Rupture of membranes occurred 29 hours prior to delivery and fever 3 hours prior to delivery. She did not receive intrapartum antibiotics.

A comprehensive metabolic panel, complete blood count with differential, and coagulation screen were obtained.
Notably, she had hypoglycemia with serum blood glucose 36 mg/dL (2 mmol/L), corrected with total parenteral nutri-
tion (TPN) adjustments. The white blood cell (WBC) count
was 21.2 \times 10^9/L, and the absolute lymphocyte count was
636 cells/\mu L. She had a mildly elevated partial thrombo-
plastin time with normal prothrombin time, international
normalized ratio, and fibrinogen. Blood cultures and CSF
culture were negative after 48 hours, so antibiotics were
discontinued.

On day of life (DOL) 4, the infant had persistent desatur-
tations to Oxygen saturation (SpO2) 88%, so she was placed on
supplemental oxygen and increased CPAP support. A chest
radiograph revealed prominent bilateral perihilar interstitial
markings. Remdesivir was started under compassionate use
with informed consent from both parents with a loading dose of
5 mg/kg and continued daily at 2.5 mg/kg for 10 days. Therapy
was intended for 5 to 10 days but given the infant’s persistence
of symptoms during therapy and elevated SARS-CoV-2 Ct
values at day 5, we extended it for 10 days. On DOL 5, the infant
had acute respiratory failure requiring intubation, so intrave-
nous dexamethasone 0.15 mg/kg every 24 hours was added for
3 days. On DOL 6, she required increasing ventilator support
and had episodes of bradycardia. Of note, she was receiving
dexmedetomidine at the time of sedation. An electrocardio-
gram showed prolonged Corrected QT interval (QTc) 484 milli-
seconds, an echocardiogram revealed normal anatomy and no
evidence of pulmonary hypertension, and serum troponin was
0.03 ng/mL. Repeat chest radiograph revealed prominent in-
terstitial markings. An endotracheal tube aspirate was without
WBCs and culture grew \textit{Staphylococcus lugdunensis}. On DOL
7, serum SARS-CoV-2 Immunoglobulin G (IgG) N protein test
was negative, and serum SARS-CoV-2 RT-PCR Ct value was
34.7, consistent with detection at low limits.

She deteriorated requiring increased Positive end-expiratory
pressure (PEEP) and FiO₂, so convalescent COVID-19 plasma
was administered under compassionate use on DOL 8. After pa-
rental consent, she received 10 mL/kg and then 15 mL/kg 24
hours later. On DOL 19, she continued to decompensate, and
a new tracheal aspirate was obtained, which grew meticillin-
susceptible \textit{Staphylococcus aureus}. We decided to treat both re-
covered staphylococci with vancomycin and nafcillin for a total
of 10 days. Bradycardia resolved and QTc was normal on repeat
Electrocardiogram (ECG). She was kept intubated and venti-
lated for a total of 13 days and was on positive pressure support
including nasal CPAP for a total of 30 days. She was eventually
weaned off respiratory support, where she remains in room air.
Daily serum creatinine and transaminases remained normal while
on remdesivir. She developed the late onset cholestatic jaundice
with direct bilirubin 5.6 mg/dL and gamma glutamyltransferase
105 units/L thought due to TPN, which she received for 28 days.
Repeated NP swabs for SARS-CoV-2 demonstrated increasing Ct
values (Figure 1).

**DISCUSSION**

We report a case of presumed vertically acquired COVID-19
in an infant born to an asymptomatic SARS-CoV-2-positive
mother. This infant’s respiratory distress leading to respiratory
failure was most likely due to COVID-19, as other causes of ne-
onatal sepsis were ruled out and an initial normal chest X-ray.
With a reported incubation period of 2–14 days [4], postnatal SARS-CoV-2 transmission was considered unlikely.

There are now a few case reports of suspected vertical transmission of COVID-19 [1–3]. A study of mothers with COVID-19 reported 2 infants with SARS-CoV-2 Immunoglobulin M (IgM) after birth, suggesting in utero infection since IgM is not transferred across the placenta. Of note, 5 infants in the study had positive SARS-CoV-2 IgG, which may have been of maternal origin [1]. Our infant did not have IgM tested; SARS-CoV-2 IgG was negative on DOL 7. The absence of SARS-CoV-2 IgG may suggest the mother was in the early phase of COVID-19; unfortunately, maternal SARS-CoV-2 IgG was not tested. Viremia is usually highest in the first few days of SARS-CoV-2 infection [5]. We speculate that a high level of maternal viremia may have resulted in fetal infection.

