Case Report

Perinatal Treatment of Refractory Atrial Flutter with Hydrops Fetalis: A Case Report

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Objective: *Highlight the management of a critically ill premature hydropic baby with refractory atrial flutter (AF) and successful outcome without neurologic sequel at 1 year of follow-up.*
Case: *A 23-year-old pregnant woman, G1P0, presented with fetal tachycardia at 32 weeks.*
Results: *Ultrasound revealed a hydropic fetus with fetal atrial rate (FHR) of 440 bpm and A:V block of 2:1. Transplacental therapy resulted in a temporary response with the combination of digoxin and flecainide, and subsequently digoxin plus sotalol. Termination of pregnancy at 34 weeks was performed for postnatal treatment, giving birth to a premature hydropic baby, weighing 3,320 grams. At birth flecainide failed to control the AF. Therefore, intravenous adenosine was started and successful conversion to normal sinus rhythm was temporally achieved. Finally, conversion to normal sinus rhythm with amiodarone plus digoxin was satisfactorily achieved and then long-term control with only oral flecainide. The hydropic signs gradually disappeared without any significant sequelae. The baby was healthy at one year of follow-up without any neurological sequelae.*
Conclusion: *This case may be evidence that combined therapy with amiodarone and digoxin is probably effective in treatment of refractory AF with hydropic changes, at least in some cases.*

Keywords: *Atrial flutter, Hydrops fetalis, Ultrasound*

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Fetal atrial flutter (AF) is defined as a rapid regular atrial rate of 300-600 beats/min accompanied by variable degrees of atrioventricular (AV) conduction block, resulting in slower ventricular rates[1]. The outcome of fetal tachyarrhythmias primarily depends on the presence or absence of hydrops fetalis rather than the type of arrhythmia[2]. AF accounts for approximately one fifth to a third of all clinically relevant tachyarrhythmia[1]. Though intrauterine treatment of AF is often successful in non-hydropic fetuses, it is rarely satisfactory in hydropic fetuses[1,3]. Among hydropic fetuses, intrauterine treatment with digoxin combined with flecainide, sotalol, or amiodarone is often required as first line treatment[4,5]. To the authors' best knowledge, there is no ideal treatment protocol for these fetuses.

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The case presented here was unusual due to unresponsive to intrauterine treatment and difficulty to control postnatally but finally response to the combination of amiodarone and flecainide with complete disappearance of hydropic changes. The objective of the present report was to highlight the management of a critically ill premature hydropic baby with refractory AF and the successful outcome without neurologic sequelae at one year of follow-up.

Case Report

A 23-year-old pregnant woman, G1P0, attended the antenatal care clinic at the gestational age of 32 weeks. Physical examination revealed a large-for-date uterine size and fetal tachycardia. Screening basic laboratory investigations of pregnancy were all unremarkable.

Ultrasound examination demonstrated a normally formed fetus with polyhydramnios, amniotic fluid index of 30 cm. The biparietal diameter was consistent with 32 weeks of gestation. The fetus had markedly hydropic changes, including pericardial

effusion, marked cardiomegaly with a cardio-thoracic ratio of 0.75 (Fig. 1A), generalized subcutaneous edema, especially scalp edema and ascites (Fig. 1B) with hydrocele. Placental thickness was 2.7 cms in width. Fetal echocardiography revealed atrial flutter (AF) with fetal atrial rate (FHR) of 440 bpm and A:V block of 2:1 at gestational age of 32 weeks (Fig. 1C).

The couple decided to have intrauterine therapy with maternal administration of anti-arrhythmic medications. Digoxin and flecainide of dosage described elsewhere[6] was started at 32 weeks of gestation. Cardioversion to normal sinus rhythm was temporarily observed in two days. However, four days after the initiation of therapy AF recurred in spite of intrauterine treatment, the combination of digoxin (0.5 mg/d) and sotalol (160 mg/d) were administered transplacentally instead. Cardioversion was temporarily successful again. However, no satisfactory response was observed.

