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Refractory Fetal Supraventricular Tachycardia with Hydrops Successfully Converted by Intraperitoneal Flecainide in the Fetus: A Case Report

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Established Facts

- Supraventricular tachycardia is the most common fetal tachyarrhythmia.
- It is often associated with fetal hydrops that can lead to death.
- It can, to some extent, be treated with different transplacental drugs and also directly into the fetus.

Novel Insights

- A new modality for treating refractory supraventricular tachycardia with intraperitoneal flecainide.

Keywords
Refractory fetal supraventricular tachycardia · Intraperitoneal flecainide · Fetal intervention

Abstract

Introduction: Supraventricular tachycardia is the most common fetal tachyarrhythmia and if persistent often associated with fetal hydrops which can cause intrauterine and neonatal death. ***Case Presentation:*** We present a case of early second trimester supraventricular tachycardia in a hydropic fetus, initially refractory to transplacental treatment. ***Conclusion:*** The supraventricular tachycardia was successfully treated when supplemented with intraperitoneal flecainide in the fetus.

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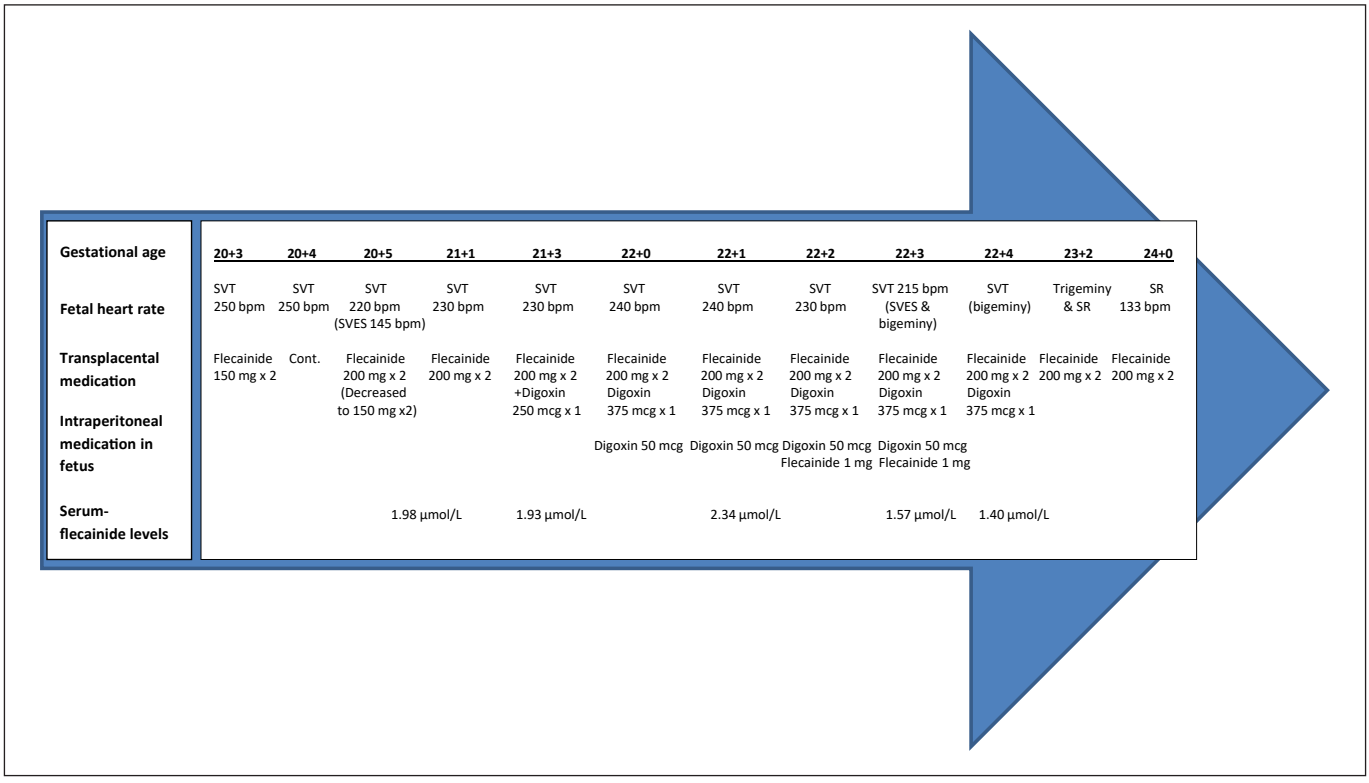

