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Second-Trimester Miscarriage in a Pregnant Woman With SARS-CoV-2 Infection

No data exist regarding the effect on fetuses of maternal severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection during the first or second trimester of pregnancy, and data are limited regarding infections that occur during the third trimester. However, reports of newborns with fetal distress or requiring admission to the intensive care unit[1,2] and a stillbirth after maternal coronavirus disease 2019 (COVID-19)[3] in the third trimester suggest the possibility of COVID-19–induced placental pathology.

We present a case of miscarriage during the second trimester in a pregnant woman with COVID-19.

Methods | A pregnant woman in her second trimester who had a miscarriage was evaluated at Lausanne University Hospital on March 20, 2020. Institutional review board approval and written informed consent were obtained. Information was obtained from medical records. Reverse transcriptase–polymerase chain reaction (RT-PCR) to detect SARS-CoV-2 and cultures to detect bacterial pathogens and PCR for *Chlamydia trachomatis, Neisseria gonorrhoeae, Mycoplasma hominis*, and *Ureaplasma urealyticum* were performed on samples from the mother, fetus, and placenta (**Table**). Placental histological examination and fetal autopsy were performed by 2 experienced perinatal pathologists (C.G. and E.D.). Hematoxylin-eosin, myeloperoxidase immunohistochemistry, Gram, and periodic acid–Schiff colorations were performed on the placenta.

Results | A 28-year-old obese, primigravida woman presented at 19 weeks' gestation with fever (102.5 °F [39.2 °C]), myalgia, fatigue, mild pain with swallowing, diarrhea, and dry cough for 2 days. A nasopharyngeal swab was positive for SARS-CoV-2. She was given oral acetaminophen and discharged home.

Table. SARS-CoV-2 RT-PCR Results[a]

Sample type	SARS-CoV-2 results	Bacterial culture and RT-PCR
Maternal		
Deep nasopharyngeal (March 18)	Positive	
Deep nasopharyngeal control (March 22)	Positive	
Vagina (March 20 and March 22)	Negative	Normal flora
Blood (March 22)	Negative	
Fetus (March 20)		
Umbilical cord blood	Negative	
Amniotic fluid	Negative	Sterile
Fetal mouth	Negative	
Fetal armpit (2 samples)	Negative	
Placental submembrane	Positive	Sterile
Placental cotyledon	Positive	Sterile
Fetal anus	Negative	
Fetal liver	Negative	
Fetal thymus	Negative	
Fetal lung	Negative	

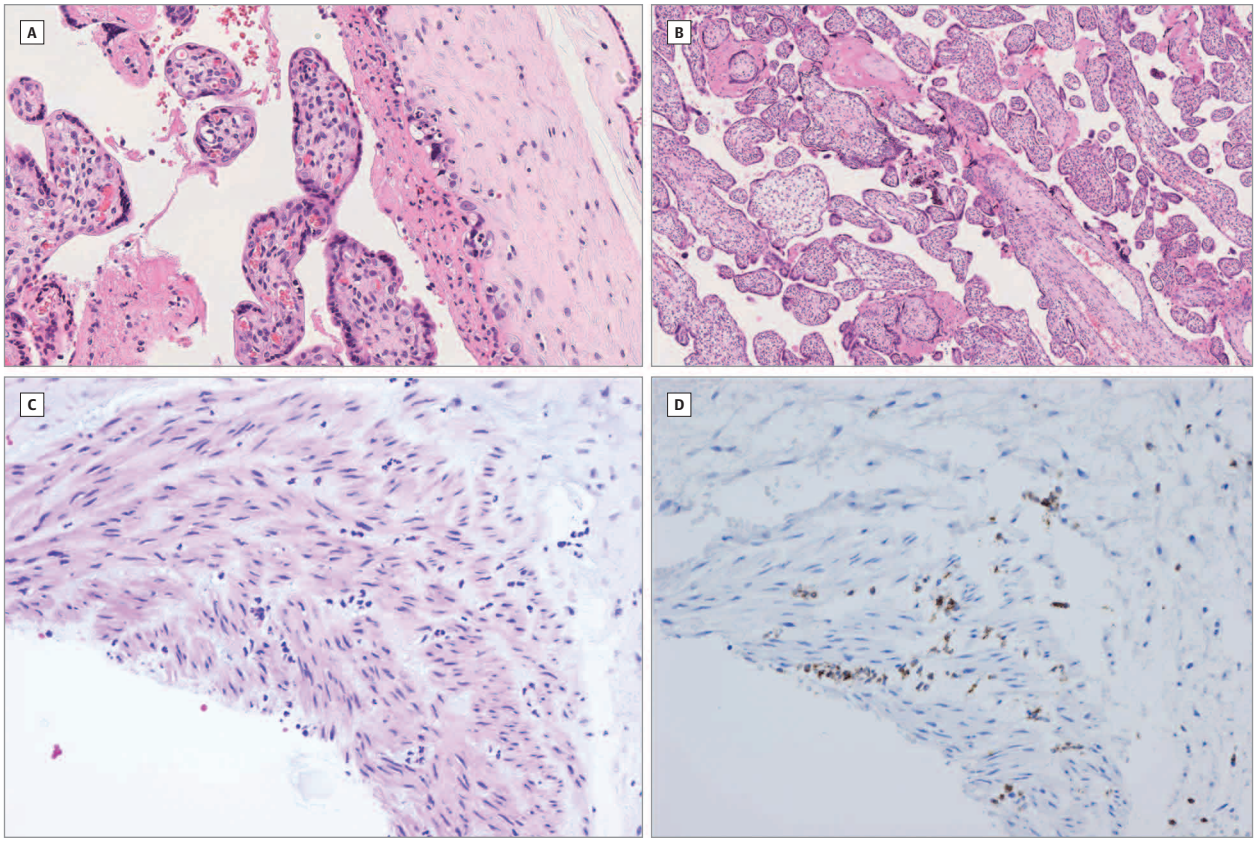
[a] Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) was detected by coupling a MagNA Pure (Roche) RNA extraction to a 1-step reverse transcriptase–polymerase chain reaction (RT-PCR) targeting the gene coding for the E protein of the virus.

