Case report

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Placental calcifications after coronavirus disease 2019 in first trimester of pregnancy: ultrasound and pathology findings

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Abstract

The effect of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) on placental tissue is unclear. We present a case of symptomatic first trimester SARS-CoV-2 infection in which longitudinal ultrasound images demonstrated diffuse areas of echogenic foci. Her 39-week delivery, following an elective induction of labor, was uncomplicated, and placental pathology evaluation noted extensive calcifications. Such findings are sometimes seen in late and post-term pregnancies and those complicated by smoking, hypertensive disorders, diabetes, and viral infections. In this case, no other potential etiology was identified. Thus, we conclude that placental calcifications may be associated with SAR-CoV-2 infection in early pregnancy.

Keywords: placental calcifications; SARS-CoV-2; pregnancy; ultrasound

Introduction

The effect of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) on placental tissue has been studied since the beginning of the coronavirus disease 2019 (COVID-19) pandemic. Some authors have reported markers of maternal vascular malperfusion (MVM) in placentas of patients with COVID-19, including increased fibrin deposition, villous agglutination, intervillous thrombi, atherosis, and increased syncytial knotting [1,2]. However, these findings can also be seen in the absence of maternal infection, and studies have not identified specific histologic changes in placentas from patients with COVID-19 [3]. There are few reports of placental ultrasound findings in pregnancies complicated by COVID-19 [4,5].

We present a case of COVID-19 in early pregnancy in which placental calcifications were identified on second trimester ultrasound and confirmed on placental pathology evaluation.

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Case report

A 40-year-old, non-Hispanic white, obese, multigravida developed nausea, vomiting, headache, and fever at 11 weeks of gestation. She denied cough, body aches, fatigue, loss of smell or taste, sore throat, shortness of breath, or lower gastrointestinal symptoms. She was positive for SARS-CoV-2 on polymerase chain reaction (PCR) testing. She had an initial dating ultrasound at 8 weeks 5 days and an ultrasound for nuchal translucency at 13 weeks, which revealed a homogeneous placenta with normal echotexture (fig 1a). The standard prenatal laboratory test results were normal. A non-invasive prenatal genetic screening test reported a low risk for fetal aneuploidy. The patient is Rhesus positive, immune to hepatitis B, Rubella, Measles, Varicella, and Mumps. Serological testing for cytomegalovirus, Parvovirus B19, toxoplasmosis, hepatitis C, and human immunodeficiency virus were negative. She was taking prenatal vitamins and no other medications. Her past medical history was significant for having a pelvic kidney. She denied smoking, alcohol, or drug use.

She underwent a detailed anatomy scan at 20 weeks of gestation, which revealed a male fetus in breech pres-

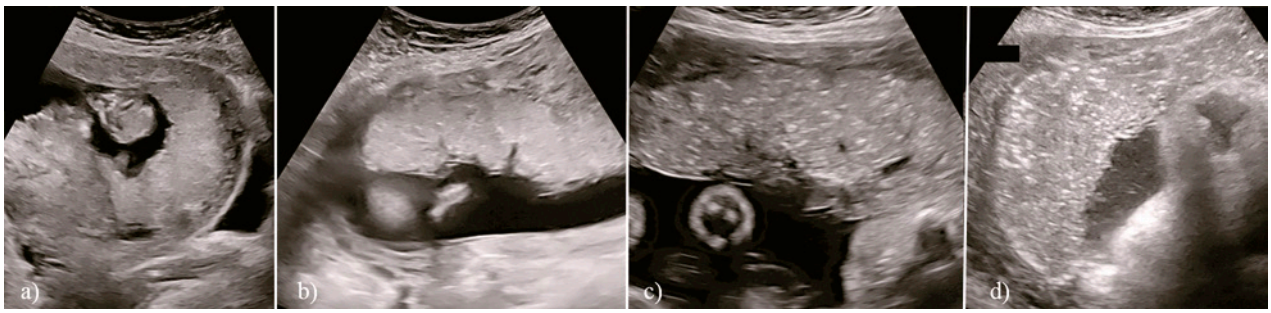

Fig 1. a) Normal homogeneous appearing placenta at 13 weeks gestation; b) placenta at 20 weeks gestation with a few areas of echogenicity; c) placenta at 29 weeks gestation with diffused echogenic foci; d) placenta at 39 weeks gestation with multiple echogenic foci.

entation, normal anatomy, normal amniotic fluid, and a low-lying placenta with areas of echogenic foci (fig 1b). A third trimester ultrasound showed an appropriately grown fetus, and the placenta was no longer low lying. The placenta however, showed diffuse echogenic foci (fig 1c). She had follow-up imaging for fetal growth and weekly biophysical profile (BPP) assessments starting at 36 weeks. The placental images continued to demonstrate diffuse echogenic foci (fig 1d). The fetal growth remained appropriate during the pregnancy and the BPP scores were reassuring.

