Title

Placental abruption in a twin pregnancy at 32 weeks' gestation complicated by COVID-19, without vertical transmission to the babies.

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The authors report no conflicts of interest.

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Condensation: A twin pregnancy, with COVID-19 and superimposed pneumonia with a placental abruption requiring a caesarean section.

Short title: A twin pregnancy complicated by COVID-19 and placental abruption.

Key words: COVID-19, SARS-COV-2, twin pregnancy, placental abruption, preterm.

Objective

Pregnant women have been recommended to be stringent in avoiding infection based on concerns of worse outcome associated with other viral infections, such as Middle East Respiratory Syndrome (MERS) and Severe Acute Respiratory Syndrome (SARS), in the third trimester, rather than linked to COVID-19. Other coronavirus spectrum infections have been associated with miscarriage, preterm birth, preeclampsia, caesarean delivery, perinatal death, fetal growth restriction, and placental abruption.[1,2]

There have only been a few reports evaluating vertical transmission from mother to baby of COVID-19, and it seems unlikely that it occurs. In four possible cases of vertical transmission reported, two were premature at 31 and 34 weeks. [3,4] Viral transfer has been linked to prematurity with HIV and other viral infections in pregnancy.

False negative COVID-19 polymerase chain reaction (PCR) tests are reported and the need for and timing of repeat tests in negative symptomatic patients is unknown. This maybe related to cite of sampling.[5]

We report a case of a monochorionic diamniotic twin pregnancy who presented at 32 weeks of gestation with cough, fever and shortness of breath, and tested positive for COVID-19, having had a negative swab two weeks prior, when she initially presented with symptoms. She was delivered by emergency caesarean section at 32^{+6} weeks due to an antepartum haemorrhage, with placental abruption confirmed clinically at delivery, and placental pathology demonstrating hypoperfusion, which may have been related. Both babies were negative for COVID-19 at testing on postnatal days 3 and 5.

We present this case to highlight the following important issues; potential association between COVID-19 infection with placental abruption, and placental pathology; the absence of vertical transmission in the context of preterm birth and placental abruption; need for repeat testing with worsening or persistent symptoms, and the importance of clinical preparedness for obstetric emergencies in the context of COVID-19.

Study Design

A thirty-year-old gravida two, para nought plus one (previous early miscarriage <12 weeks gestation), BMI 23, with monochorionic diamniotic (MCDA) twins presented at 30^{+4} weeks of gestation with an unprovoked antepartum haemorrhage (APH), with ongoing fresh vaginal bleeding (50ml), associated with lower back pain. She was a non-smoker, with no history of alcohol or recreational drug use and was normotensive at booking (120/54mm/Hg) and on admission (103/68mm/Hg).

She had been reviewed fortnightly in the Multiple Pregnancy Clinic and there were no concerns of shared placentation from serial growth scans (inter-twin discordance 3-4%, and normal amniotic fluid, with both twins growing around the 50^{th} centile). The placenta was reported as anterior high. A glucose tolerance test performed at 26 weeks', due to her ethnicity, family history of diabetes, and multiple pregnancy, was negative for gestational diabetes. In 2014 she had a thyroidectomy following a papillary cell carcinoma and was clinically euthyroid on thyroxine 200mcg (which was titrated in pregnancy to her TSH levels).

On the day she presented with an APH, it was noted that her husband had visited the Accident and Emergency Department (A&E) and received antibiotics for a chest infection the previous day. Upon arrival in the Maternity Assessment Unit, on examination, her abdomen was soft, with clots seen on vaginal speculum examination, with normal maternal observations (see table). The haemoglobin result was 111g/l, blood group rhesus positive, with no atypical antibodies. She was admitted, and her partner advised to return home to self-isolate (he had not been tested for COVID-19.) His COVID-19 PCR test was subsequently sent but was negative.

Although the woman did not meet criteria for testing, a COVID-19 PCR was sent to plan delivery, in case of contact. A course of antenatal corticosteroids for fetal lung maturity, (intramuscular dexamethasone 9·9mg) was given on the 12th and 13th March. On the second day of her admission, she developed a sore throat and shortness of breath; her COVID-19 PCR was reported as negative (throat swab) and she was discharged home, with advice to self-isolate for 14 days.

Two weeks later, she attended the hospital for her 32-week growth scan and to discuss her birth plan. She reported some itching on the day, and bloods were sent to rule out Obstetric Cholestasis. When she was contacted later that day with the blood test results in a virtual consultation she reported feeling weak and feverish, with pink coloured urine. She was advised to return to hospital.

Results

On admission she looked unwell, with a pulse rate of 128 bpm, and temperature of 37·1^{o}C. Laboratory urinalysis was unremarkable. She gave a one-day history of cough, fever and

mild shortness of breath. Chest x-ray revealed a right sided pleural effusion, and an enlarged globular heart. An echocardiogram performed the same day showed a mild pericardial effusion, and NT-BNP was 28pg/ml (normal <100pg/ml) (done to rule out cardiac failure or cardiomyopathy). Her lymphocytes and platelets had dropped (see table). On this admission her COVID-19 PCR was repeated (nasal swab) and was positive. She was nursed in isolation, and did not require oxygen.

