Prenatal Diagnosis of a Placental Infarction Hematoma Associated with Fetal Growth Restriction, Preeclampsia and Fetal Death: Clinicopathological Correlation

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Established Facts

- Placental infarcts can be manifested as placental cystic lesions.
- Preeclampsia and intrauterine growth restriction can be associated with placental cysts.

Novel Insights

- Ultrasound characteristics of a placental cystic lesion might suggest the presence of a hematoma within an infarcted placental area.
- Acute fetal hemodynamic deterioration can be related with the progressive development of a hematoma within the cystic lesion.

Key Words

Stillbirth · Placental lesions · Ultrasound · Doppler velocimetry

Abstract

The lesion termed ‘placental infarction hematoma’ is associated with fetal death and adverse perinatal outcome. Such a lesion has been associated with a high risk of fetal death and abruption placentae. The fetal and placental hemodynamic

changes associated with placental infarction hematoma have not been reported. This paper describes a case of early and severe growth restriction with preeclampsia, and progressive deterioration of the fetal and placental Doppler parameters in the presence of a placental infarction hematoma.

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Introduction

The lesion termed ‘placental infarction hematoma’ is associated with fetal death and adverse perinatal outcome. Such a lesion was first described by Bendon [1] when reporting the gross and histopathologic findings of the placenta from 6 pregnant women who had spherical blood clots in the placental mass surrounded by infarcted placental tissue. Five of the 6 cases had a fetal death, and the only surviving fetus was born by emergency cesarean section due to abruptio placentae. The fetal and placental hemodynamic changes associated with placental infarction hematoma have not been reported. This communication describes a case of early and severe growth restriction with preeclampsia and progressive deterioration of the fetal and placental Doppler parameters in the presence of a placental infarction hematoma.

Case Description

A 20-year-old African-American, gravida 3, para 1, abortion 1, with no previous history of chronic diseases, preeclampsia, or fetal growth restriction in the previous pregnancy, was first seen at 8 weeks of gestation. The fetal size was appropriate for dates. At 19 weeks and 6 days the estimated fetal weight was at the 22nd percentile, there was normal amniotic fluid, and end-diastolic velocity was present in the umbilical artery. There was a bilateral notch in the uterine arteries, and increased pulsatility index (PI). A rounded cystic area measuring 13 × 14 mm was observed in the placental mass. Maternal blood pressure was within normal range. At 20 weeks and 5 days, the patient was admitted with severe headache, hypertension, and proteinuria, and was treated with hydralazine and magnesium sulfate. Ultrasound examination showed a live fetus with an estimated fetal weight below the 5th percentile, absent end-diastolic velocity in the umbilical artery, reversed atrial flow in the ductus venosus, and decreased PI in the middle cerebral artery. There was reversal of flow during diastole in the aortic isthmus, bilateral uterine notching, and increased uterine artery

Fig. 1. Doppler parameters at the time of hospital admission (20 weeks and 5 days) when fetal growth restriction and preeclampsia were diagnosed. **a** Absent diastolic velocities in the umbilical artery. **b** Increased diastolic velocities in the middle cerebral artery.

c Reversed atrial velocity in the ductus venosus. **d** Reversed diastolic velocities in the aortic isthmus. **e** Continuous flow in the umbilical vein. **f** Uterine artery notch.

PI (fig. 1). The placental cyst measured 14.3×12.7 mm with an echogenic central area; no blood flow was observed inside or around the placental lesion. The amniotic fluid volume was considered to be within normal range, with a largest vertical pocket of 3.5 cm [2]. Due to the early gestational age, conservative management was undertaken.

During hospitalization, sonographic examinations were performed daily. There was progressive deterioration of Doppler parameters. At 20 weeks and 6 days, the mother remained hypertensive despite treatment with the highest registered blood pressure of 178/103 mm Hg, and proteinuria of 8.2 g/24 h. At 21 weeks and 4 days a fetal death was diagnosed. The last Doppler examination prior to the diagnosis of fetal death done at 21 weeks and 3 days showed signs of severe fetal-placental hemodynamic deterioration such as: reverse diastolic velocities in the umbilical artery [2, 3], biphasic umbilical vein pulsations [4–6], bilateral uterine notching and increased uterine artery PI [7–9], reduced middle cerebral artery PI [10], abnormal ductus venosus waveform with reverse atrial flow [11–13], and reduced intermediate flow between the systolic and diastolic components of the waveform [14], reversed diastolic flow in the aortic isthmus [15–18], and coronary artery vasodilatation [19–21] (fig. 2). Representative changes of Doppler

interrogation of the different vessels are shown in figure 3. The placental cyst measured 16×14 mm with central areas of mixed echodensity (fig. 4a–c); additional small cystic lesions were observed in the placenta (fig. 4d). Labor was induced and the patient delivered a non-viable female weighing 299 g. The autopsy showed a preterm stillborn with no structural anomalies. The mother was discharged 3 days after delivery with normal blood pressure.

