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Early prenatal management of a fetal ventricular tachycardia treated *in utero* by amiodarone with long term follow-up

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Fetal cardiac arrhythmias are one of the causes of intra-uterine congestive heart failure and non-immune hydrops fetalis leading to fetal death. As ventricular tachycardia (VT) is rarely diagnosed *in utero*, it leads to emergency deliveries. We report a prenatal diagnosis of fetal tachycardia at 20 weeks of gestation associated with non-immune hydrops fetalis. The tachycardia seemed to be supraventricular and was initially treated by digoxin and sotalol. The hydrops increased and sotalol was stopped in order to give the mother a high dose of amiodarone by mouth over a long period. Although the tachycardia, which the ECG recorded at birth revealed to be of ventricular origin, persisted but at a lower rate, the new treatment proved successful. The child is three years old now and health, though with persistent VT. In conclusion, fetal tachycardia with similar ventricular and atrial rates can be a VT and the drug of choice in this case seems to be amiodarone.
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KEY WORDS: fetal arrhythmia; ventricular tachycardia; prenatal diagnosis; amiodarone; pregnancy

INTRODUCTION

Fetal arrhythmias are rare and usually have a supraventricular origin. Cases of fetal ventricular tachycardia (VT) are especially rare. To our knowledge, only seven cases have been previously documented in the antepartum period. Fetal electrocardiography (ECG) recording is not available and the prenatal diagnosis is usually made by demonstrating atrio–ventricular dissociation using Doppler ultrasound (Sherer *et al*., 1990). But the diagnosis can be difficult and a VT can initially be considered of supraventricular origin. All reported cases were diagnosed after 32 weeks of gestation and evolved favourably spontaneously or led to emergency caesarean section. There has been no case of prolonged treatment *in utero* of fetal VT. We report the first case of fetal VT, requiring prolonged management *in utero* using amiodarone with a favourable long term outcome.

CASE REPORT

A 34-year-old woman, gravida 3 para 1, abortion 1, was referred to our outpatient clinic in her 20th week of pregnancy following the discovery of hydrops fetalis associated with fetal tachycardia at 210 beats per minute (bpm). Her past medical history was marked by an abortion for non-immune hydrops fetalis during her second pregnancy. All the data recorded during this second pregnancy, including morphologic echography, monitoring of fetal heart rate and post-mortem examination were normal. The third pregnancy was without any problem until the discovery of a hydrops fetalis associated with fetal tachycardia at 210 bpm during a systematic examination in the 20th week of pregnancy. Ultrasonographic investigation revealed polyhydramnios without associated fetal malformation and with growth measurements corresponding to the gestational age. Fetal echocardiography and Doppler were performed using a Hewlett-Packard Sonos 1000 echocardiogram with a 5 MHz transducer. The heart had a normal structure. As the fetal heart rate was regular between 200 and 220 bpm and the atrial and ventricular rhythms apparently similar on Time Motion (TM) mode examination, the tachycardia was considered to be of supra-ventricular origin. Laboratory data at this time indicated that the maternal blood type was O, Rh-positive and the antibody screen was negative. Her haemoglobin level was 12.3 g/dl and blood tests (calcium, potassium, magnesium, thyroid stimulating hormones, thyroid hormones) were normal. The maternal ECG was normal.

Transplacental treatment was started by giving the mother 0.75 mg of digoxin orally per day. Echocardiography, performed three days after digoxin was given, showed a worsening of the hydrops and persistence of the tachycardia. Sotalol by mouth was started, in addition to digoxin, at a dosage of 160 mg per day. The level of digoxin in the maternal serum was within the therapeutic range (2 ng/ml) with signs of digitalisation on the maternal ECG. Because of persistent tachycardia, we increased the dosage of sotalol to 240 mg per day. At 22 weeks of pregnancy, the polyhydramnios worsened in spite of partial control of the fetal heart rate (180 bpm instead of 220 bpm). Sotalol was stopped (a week after this drug was started and five days after the dose was increased

