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Complete Fetal Atrioventricular Block Associated with Maternal Autoinflammatory Diseases: Case Report and Literature Review

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INTRODUCTION

Cardiac arrhythmias, are shown to occur due to abnormal rhythm of the heart. Studies show that voltage-gated ionic channels mutations play an important role in generation of severe cardiac arrhythmias and it is suspected that mutations in voltage-gated potassium channels are more important in generation of arrhythmias.[1]

Maternal autoimmune diseases are well known to cause deformation in the fetal heart. Transplacental passage of anti-Ro/SSA and/or anti-La/SSB antibodies may cause destruction of the conduction system of fetal heart, manifesting as congenital heart block (CHB). Mothers of fetuses with CHB are often asymptomatic, with some having undifferentiated connective tissue disease.[2]

It has been shown that 1%-3% of fetuses from mothers with anti-Ro/SSA and/or anti-La/SSB antibodies develop atrioventricular (AV) block.[3] CHB is mostly detected between the 20th and 24th gestational weeks. CHB may progress to different stages but is most frequently detected in the form of complete CHB. Half of fetuses with complete CHB have no related heart disease and are defined as "isolated" CHB cases.[3] Newborns with CHB with associated structural heart disease have poorer prognosis than those defined as isolated CHB cases.

We have presented the cases of two newborns with complete CHB related to maternal autoantibodies diagnosed during the second trimester of pregnancy.

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CASE REPORT

Case 1

A 32-year old, gravidity: 1 parity: 0 woman, at 25th gestational week, was referred to our hospital's high-risk pregnancy unit due to fetal sustained bradycardia. Fetal anomaly screening was within normal limits at 20th gestational week, but fetal bradycardia was detected at 24th gestational week. Further investigations showed that the mother had antinuclear antibody and anti-cardiolipin antibody positivity with strong anti-Ro/SSA and anti-La/SSB positive status. She was not receiving any medication potentially associated with bradycardia. She was consulted and was evaluated at the pediatric cardiology department; secundum atrial septal defect (ASD) and fetal complete AV block with a heart rate of 57 beats per minute (bpm) were detected on M-mode fetal echocardiography. Differential diagnosis of bradycarida were studied (chromosomal abnormalities, congenital infections) and no additional fetal and maternal abnormality were detected. The fetus was weekly followed with serial ultrasonography and findings were discussed in the council of perinatology with members from perinatology, neonatology, and pediatric cardiology departments. The fetus developed slight cardiomegaly but with no hydrops. At the 36th gestational week, the mother delivered a male newborn weighing 2640 g through cesarean section due to oligohydramnios. The newborn was transferred to the neonatal intensive care unit (NICU) with pre-diagnosis of neonatal lupus and neonatal bradycardia. First examination revealed a weight of 2640 g (10-25 percentile) and a head circumference of 34.2 cm (25-50 percentile). Heart rate was 52-62 bpm. Respiratory rate was 52 breaths per

minute and blood pressure was 76/44 (mean: 51) mmHg. No rash or eruption was detected. Cardiovascular examination revealed no murmur. To identify the etiology of bradycardia, laboratory examinations were performed; hemogram were normal, and no pathology was observed in biochemical parameters. Acute-phase parameters were investigated to differentiate sepsis entity, which were all normal. Additionally, thyroid function was normal.

Telecardiography showed minimal enlargement in cardiothymic silhouette. A 12-lead electrocardiogram (ECG) revealed "complete AV block", which was confirmed by Holter ECG (heart rate, 50-61 bpm). Echocardiographic examination revealed secundum ASD and minimal tricuspid insufficiency. Serological testing showed a strong positivity foranti-Ro/SSA and anti-Ro52 antibodies. During close follow-up at NICU, no hemodynamic failure developed and the heart rate was between 48 to 66 bpm. On postnatal day 13, pacemaker implantation was performed according to "2002 guideline update for implantation of cardiac pacemakers and antiarrhythmia" criteria, with no complications.[4] The newborn was discharged on postnatal day 20 with stable heart beat of 130 bpm.

Case 2

A 28-year old, gravidity: 1 parity: 0 woman, was admitted to our hospital's high-risk pregnancy unit at 21st gestational week. She had been diagnosed with Sjogren Syndrome 4 years ago and received cyclosporine therapy till 12th gestational week for 1 month. Fetal anomaly screening results were normal, but Doppler ultrasonography revealed a fetal heart rate of 51-65 bpm, and thus fetal AV block was diagnosed. Maternal anti-Ro/SSA and anti-La/SSB were found to be strongly positive. The woman was consulted to the pediatric cardiology department and M-mode fetal echocardiography revealed, "complete AV block with structurally intact fetal heart". The condition of both mother and fetus was regularly followed. Other causes of fetal bradicaria (chromosomal abnormalities, congenital infection etc.) were evaluated. No additional maternal and fetal morbidity were defined. Findings were discussed in the council of perinatology with members from the perinatology, neonatology, and pediatric cardiology departments. At the 36th gestational week, the woman delivered a male newborn weighing 2950 g through cesarean section due to early membrane rupture. The baby was transferred to NICU with pre-diagnosis of neonatal lupus and neonatal bradycardia. First examination revealed a weight of 2950 g (25 percentile) and a head circumference of 35 cm (50 percentile). Heart rate was 55-74 bpm. Respiratory rate was 50 breaths per minute, and blood pressure was 67/33 (mean: 45) mmHg. No rash or eruption associated with neonatal lupus was detected. Cardiovascular examination revealed no murmur. Laboratory examinations were performed to identify the etiology of bradycardia; a normal hemogram as well as biochemical parameters were detected. To differentiate sepsis entity, acute-phase parameters were examined and found to be normal. Thyroid function was normal.