Placental Pathology

The placenta weighed 100 g and measured $8 \times 7 \times 2$ cm. There were three vessels in the umbilical cord. Sections of the placenta showed pale surfaces (fig. 5a, b). A cystic hemorrhagic area with a yellow rim, measuring $3 \times 3 \times 2$ cm, was observed involving approximately 20% of the placenta. Two additional small yellow lesions were noted and confirmed to be infarcts on microscopic examination. The largest lesion was a hematoma surrounded by a rim of infarcted placental tissue. Microscopic evaluation of the placenta also showed persistent muscularization (fig. 5c), atherosclerosis (fig. 5d), persistent endovascular trophoblast, mural hypertrophy and thrombi in decidual vessels, as well as abnormal villous morphology including distal villous hypoplasia (fig. 5e) and foci of villous dysmaturity.

Fig. 2. Doppler parameters before fetal demise (21 weeks and 3 days). **a** Reversed diastolic velocity in the umbilical artery. **b** Increased diastolic velocities in the middle cerebral artery. **c** Reversed atrial flow in the ductus venosus and reduced velocity between the

systolic and diastolic components of the waveform. **d** Reversed diastolic velocities in the aortic isthmus. **e** Umbilical vein pulsations. **f** Visualization of the coronary flow with double peak in the diastolic component.

Fig. 3. Changes in the pulsatility index of the umbilical artery (UA), middle cerebral artery (MCA), uterine arteries (Ut Art) and ductus venosus (DV) during hospitalization.

Fig. 4. a–c Progressive changes in the echogenicity of the placental lesion in relation to gestational age. The area inside the cyst became more echogenic as gestation progressed (arrows). **d** Additional small cystic areas are shown.

Color version available online

Fig. 5. Pathological examination of the placenta. **a** The maternal surface shows an ill-defined area (arrows) which coincided with the infarction hematoma. **b** Cut sections of the placenta show a large round hemorrhagic lesion surrounded by infarcted placental tissues. Two additional small infarcts (arrows) are also present.

c Basal decidual vessels with thick muscularized walls (arrows) and absent physiologic remodeling (persistent muscularization). **d** Fibrinoid deposition (arrow) in the arterial walls (atherosis). **e** Decreased number of distal villi with increased syncytial knots and prominent stem villi.

Comment

This case report shows the rapid deterioration of Doppler parameters in a fetus diagnosed to be growth-restricted and the development of early-onset preeclampsia associated with a placental infarction hematoma. In a period of 6 days, there was cessation of fetal growth and multiple signs of hemodynamic deterioration became apparent. Subsequent sonographic examinations showed worsening of all Doppler parameters consistent with increased impedance to flow in the placenta, abnormal venous Doppler velocimetry, and decreased impedance to flow in the middle cerebral and coronary arteries. The cystic image in the placenta evolved from a predominantly echolucent to a heterogeneous echodense lesion. Acute fetal deterioration may have been associated with the development of the hematoma within the infarcted area of the placenta. The placenta showed extensive lesions of decidual vasculopathy including atherosclerosis and persistent

muscularization. Decidual vasculopathy can cause a reduction in uteroplacental blood flow leading to placental ischemia, placental infarcts and lesions of placental underperfusion including, increased syncytial knots, and distal villous hypoplasia [22]. Two smaller infarcts accompanied the infarction hematoma, reinforcing the probability of severe uteroplacental disease. The acute evolution in this case is most likely a result of progressive worsening of uteroplacental disease.

The proposed pathophysiology of placental infarction hematoma is occlusion of a spiral artery leading to a placental infarction and subsequent recanalization of the vessel. This may result in the hematoma within the placental mass [1]. Placental infarction hematoma has been associated with preeclampsia and intrauterine growth restriction (IUGR). However, only a few cases with such conditions have been reported in the literature. Our impression is that this is due to underreporting. The ultrasound appearance shows an echodense region inside an

echolucent area, which can correspond to a recently formed hematoma. Old hematomas within an infarcted area might not be identified by ultrasound as they tend to appear echolucent with time [23]; a definitive diagnosis can only be made through histopathologic examination of the placenta [24].