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to 240 mg per day) in order to administer amiodarone orally, 1000 mg per day for three days then 600 mg per day in association with digoxin 0.75 mg per day. Five days later, the fetal heart rate was in the normal range at 130 bpm. Further development was then satisfactory with normal growth measurements, regression of ascites and the oedematous placenta. The dosage of amiodarone was progressively decreased to 400 mg per day at 26 weeks of pregnancy and to 200 mg per day at 31 weeks of pregnancy. During this time, the serum levels of amiodarone, N-desethyl-amiodarone and digoxin were within their therapeutic ranges. The dosage of digoxin was adapted to the maternal serum level at 0.5 and then 0.375 mg per day. No sampling of the fetal cord blood was performed.

A vaginal delivery was planned at 40 weeks of gestation. A male child weighing 3.235 g, with Apgar scores of 9 and 9 at 1 and 5 min respectively (cyanosis requiring oxygen therapy for a few minutes), was delivered. Clinical examination was normal without goitre or cardiac failure. The investigations carried out, including chest X-ray, blood tests (calcium, potassium, magnesium, thyroid stimulating hormones, thyroid hormones), were normal. An ECG was performed (Figure 1) a few hours after birth. It showed a VT (atrio–ventricular dissociation with a ventricular rate at 170 bpm), and the QT interval was measured at 0.34 s. In fact, there are two different morphologies of VT: right bundle branch block morphology—left axis deviation; and left bundle branch block morphology—left axis deviation. The child was given amiodarone (250 mg/m^2). Propranolol was added because of the persistence of intermittent VT (2 mg/kg and progressively 5 mg/kg). These different treatments controlled the ventricular rate at 110–120 bpm but prolonged periods of VT were still recorded. The echocardiography was unremarkable when the child was at a normal rate but showed ventricular dyskinesia when the rhythm was not controlled. An invasive electrophysiological study with two catheters allowing simultaneous registration of atrial, His bundle and ventricular activities confirmed the ECG findings: the existence of a VT, probably fascicular. When the child was one year old, the rhythm looked sinusal and so the treatment was stopped for a few weeks, but VT promptly reoccurred and reached 200 bpm with signs of cardiac failure, and the treatment had to be resumed. Since then, he has received permanent treatment with amiodarone and propranolol. Holter ECGs are regularly performed and show permanent VT with one predominant morphology (right bundle branch block morphology—left axis deviation). The child is now nearly three years old; he is health, euthyroid, and his growth is normal.

