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Case Report

Vertical Transmission of SARS-CoV-2 in a Twin Pregnancy

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Abstract

Description

Transmission of the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) was first identified in 2019 and rapidly evolved into the global coronavirus disease 2019 (COVID-19) pandemic. The emergence of a highly morbid disease has posed ongoing challenges in the diagnosis, management, and prevention of COVID-19. The uncertainty underlying medical decision making is further compounded by preexisting conditions, including pregnancy. Here, we report a twin pregnancy complicated by maternal COVID-19 and the vertical transmission of SARS-CoV-2. We hope that our experiences contribute to a better understanding of the disease in pregnancy and, ultimately, guide the development of effective treatment and prevention strategies.

Keywords

COVID-19; SARS-Cov-2; vertical transmission; twin pregnancy; preterm birth; perinatal outcomes; neonatal mortality

Background

The normal cardiopulmonary and immune system changes of pregnancy increase susceptibility to infection, including the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2 virus).[1] The first and third trimesters of pregnancy are associated with a shift towards a pro-inflammatory environment,[2] which may be further induced by the cytokine-storm associated with coronavirus disease 2019 (COVID-19).[1]

Pregnant women diagnosed with COVID-19 are at increased risk of preterm delivery and stillbirth.[3,4] These recent findings are compounded by the potential for vertical transmission to the neonate. There are limited and conflicting data on vertical transmission. Some studies report no evidence of vertical transmission, despite thorough analysis of placental pathology, cord blood serology, and culture of amniotic fluid.[5] However, a systematic review of 38 studies found potential vertical transmission in 3.2% of infected mothers in the third trimester, with the earliest positive test of a newborn at 16 hours of life.[6] Proposed mechanisms of vertical transmission include the direct infection of syncytiotrophoblasts, a passage from the maternal circulation to extravillous trophoblasts, a passage through maternal immune cells, and an ascending vaginal infection.[7]

In this report, we present a case of maternal COVID-19 infection with monochorionic-diamniotic twin gestation in Louisiana and subsequent neonatal COVID-19 infection confirmed in both twins at 24 hours of life.

Case Presentation

In November 2020, a 22-year-old primiparous female with an uncomplicated monochorionic-diamniotic twin pregnancy at 27 weeks and 1 day of gestational age presented to labor and delivery triage with symptoms concerning for COVID-19. Prior to this presentation,

the patient received regular prenatal care and had traveled over 200 miles to visit family when her symptoms began. Outside prenatal records were requested, but due to the acute and fulminant clinical course, the records were not available. She reported a 4-day history of exertional dyspnea, headache, and myalgias. These symptoms initially improved with acetaminophen, guaifenesin, and diphenhydramine. Forty-eight hours after the initial onset of symptoms, she had a positive COVID-19 test result. After an additional 48 hours, she noted persistent fever, prompting evaluation in labor and delivery. She denied obstetric complaints, including contractions, vaginal bleeding, decreased fetal movement, or leaking of fluid.

She reported a history of asthma, last requiring an albuterol inhaler over 5 years ago. Her previous gynecologic, surgical, family, and social histories were unremarkable.

On arrival, she was febrile to 100.9 °F, tachycardic to 135 bpm, but normotensive. Oxygen saturation initially remained at 96-99% without the use of supplemental oxygen. She appeared mildly dyspneic with conversation. The remainder of the physical examination was unremarkable, including lung spaces that were clear to auscultation. Initial chest radiograph showed bibasilar patchy lung opacities concerning for early airspace disease (**Figure 1**). Maternal laboratory results are presented in **Table 1**. Laboratory testing revealed a mildly elevated aspartate aminotransferase, lymphopenia, and an elevated erythrocyte sedimentation rate, a prothrombin time of 9.3 seconds, and an activated partial thromboplastin time of 32.3 seconds. Urinalysis was unremarkable.

External fetal heart rate monitoring showed both twins had fetal tachycardia with a baseline in the range of 190-200 bpm, moderate variability, and intermittent variable and late decelerations. External uterine tocodynamometer showed uterine contractions every 1-2 minutes that resolved with intravenous fluid resuscitation. The patient was admitted for symptomatic management of COVID-19 and continuous fetal monitoring.