Placental infarcts are mainly due to (a) occlusion of spiral arteries by thrombus, or due to under perfusion of secondary to decidual vascular disease [22, 25–28]. Placental infarcts can be documented in approximately 20% of uncomplicated pregnancies and in 70 and 40% of patients with severe and mild preeclampsia, respectively [29–31]. Vinnars et al. [30] reported that infarcts involving more than 5% of the placenta can be observed in 39% of patients with severe preeclampsia. The association of placental infarctions with acute fetal deterioration was reported by Barclay et al. [32] in a patient at 27 weeks of gestation with acute reduction of amniotic fluid volume, lack of fetal growth, and abnormal fetal heart rate tracing, in the presence of multiple placental cystic areas suggestive of infarcts, which were confirmed after the delivery.

Sonographic images associated with placental lesions include cystic areas [33–35], heterogeneous appearance of the placental mass [36–39], and thick [40] or thin [41] placentas. Cystic areas are frequently observed in association with preeclampsia, growth restriction and fetal demise [31, 42–46]. Fitzgerald et al. [47] reported that well-defined rounded cystic areas in the placenta were associated with a higher risk of preeclampsia and IUGR. The authors referred to this as ‘*rounded intraplacental hematomas*’ and reported that more than 50% of these cystic lesions were associated with placental infarcts reflecting maternal vascular underperfusion. Viero et al. [48] studied the sonographic placental features of 59 fetuses with absent end-diastolic flow in the umbilical artery, and reported cystic images highly suspicious of placental lesions in 43 of 59 pregnancies. Echogenic cystic lesions had a 37% sensitivity for confirmed villous infarcts, and when combined with abnormal uterine artery Doppler velocimetry, there was a 53% positive predictive value for fetal death. The authors emphasized the potential value of other imaging techniques of the placenta such as magnetic resonance imaging (MRI) and the possibility of treatment with heparin. Messerschmidt et al. [49] reported the results of MRI examination of the placenta in 50 patients with early IUGR, abnormal umbilical artery Doppler velocimetry or oligohydramnios. The prevalence of placental infarcts with or without hemorrhage was 35 and 89% for subchorionic thrombi. Fetal death occurred in 36% of cases and surviving fetuses were delivered at a mean ges-

tational age of 29 weeks. The authors proposed that MRI may have the potential for the prenatal diagnosis of placental infarctions in cases of early placental insufficiency.

Detailed sonographic evaluation of the placenta and histopathological confirmation after birth are used to identify lesions associated with preeclampsia, IUGR and adverse short- and long-term perinatal outcome [25, 50–58]. The presence of cystic images in the placenta is not uniformly associated with adverse perinatal outcome [59]. Detailed sonographic evaluation of cysts includes evaluation of shape, size and content as well as the absence/presence of blood flow around or inside the cyst. The presence of hypoechogenic images with a regular shape, with a hyperechogenic rim and the lack of demonstrable blood flow, suggests the presence of placental pathology and, specifically, a placental infarction hematoma [60, 61]. MRI may improve the diagnosis of placental cystic structures [49, 62]. Placental vascular lesions consistent with underperfusion and fetal thrombotic vasculopathy have been associated with abnormal neurodevelopment in surviving fetuses [54, 63, 64].

At present, there is no treatment for placental infarction hematomas. Alkazaleh et al. [65] proposed the use of low-molecular-weight heparin and aspirin when placental lesions suggestive of infarcts are observed in the ultrasound scan. They evaluated pregnant women at 18–20 weeks of gestation with a history of previous fetal death, preeclampsia and/or IUGR. The authors identified 6 patients with echogenic cystic areas in the placenta and abnormal uterine artery Doppler, but still with normal fetal growth; all were treated with low-molecular-weight heparin (dalteparin 5–10,000 units/day s.c.) and 81 mg of aspirin daily. All patients had a live birth (33–37 weeks of gestation). However, the authors did not offer treatment when fetal growth restriction was diagnosed. The study of Alkazaleh et al. [65] is interesting and suggests that the identification of placental lesions with ultrasound in the absence of fetal growth restriction may be amenable to treatment. However, this concept requires additional studies.

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