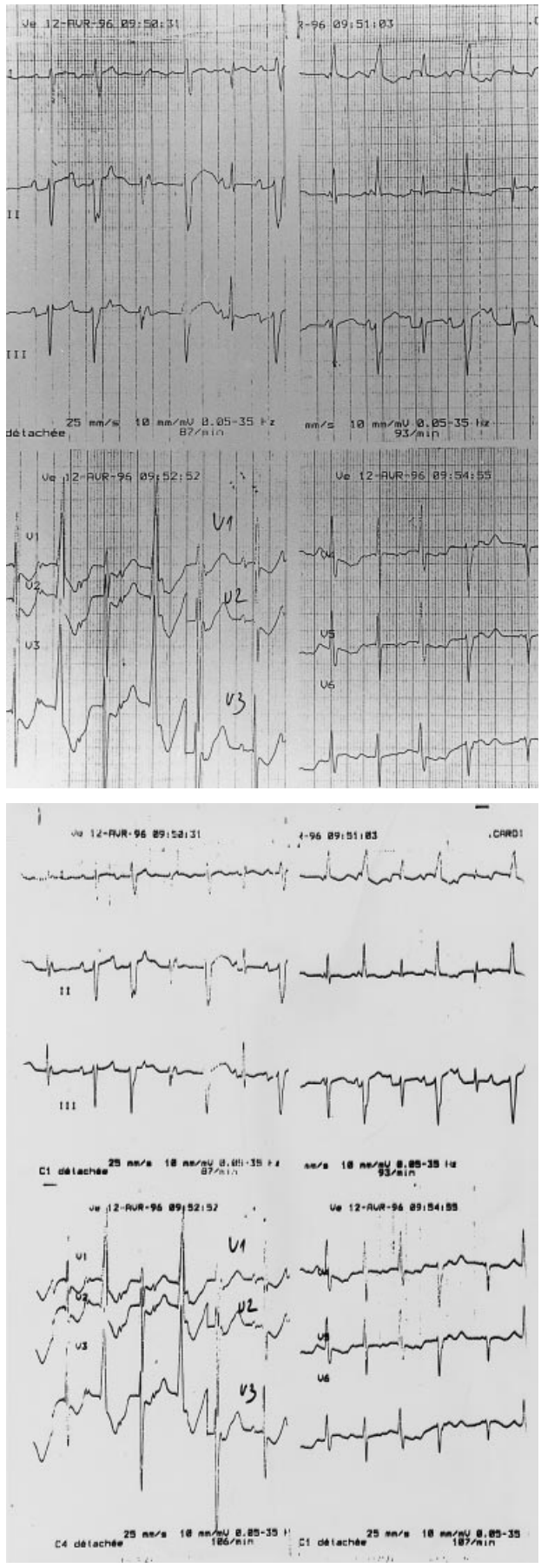

Figure 1—Twelve leads ECG recorded at birth showing the ventricular tachycardia with atrio–ventricular dissociation. There are two different morphologies of VT: right bundle branch block morphology—left axis deviation; and left bundle branch block morphology—left axis deviation

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DISCUSSION

Fetal VTs are very rare. Fetal ECG is not available for a most of the pregnancy owing to the presence of vernix caseosa. Fetal echocardiography allows early diagnosis of fetal tachycardia. Seven cases of VT have been reported in the literature (Table 1). The first two cases of fetal VT reported were diagnosed on fetal ECGs, at term or on fetal scapl ECG during labour (Shenker, 1979). The outcome was unfavourable in the first case with associated cardiac malformation, and favourable for the second with regression of the VT, the child receiving propranolol for a few days. In the first case diagnosed by fetal ECG, atrio–ventricular dissociation was demonstrated by Doppler flow taken on a four-chamber view of the fetal heart in the 30th week of pregnancy. The evolution was unfavourable and the child died a few hours after an emergency caesarean section in spite of attempted transplacental treatment by quinidine (Sherer *et al*., 1999). Two other cases were diagnosed using M-mode ECG belatedly in pregnancy (36 weeks) and a spontaneously favourable evolution was observed without any antiarrhythmic treatment (Van Engelen *et al*., 1994). Another case was diagnosed using M-mode ECG at 31 weeks of pregnancy; the evolution was favourable with emergency caesarean section, and the child received propranolol, isoproterenol and lidocaine for a few days. There was a prolonged QT interval in the neonatal period and the arrhythmia gradually disappeared during the first month (Ikeda *et al*., 1995). The last case reported, to our knowledge, was diagnosed at 38 weeks of gestation using M-mode ECG. The evolution was favourable after emergency caesarean section, and vagal stimulation (induced by suctioning) converted the tachycardia into a sinus rhythm; six days later the tachycardia reoccurred and was reduced using verapamil. Then, the child received amiodarone for two years and the treatment was stopped because he was in permanent sinus rhythm (Lopes *et al*., 1996).

In the antepartum period, when a direct fetal ECG is not available, prenatal diagnosis of fetal ventricular tachycardia should be based upon fetal echocardiography aided by M-mode and Doppler flow. We thought the tachycardia was supraventricular in origin and careful examination was necessary for the diagnosis of this rare arrhythmia. A tachycardia with an atrial rate very close to the ventricular rate can be a VT with cardiac failure and reactional sinusal tachycardia, especially when the frequency is close to 220 bpm. In the case of a VT with 1 : 1 ventriculo–atrial conduction, the diagnosis can be very difficult.

