Clinical Case Report

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Two case reports of neonatal autoantibody-associated congenital heart block

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Abstract

Rationale: Neonatal lupus erythematosus (NLE) is an infrequent disease caused by transplacental maternal autoantibodies. The most common effects of NLE include cutaneous involvement and congenital heart block (CHB), although it might involve multiple organs, such as the liver, lungs, blood, and nervous or digestive systems. Izmirly PM1 and Tonello et al recently reported cutaneous manifestations of neonatal lupus and risk of subsequent CHB. The most serious complication of NLE is complete atrioventricular (AV) block.

Patient concerns: We experienced 2 cases of NLE that were diagnosed in the past year in our Neonatal Intensive Care Unit. These cases showed 2 different clinical spectrums (CHB, multisystemic effects). One case was a 32-week pregnant woman with combined liver damage and fever, and her fetus was premature due to bradycardia and pericardial effusion. The second case was a young pregnant woman who had systemic lupus erythematosus for 2 years and had been taking methylprednisolone and hydroxychloroquine for a long time since her illness. When prenatal testing at 28 weeks of pregnancy showed that the fetus had CHB, the mother began taking dexamethasone.

Diagnosis: The first case was diagnosed as NLE with CHB after birth, while the second was diagnosed as NLE with CHB, ductus arteriosus, and atrial septal defect when she was born at 34 weeks.

Interventions: Both of 2 cases were treated with steroids, intravenous immunoglobulin, and a diuretic. But the second case was treated with isoprenaline in addition to the above.

Outcomes: Both of the infants was followed up and found to be clinically normal. During the clinic follow-up of the first case, the 8-month-old infant was still asymptomatic with normal growth and development. Her heart rate fluctuated from 40 to 90 beats/minute.

Lessons: Autoimmune CHB is a severe, potentially life-threatening disorder associated with passive transfer of maternal anti-Sjogren's syndrome A/Ro and anti-Sjogren's syndrome B/La autoantibodies. Mothers who are positive for these autoantibodies are recommended to have serial echocardiography and obstetric ultrasonography from the early second trimester. Newborns should be delivered at an early stage of gestation if there is evidence of pericardial effusion, ascites, increasing ventricular ectopy, reduced ventricular shortening fraction, or AV valve regurgitation. Aggressive medical management after birth should be coupled with pacemaker implantation in infants who do not respond to medical therapies alone.

Abbreviations: ANA = antinuclear antibody, anti-SSA/Ro = anti-Sjogren's syndrome A/Ro, anti-SSB/La = anti-Sjogren's syndrome B/La, AV = atrioventricular, CHB = congenital heart block, EFE = endocardial fibroelastosis, NLE = neonatal lupus erythematosus, Ro52 = Sjogren's syndrome 52.

Keywords: congenital heart block, erythematosus, neonatal lupus

1. Introduction

Neonatal lupus erythematosus (NLE) is considered as a model of passively acquired autoimmune disease characterized by the transplacental passage of anti-Sjogren's syndrome A/Ro (anti-SSA/Ro) and anti-Sjogren's syndrome B/La (anti-SSB/La) antibodies from an affected mother to her fetus. The characteristic clinical features of NLE include transient rash, congenital heart block (CHB), hepatobiliary dysfunction, and hematological, neurological and pulmonary abnormalities. The most serious, life-threatening complication of NLE is CHB.[1] Different degrees of atrioventricular (AV) block may be found in the affected fetus. First- and second-degree AV blocks may change in severity; however, third-degree AV block is irreversible.

We report 2 cases of NLE with CHB. The patients' epidemiology, pathogenesis, and clinical characteristics are briefly discussed.

2. Case reports

2.1. Case 1

A pregnant woman at 32 weeks gestation was referred at our infectious disease clinic. Fetal arrhythmia was observed for 2 months during her routine prenatal care. She had 9 days of liver dysfunction and 1 day of unexplained fever.

