CASE REPORT

Embolic stroke in a postpartum patient with Fontan physiology

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SUMMARY

In cardiac physiology, single ventricle typically refers to the presence of a dominant systemic ventricle along with a hypoplastic ventricle. The Fontan operation is used to repair the single ventricle by directing deoxygenated systemic venous flow to the pulmonary arterial circulation. Normal pregnancy physiology, particularly increased intravascular volume, increased heart rate, increased cardiac output, hypercoagulability and decreased systemic vascular resistance, can exacerbate cardiac disease in patients with Fontan circulation, leading to pregnancy complications. Despite the known risks, there are limited data addressing the question of anticoagulation in pregnant patients with Fontan physiology. Herein we present the case of a Fontan patient who had a successful pregnancy and delivery, and developed an embolic stroke in the postpartum period.

BACKGROUND

The majority of women born with congenital heart disease (CHD) reach childbearing age.¹ For many of these women, pregnancy carries significant risks. In cardiac physiology, single ventricle typically refers to the presence of a dominant systemic ventricle along with a hypoplastic ventricle. The Fontan operation is used to repair the single ventricle by directing deoxygenated systemic venous flow to the pulmonary arterial circulation. Normal pregnancy physiology, particularly increased intravascular volume, increased heart rate, increased cardiac output, hypercoagulability and decreased systemic vascular resistance, can exacerbate cardiac disease in patients with Fontan circulation, leading to pregnancy complications.² Successful pregnancies in women after the Fontan operation have been published with increasing frequency^{2–9}; however, there are few guidelines on management throughout pregnancy and corresponding pregnancy outcomes. Here, we present the case of a pregnancy in a woman with complex CHD, including double outlet right ventricle with hypoplastic left ventricle, ventricular septal defect, common atrioventricular valves, partial anomalous pulmonary venous return (PAPVR), heterotaxy syndrome with bilateral right-sidedness and levocardia, and chronic CHD-related hypoxaemia requiring continuous oxygen, status post-treatment of PAPVR, bidirectional Glenn shunt and lateral tunnel Fontan operation.

CASE PRESENTATION

A 26-year-old gravida 4, para 0 born with complex CHD presented to our maternal fetal medicine clinic at 12 and 1/7 weeks' gestation. Her obstetric history was significant for three prior first-trimester spontaneous miscarriages that did not require intervention. Her CHD was diagnosed at 23 days of age, confirmed on cardiac catheterisation at 9 months of age, and consisted of double outlet right ventricle with hypoplastic left ventricle, ventricular septal defect, common atrioventricular valves, partial anomalous pulmonary venous return in the setting of heterotaxy syndrome with bilateral right-sidedness, levocardia and asplenia. At 14 months of age, she underwent a pulmonary banding procedure. The band was taken down at 3 years of age when a bidirectional Glenn shunt was created. At 5 years of age, the Fontan circuit was completed when a lateral tunnel Fontan with fenestration was performed, notably with a side-to-side anastomosis between the main pulmonary artery and right atrium. The patient followed closely with cardiology and was maintained on amiodarone as an antiarrhythmic.

Six months prior to conception, exercise stress echocardiography revealed the patient had a New York Heart Association classification class I/II functional status with a resting oxygen saturation of 84% that decreased to 76% with exercise. Cardiac catheterisation at that time revealed acceptable post-Fontan dynamics with mild systemic desaturation. ECG demonstrated an unchanged right-bundle branch block. These findings were discussed with the patient, who had been experiencing increasing dyspnea. She was started on at-home oxygen 1 month prior to conception. Cardiology advised that pregnancy should be avoided. Long-acting reversible contraceptive options were discussed; the patient declined.

