

## Case report/Caso clínico

# Congenital complete atrioventricular block – case report and review of the literature

## Bloqueio aurículo-ventricular completo congénito – caso clínico e revisão da literatura

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### Abstract

**Introduction:** Congenital complete atrioventricular block (AVB) without cardiac malformation is a rare and potentially fatal condition. In most cases it is associated with maternal systemic lupus erythematosus through transplacental passage of antibodies anti-SSA/Ro and/or anti-SSB/La. Antenatal fluorinated-steroids have been successful in reversing first and second degree congenital AVB but inconsistent in third degree block.

**Case Report:** The authors report a case of fetal bradycardia diagnosed at 24 weeks of gestation. The fetal echocardiogram revealed a second/third degree AVB without structural heart disease. Maternal anti-SSA/Ro antibodies were detected. There was no blockage improvement with maternal oral fluorinated-steroids. An elective cesarean section was performed at term with the delivery of a healthy girl that required an epicardial pacemaker on the 8<sup>th</sup> day of life.

**Conclusion:** In this case, treatment with maternal fluorinated corticosteroids was not effective in preventing progression of the heart block.

**Keywords:** Congenital heart block; Pregnancy; anti-SSA/Ro antibodies; Anti-SSB/La antibodies; Fluorinated corticosteroids

### INTRODUCTION

Congenital complete atrioventricular block (AVB) without cardiac malformation occurs in 1-15000 to 1-20000 pregnancies<sup>1,2</sup>. It is a permanent, practically irreversible and potentially fatal complication<sup>3</sup>. In more than 90% of cases results from neonatal lupus erythematosus through transplacental passage of antibodies anti-SSA/Ro and/or anti-SSB/La<sup>2</sup>. Maternal administration of high-dose oral fluorinated steroids may reverse or inhibit progression of first and second degree AVB. However, in the presence of a third degree

AVB the therapeutical results have been inconsistent.

The authors present a case of congenital complete AVB and a review of the literature.

### CASE REPORT

A 34-year-old primiparous woman was referred to our Maternity at the 24<sup>th</sup> week of gestation, due to fetal bradycardia detected on a routine ultrasound performed two weeks earlier. The previous pregnancy resulted in a healthy child.

Her medical history was irrelevant. Our initial evaluation included a fetal ultrasound and echocardiogram and maternal autoantibody screening, with emphasis on testing anti-nuclear antibody (ANA), anti double-stranded DNA antibody (anti-dsDNA) and anti-extractable nuclear antigens (ENA), particularly anti-SSA/Ro and anti-SSB/La (Table I). Fetal ultrasound revealed normal fetal growth (25<sup>th</sup> percentile) with normal umbilical and mean cerebral artery doppler scans.

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TABLE I. AUTOANTIBODIES PANEL

Blood Test	25 <sup>th</sup> week	33 <sup>rd</sup> week	3 weeks postpartum
ANA	Positive (1/640)	Positive (1/640)	Positive (1/320)
Anti-dsDNA	Negative	Negative	Negative
Anti-SSA/Ro	Positive	Positive	Positive
Anti-SSB/La	Negative	Negative	Negative
Lupic anticoagulant	Negative	Negative	Negative
Anti-cardiolipin IgG/IgM	Negative/Negative	Negative/Negative	Uncertain/Negative
Anti-β2GP1 IgG/IgM	Negative/Negative	Negative/Negative	Negative/Negative
Reumathoid Factor	Positive	Negative	
Anti-smooth muscle	Negative	Negative	Negative
Anti-RNP	Negative	Negative	Negative
C'3	1.37 (0.90 – 1.80)	1.70 (0.90 – 1.80)	1.17 (0.90 – 1.80)
C'4	0.31 (0.10 – 0.40)	0.35 (0.10 – 0.40)	0.41 (0.10 – 0.40)
Anti-mitochondria		Negative	
Anti-nucleosome		Negative	Negative
Anti-Scl-70		Negative	Negative
Anti-centromere		Negative	Negative
Anti-histone		Negative	
C-ANCA / P-ANCA		Negative/Negative	
Anti-TPO			1.0 (<9)
Anti-TG			<0.9 (<4)

ANA: anti-nuclear antibody; Anti-dsDNA: anti double-stranded DNA antibody; Anti-β2GP1: anti beta2 glycoprotein 1 antibody; Anti-RNP: anti-ribonucleoprotein; Anti-Scl-70: anti topoisomerase I antibody; C-ANCA: Cytoplasmic antineutrophil cytoplasmic antibodies; P-ANCA: Perinuclear Anti-Neutrophil Cytoplasmic Antibodies; Anti-TPO: Anti-thyroid peroxidase antibody; Anti-TG: Anti-thyroglobulin antibody

Fetal echocardiogram showed a sinus bradycardia with heart rates of 57–60 bpm without associated structural heart defects, atrioventricular (AV) regurgitation or pericardial effusions. Maternal anti-SSA/Ro antibodies were detected.

Fetal echocardiogram repeated one week later revealed an alternating second to third degree heart block with atrial rate of 120 bpm and ventricular rate of 58–60 bpm. The mother was started on oral dexamethasone (4mg/day) on the 25<sup>th</sup> week of gestation, which was discontinued 6 weeks after, since there was no reverse in the AV block. Prior to the institution of the fluorinated steroids, 75g oral glucose tolerance test was performed within normal range values.