Fig. 1. Timeline of events.

Case Report

A 25-year-old woman referred to our department at gestational age (GA) 20 weeks and 3 days due to fetal tachycardia and fetal hydrops at the mid-trimester anomaly scan. The patient was nulliparous, healthy, and with an uncomplicated pregnancy to this point. The timeline is shown in Figure 1. Upon arrival, supraventricular tachycardia with suspected short VA interval and a fetal heart rate (FHR) of 250 bpm was seen with 1:1 conduction, pericardial effusion, dilated atria, and severe ascites. Maternal biochemistry for thyroid function and infection was normal. We initiated treatment with transplacental flecainide 150 mg twice daily with the mother on telemetry. There was no effect of the treatment on the following day (GA 20 + 4). On day 3, the flecainide dose was increased to 200 mg twice daily, and the FHR decreased to 220 bpm, but with a few, short periods of a few seconds with sinus rhythm with supraventricular extrasystoles (SVES) and FHR of 145 bpm. The mother developed significant side effects to the increased flecainide dosage with severe dizziness and nausea, and borderline prolonged QRS complexes on the ECG. Consequently, the flecainide dosage was decreased to 150 mg twice daily. Serum-flecainide was within the therapeutic range (0.48–2.41 µmol/L), and the levels are listed in Figure 1. On day 6 (GA 21 + 1), FHR was at 230 bpm with no periods of SVES, and once again transplacental flecainide was increased to 200 mg twice daily, which was now tolerated better by the mother. Unfortunately, no fetal effect was achieved, and on day 8 (GA 21 + 3), we added transplacental digoxin 250 µg daily. On day 12 (GA 22 + 0), the FHR was 235–245 bpm, and the fetus had developed general hydrops. Transplacental digoxin dosage was increased to 375 µg daily. Due to the worsening of the condition, the fetus was treated with digoxin 50 µg intraperitoneally, which was repeated on the following day (GA 22 + 1) as a result of no effect. On day 14 (GA 22 + 2), we found an unchanged FHR at 230 bpm, and the fetus was treated intraperitoneally with digoxin 50 µg for the third time, though this time combined with flecainide 1 mg intraperitoneally. Right after the administration, we observed unchanged FHR, though with frequent SVES. On day 15 (GA 22 + 3), we found a slight decrease in the FHR at 208–220 bpm and periods with SVES and bigeminy. It was suggested to change to amiodarone, but the patient declined telemetry and hospital admission, and consequently amiodarone treatment or increasing the dosage of flecainide was not an option. Changing to sotalol was also considered, but since the fetus was hydropic and thus at severe risk for IUD, it was decided to continue with flecainide as the primary drug to avoid further postponement by change in treatment strategy. Thus, the intraperitoneal combination therapy consisting of digoxin 50 µg and flecainide 1 mg was repeated. On day 16 (GA 22 + 4), the fetus still presented with tachycardia, though mostly bigeminy, unchanged fetal hydrops with severe ascites, pericardial effusion, and subcutaneous edema. On day 21 (GA 23 + 2), unchanged ascites, FHA with trigemini but also with periods of sinus rhythm for the first time, and normal ductus venosus flow were observed. Due to no signs of AV-block, the digoxin treatment was ceased. On day 26 (GA 24 + 0), the fetus had persistent sinus rhythm with FHR at 133 bpm and only a few SVES. The sinus rhythm remained stable