On presentation to the maternal fetal medicine clinic in her first trimester, the patient stated that she desired the current pregnancy and declined termination despite counselling on the morbidity and mortality associated with her condition. The patient reported she was currently using 2L of oxygen as needed and that she was experiencing increased fatigue. The pregnancy progressed and she received regular prenatal care on an outpatient basis. Amiodarone had been stopped on positive pregnancy test, and the patient remained in normal sinus rhythm throughout pregnancy. Results of a transthoracic echocardiogram at 25 and 1/7 weeks' gestation are presented in [table 1](#). Levothyroxine, amoxicillin and aspirin 81 mg were continued daily

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Table 1 Results of transthoracic echocardiography during the antepartum and postpartum periods

	Antepartum (25w1d)	Postpartum (Day 10)
Congenital	Situs inversus, levocardia. Anterior aorta with VA discordance, main PA not seen, unbalanced AV canal, unrestricted VSD, mildly hypoplastic left heart, status postlateral tunnel Fontan	
Left ventricle	Small LV cavity size, mildly reduced systolic function No concentric left ventricular hypertrophy Functionally single ventricle due to large inlet VSD Abnormal septal motion consistent with systemic right ventricle	Small LV cavity size, mildly reduced systolic function No concentric left ventricular hypertrophy Common ventricle due to unrestricted VSD, RV dominates No wall motion abnormalities
Right ventricle	<i>Mild</i> right ventricular dilation with systolic function at lower limits of normal Right ventricular hypertrophy	<i>Moderate</i> right ventricular dilation with systolic function at lower limits of normal Right ventricular hypertrophy
Atria and atrial septum	Common atrium Lateral tunnel, unrestricted ASD. Small fenestration with right to left shunt	Common atrium Lateral tunnel, unrestricted ASD. Small fenestration with right to left shunt
Aorta	Mild aortic root dilation with reduced excursion Aorta at sinuses diameter 3.4 cm (normal 2.1–3.5 cm) Unrestricted aortic arch	Mild aortic root dilation Aorta at sinuses diameter 3.6 cm (normal 2.1–3.5 cm) Unrestricted aortic arch
Vessels	No evidence of pulmonary venous obstruction Normal pulmonary venous inflow pattern	No evidence of pulmonary venous obstruction Normal pulmonary venous inflow pattern
Pericardium	No pericardial effusion	No pericardial effusion
Valves	Aortic valve: mild central aortic regurgitation Mitral valve: see tricuspid valve Pulmonary valve: not visualised Tricuspid valve: common AV valve with moderate regurgitation E/A ratio: 1.10/0.20 Regurgitation: 1 (0–4)	Aortic valve: mild aortic regurgitation Mitral valve: see tricuspid valve Pulmonary valve: not visualised Tricuspid valve: common AV valve with moderate regurgitation E/A ratio: 0.99/0.7 Regurgitation: 2 (0–4)

Compared with the antepartum study, the right ventricular function and tricuspid regurgitation were the same to slightly worse in the postpartum study. Abbreviations: VA - ventriculo-arterial; AV - atrioventricular; VSD - ventricular septal defect; LV - left ventricle; RV - right ventricle; ASD - atrial septal defect; PA - pulmonary artery

for hypothyroidism, asplenia and venous thromboembolism prophylaxis, respectively. Fetal anatomic ultrasound and fetal echocardiogram were both normal. At 29 and 1/7 weeks' gestation, the patient presented to clinic with worsening shortness of breath. Her SaO₂ in the clinic was 89%. The decision was made to admit the patient to the hospital for maternal and fetal surveillance until delivery.

The patient was admitted to the maternal fetal medicine service without obstetric complaints. Adult congenital cardiology, anaesthesia and neonatal intensive care unit (NICU) were consulted; an interdisciplinary care plan was in place for the duration of her stay. Antenatal testing consisted of daily non-stress tests and twice-weekly amniotic fluid assessment, which were consistently reassuring. Interval growth ultrasounds were performed, revealing a normally grown fetus. Heparin was started in addition to the patient's baseline aspirin 81 mg for venous thromboembolism prophylaxis. She received two complete courses of betamethasone 2 weeks apart to promote fetal lung maturity. From admission to the day of delivery, the patient's antepartum course was without any acute events. However, she experienced increasingly persistent shortness of breath culminating in a requirement of 10L of continuous oxygen at rest. Given this progressive functional decline, a multidisciplinary team decision was made to begin induction of labour at 34 weeks.