Regular fetal echocardiograms confirmed complete AV block without heart failure, pericardial effusions or atrioventricular impairment. At the 31<sup>st</sup> week of gestation a fetal brain magnetic resonance imaging showed normal brain, cerebellum and brain stem morphology, with no signs of intracranial hemorrhage or encephaloclastic lesions. A mild asymmetry of the la-

teral ventricles was identified.

At the 35<sup>th</sup> week of gestation there was a slight increase in maternal arterial blood pressure (140/90 mmHg) without proteinuria. Fetal growth fell to 15<sup>th</sup> percentile with normal umbilical and mean cerebral artery doppler scans. There was no fetal hydrops or signs of heart failure throughout the entire pregnancy.

Due to a fall in atrial and ventricular rates (110 bpm and <50 bpm, respectively) an elective cesarean section was performed at 37 weeks of gestation. The newborn had an Apgar score of 8/8 and weighted 2320g. Heart rate at birth was above 50 bpm. The newborn was transferred immediately to our Pediatric Cardiology Unit. Electrocardiogram confirmed a complete AVB with a stable heart rate of 40–50 bpm. On the 8<sup>th</sup> day of life an epicardial pacemaker was implanted. Post-natal echocardiogram reaffirmed the absence of structural heart defects or signs of heart failure. The newborn was discharged at the 20<sup>th</sup> day.

Maternal blood pressure normalized in the postpartum period.

The child is now one year old has attended regular follow up in a Pediatric Cardiology and is doing well.

## DISCUSSION

Virtually all mothers of fetuses with isolated AVB will have a connective tissue disease – Systemic Lupus Erythematosus (SLE) or Sjögren Syndrome. Although some may be completely asymptomatic<sup>4</sup>, the increased risk of developing a connective tissue disease requires a tight surveillance. Anti-SSA/Ro and Anti-SSB/La are the maternal autoantibodies most frequently associated with AVB<sup>3,5-9</sup>. These autoantibodies, cross the placenta during the second trimester of pregnancy, bind to fetal cardiac myocytes that undergo apoptosis with subsequent opsonization, altering calcium homeostasis and promoting a proinflammatory reaction that may lead to conduction disturbances, myocarditis and arrhythmogenicity<sup>3-5,7,10</sup>. Intrauterine mortality is higher when complete AVB is diagnosed before 20 weeks of gestation, ventricular rate is below 50 bpm or when hydrops or impaired left ventricular function are present<sup>1</sup>.

Once a complete AVB is established, pharmacological attempts at reversal have never been successful. However, first and second degree AVB may still be reversible with *in utero* treatment, suggesting that severe fibrosis has not yet occurred<sup>8</sup>. Various therapeutic approaches have been reported, such as plasmapheresis, steroids, intravenous gamma globulin (IV-Ig), beta-adrenergic agents, cyclophosphamide, extracorporeal immunoabsorption, azathioprine, hydroxychloroquine and B cell depletion therapies. Most of them involve single case reports<sup>1,8</sup>.

Several studies suggested that fluorinated steroids (betamethasone or dexamethasone), which cross the placenta in their active form, would prevent progression of the AVB or even promote its reduction<sup>2,4,5,11</sup>. So far, there is not enough evidence that supports benefit in complete AVB. Side-effects on the fetus – oligohydramnios, fetal growth restriction and reduced cerebral growth – and on the mother – diabetes, hypertension and adrenal insufficiency<sup>1,5,10</sup> – have to be considered before initiating steroid therapy.

Few non-randomized, multi-center studies of antenatal IV-Ig on AVB are available. In 2010 Friedman published a study of 20 pregnant women with anti-SSA/Ro and/or anti-SSB/La antibodies treated with IV-Ig. To enroll in the study, a previous child with con-

genital AVB or SLE-associated rash, concomitant treatment with prednisone and gestational age under 12 weeks were required. The authors concluded that IV-Ig was ineffective in preventing congenital AVB or reducing maternal antibodies titers<sup>8,12</sup>. In the same year, Pisoni published a similar study with 24 pregnant women whose offspring in prior pregnancies developed congenital AVB. Gestational age under 12 weeks and positive anti-SSA/Ro and/or anti-SSB/La were mandatory criteria for enrollment. Likewise, efficacy of IV-Ig in preventing congenital AVB was not established<sup>8,13</sup>.

Hydroxychloroquine is the most recent line of investigation for congenital AVB treatment. In 2010, a retrospective case-control study involving 50 children whose mothers had SLE and documented anti-SSA/Ro and/or anti-SSB/La antibodies and 151 controls found no significant differences in pregnancy outcomes between the group treated with hydroxychloroquine and the control group. Nevertheless, the authors suggested that hydroxychloroquine may decrease the risk of developing neonatal cardiac SLE<sup>8,14</sup>.

Currently available data does not demonstrate efficacy of any pharmacological treatment in preventing or avoiding progression of congenital heart block. Two-thirds of these children will require a pacemaker within the first year of life and some will develop cardiomyopathy<sup>1,2,9</sup>. After an affected pregnancy, the risk of another fetus with congenital AVB increases at least 10-fold<sup>8</sup>.

In our case fluorinated corticosteroids were not effective in preventing progression to third degree AVB. The lack of prospective and randomized controlled trials that support a beneficial effect of steroids, IV-Ig or hydroxychloroquine for treatment of complete congenital AVB requires a careful risk-benefit analysis before initiating therapy.

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