Chapter

Neurological Outcome of Children who were Treated for Fetal Tachycardia Complicated by Hydrops

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Abstract

Background
Fetal tachycardia is a condition associated with congestive heart failure and development of fetal hydrops, which may result in neurological morbidity and mortality. Limited data exists on the long-term outcome of hydropic fetuses.

Methods
A retrospective study on cognitive and neurological functioning of 11 infants, aged 0.5 to 12 years, who experienced fetal tachycardia complicated by hydrops.

Results
Seven fetuses had supraventricular tachycardia, 3 had atrial flutter and 1 had ventricular tachycardia. Nine fetuses converted to sinus rhythm in a mean time of 7.9 days; resolution of hydrops was achieved in 6 of these patients in a mean time of 7.4 days. Mean GA at birth was 35 weeks and 4 days. Neonatal cranial ultrasound was normal in 7 infants and all but one of these were normal at follow-up: one infant who initially had no abnormalities developed multiple cerebral lesions as a result of a malignant LQTS and died at the age of 2 years. The remaining 4 infants all had flaring on neonatal cranial ultrasound, one complicated by a pseudocyst and one by a porencephalic cyst. One of these infants was normal at follow-up, one died two days after birth and two infants had neurological abnormalities at follow-up, consisting of mild hemiplegia with normal cognitive function in one, and a cognitive developmental delay in the other.

Conclusions
Fetal tachycardia complicated by hydrops predisposes the unborn child to neurological damage. However, in this series 8 out of 11 infants were neurologically normal. Prognosis seems particularly good in case of successful treatment and delivery at term, and initiation of therapy should not be withheld or delayed on the assumption of poor neurological outcome.
Introduction

Fetal tachycardia is a serious condition in which the fetus is at risk for congestive heart failure and subsequent development of hydrops. This situation is associated with significant morbidity and mortality. Neurological morbidity has been linked to fetal tachycardia in several reports and is probably the result of dysfunction of the cerebrovascular autoregulation in hemodynamically compromised fetuses. This makes the prevention and management of fetal tachycardia complicated by hydrops most important. Intrauterine therapy is to be preferred over preterm delivery and postnatal treatment, in avoidance of neonatal complications of prematurity additional to the arrhythmia. Several management protocols have been proposed in the last years of which treatment with flecainide or amiodarone and digoxin seem to be the most successful in SVT, and sotalol the most successful in AF. However, little is known on the neurological follow-up of these children. We present a retrospective study on 11 cases that were treated for fetal tachycardia complicated by hydrops, with special focus on neurological outcome.

Methods

All cases with fetal tachycardia complicated by hydrops and treated at our hospital from 1991 until 2002 were reviewed. Two of these patients have been described in a previous study. Fetal tachycardia was defined as a ventricular heart rate exceeding 180 beats per minute (bpm). Supraventricular tachycardia (SVT) was defined by 1:1 atrioventricular conduction and atrial flutter (AF) was defined as an atrial rate > 250 bpm with a fixed or variable AV block, resulting in a variable ventricular response. Fetal hydrops was defined by clear fluid accumulation in 2 or more of the compartments in the fetal body, such as pericardial effusion, pleural effusion, ascites and skin edema.

Treatment differed between cases as a result of the time span of this study and due to the progressing insights on therapy.

Neurological follow-up

All records, both prenatal and postnatal, were reviewed. All 11 neonates had cranial ultrasounds performed shortly after birth. Neonates who were diagnosed to have neurological abnormalities were accurately documented and enrolled in the neurological follow-up. Neonates who
showed no signs of neurological damage, both at cranial ultrasound and during the neurological follow-up in the first year of life, were discharged from further neurological follow-up. Further development was noted at cardiological follow-up.

At the time of this follow-up study, the patients were invited at our out-patient clinic. They were asked for possible signs and symptoms of any disease, medication, level of education and participation in sports. A full standardized neurological investigation was performed by one neurologist (RHJMG). Normal neurological outcome was defined by adequate cognitive functioning, as defined by a normal level of education and no abnormalities at neurological investigation. Statistical difference in GA at presentation and delivery between groups was made by the Mann-Whitney-U test. A p value of 0.05 was considered significant.