At 33 and 6/7 weeks' gestation, heparin was held and an arterial line was placed. Ampicillin was initiated for endocarditis prophylaxis. At 34 weeks' gestation, the patient was transferred to labour and delivery. Induction of labour was started with placement of 25 µg of vaginal misoprostol, followed by Foley bulb placement and augmentation with intravenous oxytocin. Artificial rupture of membranes occurred after 5 hours of no cervical dilation while on oxytocin. Five hours after rupture of membranes, the patient became febrile, and the fetus became tachycardic, leading to

a diagnosis of chorioamnionitis. Treatment with ampicillin, gentamicin and clindamycin was initiated, and the fetus developed non-reassuring fetal heart tones and the decision was made to proceed with caesarean section. Epidural was in place for anaesthesia. A primary low-transverse caesarean section at 34 and 1/7 weeks' gestation was performed with delivery of a viable male infant weighing 2330 g with Apgar scores of 8 and 9 at 1 and 5 min, respectively. Bilateral tubal ligation took place at time of delivery per patient request for permanent contraception. The patient was stable during and after surgery, and was admitted to the surgical intensive care unit (SICU) per delivery plan. She was downgraded from SICU approximately 24 hours after the time of caesarean section. The remainder of the patient's hospital course was uneventful and she was discharged to home on postpartum day 4, stable on 3–4L continuous oxygen. Thromboprophylaxis with aspirin was initiated on discharge. The infant was taken to NICU for prematurity after delivery and was discharged home on day of life 12.

On postpartum day 13, after awakening from a nap, the patient was noted to have trouble talking, left facial droop and left-sided weakness. She presented to an outside hospital where physical examination confirmed these findings and non-contrast head CT showed an intra-arterial thrombus in the right middle cerebral artery (MCA). The patient was within the window for fibrinolysis with tissue plasminogen activator (tPA), although it was absolutely contraindicated given her caesarean section 13 days prior. Thus, the patient went immediately for mechanical thrombectomy. After thrombectomy, the left-sided deficit resolved and there was no evidence of dysarthria or aphasia. The patient was then

stable and transferred to our institution without any neurological deficits.

OUTCOME AND FOLLOW-UP

The patient was directly admitted to the neurological intensive care unit. Stroke work-up was initiated by neurology and cardiology. A brain MRI showed evidence of an acute ischaemic stroke in the right basal ganglia, likely secondary to an embolus lodging into the right MCA and lenticulostriate vessels. Vessel imaging of the head and neck with a Magnetic Resonance Angiogram (MRA) was unremarkable. Transthoracic echocardiogram demonstrated the known ventricular septal defect without any vegetations (table 1). A deep venous thrombosis scan was negative. However, a high suspicion remained for a paradoxical embolus given her history of fenestrated Fontan anatomy. Blood flow through the Fontan circuit is a slow, passive process without ventricular propulsion, thereby there is an increased propensity for thrombosis formation. If an embolus were to result, it may travel to the arterial system via a right-to-left shunt: through the patient's ventricular septal defect, fenestration in the lateral tunnel conduit or pulmonary arteriovenous shunts, a common complication in Fontan patients. At the time of readmission for stroke work-up, the patient's haematocrit was 32.1% and platelet count was 613×10^9 per litre; both had been in the normal range throughout pregnancy and the immediate postpartum period. Per cardiology, the patient was started on warfarin with enoxaparin bridge, in addition to her home aspirin. The patient's lipid profile revealed dyslipidaemia warranting treatment; however, she was not started on a statin because she was breastfeeding. Likewise, amiodarone was held while breastfeeding in the postpartum period as the patient continued to be in normal sinus rhythm. Consideration was given to closing the fenestrated lateral Fontan. The need for closure was decided to not be emergent and could be pursued as an outpatient in the future. The patient was discharged to home on hospital day 4 in stable medical and neurological condition, on 6L of continuous oxygen. Most recently, the patient was seen for her 6-week postpartum visit, at which her only neurological deficit was a very slight left facial droop and her SaO_2 was 86% on room air.

