Recurrent placental chorioangioma in the setting of Fontan circulation: A case report

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ABSTRACT

Introduction: The incidence of cardiac disease in pregnancy continues to increase, particularly pregnancy with complex congenital heart diseases. Fontan circulation is a unique circulation surgically created for individuals with single ventricle physiology, effects of which on developing placenta and fetus are not completely understood. Chronic placental hypoxia in Fontan circulation might explain increased incidence of chorioangioma in those patients.

Case Report: We present the case of a 28-year-old female with congenital pulmonary atresia and an extracardiac Fontan circulation with fenestrations and chronic right to left shunting, with baseline oxygen saturation of 87–91%. She had three successful pregnancies. Placentomegaly has been noted in all her pregnancies, with recurrent chorioangioma noted in her first and last pregnancy.

Conclusion: Fontan circulation with chronic hypoxia may be associated with increased risk of giant chorioangioma with potential for adverse perinatal outcomes. Ultrasound screening for large chorioangioma therefore may be beneficial in this subset of patients.

Keywords: Chorioangioma, Congenital heart disease in pregnancy, Fontan circulation in pregnancy, Placentomegaly

INTRODUCTION

The incidence of cardiac disease in pregnancy continues to increase with associated increasing prevalence of obesity, advanced maternal age, and comorbidities like diabetes. Advances in management of congenital heart disease have improved survival for individuals with complex congenital heart anomalies, resulting in survival to reproductive age. As a result, novel effects of the physiology of repaired congenital cardiac disease are presenting as previously unreported findings on the placenta and developing fetus [1].

Fontan circulation is a unique circulation surgically created for individuals with single ventricle physiology. The single ventricle is used as the systemic ventricle, with constructed caval-pulmonary circulation. Consequently, the right-sided circulation becomes a passive one, limiting systemic venous return and reactive increase in cardiac output in response to physiologic stress, including pregnancy [2]. The limited systemic venous return is particularly pronounced in patients with elevated pulmonary artery pressure. Fenestrations have been added to the Fontan procedure, first in 1990, in high risk patients, with the goal of creating a right to left shunt, to partially bypass the pulmonary circulation and assist in reducing the systemic venous congestion secondary to the passive circulation. This development comes at the
expense of causing chronic hypoxemia due to the mixed oxygenated and deoxygenated circulations [3].

When examining the effects of Fontan circulation on developing fetus and placenta, data are expectedly limited. An increased risk of miscarriage and preterm deliveries, whether spontaneous or iatrogenic, has been reported in the literature [4]. Given the lack of autoregulation in placental vessels, there is no doubt that the unusual hemodynamics of a Fontan directly influence placental development. A case series reported global increase in subchorionic fibrin deposition in those pregnancies, which is hypothetically related to the increased venous congestion, potentially causing small bleeding and fibrin deposition [5].

An important additional factor that would theoretically impact placental development is the chronic hypoxemia present in Fontan circulation patients complicated by right to left shunt either iatrogenic with fenestrations or with spontaneously formed arteriovenous malformations.

Placental development is a complex process, which remains incompletely described. As the fetal oxygen requirements increase with advancing gestation, the placenta becomes more efficient at delivering oxygen. Maternal hypoxia has been associated with hypercapillarization of villous vasculature with more extensive angiogenesis as a compensatory mechanism [6]. This is mediated by the increased activity of hypoxia inducible factor-1 which increases transcription of angiogenic factors [7]. A similar placental change has been seen in high altitude placenta, where chronic hypoxia stimulates more pronounced branching angiogenesis [8].

Chorioangioma is the most common nontrophoblastic tumor of the placenta. It is present in 1% of pregnancies [9]. Pathologically diagnosis can be missed unless careful sectioning and examination of the placenta is performed. Most chorioangiomas are small or microscopic, with no adverse implications to the pregnancy. However, large chorioangiomas >4–5 cm have been associated with adverse fetal outcomes secondary to hyperdynamic circulation and fetal cardiovascular stress [10]. Chorioangiomas are usually sporadic and not well recognized. A higher incidence of chorioangioma has been reported in high altitude, which could potentially be related to the relative chronic placental hypoxia [11].

We present a unique case of a patient with Fontan circulation with fenestrations, chronic hypoxia, and recurrent placentomegaly and chorioangioma, which could represent an exaggerated increase in branching angiogenesis.

**CASE REPORT**

The patient was a 28-year-old G5P3023 with congenital pulmonary atresia with intact interventricular septum. She had extracardiac Fontan with fenestrations and chronic right to left shunting. Her baseline oxygen saturation was 87–91%.

Care in her three pregnancies was provided by maternal-fetal medicine and cardiology, it was highlighted by immediate postpartum recovery on the cardiology unit with close monitoring and therapeutic Lovneox through six weeks postpartum. Her cardiac status remained stable through all her pregnancies. Obstetric outcomes were presented by pregnancy.

**First pregnancy**

Enlarged placenta measuring 8.16 cm was noted on anatomy ultrasound (Figure 1). Fetal growth restriction (FGR) with estimated weight <3rd percentile and elevated systolic to diastolic ratio on umbilical artery Doppler (UAD) was noted. At 35 weeks, the patient was admitted for delivery due to concern of non-reassuring fetal heart monitoring. Induction of labor was attempted. However, the patient underwent an uncomplicated primary cesarean delivery secondary to fetal intolerance to labor. The patient delivered a live female neonate weighing 1625 grams with APGARS scores of 5, 6, and 9 at 1, 5, and 10 minutes, arterial blood gas PH 7.18, PO2 19 mmHg, PCO2 60 mmHg, venous blood gas PH 7.27, PO2 29 mmHg, PCO2 49 mmHg. On pathologic evaluation, the placenta was noted to weigh 243 grams, consistent with <10th percentile, and measured 13.5 × 10.8 × 3.3 cm with subchorionic fibrin disposition in 15%. A small chorioangioma measuring 0.2 cm in diameter was also noted.