**Results**

**Prenatal situation**

Eleven hydropic patients were included in this study. The mean gestational age at the time of presentation was 30+3 weeks (range 24+4 – 38+4 weeks). Seven patients had SVT, 3 had AF and 1 patient had ventricular tachycardia (VT). Table 1 shows the patient characteristics. In nine patients, conversion to sustained sinus rhythm was achieved in a mean time of 7.9 days (SD 6.0). In 6 of these patients, resolution of hydrops was achieved in a mean time of 7.4 days (SD 3.8) after conversion to sinus rhythm. Of the remaining three patients that converted to sinus rhythm, two went into preterm labour before the hydrops was dissolved (case 9 and 10), and one was delivered at 39 weeks after several days of sinus rhythm (case 5), although still hydropic.

One case that converted to sinus rhythm without treatment was included in the group that converted to sinus rhythm (case 4). This was a twin pregnancy presenting at 31 weeks, with one fetus with SVT at 300 bpm and massive hydrops, and one unaffected twin. In view of the minimal cardiac output and expected poor neurological prognosis, it was decided in conjunction with the parents, not to initiate therapy. However, at follow-up at 32+4 weeks, the heart of the affected twin showed a normal sinus rhythm and signs of decreasing hydrops. Hydrops was completely resolved at 33+2 weeks and the biophysical profile was satisfying. At 35 weeks, relapse of the tachycardia occurred at 300 bpm, and at this point we decided to perform a caesarean section (S.C). Two healthy daughters
were born with good Apgar scores and birth weights of 2500 and 3000 gram.
Two patients did not convert to sinus rhythm. One patient had intermittent VT at 260-280 bpm, and was treated with sotalol and digoxin. As no conversion to sinus rhythm occurred and hydrops was progressing, it was decided to perform a S.C. at 31+1 weeks. A daughter was born with an Apgar score of 5/8 and a birth weight of 2180 gram. She was diagnosed to have long QT syndrome (LQTS) type 3 (case 7). The other patient not converting to sinus rhythm had AF at 300:150 bpm and intermittent 1:1 conduction at 300 bpm. Although not converted to sinus rhythm, on therapy, no 1:1 conduction was seen anymore. Hydrops resolved in 14 days (case 8). Six fetuses were delivered vaginally and 5 by caesarean section (S.C.) Indications for S.C. included breech presentation (n=2), therapy resistance (n=1), relapse (n=1) and emergency S.C. (decreased fetal movements and reduced FHR variability; n=1).

<table>
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<tr>
<th>Case</th>
<th>GA (weeks)</th>
<th>Mechanism</th>
<th>Int/continuous</th>
<th>FHR</th>
<th>Therapy</th>
<th>T to conv (days)</th>
<th>T to resolution (days)</th>
<th>Delivery</th>
<th>GA</th>
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<td>Delay</td>
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</table>

*Table 1*

Postnatal situation

Mean G.A. at birth was 35+4 weeks (range 31 – 41+2). Neonatal cranial ultrasound was normal in 7 infants (group 1) and abnormal in 4 (group 2). The infants of group 1 had a mean GA at presentation of 30,5 weeks (SD 4,2), as compared to a mean GA of 28,8 weeks (SD 3,4) in group 2 (not significant). However, there was a significant difference between the groups in gestational age at delivery (mean 37, SD 3,5 vs mean 33, SD 1,4; p = 0,047).

The infants of group 2 were neurologically abnormal shortly after birth and another one became neurologically abnormal later on, due to ongoing cardiac problems. Two of these five infants died. All together there were 9 survivors, two of whom with neurological sequelae.
Six of the seven infants with a normal neonatal cranial ultrasound were normal at follow-up. One is at present 8 months old with normal neurological results and a normal MRI scan. The other 5 infants are 6 to 12 years old at present. The one patient from this group, who developed abnormally (case 7), had runs of polymorphic tachycardia shortly after birth and a QTc of 0,51 (prolonged) and she was diagnosed to have congenital LQTS. A ventricular pacemaker was implanted and propranolol therapy was initiated. Convulsions were present in the first two weeks of life and a repeated cranial ultrasound performed at two weeks of age showed a small infarction in the left thalamus. A MRI at two months of age showed a small cyst in the left-sided nucleus lentiformis. Neurological development however, was good up to one year of age. At this point in time, the cardiac condition was critical with several periods of ventricle fibrillation and need for resuscitation. A cardioverter defibrillator was implanted, but repeated shocks were required and signs of heart of failure developed. The neurological condition deteriorated and the infant died at 2 years of age of intractable ventricle fibrillation.