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Echocardiography showed fetal bradycardia. The ventricular rate was 55 to 60 beats/minute and pericardial effusion was found. The next day, a 1420-g female neonate was delivered by cesarean section with Apgar scores of 10 and 10 at 1 and 5 minutes, respectively. An electrocardiogram confirmed the diagnosis of second-degree AV block, with a ventricular rate of 55 beats/minute and an atrial rate of 128 beats/minute. A 2-dimensional echocardiogram showed normal cardiac anatomy with a diminished contractility and mild pericardial effusions. Subsequent tests were performed. All results were normal, except for thrombocytopenia (83,000 platelets). Antinuclear antibody (ANA) was reactive at 1:320. Anti-SSA, anti-SSB and Sjogren's syndrome 52 (Ro52) antibodies were positive. A laboratory investigation of the mother showed reactive ANA (1:1000), and anti-SSA, anti-SSB, and Ro52 antibodies were the same as those found in the newborn.

Treatment of the newborn included steroids (methylprednisolone succinate sodium and prednisone), intravenous immunoglobulin, and a diuretic (furosemide). On the 22nd day, we found annular erythema and scaly lesions on the right face and trunk of the neonate. The final diagnosis was NLE with cardiac, cutaneous, and hematological involvement. The infant was discharged with an uneventful observation in the nursery during the following 26 days.

During her last clinic visit, the 8-month-old infant was still asymptomatic with normal growth and development. Her heart rate fluctuated from 40 to 90 beats/minute.

2.2. Case 2

A 26-year-old gravida 2, para 0 woman was referred at 22 weeks' gestation for evaluation of sustained fetal bradycardia, ranging from 80 to 85 beats/minute. She had a 2-year history of systemic lupus erythematosus and had taken methylprednisolone and hydroxychloroquine. Her previous pregnancy resulted in miscarriage.

Fetal echocardiography was performed at 28 weeks gestation. The diagnosis of CHB was made, with a ventricular rate of 75 to 78 beats/minute and an atrial rate of 126 to 138 beats/minute. The mother started taking dexamethasone 3.75 mg/day.

At 34 weeks of gestation, a 2500-g female neonate was delivered by cesarean section, with Apgar scores of 7 and 9 at 1 and 5 minutes, respectively. An electrocardiogram confirmed the diagnosis of CHB with a ventricular rate of 58 beats/minute and an atrial rate of 123 beats/minute. A 2-dimensional Doppler echocardiogram showed a patent ductus arteriosus (0.4 cm) with atrial septal defect (0.3 cm).

Treatment of the neonate included steroids (methylprednisolone succinate sodium and prednisone), intravenous immunoglobulin, isoprenaline, and a diuretic (furosemide). Her subsequent hospital course was uneventful. During her last clinic visit, the infant appeared clinically well. The mother and her infant were positive for ANA, SSA, and Ro52 antibodies.

Informed written consent was obtained from the patient's mother for publication of this case report and accompanying images. The protocol was approved by the ethics committee of The Affiliated Hangzhou First People's Hospital, Zhejiang University School of Medicine (scientific research and medical ethics review no. 109–01, 2018)

3. Discussion

Congenital autoimmune AV block usually occurs in association with autoimmune antibodies in the mother that cross the placenta and damage the AV node of the fetus. The incidence of CHB is 2% in cases of maternal anti-SSA/Ro antibody positivity, and 3% when both anti-SSA/Ro and anti-SSB/La are positive.[1–2] In subsequent pregnancies, the risk of CHB again in the fetus is 6 to 10 times higher.[2] In contrast, Tonello et al[3] recently reported a surprisingly high occurrence rate of CHB at 19.8%.

Nearly half of the mothers carrying autoantibodies of systemic lupus erythematosus are not aware of this disease until their children are born with CHB. These mothers are asymptomatic at delivery and are identified only by the birth of an affected child.[4] In case 1, fetal arrhythmia was observed for 2 months during routine prenatal care. The pregnant woman had hepatobiliary dysfunction for 9 days and a fever for 1 day. Her illness failed to respond to protection of the liver and to antibiotic treatment that was administered during hospitalization at a local hospital. She was then transferred to our hospital and diagnosis of CHB was confirmed. A laboratory investigation of the mother showed reactive ANA (1:1000), and the antibodies were the same as those found in the newborn. Therefore, incidental detection of fetal bradycardia in antenatal ultrasound indicates that further screening of maternal anti-SSA/Ro and anti-SSB/La antibodies should be performed.