Approximately 3 hours after arrival, there was an abrupt onset change in the fetal status of both twins. Twin A had recurrent late decelerations with a decrease in variability, followed by prolonged fetal heart rate deceleration that was refractory to in-utero resuscitation methods. Twin B's fetal heart rate could not be traced continuously as a loss of signal was noted. However, late decelerations were evident. Due to the non-reassuring fetal heart rate tracing for both twins, the decision was made to proceed with an emergent cesarean delivery. She delivered viable twin female infants weighing 940g and 730g, respectively. Twin A had APGAR scores of 1 at 1 minute, 3 at 5 minutes, and 4 at 10 minutes. Twin B had APGAR scores of 2 at 1 minute and 7 at 5 minutes (**Table 2**). Placental pathology was notable for focal acute chorioamnionitis of the fetal membranes and a slightly increased perivillous fibrin deposition.

Both infants were immediately handed off to the Neonatal intensive care unit (NICU). Neonatal statuses at delivery are presented in **Table 2**. Both twins were intubated and admitted to the NICU for respiratory distress syndrome and nutritional support. Both neonates tested positive for COVID-19 at 24 hours, 48 hours, and

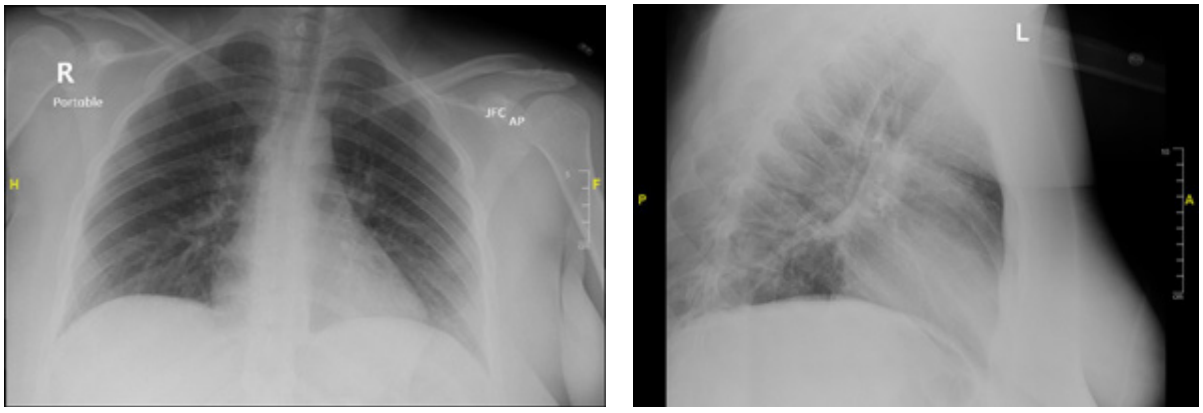

Figure 1. Posteroanterior and lateral radiographs of the patient's chest on the day of presentation show bilateral airspace opacities.