**Second pregnancy**

Similar to her first pregnancy, a thickened placenta measuring 8.7 cm was observed on anatomy scan (Figure 2). The fetus was followed for severe FGR with estimated weight <3rd percentile, with normal UAD. The patient underwent an uncomplicated repeat cesarean delivery at 37 4/7 weeks gestation. A live female neonate was delivered weighing 2110 grams with APGARS of 9 and 9 at 1 and 5 minutes, arterial blood gas PH 7.25, Base excess –3.7, PO2 13 mmHg, PCO2 58 mmHg, venous blood gas PH 7.34, base excess –3.2, PO2 24 mmHg, PCO2 43 mmHg. On pathologic evaluation, the placenta weighed 278 grams, consistent with <10th percentile and measured 11.5 × 10.8 × 1.9 cm. Of note, no chorioangioma was identified at that time.

**Third pregnancy**

Unlike the other pregnancies, normal placenta was noted at the time of anatomy ultrasound. However, at 28 weeks gestation, the placenta was thickened 6.2 cm with vascular mass close to placenta cord insertion measuring 2.9 cm, and was concerning for chorioangioma. Fetal growth restriction was simultaneously noted with estimated weight at the 3rd percentile with normal UAD. On serial ultrasound, the placental thickness increased to 8 cm with minimal growth of vascular mass to 4 cm at 36 weeks gestation (Figure 3). She underwent an
uncomplicated repeat cesarean delivery and bilateral tubal ligation at 37 weeks following admission for spontaneous rupture of membranes. At that time, a live male neonate was delivered weighing 2440 grams with APGARS of 7 and 9 at 1 and 5 minutes, arterial blood gas PH 7.22, base excess -9.5, PO$_2$ 56.5 mmHg, PCO$_2$ 45 mmHg, venous blood gas PH 7.3, base excess 8.4, PO$_2$ 62 mmHg, PCO$_2$ 36 mmHg. On pathologic evaluation, the placenta weighed 433.6 grams, consistent with 67th percentile, and measured 17.4 × 16.5 × 2.8 cm with attached 10.5 × 7.0 × 3.5 cm accessory lobe. Subchorionic discoloration was noted along 30% of maternal placental surface and microscopically chorioangioma was noted. The gross and microscopic pictures of placenta from third pregnancy is shown in Figure 4.

DISCUSSION

Fontan circulation in pregnancy and chorioangiomas are both rare, particularly when they occur simultaneously in a recurrent manner.

Fontan circulation is a common pathway for many repaired complex congenital heart diseases. It involves a single ventricle circulating systemic circulation. The pulmonary circulation is maintained in acardiac fashion, where the superior vena cava and inferior vena cava are directly connected to pulmonary arteries. The acardiac right-sided circulation has limited adaptability to physiologic stress, with restricted ability to increase venous return. Fenestrations between right and left circulations are sometimes performed to decompress right side and allow a degree of right to left shunting. Fenestrations improve hemodynamic flow and decrease venous congestion, but at the expense of chronic hypoxia owing to mixing of oxygenated and unoxygenated blood [2, 3].

The effects of Fontan circulation on pregnancy has been documented in limited studies in the literature, given the rarity of diagnosis. There is an association between Fontan circulation and increased risk of miscarriage, preterm deliveries, fetal growth restriction, intrauterine fetal demise, cesarean deliveries, and neonatal intensive care unit (NICU) admission [12]. Fontan circulation with
chronic hypoxia can theoretically increase all those risks, with live birth rate of less than 12% if resting oxygen saturation is less than 85% [13].

Oxygen is an important regulator of placental development. Preplacental hypoxia has been shown to increase synthesis of angiogenic factors in the placenta through hypoxia inducible factor-1, which translates into increased villous branching, as an attempt to oxygenate the fetus and compensate for chronic hypoxia. This phenomenon has been documented in pregnancies at high altitude [6–8].

When reviewing the obstetric history of our patient, recurrent thickened placenta with chorioangioma has been noted in her pregnancies. We hypothesize that this finding may be an exaggerated angiogenic response to chronic hypoxia in our patient, and therefore believe this population of obstetric patients with Fontan circulation may be at increased risk of similar findings on ultrasound and pathologic evaluation.

Chorioangioma is the most common nontrophoblastic tumor of the placenta [9]. It is present in 1% of pregnancies, considered an uncommon occurrence that is not known to be recurrent. The fact that it is recurrent in our patient, supports the hypoxia induced vascular proliferation hypothesis. Chorioangiomas are more commonly microscopic or small, which does not usually affect pregnancy management or outcomes. However, when chorioangiomas get to a size >4–5 cm, they are characterized as giant and can exert stress on fetal cardiovascular system. The estimated complication rate for giant chorioangiomas is about 30–50% with increased risk for polyhydramnios, fetal growth restriction, fetal hydrops, and demise [10]. It is noteworthy that thickened placenta and FGR are co-occurring in this population, while FGR resulting from other etiologies is often found in conjunction with a small placenta.

**CONCLUSION**

Fontan circulation with chronic hypoxia may be associated with increased risk of giant chorioangioma with potential for adverse perinatal outcomes. Ultrasound screening for large chorioangioma therefore may be beneficial in this subset of patients.

**REFERENCES**


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**Author Contributions**

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Erin M Cleary – Design of the work, Drafting the work, Revising the work critically for important intellectual content, Final approval of the version to be published, Agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved

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