Vivanti et al [2] demonstrated placental tissue positive by RT-PCR for SARS-CoV-2, immunostaining, and histology consistent with SARS-CoV-2 infection. They postulated that neonatal viremia occurred following placental infection given that infant blood and bronchoalveolar lavage fluid were positive for SARS-CoV-2 by RT-PCR [2]. Sisman et al [3] reported an infant with SARS-CoV-2 in NP samples as well as placental tissue by immunohistochemistry and electron microscopy, which strongly suggested transplacental transmission. We were unable to test the placenta or amniotic fluid for SARS-CoV-2. Infection prevention practices were consistent with Centers for Disease Control and Prevention (CDC) guidance and with those reported by Salvatore et al [6], where none of the 80 newborns from SARS-CoV-2-positive mothers acquired infection. In light of this evidence gathered by others and the clinical presentation of our infant, with limited contact with her mother and development of symptoms at 25 hours of life, we conclude that our patient most likely acquired COVID-19 by vertical transmission.

Treatment decisions were guided by the National Institutes of Health (NIH) treatment guidelines for COVID-19 [7] and the best available evidence [8–10]. The benefits and risks of each treatment were carefully weighed given the clinical deterioration of our patient and the paucity of evidence available in treating neonates with COVID-19. We decided to use remdesivir once the infant required supplemental oxygen, which is the strongest indication for remdesivir [7]. Han et al [9] recently described the viral kinetics in an infected newborn with viral shedding for 11 days. Our patient had prolonged detection with a progressive decline in viral load. Remdesivir therapy likely contributed to the decreased viral load, though we cannot speculate to what degree as the natural progression of viral load is to decrease over time. We opted to use remdesivir for 10 days to support the putative immature immunity with a direct antiviral agent [10]. We monitored serum creatinine and transaminases and they were within normal limits for age throughout treatment with remdesivir, which was tolerated well.

After intubation, the infant was started on dexamethasone, which at the time showed a marginal benefit in mechanically ventilated patients [7]. After 3 doses of dexamethasone, the infant was not showing clinical improvement, so it was stopped due to its high side-effect profile and the theoretical disadvantages of using corticosteroids in the setting of an acute viral infection in an infant with immature cellular immunity. We were especially concerned with the possibility of delayed viral clearance that has been described in patients with other causes of viral pneumonia that received corticosteroids [8].

With ongoing clinical deterioration and absent specific IgG, we decided to give her COVID-19 convalescent plasma with the goal of providing neutralizing antibodies, thereby suppressing viral replication and possibly modifying the host immune response. It has shown to have a modest beneficial effect in improving oxygen requirement and improving survival, while being overall safe [7]. Our patient tolerated the plasma transfusions well without evidence of adverse events. Notwithstanding, we did not observe an immediate improvement as it has been described in adult patients with severe respiratory COVID-19.

We must comment on the possible role of staphylococcal superimposed bacterial pneumonia. The initial sputum culture with S. lugdunensis was thought to be secondary to respiratory colonization given the lack of WBCs in the sample and chest X-ray with diffuse interstitial infiltrates. A repeat sputum culture after reintubation was positive for Methicillin-susceptible Staphylococcus aureus (MSSA). Due to her ongoing respiratory deterioration, we initiated antibiotics. It is difficult to discern the role of bacterial pneumonia and its treatment played in interpreting this infant’s clinical course and response to COVID-19 targeted therapy.

It is unclear whether the use of treatments for acute COVID-19 infection was of benefit; however, it is reassuring that we did not observe any adverse effects of these therapies. Studies to guide treatment in infants with congenital or neonatal COVID-19 are urgently needed.

### Supplementary Data

Supplementary materials are available at the Journal of the Pediatric Infectious Diseases Society online (http://jpids.oxfordjournals.org).

### Note

**Potential conflicts of interest.** All authors: No reported conflicts. All authors have submitted the ICMJE Form for Potential Conflicts of Interest. Conflicts that the editors consider relevant to the content of the manuscript have been disclosed.
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