Table 1. Maternal Laboratory Data

	On admission				
Laboratory test	**Day 1**	**Day 2**	**Day 3**	**Day 4**	**Reference range**
Hematology					
White blood cell count, K/μL	5.3	5.7	4.4*	5.2	4.5 – 11.0
Hemoglobin, g/dL	12.4	10.1*	10.7*	11.0*	12.0 – 16.0
Hematocrit, %	38.5	31.0*	33.9*	35.1*	36.0 – 46.0
Mean corpuscular volume, fL	85.4	85.6	87.4	86.7	80.0 – 100.0
Mean corpuscular hemoglobin concentration, g/dL	32.2	32.6	31.6*	31.3*	32.0 – 35.0
Red cell distribution width, %	16.2*	16.1*	16.9*	17.1*	12.0 – 15.0
Platelet count, K/μL	199	170	175	214	160 – 420
Absolute Gran	0.10	0.08	0.06	0.07	
Immature Gran, %	1.9	1.4	1.4	1.4	0 – 3
Neutrophils, %	87*	81*	59	51*	52 – 70
Lymphocytes, %	6*	10*	30	39	20 – 44
Monocytes, %	5	8	8	8	0 – 10
Eosinophils %	0	0	1	1	1 – 5
Basophils, %	0	0	1	0	0 – 2
Erythrocyte sedimentation rate, mm/hr	27*	---	---	---	0 – 20
Chemistry					
Sodium, mmol/L	134	134	139	140	134 – 144
Potassium, mmol/L	4.0	3.9	3.9	3.8	3.6 – 5.2
Chloride, mmol/L	100	102	107	108	96 – 107
Carbon dioxide, mmol/L	26	25	28	26	21 – 32
Urea nitrogen, mg/dL	4	7	10	10	5 – 23
Creatinine, mg/dL	0.7	0.7	0.7	0.6	0.6 – 1.0
Glomerular filtration rate	111	111	111	132	
Glucose, mg/dL	72	90	72	68	68 – 106
Lactic acid, mmol/L	1.5	---	---	---	0.67 – 2.47
Uric acid, mg/dL	4.4	---	---	---	3.0 – 5.8
Calcium, mg/dL	9.3	7.8	8.3*	8.4	8.4 – 10.4
Phosphorus, mg/dL	3.7	4.8*	---	---	2.5 – 4.2
Magnesium, mg/dL	1.5*	---	---	---	1.6 – 2.5
Ferritin, μ/L	---	---	127	---	8 – 252
Total bilirubin, mg/dL	0.3	0.2	0.2	0.3	<1.1
Direct bilirubin, mg/dL	---	0.1	0.1	---	<0.4
Aspartate aminotransferase, U/L	46*	135*	117*	84*	<35
Alanine aminotransferase, U/L	46*	60*	74*	63*	30 – 65
Alkaline phosphatase, U/L	105	66	55	58	40 – 120
Lactate dehydrogenase, U/L	220	---	---	---	81 – 234
Troponin I, ng/mL	<0.017	---	---	---	0.000 – 0.056
N-terminal pro-B-type natriuretic peptide, pg/mL	129	---	---	---	0 – 450
Total protein, g/dL	6.8	5.1	5.3	5.6	6.3 – 8.2
Albumin, g/dL	2.7*	1.9*	2.0*	2.1*	3.4 – 5.0
Albumin/Globulin ratio	0.6	---	0.6	0.6	
Coagulation					
Prothrombin time, sec	9.3*	---	---	---	9.5 – 12.0
International normalized ratio	0.91	---	---	---	0.9 – 1.1
Activated partial thromboplastin time, sec	32.3*	---	---	---	21.0 – 32.0
Fibrinogen, mg/dL	512*	---	---	---	168 – 404
D-dimer, mg/mL	---	6.41*	---	---	0 – 0.59

*Indicates abnormal result.

Table 2. Neonate Findings

Variable	Twin A	Twin B
Birth		
Sex	Female	Female
Birth weight, g	940	730
Birth weight percentile, %	55.2	17.9
APGARs at 1, 5, and 10 min	1, 3, 4	2,7
Presentation	Cephalic	Breech
Vital signs		
Temperature, °F	99.5	102.9
Heart rate, beats/min	173	192
Respiratory rate, respirations/min	75	65
Blood pressure, mmHg	45/44	43/26
Laboratory data		
White blood cell count, K/μL	14.6	11.7
Hemoglobin, g/dL	13.7	13.5
Hematocrit, %	42.2	40.6
Platelet count, K/μL	160	159
Arterial blood gases		
Sample site	Arterial line	Arterial line
pH	7.168*	7.249
pCO_2	58.3*	44.3
pO_2	33.4*	45.1*
HCO_{3-}	21.2	19.4
Base excess	-8.0*	-7.7*
FiO_2	60	30
O_2 saturation	67.0	27
PO_2/FiO_2 ratio	55.6*	150.3*
Length of stay, days	7*	88*

*Indicates abnormal result

day 8 of life through a nasopharyngeal swab. On day 8, twin A passed away from pseudomonas sepsis. Twin B was discharged to home in stable condition at 88 days old.

After delivery, on postoperative day 1, the patient developed shortness of breath and hypoxemia, requiring supplemental oxygen at a rate of 3 liters per minute to maintain her oxygen saturation above 94%. Due to persistent symptoms, the patient received intravenous 6 mg of dexamethasone daily until hospital discharge on postoperative day 3. Persistent radiographic evidence of respiratory disease was demonstrated on sequential chest radiographs. The patient declined the use of intravenous remdesivir therapy. Her serum D-dimer level was noted to be elevated in the absence of symptoms suspicious of venous thromboembolism or a personal history of thrombosis. However, due to multiple obstetrics risk factors, including recent cesarean delivery of a preterm multifetal gestation pregnancy, and ongoing systemic infection with COVID-19 requiring hospitalization, thromboprophylaxis with unfractionated heparin was initiated. On postoperative day 2 (hospital day 3), her respiratory status improved, no longer requiring supplemental oxygen, which was subsequently discontinued, and adequate oxygenation was maintained on room air. By postoperative day 3 (hospital day 4), she met all milestones and was discharged home.