Termination of pregnancy at 34 weeks was performed for more effective postnatal treatment. The premature hydropic baby was born by cesarean section, weighing 3,320 grams, surviving with ventilatory support. The baby had generalized edema with ascites but no gross anomalies. Shortly after birth echocardiogram showed the same as prenatal findings and ventricular rate was about 228 bpm with poor ejection fraction (10%). Flecainide(100 mcg/m^2/d) was administered after birth but failed to control the AF and intravenous adenosine (200 micrograms per kilogram) was subsequently started, resulting in temporary conversion to normal sinus rhythm with rapid recurrent AF. On day 5, oral amiodarone (5 mg/kg) was administered but conversion to normal sinus rhythm was not achieved yet. Finally, oral digoxin was added (0.2 ml oral OD) to amiodarone and satisfactory response was observed. Normal sinus rhythm was achieved and then long-term control with only oral flecainide. On day 11, echocardiogram showed improved ventricular function, ejection fraction of 51%. Ejection fraction on day 18 was normal at 75%. The hydropic signs were gradually disappeared without any significant sequelae. The baby was discharged on the day 36, weighing 2,710 grams but needed flecainide to control. The baby was healthy at one year of follow-up without any neurological sequelae.

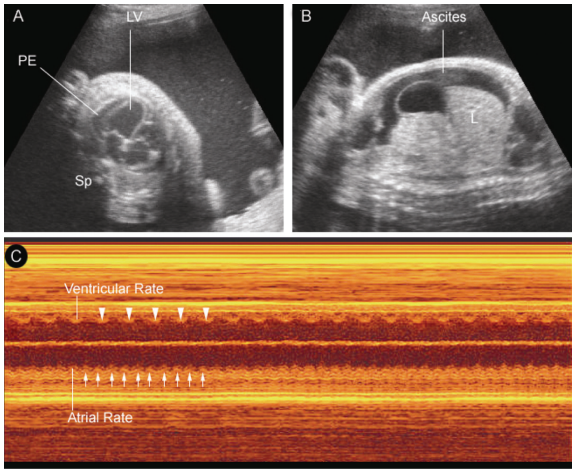

Fig. 1 A) Four-chamber view shows marked cardiomegaly with pericardial effusion (PE) (LV; left ventricle, Sp; spine). B) Sagittal scan of the fetal abdomen shows ascites (L; liver). C) M-mode shows atrial rate of of 420 bpm with A:V block 2:1 (small arrows: atrial beats, arrow heads: ventricular beats)

Discussion

The most important prognostic factor for a fetus with AF is the presence or absence of fetal hydrops. The prognosis for hydropic fetuses is obviously worse. The response to transplacental therapy is generally less successful in a hydropic group. Although digoxin remains an effective first-line therapy in the treatment of fetal AF, digoxin as a single therapy, however, it is often unsuccessful in fetal AF with hydrops fetalis[2,7,8]. Flecainide is an effective second-line therapy, especially in the face of fetal hydrops, with a reported success rate of up to 60%[2]. Firstly, the authors chose the combination with flecainide since it has been the most studied medication used in the transplacental treatment of AF. Additionally, the time taken to convert the fetus to sinus rhythm is usually shorter. Effective transplacental therapy of hydropic fetuses with amiodarone[9-11] and sotalol[8] has also been reported, though the experience has been very limited in the literature. Some drugs, such as digoxin, which are effective in the non-hydropic fetus, may not cross the hydropic placenta adequately to the hydropic fetus[12] and therefore treatment may fail because insufficient drug reaches the fetus to convert the baby to sinus rhythm. This may be a reason of unsuccessful transplacental therapy in the case presented here, though it showed a temporary response to flecainide and somewhat improvement of hydrops. With flecainide, conversion into sinus rhythm is usually seen in three days after initiation of treatment, though it can take up to two weeks[1]. Therefore the treatment

should be continued beyond three days, especially when an initial decrease of fetal heart rate is noted[1]. When flecainide cannot restore sinus rhythm and hydropic appearance persisted, amiodarone therapy may an alternative to be converted prenatally[11]. Unusually, AF in the present case was rather refractory and showed unsatisfactory response to several drugs at 34 weeks. Therefore, termination of pregnancy for postnatal effective therapy was justified.

