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Case Report

Discordant immune complete heart block and growth restriction in dichorionic twin pregnancy with permanent pacemaker implantation of an 1140 g neonate

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ABSTRACT

Fetal atrioventricular block is a rare pathology, mostly due to placental transmission of maternal SSA/Ro and SSB/La antibodies, and can lead to severe fetal or neonatal outcomes. We report a case of dichorionic, diamniotic twin pregnancy, with maternal SSA/Ro antibodies. Isolated complete atrioventricular block was diagnosed at 23 weeks in one fetus (Twin A), while the second fetus (Twin B) remained in normal sinus rhythm. Severe asymmetric intrauterine growth restriction occurred in Twin A. Delivery was by caesarean section at 32 + 2 weeks. Neonatal permanent pacemaker was inserted on the first day after birth in 1140 g neonate. Discordant heart block in twin pregnancy has already been reported in a few dichorionic pregnancies, but the pathway of discordant disease expression remains unclear. Extraction decision is a dilemma between cardiac failure prevention and prematurity associated twin morbidity. This case shows a successful pacing in a very low birth weight neonate.

Introduction

Congenital fetal heart block is a rare obstetrical pathology, occurring in 1/20000–30000 live births. The main etiology is transplacental transmission of maternal SSA/Ro and SSB/La antibodies secondary to rheumatic disease such as Lupus or Gougerot-Sjögren syndrome [1]. Only 1–2% of fetuses exposed to maternal SSA/Ro antibodies develop heart block, even if more 80% are antibody positive at birth. In addition, the risk of recurrence of heart block is 10 times higher in subsequent pregnancies suggesting a genetic predisposition for congenital heart block [1]. Moreover, a few cases of discordant expression after antibodies placental transfer in twin pregnancies have been described, strongly suggesting that block occurrences also depends on fetal and environmental factors [2,3]. We report the case of a dichorionic, diamniotic twin pregnancy (female Twin A and female Twin B) whose mother suffered from Lupus with SSA/Ro antibodies resulting in discordant atrio-ventricular block and severe growth restriction.

Case report

A 35 year-old woman with confirmed diagnosis of dichorionic diamniotic twin pregnancy, patient is a known case of Lupus (limited to the skin and joint) with DNA-native antibody SSA/Ro, with a history of pulmonary embolism ten years ago. During her early pregnancy patient was treated with Hydroxychloroquine 400 mg/d, Acetylsalicylic Acid 75 mg/d and Enoxaparin 4000 UI/d. SSA/Ro antibodies level was 63 UI/L (units/ml). Congenital complete atrioventricular block (CCAVB) was diagnosed in Twin A at 23 weeks with stable heart rate 55 bpm, while female Twin B remained in normal sinus rhythm with normal mechanical PR interval. Both twins showed normal cardiac structure. According to our protocol, the patient received 4 mg of Dexamethasone orally per day. Her weekly follow up echocardiograph showed no signs of hydrops fetalis or endocardial fibro-elastosis (EFE). Heart rate was stable at 55 bpm. Severe asymmetric growth restriction was diagnosed at 28 weeks in Twin A with abdominal and femoral

Abbreviations: CAVB, Complete atrioventricular block; CCAVB, Congenital complete atrioventricular block; DCM, Dilated cardiomyopathy; EFE, Endocardial fibro-elastosis; HLA, Human Leukocyte Antigen.