Complete congenital fetal heart block related to maternal anti-SSA/Ro autoantibodies typically occurs during 20 to 24 weeks of gestation (case 2). In anti-SSA/Ro and anti-SSB/La antibody-positive mothers, serial echocardiography and obstetric ultrasonography should be performed from the early second trimester. In pregnant women at high risk, such as women with previously affected newborns, weekly monitoring beginning from the early second period of gestation and bi-weekly monitoring between 24 to 36 weeks should be performed[5]

CHB with a structurally normal heart is frequently associated with maternal autoantibodies to SSA/Ro and SSB/La. A mosaic of maternal, fetal, and possibly environmental factors might be involved in inducing CHB, but also the combination of such factors might induce onset of CHB.[6] Tissue injury in the fetus is presumed to be dependent on Fc γ R-mediated transplacental passage of maternal immunoglobulin G autoantibodies. Anti-SSA/Ro and anti-SSB/La antibodies bind to fetal cardiocytes and inhibit the normal physiological removal of apoptotic cells. This results in inflammatory reactions and fibrosis of the cardiac conduction system.[5,7] Damage to the AV node, including calcification and collagen deposition, is the main finding in autopsy reports. CHB may also affect other conduction systems, including the sinoatrial node and the bundle of His.[8]

The clinical features of neonates with CHB depend on the effect of heart rate on cardiac output. At birth, the infant may present with congestive heart failure (case 1), anasarca, hepatomegaly, and metabolic acidosis requiring emergent pacing. A low heart rate may result in fetal hydrops or neonatal heart failure. Some newborns can compensate by having a low heart rate, although most of them might require pacemaker implantation.

Newborns with AV block should be admitted to the intensive care unit soon after birth if they have impaired cardiac function and a low cardiac output for further central line placement, optimization of acid/base status, inotropic drug infusions, and mechanical ventilation if necessary. Planned early pacing of high-risk neonates with CHB potentially reduces the adverse consequences of profound bradycardia and asystole soon after birth in the milieu of increasing metabolic demands. According to a study by Glatz et al,[9] early diagnosis, use of maternal steroids, close follow-up, and early placement of temporary epicardial

pacing for severely affected newborns with isolated CHB are recommended after planned deliveries.

Sustained reversal of third-degree CHB has never been achieved. There is no approved medication for treatment or prevention of this disease. CHB carries a significant risk of morbidity and mortality, especially in utero or in the first few months of life. The severity of autoimmune CHB is shown by a 20% global mortality rate and 64% of live births require pacemakers.[10] Identified factors for a poor prognosis of CHB include the following: hydrops fetalis, low heart rate (<50–55 beats/minute) or a sudden rapid drop in heart rate, endocardial fibroelastosis (EFE), dilated cardiomyopathy, valvular dysfunction, low birth weight, male sex, delivery at <34 weeks of gestation, and complications from prematurity or neonatal lupus. Hydrops and EFE are the only significant echocardiographic predictors of mortality.[5,11]

Unlike CHB, noncardiac symptoms of NLE usually resolve within a few months after birth. This disappearance of symptoms coincides with clearance of maternal antibodies from the child's circulation.

4. Conclusion

Autoimmune CHB is a severe, potentially life-threatening disorder associated with the passive transfer of maternal anti-SSA/Ro and anti-SSB/La autoantibodies. Anti-SSA/Ro and anti-SSB/La antibody-positive mothers should have serial echocardiography and obstetric ultrasonography performed from the early second trimester. Newborns should be delivered at an early stage of gestation if there is evidence of pericardial effusion, ascites, increasing ventricular ectopy, reduced ventricular shortening fraction, or AV valve regurgitation. Aggressive medical management after birth should be combined with pacemaker implantation in infants who do not respond to medical therapies alone.

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