Two days later, she presented with severe uterine contractions, fever, and no improvement of her symptoms. Physical examination did not reveal any signs of pneumonia. Vaginal examination demonstrated bulging membranes through a 5-cm dilated cervix. Active fetal movements; fetal tachycardia (180/min); and normal fetal morphology, growth, and amniotic fluid were detected on ultrasound. Prophylactic amoxicillin–clavulanic acid and regional anesthesia were started. The patient wore a mask throughout her labor, as did 2 health care professionals who both tested negative for SARS-CoV-2. Amniotic fluid and vaginal swabs sampled during labor tested negative for SARS-CoV-2 and bacterial infection (Table).

A stillborn infant was delivered vaginally after 10 hours of labor. Swabs from the axillae, mouth, meconium, and fetal blood obtained within minutes of birth tested negative for SARS-CoV-2 and bacterial infection. Fetal autopsy showed no malformations, and fetal lung, liver, and thymus biopsies were negative for SARS-CoV-2.

Within minutes of placental expulsion, the fetal surface of the placenta was disinfected and incised with a sterile scalpel, and 2 swabs and biopsies (close to the umbilical cord and peripheral margin) were obtained. All were negative for bacterial infection but were positive for SARS-CoV-2. At 24 hours, the placenta remained positive for SARS-CoV-2. At 48 hours, maternal blood, urine, and vaginal swab were all negative for SARS-CoV-2, whereas a nasopharyngeal swab remained positive. Placental histology demonstrated mixed inflammatory infiltrates composed of neutrophils and monocytes in the subchorial space and unspecific increased intervillous fibrin deposition (**Figure**). Funisitis (inflammation of the umbilical cord connective tissue suggesting fetal inflammatory response) was also present. Gram and periodic acid–Schiff

Figure. Placental Histology



A, Neutrophils and macrophages in the subchorial space indicating acute subchorionitis (hematoxylin-eosin ×20). B, Increased intervillous fibrin deposit and syncytial knots (hematoxylin-eosin ×10). C, Funisitis and umbilical cord vasculitis (hematoxylin-eosin ×20). D, Funisitis with neutrophil-specific staining (myeloperoxidase immunohistochemistry ×20).

staining of the placenta, PCR, and culture did not identify any bacterial or fungal infections.