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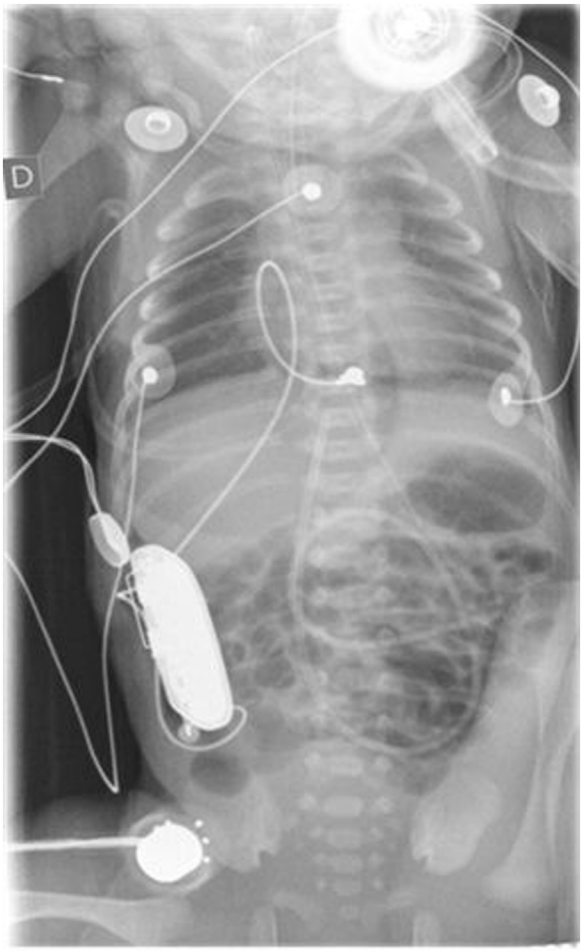
biometry and global weight <3rd percentile on Hadlock and Gardosi curves. Twin B's growth stayed normal. Dexamethasone was stopped at this time, and the patient was admitted to the obstetrical unit. Patient received 12 mg of Bethametasone intramuscularly for fetal lung maturation. Monitoring consisted in daily echography with cardiac frequency, hydrops research and Manning's score. At 31 weeks ultrasound showed a stagnation of the fetus weight (1100 g). Multidisciplinary discussion at this time recommended a fetal extraction by cesarean section at 31 + 2 weeks. Twin A (female) weight 1140 g APGAR score of 10/10/10, and Twin B (female) 1650 g weight APGAR score of 8/9/10 were delivered. Twin A's heart rate was 50 bpm. Echocardiogram confirmed a structurally normal heart with mild ventricular dilatation, but without EFE. Complete atrioventricular block was confirmed by electrocardiogram. Heart rate was not increased by Isuprenalin, and permanent ventricular demand inhibited pacemaker ST JUDE MEDICAL MICRONY II SR+® was implanted at the first day after birth (Picture 1) without any post-operative complication. The newborn was discharged 20 days after surgical intervention. The child is now 12 months old, has normal growth without any cardiac symptoms.



Picture 1- Neonatal radiography showing permanent ventricular demand inhibited pace maker implantated at first day after birth.

Picture 1. Neonatal radiography showing permanent ventricular demande inhibited pace maker implantated at first day after birth.

Discussion

Atrioventricular block discordance due to maternal SSA/SSB antibodies has been described in dizygotic or monozygotic twin pregnancies, but the physiopathology remains unclear. Antibody transplacental transmission is necessary for the endomyocardial injury that leads to atrioventricular block, but is not sufficient, because antibody levels are usually identical at birth in both twins. Fetal factors such as Human Leukocyte Antigen (HLA) markers, TGF B cytokine expression, and tissular receptors have been proposed to explain pathogenesis in twins [4]. A few cases of discordance in monozygotic twins pregnancy have however been reported, strongly suggesting that expression also depends on environmental and maternal factors during intra-uterine period [5,6].

Fetal atrioventricular block detection is a challenge in SSA/SSB antibody positive pregnancy. Only 1–2% of fetuses exposed to SSA/SSB antibodies will develop heart block [1]. Mechanical PR interval measurement between 16 and 28 weeks was initially thought to be useful in predicting second and third block occurrences, but there is now evidence that complete block, occurring in a matter of days without prior first degree block, is found in 10–30 % of these pregnancies [7]. Complete heart block remains the most frequent initial presentation in some studies. Since block occurs due to myocardial inflammatory mechanisms, dexamethasone administrated to the mother has been suggested to reverse first and degree block, but this point is controversial [8,9]. Third degree block is considered to be irreversible. In our case, we continued maternal corticosteroids to 28 weeks in order to protect the unaffected twin, but stopped it when Twin A's growth restriction was diagnosed, since prolonged corticotherapy has been suggested to reduce fetal growth.