Discussion

These findings highlight the risk of preterm delivery due to fetal distress and neonatal SARS-CoV-2 infection in a pregnancy complicated by maternal COVID-19. Pregnant women infected with SARS-CoV-2 are known to be at increased risk of cesarean delivery and preterm delivery, as in this case.[9] The increased risk of preterm birth is most strongly associated with active infection during the third trimester, and future studies may need to investigate whether adverse early trimester outcomes are increased in patients who have preexisting risk factors for preterm delivery, such as the multiple gestation seen in this patient.[9-12]

While other studies at the time of this case have shown most infants born to mothers infected with SARS-CoV-2 do not have detectable levels of viral RNA in the nasopharynx or other COVID-19 signs and symptoms, our case of SARS-CoV-2 infection in twin neonates indicate the potential for vertical transmission in a mother with COVID-19. Based on studies at the time of this case, the mean incubation period for COVID-19 following exposure is 5.6-6.7 days.[7] A meta-analysis of 32 studies published in November 2020, found that the highest percentage of virus detection from reverse transcription polymerase chain reaction occurs during days 0-4 of symptom onset.[8] Though limited data exists regarding the COVID-19 post-exposure incubation period for neonates, these findings may suggest that the twins' positive 24-hour nasopharyngeal swabs indicate exposure prior to delivery.

It appears vertical transmission may be possible with COVID-19 infection, and a meta-analysis has demonstrated that infection rates of 3.2% are similar to those of other vertically-transmitted diseases.[13] Further research into the characteristics and potential mechanisms for SARS-CoV-2 vertical transmission is warranted to better understand the risk of adverse neonatal outcomes, including preterm delivery and stillbirth, in pregnant patients with severe COVID-19[14] and asymptomatic COVID-19.[15]

Ascertaining evidence of vertical transmission in early trimesters may be difficult, since COVID-19 IgG antibodies could be of maternal origin, and IgM antibodies (which do not cross the placenta) decrease 15-28 days after recovery.[16] Additionally, there is evidence that production of fetal IgM does not occur until approximately twenty weeks gestation.[18] Though preliminary studies indicate that severe cases of neonatal COVID-19 are rare, future studies may need to explore whether vertical transmission has an effect on the severity of the infection and the incidence of adverse long-term outcomes.[19,20] In general, data are currently limited regarding general maternal and neonatal outcomes following first- or second-trimester SARS-CoV-2 infection.[17]

Such adverse neonatal outcomes are further compounded by the risk of increased maternal COVID-19 severity in pregnancy, including venous thromboembolism, maternal death, and need for ICU admission.[14] In non-pregnant patients, severe COVID-19 has been associated with coagulopathy and elevated D-dimer levels,[21] both of which are inherently increased in pregnancy. However, D-dimer levels can be elevated in pregnancy, providing limited utility in reliably excluding venous thromboembolism, and, therefore, are not recommended for use in pregnancy.[22,23] At the time of this case, venous thromboembolism prophylaxis was not recommended in pregnancy; beginning December 17, 2020, prophylaxis was recommended for pregnant patients with severe COVID-19.[24]

Conclusion

The findings from this case suggest the risk of adverse outcomes of a pregnancy complicated by maternal SARS-CoV-2 infection and the potential for exposure to fetuses in utero as well as long-term sequelae of neonatal SARS-CoV-2 infection. Further investigation of the pathophysiology of vertical transmission and longitudinal studies of developmental outcomes of neonates exposed to SARS-CoV-2 are warranted. Since pregnant women have known increased susceptibility to COVID-19 and increased risk of adverse outcomes following infection, preventative measures to limit exposure through social distancing and the COVID-19 mRNA vaccine, which has been shown to transfer maternal IgG to fetuses, should be encouraged.[1,25]

Conflicts of Interest

The authors declare that they have no conflicts of interest.

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