DISCUSSION

The Fontan procedure is a palliative operation that was first used in a patient with congenital tricuspid atresia and hypoplasia of the right heart.² Since its origin in 1971, the Fontan procedure has expanded to treat a wide variety of CHDs. The idea of Fontan palliation is that adequate circulation can be achieved by directing systemic venous return directly into the lungs without the need for ventricular contraction and propulsion forward. In doing so, the pulmonary and systemic circulations are separated to eliminate arterial hypoxaemia seen in untreated CHD and normalise the volume load of the functional single ventricle.¹⁰

An unfortunate consequence of Fontan circulation is that the blood flow through the Fontan circuit is slow and passive in the absence of a ventricular pump, thereby increasing the propensity for thrombus formation.¹¹ Rates of thromboembolic events in patients following the Fontan procedure vary widely, with incidence ranging from 4% to 20% in various studies, likely due to differing methods of detection and methods of Fontan repair.¹¹ Herein we presented the case of a patient who had a lateral tunnel Fontan repair. This type

Figure 1 Illustration of a single-ventricle heart prior to Fontan repair (A) and a single-ventricle heart following a lateral tunnel Fontan procedure (B). In an uncorrected single-ventricle heart, there is mixing of the arterial and venous blood resulting in significant hypoxaemia. In patients with a Fontan repair, the systemic venous return is redirected to the pulmonary circulation without the need for ventricular contraction and propulsion forward. In a lateral tunnel Fontan repair, this is accomplished by interposing a patch to construct a tunnel within the right atrium to connect the inferior vena cava and superior vena cava, and connect their confluence with the right pulmonary artery. In doing so, the pulmonary and systemic circulations are separated to eliminate arterial hypoxaemia seen in untreated CHD and normalise the volume load of the functional single ventricle. (Adapted with permission from Diller GP, Breithardt G, Baumgartner H. Congenital heart defects in adulthood. *Dtsch Arztebl Int* 2011; 108(26): 452–9. DOI: 10.3238/arztebl.2011.0452).

of repair involves interposing a patch to construct a tunnel within the right atrium between the inferior vena cava and superior vena cava, and their confluence with the right pulmonary artery (figure 1). In one study of the long-term outcomes of 220 patients who underwent lateral tunnel Fontan repair, two patients experienced stroke and hemiplegia, and a third patient died of massive cerebral thromboembolism within a 10-year postoperative period.¹² In a different retrospective review of 592 patients who underwent Fontan surgery, the majority (82%) of which underwent lateral tunnel Fontan, the freedom from thrombus was 92%, 90%, 84% and 82% at 1, 3, 8 and 10 years after the operation, respectively.¹³ Thus, the risk for thromboembolism following the Fontan operation is persistent throughout the patient's lifetime.

The risk of thromboembolism in Fontan patients is multifactorial. In addition to the aforementioned sluggish flow through the Fontan circuit, a hypercoagulable state develops in patients following the procedure: the levels of protein C, protein S and antithrombin III are low, while the level of factor VIII is elevated.¹⁴ The pathogenesis behind this imbalance is not fully understood. Some studies suggest factor VIII is elevated simply as an acute-phase reactant, whereas others hypothesise the increased levels may represent endothelial dysfunction. Additionally, some studies suggest the thrombophilia seen in Fontan patients is a function of abnormal coagulation and reflects platelet hyper-reactivity. This idea has led to the comparison of warfarin and aspirin for potential thromboprophylaxis in Fontan patients. A recent meta-analysis demonstrated no statistically significant difference in

thrombotic and embolic events in patients taking warfarin versus aspirin ($P=0.54$).¹⁴