When complete heart block is diagnosed, weekly echocardiograms should be performed in order to look for extraction criteria. Heart rates over 55 bpm are generally well tolerated, but a rapid decrease or rate lower than 50 bpm leads to hydrops fetalis and cardiac failure. Hydrops fetalis is the worst outcome predictor, with a fetal or neonatal mortality rate of 83% to 100%. EFE occurs in 7% of CAVB, indicates myocardial dysfunction and is associated with cardiac failure despite neonatal pacing [1]. Recent reports suggest that isolated EFE could be a presentation of antenatal and neonatal lupus. Our case presents without any sign of EFE, only mild ventricular dilatation. Dilated cardiomyopathy (DCM) associated with CCAVB can be present at birth or can occur late after pacing. Moak et al [10] followed 16 paced infants with CAVB and normal left ventricular function at birth, 75% of which developed DCM and heart failure before the age of 2. These data remind us that although there may be a reassuring short-term evolution, early pacemaker insertion can be associated with significant morbidity and mortality.

The association between intra uterine growth restriction, maternal connective tissue disease and CCAVB is well documented and growth restriction with concordant CCAVB has already been described in twin pregnancy [11]. The most common etiologies of discordant growth restriction in dizygotic twins are vascular or placental dysfunction, but hemodynamic changes due to prolonged severe bradycardia and low cardiac output could also have a role in physiopathology. One candidate environmental stress factor is hypoxia that is capable of amplifying the myofibroblast transdifferentiation of a fetal cardiac fibroblast that has already been subjected to an inflammatory injury initiated by circulating maternal anti SSA/Ro antibodies [12]. Our case shows a rare association between discordant CCAVB and discordant growth restriction, which seems to possibly suggest fetal cardiac involvement in the onset of growth restriction. The association of CCAVB and growth restriction complicates fetal monitoring, because umbilical and cerebral Doppler index and fetal rhythm analysis are

useless in predicting fetal distress. Given that prematurity <32 weeks is considered a bad neonatal outcome in fetuses with CCAVB [1], we used daily Manning scores, heart rate and hydrops search to prolong pregnancy as long as possible. Some teams also use a score that deducts points for hydrops, ductus venosus pulsations, reversed umbilical diastolic flow, cardiac enlargement, and atrioventricular valve regurgitation [13].

Autoimmune CCAVB is associated with a mortality rate of 19%; the majority of deaths (70%) occurred in utero [1]. Prematurity and low birth weight are strong predictors of bad neonatal outcome in a fetus with CCAVB.

Permanent pacemaker implantation is indicated for CCHB in the following patients: those with a wide QRS escape rhythm, complex ventricular ectopy or ventricular dysfunction; in infants with a ventricular rate <55bpm or with congenital heart disease and a ventricular rate of less than 70bpm.

Initial pacing using a right ventricular epicardial lead with VVI mode is the dominant technique in neonates, when a permanent pacemaker implanted by catheter access is used after the child has grown to 10/15 kg. Permanent or temporary choice for initial neonatal pacing depends on weight at birth and the medical-surgical team's experience. Permanent pacemakers are usually implanted when the child reaches 2.0 kg. Thanks to technology improvements and close cardiac monitoring, the cumulative probability of survival at 10 years reaches up to 73% [14].

Successful cases of low birth weight neonate permanent pacing have been reported but remain rare [15].

Our patient who weighted 1140 g was, in our knowledge, the smallest newborn who successfully underwent early and initial permanent pacemaker implantation. The key to this success was certainly the close fetal monitoring, scheduled birth, and planned neonatal intervention with a suitable pacemaker at birth.

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