All anti-arrhythmic drugs are associated with some proarrhythmic effects[13,14], especially flecainide which may occasionally result in intrauterine death[15]. Therefore, initial administration of the medications to the mother should take place in the hospital with close eclectrocardiographic monitoring and when possible, drug levels should be monitored.

There has been no large prospective study of neurodevelopmental outcome of fetuses with AF and most series do not report neurologic outcome at all. In one series, two hydropic fetuses (1.6%) had significant neurologic impairment[2]. However, Schade et al[16] reported that three of eight hydropic fetuses had abnormalities on cranial ultrasound scan performed in the immediate postnatal period. It is difficult in some cases to disentangle the direct effects of arrhythmia versus the effects of preterm delivery, but this is clearly an area of concern that merits further study.

Conclusion

The case presented here highlights the prenatal and postnatal management of a critically ill premature hydropic baby with refractory AF, and the successful outcome without any neurologic abnormalities at one year of follow-up.

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การรักษาทารกบวมน้ำในครรภ์จากภาวะหัวใจเต้นผิดจังหวะชนิด atrial flutter

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รายงานความสำเร็จในการดูแลรักษาทารกบวมน้ำในครรภ์ที่คลอดก่อนกำหนดเนื่องจากมีภาวะหัวใจเต้นเร็วชนิด arial flutter (af) โดยปราศจากภาวะแทรกซ้อนที่รุนแรงทางระบบประสาทในช่วง 1 ปี หลังคลอด ในผู้ป่วยรายนี้เป็นสตรีตั้งครรภ์แรก อายุ 23 ปี ตรวจพบทารกมีหัวใจเต้นเร็วผิดปกติตอนอายุครรภ์ 32 สัปดาห์ การตรวจด้วยคลื่นเสียงความถี่สูงพบทารกบวมน้ำ หัวใจเต้นด้วยอัตราเร็ว 440 ครั้งต่อนาที เป็นชนิด atrial flutter โดยมีจังหวะการเต้นระหว่าง atrium: ventricle ในอัตรา 2:1 ทารกในครรภ์รายนี้ได้รับการรักษาด้วยยาผ่านทางรก โดยให้ digoxin ร่วมกับ flecainide ซึ่งได้ผลชั่วคราวและมีการกลับเป็นซ้ำ จึงได้เปลี่ยนเป็น digoxin ร่วมกับ sotalol และพิจารณายุติการตั้งครรภ์ ณ อายุครรภ์ 34 สัปดาห์ เพื่อให้การรักษาทารกหลังคลอด ได้ทารกมีลักษณะบวมน้ำ น้ำหนัก 3,320 กรัม โดยหลังคลอดพบว่าไม่ตอบสนองต่อ flecainide จึงเปลี่ยนมารักษาด้วย adenosine ฉีดเข้าทางหลอดเลือด ซึ่งพบว่าให้ผลดีในการรักษา ต่อมาจึงเปลี่ยนเป็นยาชนิดรับประทานโดยให้เป็น amiodarone ร่วมกับ digoxin เมื่ออาการคงที่จึงควบคุมระยะยาวด้วย flecainide ทารกภายหลังการรักษา ภาวะบวมน้ำอาการดีขึ้น ไม่พบภาวะแทรกซ้อนโดยเฉพาะระบบประสาทโดยสรุป กรณีศึกษารายนี้มีวัตถุประสงค์เพื่อนำเสนอการรักษาภาวะหัวใจเต้นเร็วชนิด atrial flutter ด้วย amiodarone ร่วมกับ digoxin ในการรักษา refractory atrial flutter