Pregnancy adds to the hypercoagulability seen in patients with Fontan circulation. Women are five times more likely to develop a thromboembolic event during pregnancy than when not pregnant.¹⁵ Similar to post-Fontan physiology, in pregnancy levels of protein C, protein S and antithrombin III decline, while levels of factors VII, VIII, IX and X increase creating a hypercoagulable state.¹⁶ This normal physiological change in pregnancy likely has evolved to protect women from haemorrhage during delivery. This hypothesis could potentially explain why the risk of venous thromboembolism is higher post partum than during pregnancy, with highest risk occurring immediately post partum through the first week.¹⁶

There are limited data to address the question of anticoagulating Fontan patients in the context of pregnancy. The largest retrospective multicentre analysis of pregnant patients post-Fontan came from Gouton *et al*,³ which followed 59 pregnancies with a median follow-up of 2 years.³ Thromboembolic events occurred in two women antepartum and one woman postpartum. Two of the three thromboembolic events occurred in patients without anticoagulation. However, there were risks to anticoagulation. Two of three postpartum haemorrhages occurred in patients treated with therapeutic anticoagulation that had been stopped at least 12 hours prior to delivery. Additionally, anticoagulation was associated with a statistically significant increase in neonatal complications (listed as prematurity and small-for-gestational-age neonates) compared with no anticoagulation or antiplatelet treatment alone ($P<0.01$). There was only one report of cerebrovascular attack that occurred 18 months post partum to a patient maintained on antiplatelet therapy alone. The authors ultimately advised that anticoagulation should be used during the antepartum and postpartum periods in all women with Fontan physiology to avoid Fontan failure and catastrophic consequences.

An additional well-documented complication associated with Fontan palliation is the development of arrhythmias that can occur both early and long term after the procedure.^{2 3 12 17} Post-Fontan bradyarrhythmias and tachyarrhythmias have been reported and are associated with atrial scars near the sinus node.¹⁷ Tachyarrhythmias, particularly supra-ventricular tachycardia, are the most troublesome and are associated with a risk of thrombotic and embolic complications. In the review performed by Gouton *et al* of Fontan patients in pregnancy, the cardiac complication rate was 10%, with atrial arrhythmia being the most common. The only predictive factor identified for arrhythmia during pregnancy was a history of pre-pregnancy arrhythmias.³ Fortunately, in this case, our patient remained in normal sinus rhythm throughout pregnancy and the postpartum period despite having a history of pre-pregnancy atrial arrhythmia.

In summary, the rising number of women with complex CHD who are considering pregnancy requires maternal fetal medicine specialists as well as cardiologists and primary care physicians to be prepared to take part in their care. We recommend that providers reference guidelines such as the WHO pregnancy risk categories¹ when providing preconception counselling to complex cardiac patients of reproductive age. Patients with Fontan palliation performed for any cause are automatically categorised as class III: significantly increased risk of mortality or severe morbidity. If pregnancy is achieved and desired in a Fontan patient, the risks should be clearly communicated with the patient. As the pregnancy progresses, risk stratifying the

patient for likelihood of thromboembolic event should guide the use of prophylactic or therapeutic anticoagulation. Here, we presented the case of a Fontan patient who had an embolic stroke in the postpartum period while on aspirin alone, who was then transitioned to anticoagulation.

Learning points

- The Fontan procedure is used to palliate single-ventricle cardiac physiology by directing deoxygenated systemic venous blood directly to the pulmonary arterial circulation without the need for ventricular contraction, thereby increasing systemic arterial oxygenation and normalising the volume load of the single functional ventricle.
- Normal pregnancy physiology can exacerbate cardiac disease in patients with Fontan circulation, leading to pregnancy complications.
- A major concern for patients with Fontan palliation is the risk of thromboembolism, which can be precipitated by the development of atrial arrhythmias.
- Risk stratifying the pregnant Fontan patient for likelihood of thromboembolic event should guide the use of prophylactic or therapeutic anticoagulation.
- Specialist multidisciplinary care teams are recommended for the management of complex cardiac conditions in pregnancy.

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