On the second day of admission she had a further vaginal bleed (200mls measured quantity of fresh blood), and a category two caesarean section was arranged under regional analgesia. There was a delay of 110 minutes in the delivery, in part, due to the donning of full PPE (FFP3 masks, visors, long sleeve gowns and gloves). In this period, she remained stable with no oxygen requirement and the fetal heart traces were normal. During the procedure there was clear evidence of placental abruption, with significant intra-uterine clots on entry to the uterus and a 400ml retroplacental blood clot. The blood loss was 1·7 litres, excluding the APH. She did not require a blood transfusion and was managed postnatally in isolation with one to one care.

Both twins required positive pressure respiratory resuscitation, twin one by endotracheal tube and twin 2 by mask. The Apgar scores were 5, 8, 8 and 8, 9, 9 for twin one (2190g) and two (2160g) respectively and umbilical cord pH as follows: twin one arterial, base excess: 7.215, -3.2 ; venous, base excess: 7.319, -2.9 and twin 2 arterial, base excess: 7.285, -2.9; venous, base excess: 7.30, -2.7

Both were intubated in neonatal intensive care unit. The mother expressed breastmilk. Both babies were negative for COVID-19 PCR on postnatal days three and five. The placental

histology report described accelerated villous maturation with evidence of mild hypoperfusion.

Conclusion

We report the first case of significant placental abruption in a woman diagnosed with COVID-19, requiring a category two caesarean section with good maternal and neonatal outcomes.

Abruptions are rare in MCDA twins, in an otherwise normal pregnancy as was the case here (<2%).[6] The association between placental abruption and COVID-19 infection in pregnancy is uncertain. However, our patient had no recognised risk factors for placental abruption, (30 years old, BMI 23, non-smoker, with no history of alcohol or recreational drug use, normotensive at booking (120/54) and on admission (103/68), anterior high placenta), and cases of abruption have been reported with other coronavirus spectrum infections.[6] The abruption maybe incidental but as COVID-19 can affect maternal haemostatic parameters, we advise further caution with careful surveillance with antepartum haemorrhage in positive women until more data are available.

Placental histology did not show any maternal or fetal inflammatory response or lymphocytic inclusions, as is commonly noted in acute viral infections but there was evidence of accelerated villous maturation suggesting hypoperfusion over days, which we believe is the first description of placental pathology in the context of COVID-19. These are non-specific placental changes which can occur in other conditions, e.g: Pre-eclampsia, but given the absence of additional features like decidual vasculopathy and partial agglutination of the villi, often present in pre-eclampsia, and normal growth of both twins on serial scans, it is

plausible that changes could be due to a mild COVID-19 infection causing abruption and hypoxic changes in the placenta.

Postnatally, the mother was relatively well and not requiring oxygen, but had thrombocytopenia and lymphocytopenia typically associated with COVID-19, abnormal chest X-Rays, with a mild pericardial effusion on cardiac echo. We believe the pericardial effusion was unrelated to COVID-19 as the BNP was normal. Neither the abruption or preterm birth was associated with vertical transmission to the baby.

This was the first case of an obstetric emergency where the mother was known to have COVID-19 in our hospital. Full PPE was donned but took time, and we advise training for such emergencies, as placental abruption can often be associated with acute fetal distress requiring urgent delivery in minutes.

Initial COVID-19 PCR was negative, when taken from the throat, soon after developing typical symptoms. False negative results have been reported with a poorer positive predictive value for throat swabs (her first swab), compared to nasal swabs (her second swab), 24% v 57% respectively.[5] Tests five to six days following symptoms are most likely to identify the disease. Reorganization of the delivery of obstetric care in the current pandemic (e.g. virtual consultations) has re-emphasised the value of comprehensive history taking, and triaging for a face-to-face attendance, including repeat testing, where there is any suspicion of deterioration of symptoms.

Author Statement:

Katy Kuhrt: Writing – original draft, writing – review and editing, visualization; **Jess McMicking:** Conceptualization, writing – review and editing; **Surabhi Nanda:** Conceptualization, writing – review and editing; **Catherine Nelson-Piercy:** writing - review and editing; **Andrew Shennan:** Conceptualization, supervision, writing – review and editing.

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	Timeline					
	30+4	**32+4**	**32+6**	**Day 1 Postnatal**	**Day 3 postnatal**	**Day 5 postnatal**
	12/03/20	**26/03/20**	**28/03/20**	**29/03/20**	**31/03/20**	**02/02/20**
Event	APH (50ml), 1ST Admission	Fever, pink stained urine, 2ND Admission	APH (200ml) Delivery			
Symptoms	Sore throat, short of breath	Feverish, Cough, short of breath				
COVID-19 PCR	Negative	Positive				
Twin 1 COVID-19 PCR					Negative	Negative
Twin 2 COVID-19 PCR					Negative	Negative
Maternal platelets	154	108	88	104	114	191
Maternal Lymphocytes	1.3	0.9	1.1	1.5	1.2	1.3
Maternal Ferritin			42		119	86
Magnesium				0.62	0.63	0.61
ALT		8		11		15
Albumin		32		24		26
LDH					428	363
CRP		32	47	74	102	40
Temp	36·8	37·1	36·5	37·5	36·8	36·2
PR	101	128	72	90	67	58
SBP	121	109	109	128	108	108
DBP	64	67	69	80	64	74
RR	16	28	15	18	16	17
O2 sats (%)	99	99	96	94	100	98

Table shows swab results, and trends in blood tests and observations over time. Pulse rate (PR); systolic blood pressure (SBP); diastolic blood pressure (DBP); respiratory rate (RR).