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

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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
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 x 10.8 x 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 x 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 unoxygeated 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

1. Elkayam U, Goland S, Pieper PG, Silversides CK. High-risk cardiac disease in pregnancy: Part II. J Am Coll Cardiol 2016;68(3):502–16.
2. ACOG Practice Bulletin No. 212 Summary: Pregnancy and heart disease. Obstet Gynecol 2019;133(5):1067–72.
3. Lemler MS, Scott WA, Leonard SR, Stromberg D, Ramaciotti C. Fenestration improves clinical outcome of the fontan procedure: A prospective, randomized study. Circulation 2002;105(2):207–12.
4. Gouton M, Nizard J, Patel M, et al. Maternal and fetal outcomes of pregnancy with Fontan circulation: A multicentric observational study. Int J Cardiol 2015;187:84–9.
5. Phillips AL, Cetta F, Kerr SE, et al. The placenta: A site of end-organ damage after Fontan operation. A case series. Int J Cardiol 2019;289:52–5.
6. Kingdon JC, Kaufmann P. Oxygen and placental villous development: Origins of fetal hypoxia. Placenta 1997;18(8):613–21.
7. Myatt L. Placental adaptive responses and fetal programming. J Physiol 2006;572(Pt 1):25–30.
8. Zamudio S. The placenta at high altitude. High Alt Med Biol 2003;4(2):171–91.
9. Liu H, Gu W, Li X. Natural history and pregnancy outcome in patients with placental chorioangioma. J Clin Ultrasound 2014;42(2):74–80.
10. Zanardini C, Papageorghiou A, Bhide A, Thilaganathan B. Giant placental chorioangioma: Natural history and pregnancy outcome. Ultrasound Obstet Gynecol 2010;35(3):332–6.
11. Reshetnikova OS, Burton GJ, Milovanov AP, Fokin EI. Increased incidence of placental chorioangioma in high-altitude pregnancies: Hypobaric hypoxia as a possible etiologic factor. Am J Obstet Gynecol 1996;174(2):557–61.
12. Afshar Y, Tan W, Jones WM, et al. Maternal Fontan procedure is a predictor of a small-for-gestational-age neonate: A 10-year retrospective study. Am J Obstet Gynecol MFM 2019;1(3):100036.
13. Presbitero P, Somerville J, Stone S, Aruta E, Spiegelhalter D, Rabajoli F. Pregnancy in cyanotic congenital heart disease. Outcome of mother and fetus. Circulation 1994;89(6):2673–6.

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Author Contributions

Mahmoud Abdelwahab – Conception of the work, Design of the work, Drafting the work, 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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Conflict of Interest
Authors declare no conflict of interest.

Data Availability
All relevant data are within the paper and its Supporting Information files.

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