She had an elective induction of labor at 39 weeks of gestation. She had an uncomplicated vaginal birth of a male infant weighing 4,045 grams with APGAR scores of 9 and 9 at 1 and 5 minutes. The umbilical artery blood gas was within normal limits: (pH 7.21 / pCO_2 62.9 mmHg/ pO_2 17.1 mm Hg / HCO_3 19 mmol/L). The estimated blood loss was 350 mL.

The placenta weighed 598 grams, which was at the 75-90th percentile for gestational age, and a three-vessel umbilical cord was noted. It was 75% circumvallate with the ridge measuring 2 cm from the disc ridge. The membrane was complete, pink tan, and opaque. The maternal surface of the placenta showed complete cotyledons. The parenchyma was dark red and spongy with a 0.7 cm luminal space lined by pink-tan soft tissue containing mucoid material (fig 2a). Histologic assessment showed findings of mature villi, chorangiosis, focal distal villous hypoplasia, intramural fibrin deposition in subchorionic stem vessels, and excessive calcifications (fig 2b). These calcifications were found in all regions of the disc, from the chorionic plate to the basal plate. Most of these calcifications were found in the stem vessels with few focally present in an aggregate of trophoblast deep in the chorionic plate. There were no viral cytopathic effects, microorganism, villitis, or excessive fibrin associated with these calcifications. The placental tissue was not tested for SARS-CoV-2. The neonate had an unremarkable hospital course. He was not tested for SARS-CoV-2 and was discharged with the mother on day 2 of life.

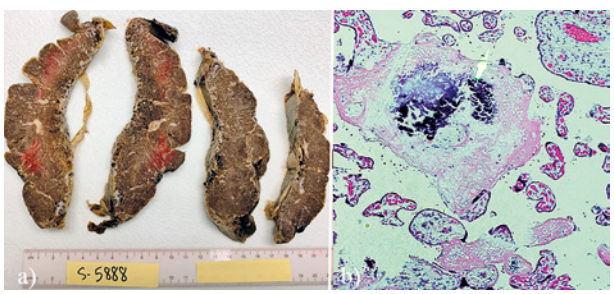

Fig 2. a) Gross appearance of the placenta; b) placenta histology: high power magnification 40X, excessive calcification of villi and villous hypoplasia-rare density.

Discussion

We report the ultrasound finding of placental echogenic foci in a pregnancy with mild COVID-19 during the first trimester. These echogenic foci were confirmed as placental calcifications on histologic assessment. Placental calcifications are calcium hydroxyapatite and phosphorous crystals, which are observed in late and post-term pregnancies, placentas of smokers, patients with hypertensive disorders of pregnancy, diabetes, and infections [6]. They have been reported in pregnancies complicated by viral infections such as Rubella, Varicella, Parvovirus B19, Herpes simplex, Zika, and Cytomegalovirus [7]. The significance of placental calcifications in the absence of viral infections is still debated. Some studies have shown that calcifications are associated with hypertensive disorders of pregnancy and adverse fetal outcomes [8]. Other studies have reported that calcifications are a sign of placental maturity but do not increase the risk for adverse fetal or neonatal outcomes [9].

In one case report of mild COVID-19 in pregnancy, a complaint of decreased fetal movement prompted a 29-week ultrasound which demonstrated oligohydramnios, absent end-diastolic velocity on umbilical artery Dop-

plers, and placental calcifications which were described as comma-like densities and indentations corresponding to Grannum grade 2-3 [5]. The patient had a cesarean delivery due to reduced fetal heart rate variability. Placental histology evaluation revealed intervillous fibrin deposition with ischemic necrosis of villi and histiocytic intervillositis with no mention of calcifications. Another report by Bouachba et al described placentas from 3 cases of fetal death and 2 very preterm deliveries from patients with COVID-19 [4]. The adverse pregnancy outcomes were attributed to massive perivillous fibrin deposition, large intervillous thrombi, and histiocytic intervillositis. One of the patients was a grand multiparous smoker with a pregnancy complicated by early-onset fetal growth restriction that resulted in a 26-week delivery secondary to abnormal fetal Doppler studies. Ultrasound examination prior to delivery showed placental hypoechoic lacunae and focal hyperechoic lesions suggestive of calcifications. These hyperechoic areas were attributed to large intervillous thrombi on histologic examination of the placenta.

In our case, ultrasound images of the placenta demonstrated diffuse punctate echogenic foci involving the entire placenta which is an unusual finding and differs from the aforementioned cases whose findings are seen in many pregnancies even in the absence of COVID-19. Furthermore, the placental echogenic foci in our case were confirmed to be calcifications on pathology evaluation rather than intervillous thrombi. Nevertheless, it remains unclear whether these findings are caused by SARS-CoV-2. Our patient had an uncomplicated pregnancy course and delivered a full-term, healthy, large for gestational age, male infant.

In conclusion, placental calcifications may be associated with SAR-CoV-2 infection in early pregnancy.

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