Discussion | This case of miscarriage during the second trimester of pregnancy in a woman with COVID-19 appears related to placental infection with SARS-CoV-2, supported by virological findings in the placenta. Contamination at the time of delivery, sampling, or laboratory evaluation is unlikely, as all other swabs were negative for SARS-CoV-2. No other cause of fetal demise was identified. There was no evidence of vertical transmission, but absence of the virus is not surprising given the stage of fetal development and short time of maternal infection. Whether SARS-CoV-2 crosses the placental barrier warrants further investigation.[4]

Limitations include the single case and that other causes of miscarriage, such as spontaneous preterm birth, cervical insufficiency, or undetected systemic or local bacterial infection, cannot be ruled out.

Infection of the maternal side of the placenta inducing acute or chronic placental insufficiency resulting in subsequent miscarriage or fetal growth restriction was observed in 40% of maternal infections with Middle East respiratory syndrome coronavirus and severe acute respiratory syndrome coronavirus.[5,6] Additional study of pregnant women with COVID-19 is warranted to determine if SARS-CoV-2 can cause similar adverse outcomes.

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Case Series of Transcutaneous Magnetic Stimulation for Ventricular Tachycardia Storm

Numerous studies suggest the therapeutic benefit of autonomic neuromodulation to reduce cardiac sympathetic input in patients with ventricular tachycardia storm.[1] Neuromodulation includes local blockade of the left stellate ganglion, a significant source of cardiac sympathetic innervation.[2] Transcutaneous magnetic stimulation (TCMS) has a role in noninvasive and nondestructive modulation of nervous system activity.[3,4] Animal studies have demonstrated the ability of magnetic stimulation to modify arrhythmias by targeting cardiac sympathetic innervation.[5,6] In this study, the first of its type involving human participants to our knowledge, we investigated the feasibility and adverse events of TCMS for left stellate ganglion inhibition in ventricular tachycardia storm.

Supplemental content

Methods | The institutional review board of the University of Pennsylvania approved this study, and all patients or their surrogate decision makers provided written informed consent prior to enrollment. Between March 2019 and June 2019, 5 consecutive adult patients with at least 3 episodes of sustained ventricular tachycardia (>30 seconds) in the preceding 24 hours were enrolled. Patients were excluded if they had an implantable cardiac device. A figure 8 TCMS coil attached to a magnetic stimulation system was positioned lateral to the C7 spinous process in approximation of the left stellate ganglion (eFigure in the Supplement). Repetitive TCMS was delivered at 80% of the left trapezius motor threshold at 0.9 Hz frequency for 60 minutes. We compared the number of ventricular tachycardia episodes in the 72 hours after TCMS with the baseline 24-hour period. Patients were monitored during and immediately following stimulation for adverse events including hemodynamic compromise, local discomfort, or skin irritation.

Results | All patients were men aged 40 to 68 years with 3 to 53 episodes of sustained ventricular tachycardia in the baseline 24 hours **(Table 1)**. The treatment protocol was completed without any clinically important change in vital signs or electrocardiogram intervals during or following the procedure **(Table 2)**. After 17 minutes, TCMS for patient 4 was automatically shut off due to coil overheating, which could not be resolved to complete the protocol. In the 3 patients who were not under sedation, each reported no discomfort (on a 10-point scale: 0 [no pain] to 10 [worst possible pain]) from TCMS.

Compared with the baseline 24 hours, there was a lower burden of sustained ventricular tachycardia in the 48 hours

Table 1. Characteristics of the 5 Patients at Time of Enrollment

	Polymorphic resulting in cardiac arrest			Monomorphic	
Qualifying arrhythmia	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5
No. of episodes of sustained ventricular tachycardia 24 hours before TCMS	5	7	31	53	3
No. of episodes of sustained ventricular tachycardia 6 hours before TCMS	5	2	7	50	3
No. of episodes of nonsustained ventricular tachycardia 24 hours before TCMS	22	10	26	88	4
No. of external shocks 24 hours before TCMS	0	4	31	3	3
Antiarrhythmic drugs prior to TCMS	Amiodarone	Amiodarone, lidocaine, mexiletine	Amiodarone, general anesthesia	Amiodarone, lidocaine, verapamil	Amiodarone, lidocaine, general anesthesia
Hemodynamic support at the time of TCMS	None	Milrinone	Extracorporeal membrane oxygenation, phenylephrine	None	Epinephrine, norepinephrine
Left ventricular ejection fraction, %	35	25	5-10	5	10

Abbreviation: TCMS, transcutaneous magnetic stimulation.