throughout the rest of the pregnancy without any SVES, and the mother was kept on 200 mg of flecainide twice daily throughout the pregnancy. The baby was delivered at 37 weeks and 3 days of gestation after induction of labor. The delivery was uncomplicated and resulted in a healthy boy weighing 2,792 g with a full Apgar score. The boy was admitted to the neonatal unit for telemetry. The ECG was normal, though initially described with borderline prolonged QT interval, which normalized. The family was discharged 3 days postpartum with a follow-up appointment in the pediatric cardiology outpatient clinic after 6 months. The mother was contacted by phone 2.5 months postpartum for an update, and the baby boy was still thriving and developing accordingly. They had had no hospital contacts since they were discharged shortly after birth. At the follow-up at 6 months, the boy was growing accordingly, had a normal heart auscultation, and a normal echocardiography. The mother has provided written informed consent to publish the case.

Discussion

Supraventricular tachycardia is the most common fetal tachyarrhythmia and if persistent often associated with fetal hydrops which can cause both intrauterine and neonatal death [1]. The fetal hydrops is caused by the increased heart rate leading to both an increased preload and a decrease in the cardiac output resulting in imminent circulatory failure and development of fetal hydrops. It is well known that transplacental digoxin has a limited effect on tachyarrhythmia in cases with placental hydrops due to restricted passage of digoxin across the placenta [2]. On the contrary, transplacental flecainide has been shown to pass the placenta, also in cases with hydrops [3]. A meta-analysis from 2017 concludes that transplacental flecainide is superior to digoxin in cases of supraventricular arrhythmia in efficacy and without causing more maternal side effects [1]. Additionally, the antiarrhythmic effect was more pronounced in cases with hydrops. In refractory cases of fetal supraventricular tachycardia, the American Heart Association recommends either transplacental amiodarone or intramuscular digoxin [4]. Due to the increasingly hydropic fetus, we administered digoxin intraperitoneally attempting to shorten the time to conversion. The dosage recommended for intramuscular digoxin in the fetus is 88 μg/kg, why we chose to give 50 μg [4]. With no effect of the treatment and deteriorating fetal condition, a combination of intraperitoneal digoxin and intraperitoneal flecainide was attempted. It was speculated whether a deposit of intraperitoneal antiarrhythmic drug of the same type as used for transplacental treatment could increase the fetal concentration without jeopardizing the mother – who in this case had side effects and, thus, could not be increased in medication. We estimated the fetal intraperitoneal flecainide dosage of 50 mg according to the recommendations for neonatal use, where a dose of 2 mg/kg is considered safe and effective [5, 6]. The procedure-related risk of depositing an intraperitoneal drug into a large amount of ascites was considered very low – lower than into the umbilical vein. It is well known that early cordocentesis is associated with a higher loss of pregnancy rate, especially in hydropic fetuses. Further, we speculated whether the drug deposited intraperitoneally could have a prolonged effect compared to the intravascular mode. In a 21-week fetus, the muscles are very small compared to a large amount of ascites; thus, it was considered safer than an intramuscular injection. Liquid flecainide may induce local reactions of unknown risk to the fetus' muscles at early gestation. The same is the case for an intraperitoneal application, but since the concentration was diluted in the ascites, it was thought to decrease this risk of tissue damage.

No published reports on this treatment modality have been identified, but in this single case, we achieved rhythm conversion. This approach may be useful in severe refractory cases of fetal supraventricular tachycardia.

Statement of Ethics

Publication of the case has been approved by the patient, and we have obtained written permission to publish the case.

Disclosure Statement

The authors have no conflicts of interest to declare.

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Author Contributions

Treatment was discussed and planned among all authors. Treatment was carried out by K.S., N.V., and L.N.J. The manuscript was drafted by C.V. and critically reviewed by all authors. The final manuscript was approved by all authors.

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