Minimal enlargement in cardiothymic silhouette was observed with telecardiography. ECG with 12 derivation showed a complete AV block, which was confirmed by Holter ECG (heart rate: 54-72 bpm). Echocardiographic examination revealed no additional structural heart abnormalities. Serological testing showed a strong positivity for anti-Ro/SSA and anti-Ro52 antibodies. During close newborn follow-up at the NICU, no hemodynamic failure was seen. The heart rate was 54-102 bpm and therefore pacemaker implantation was not indicated and the newborn was discharged on postnatal day 13.

DISCUSSION

Fetal bradycardia is defined as fetal heart rate < 110 bpm for at least 40 minutes.[5] Identification and differentiation of fetal bradicardia have a great importance during antenatal period. A successful and a detailed differential diagnosis of fetal bradicardia may enhance qualitified observation, most suitable treatment and prevention of possible complications caused by inappropriate and missed follow-up during pregnancy.

Well-defined causes of fetal bradycardia include cord compression, fetal head compression, and contractions assumed as benign causes. M-mode echocardiography or Doppler ultrasonography is usually used to define and identify bradycardia in fetuses. M-mode echocardiography is helpful, not only in detecting fetus' heart rate, but also in understanding the relationship

between atrium and ventricles during contractions.

The sustained type of fetal bradycardia is rarely observed. A persistent ventricular rate < 60 bpm is usually associated with complete heart block and carries a substantial risk of cardiac dysfunction development.

Some studies focused mainly on identifying fetal bradycardia etiology, showing that the most frequent cause of sustained fetal bradycardia is AV block.[6] Clinical studies have shown that most fetal-isolated complete AV block cases occur when mothers have connective tissue diseases. Mothers with anti-SSA/Ro positivity (in presence or absence of anti-SSB/La) have a risk of complete AV block in 1%-7.5% of fetuses.[3]

Destruction of fetal cardiac conduction system by maternal autoantibodies is a well-known cause of isolated CHB with structurally normal heart. Maternal autoantibodies are presumed to cross the placenta and damage the fetal conduction system.[7] Most prevalent initial presentation of fetuses contacting with maternal autoantibodies is complete AV block.[7]

Treatment modalities for cases of fetal AV block during pregnancy have evolved, with beta adrenergic stimulants and steroids reportedly being effective.[8] Beta adrenergic stimulants (i.e., terbutaline) have been successfully used to increase fetal heart rate>55 bpm. These agents have also reversed hydrops in some fetuses. However, they showed no impact in fetal or neonatal death risk.[9] In addition to conventional modalities, the concept of a "biological pacemaker" has emerged as an alternative method for the treatment of bradyarrhythmias, originated with the idea of using a viral gene delivery mechanism with gene therapy, followed by the combination of gene and cell therapies.[9]

Reportedly, steroids may improve first- and second-degree AV block when administered immediately after detection. As no treatment modality exists for third degree AV block, steroid use is only recommended when myocarditis and/or hydrops are present.[8] In the present complete AV block cases, steroid therapy was not used because close and serial Doppler examinations revealed no signs of hemodynamic instability (i.e., no myocarditis or hydrops). Additionally, existing concerns about neurological adverse effects and growth restriction in fetuses and maternal adverse effects related with steroid therapy suggest the need for further research.[10]

Postnatal pacemaker implantation has become the best option for AV block treatment. The most important indication for pacemaker implantation is sustained fetal heart rate below 55 bpm.[4] Fetal complete AV block with structurally normal heart may require urgent pacemaker implantation. Prenatal pacemaker implantation has also been reported in the literature.[11]

In our cases, the close Doppler follow-up during the second pregnancy trimester identified two fetuses with complete AV block due to maternal autoimmune diseases (Lupus and Sjogren's disease). M-mode echocardiography was performed to determine the presence of any additional structural heart abnormalities; none were found. We discussed the possibility of premature deliveries in order to early-start for follow up and theraphy. Fetuses were reactive and hemodynamically stable during close Doppler follow-up. No beta sympathomimetic agents or steroids were administrated. No complications were detected (cardiac failure, hydrops, myocarditis) and therefore, heart associated preterm delivery was not indicated. After delivery, newborns were followed up in the NICU. Pacemaker implantation was necessitated for one newborn according to the updated guidelines for cardiac pacemaker implantation.[4]

LEARNING POINTS

- Fetal complete AV block due to maternal antibodies remains a substantial cause of fetal morbidity and mortality.
- Timely diagnosis, close multidisciplinary follow-up for well-being and complications, delivery in a tertiary facility where comprehensive neonatal cardiac care is available, and urgent pacemaker implantation when needed are important issues toward a successful outcome.
- Further studies are warranted to develop prenatal intervention modalities for fetuses with complete AV block.

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CONFLICT OF INTEREST

All the authors declare no conflict of interest.

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