There were four infants with an abnormal neonatal cranial ultrasound. Two infants had severe flaring (case 3 and 9) and the other two had mild flaring, with a pseudocyst (case 11) and a porencephalic cyst (case 2). Only case 11 did well. This infant is at present 6 months old, has no abnormalities on repeated cranial scans and is also neurologically developing normal. The other 3 cases are discussed below.
Case 3 initially developed well, but proved to have psychomotor retardation at the age of 16 months when he was functioning conform the age of 9-10 months, determined with the Griffiths developmental assessment scale (63 out of 100). No subsequent follow-up could be
obtained as a result of emigration shortly after the last visit (described in a previous study 4).

Case 2 showed signs of dilatation of the left cerebral ventricle and a shift of the midline at two months of age. These findings were confirmed on MRI, and a ventriculoperitoneal drain was placed. At the time of this study, he is 7.5 years old, has a mild hemiplegia on the right side and requires physical therapy, although development is well and quality of life is not hampered by the mild hemiplegia. Cognitive functioning is normal (described in a previous study 4).

Case 9 was born preterm with massive hydrops at 33 weeks and 3 days of gestation, as a result of preterm contractions. In addition to the severe flaring, a precysteus periventricular leucomalacia was seen and convulsions occurred. In view of the poor prognosis it was decided to abstain from therapy. The infant died at the second day of life.

**Discussion**

Fetal tachycardia is a situation in which the fetus is predisposed to neurological abnormalities probably as a result of hemodynamical compromise. These abnormalities are only present in hydropic fetuses and therefore seem to be related to situations in which such a hemodynamical compromise is severe. Hemodynamic compromise as a result of a disturbance in rhythm predisposes the fetus to cerebral ischemia in periods of moderate hypotension and to intracranial hemorrhage in periods of moderate hypertension 4. The gestational age at presentation of the tachycardia has been proposed as a risk factor for neurological complications, but we could not demonstrate this in our study. A significant difference however, was present in GA at the time of delivery between infants with normal and abnormal neonatal brain scan, probably as a result of the severity of the condition (preterm delivery as a result of polyhydramnios in three cases and induced preterm delivery because of therapy resistance in one case).

Case reports have suggested an association between fetal hydrops due to tachycardia and neurological abnormalities 6-10, but the outcome of a consecutive series is not known. Three of the 11 patients of our study proved to have neurological complications related to the prenatal tachycardia, and in one of them these complications were severe enough, to decide to abstain from further treatment. One patient had
a marked mental retardation and one a mild hemiplegia with a good quality of life. One further case initially was neurologically normal, but deteriorated as a result of the critical cardiological condition. Outcome of the group as a whole was above our expectations and compares favorably with that of other causes of fetal hydrops. However, publications on outcome are mostly focused on mortality rates. In severe immune fetal hydrops a mortality rate of 45% has been reported, even after intrauterine treatment. Outcome in non-immune fetal hydrops related to other causes is poor with perinatal mortality rates of 80 – 100% \(^{17,18}\). In one study, outcome of 126 surviving infants who had suffered from anemia prenatally, induced by red blood cell-alloimmunization, has been studied. In 21% of infants who had been severely hydropic prenatally, visits to neurology and rehabilitation departments were reported, suggesting neurological abnormalities. A percentage of neurological impairment that is comparable to our findings. In addition, they reported a trend towards behavioural problems in the group with severe hydrops \(^{19}\).

Our data indicate that the majority of fetuses apparently seem capable of handling fetal tachycardia at least for a certain amount of time, and adequate blood flow to the fetal brain must be assumed in these cases. Initiation of therapy should therefore never be withheld or delayed based on the unfounded assumption of poor neurological outcome. Even in cases in which it might take several weeks to achieve a sinus rhythm and a subsequent resolution of hydrops, outcome is not necessarily poor (case 11). Only in situations in which obvious neurological lesions are detected in utero one may opt, in conjunction with the parents, to abstain from therapy. Our data do not provide a clue as to which hydropic fetus will develop favorably or otherwise.

**Conclusions**

Fetal tachycardia complicated by hydrops predisposes the unborn child to neurological damage. In our population of 11 fetuses, two deaths occurred, one shortly after birth as a result of the fetal tachycardia and its complications, and one at 2 years of age related to the arrhythmia. The neurological abnormalities encountered in this study, were mild hemiplegia with normal cognitive function in one patient and a cognitive developmental delay in the other. However, neurological outcome of the hydropic group as a whole was reasonably good with no neurological abnormalities in 73% of cases. At long term follow-up, cognitive
function was normal in all surviving infants. Prognosis seems particularly excellent in case of successful treatment and delivery at term. Therefore, initiation of therapy should not be withheld or delayed based only on the assumption of poor neurological outcome.
References


