

Transplacental digoxin therapy for fetal atrial flutter with hydrops fetalis

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Background: Without timely treatment, fetal atrial flutter (AF) could result in congestive heart failure, hydrops fetalis and even fetal demise.

Methods: Prenatal echocardiography was used to confirm AF and assess fetal cardiac function with cardiovascular profile score. Transplacental digoxin therapy was adopted, and the patient was followed up for 10 months.

Results: The healthy male baby was delivered with normal postnatal electrocardiogram and echocardiogram. Neither arrhythmia nor neurodevelopmental impairment was found during the follow-up.

Conclusion: Timely transplacental digoxin therapy can successfully treat fetal AF and allow the fetus to recover from AF associated fetal heart failure and hydrops fetalis prior to delivery.

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Key words: fetal atrial flutter;
heart failure;
hydrops fetalis;
transplacental digoxin therapy

Introduction

During the development of the embryonic heart, most fetal arrhythmias are transient and benign. However, sustained fetal tachyarrhythmia may result in congestive heart failure, hydrops fetalis, and fetal or neonatal death.^[1-5] In addition, because

of fluctuation of cerebral perfusion, a fetus with tachyarrhythmia and subsequent hydrops may be at risk of cerebral injury and neurodevelopmental impairment, which requires appropriate therapy.^[1,3,4] Here, we report a case of fetal atrial flutter (AF) with fetal heart failure and hydrops fetalis treated with transplacental digoxin successfully.

Case report

An audible fetal arrhythmia was detected in a healthy 35-year-old multigravida at 34 gestational weeks. Subsequent fetal echocardiography revealed an AF with atrial rate of 477 beats per minute (bpm) and ventricular rate of 226 bpm [2:1 atrioventricular conduction (Fig. A)], reduced cardiac function [cardiomegaly (Fig. B) and atrioventricular valve regurgitation], and hydrops fetalis [ascites (Fig. C) and hydrothorax]. No structural abnormalities, hydropericardium or skin edema was detected. The fetal cardiac function was assessed with cardiovascular profile score (CVPS)^[6,7] and its value was 5 points. The mother did not present with or have any following conditions including cardiac arrhythmia, viral infection, pregnancy-induced hypertension, placental aging, radiation/drug exposure, or a family history of cardiac arrhythmia and congenital heart disease.

With written informed consent, transplacental digoxin therapy was started at a dose of 0.125 mg twice per day. Maternal vital signs and electrocardiogram changes as well as fetal movement and heart rate were monitored daily. Fetal echocardiography and measurement of maternal serum digoxin level were performed every 4-7 days.

Seven days following digoxin therapy, fetal echocardiography revealed a slight reduction of hydrops fetalis and recovery of cardiac function (CVPS=7 points). However, fetal AF with a 2:1 conduction was still present. The dose of digoxin was increased to 0.25 mg twice per day. Four days later, fetal cardiac rhythm returned to sinus with a rate of 138 bpm, 1:1 atrioventricular conduction, notable alleviation of hydrops fetalis and enhancement of

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Fig. Fetal echocardiography showed an atrial flutter with 2:1 conduction (A = atrial rate: 477 bpm; V = ventricular rate: 226 bpm) (A), cardiomegaly with a cardiac area/thoracic area ratio of 0.51 (B), and the presence of fetal ascites (C).

cardiac function (CVPS=8 points). Since the fetal heart failure had not been fully corrected, we maintained the same dose for another 7 days, leading to nearly a full recovery of fetal cardiac function (CVPS=9 points). To avoid side effects, the dose of digoxin was reduced to 0.25 mg once per day. Fetal echocardiography at 37⁺⁶ gestational weeks showed a fetal heart rate of 121 bpm, 1:1 atrioventricular conduction and only localized fetal ascites. During the treatment, the mother did not experience any side-effects from digoxin, and the serum levels of digoxin are listed in the Table.

At 38 gestational weeks, a full-term delivery was achieved through cesarean section. The newborn was a healthy male with a birth weight of 3350 g and excellent Apgar scores (10 points at 0, 1, 5 and 10 minutes). The maternal, umbilical and neonatal serum digoxin concentrations were 0.51 ng/mL, 0.47 ng/mL, and 0.43 ng/mL, respectively (Table). The ratio of neonatal/maternal serum digoxin level was 84.31%. Electrocardiography showed a sinus rhythm with a rate of 102 bpm. Echocardiography revealed normal cardiac anatomy and functions [left ventricular ejection factor (LVEF): 59%; left ventricular fractional shortening (LVFS): 33%]. There were no signs of hydrothorax, hydropericardium or ascites. The infant grew and developed normally at a 10-month follow-up without arrhythmia or neurodevelopmental impairment.

Discussion

Digoxin can cross the placenta and reach a steady state within 5-7 days.^[5,6,8] Due to quick excretion without accumulation, digoxin is considered a safe option for transplacental therapy of fetal heart failure and part of fetal cardiac arrhythmia.^[5,6] In our case, digoxin therapy was given at a dosage of 0.125 mg twice per day, which was increased to 0.25 mg twice per day and maintained at 0.25 mg once per day until delivery. This therapeutic regimen was effective to convert AF to a normal sinus rhythm and correct the heart failure. The ratio

Table. Serum digoxin levels during the treatment

Serum samples	Gestational week	Digoxin level (ng/mL)
Mother	35 ⁺³	0.33
	36	0.62
	37	0.84
	37 ⁺⁶	0.56
	38 [*]	0.51
Umbilical cord		0.47
Neonate		0.43

*: intrapartum; the ratio of neonatal/maternal serum digoxin level: 0.43/0.51=84.31%.

of neonatal/maternal serum digoxin level was 84.31% at birth, which was similar to the previously reported range between 60% and 90%.^[5,6,8]

Fetal hydrops is a serious condition associated with perinatal mortality, which can be as high as 72%.^[6,7] Signs of fetal hydrops include fetal ascites, hydrothorax, hydropericardium, and skin edema.^[7] Once fetal skin edema occurs, serious hydrops develops and digoxin treatment may not be effective.^[6] Our reported fetus had ascites and hydrothorax, but did not demonstrate skin edema, so was successfully treated with transplacental digoxin therapy. This outcome is in agreement with Hofstaetter et al's observation.^[6]

As an effective semi-quantitative index for cardiac function, CVPS was adopted in this study and it reflected the outcome of the treatment. The current case report provides a useful reference to apply CVPS in the assessment of transplacental digoxin therapy for fetal AF.

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