Choosing the best treatment is also difficult because no other case of prolonged and successful management *in utero* of fetal VT diagnosed early has been reported. On the other hand, several cases of supraventricular tachycardia successfully managed *in utero* with different drugs have been reported.

Digoxin is the drug of first choice in supraventricular tachycardia but should be avoided in VT because of the risk of degradation into a malignant arrhythmia even if, as in the case we report, the mother received this drug throughout her pregnancy (Colin *et al*., 1989). Flecainide has been used with success (Allan *et al*., 1991) but is inadvisable because there is a risk of arrhythmogenesis which may be responsible for sudden fetal death *in utero* (Allan, 1996). Verapamil seems to pose similar problems. Procainamide has been used (Triedman *et al*., 1996) but has to be injected intravenously to the mother and only a few patients have been given this drug. Quinidine has been used in one case (Sherer *et al*., 1990) without good result. Propranolol is used but its transplacental passage is only 25%, and it can induce slight growth retardation (Page, 1995). Sotalol seem to be of greater interest in VT because of its superior efficacy in patients with ventricular arrhythmias. No evidence of risk in humans has been reported (Page, 1995). Transplacental passage is 45% (Colin *et al*., 1989). However in our case, this treatment was unsuccessful. Amiodarone is of great interest because this drug has been used several times for refractory fetal supra–ventricular tachycardia and for severe maternal arrhythmias at high doses. Its transplacental passage is 20% (Colin *et al*., 1989). A review of the literature has reported 31 cases where amiodarone was used during pregnancy. No cases of congenital defects have been mentioned in any of the reported cases (Foster and Love, 1988). Another study reported nine cases of

Table 1—Summary of cases of antenatal VT reported in the literature

Case no.	Gestational age (weeks) and diagnostic method	Fetal heart rate (bpm)	Treatment and outcome
1	Term/fetal ECG	Unknown	Death at 12 h old
2	Term/scalp electrode	Runs of VT	Propranolol, favourable
3	30/Doppler flow mode	Intermittent VT, 190–260	Quinidine, then emergency caesarean section, death at 5 h old
4	36/TM mode	170	No treatment, favourable
5	36/TM mode	170	No treatment, favourable
6	33/TM mode	240	Emergency caesarean section, favourable after pharmacological treatment
7	38/TM mode	230–260	Emergency caesarean section, favourable

Nos 1–2: Shenker (1979); no. 3: Sherer *et al*. (1990); nos 4–5: Van Engelen *et al*. (1994); no. 6: Ikeda *et al*., (1995); no. 7: Lopes *et al*. (1996).

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pregnant women who received amiodarone (200 mg per day) and the follow-up of their newborns. All women were clinically euthyroid at the delivery and showed normal values of thyroid hormones. Only one newborn was hypothyroid which improved spontaneously within the first month of life (Matsumara *et al.*, 1992). The frequency of hypothyroidism at birth in the cases of administration of amiodarone to the mother is 20% with favourable evolution after a few months (Laurent *et al.*, 1987; Matsumara *et al.*, 1992). Amiodarone can be used in pregnancy with assessment of thyroid function at birth (Foster and Love, 1988). It is the drug of choice for direct administration to the fetus in refractory tachycardia with severe hydrops which hampers transplacental passage of drugs (Hansmann *et al.*, 1991).

In conclusion, a fetal tachycardia with a ratio of 1 : 1 between the atrial and ventricular rate can be a VT, especially with a ventricular rate between 200 and 240 bpm, even if the best diagnostic criterion is the presence of an atrio–ventricular dissociation on M-mode echocardiography. In the case we report, the drug of choice was amiodarone but prospective studies are required before general recommendations can be given.

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