CASE REPORT

Successful Preventive Treatment of Congenital Heart Block During Pregnancy in a Woman with Systemic Lupus Erythematosus with Anti-La/Ro Antibody

Vishwakarma Pratibha^{1,2} · Shankar Kundavi¹ · Varma R. Thangam¹ · S. Ramakrishnan³

Received: 29 December 2015 / Accepted: 9 January 2016 / Published online: 11 March 2016
© Federation of Obstetric & Gynecological Societies of India 2016

About the Author

Dr. Pratibha Vishwakarma MBBS, MS (Obst & Gynae), is currently doing Postdoctoral Fellowship in Reproductive Medicine (FNB) in Institute of Reproductive Medicine & Women's Health, Madras Medical Mission Hospital from National Board of Examination, Delhi. She presented a paper on "Ultrasonographic and endoscopic evaluation of infertile couple" in FOGSI conference in 2008 in Agra. She published a paper on "Ultrasonographic evaluation of infertile couple" in UPSCOG in 2009. She sent a case report on "Enlarged ovaries following IVF/ICSI as an etiology of obstructive uropathy resulting in acute renal failure" in Indian Journal of Clinical Practice.

Dr. Pratibha Vishwakarma, MBBS, MS (Obst & Gynae) is Post doctoral Fellow in Institute of Reproductive Medicine & Women's Health, Madras Medical Mission Hospital; Dr. Shankar Kundavi, DGO, DNB, MNAMS is Senior Consultant in Institute of Reproductive Medicine & Women's Health, Madras Medical Mission Hospital; Dr. Varma R. Thangam, PhD, FRCS, FRCOG is Medical Director in Institute of Reproductive Medicine & Women's Health, Madras Medical Mission Hospital; Dr. S. Ramakrishnan, DM, Rheumatology is Senior Consultant, Appolo Hospital, Chennai.

✉ Vishwakarma Pratibha
pratibha_vish@yahoo.co.in

¹ Institute of Reproductive Medicine and Women's Health, Madras Medical Mission Hospital, A-4, Dr. J.J. Nagar, Mogappair, Chennai, Tamilnadu 600037, India

² H. No. 16/c, Medimix Avenue, Kalaivannar Colony, Anna Nagar West Extension, Chennai, Tamilnadu 600101, India

³ Department of Rheumatology, Appolo Hospital, Chennai, Tamilnadu, India

Keywords Congenital heart block · SS-A antibodies · Immunoglobulin · Systemic lupus erythematosus

Introduction

Neonatal lupus syndrome (NLS) is a classic model of passively acquired autoimmunity. Congenital heart block (CHB) is a manifestation of NLS. Pregnant women whose sera contain anti-Sjögren's syndrome A (SSA)/Ro antibodies (in the presence or absence of anti-SSB/La antibodies) have a 1–7.5 % risk of having a child with third-degree CHB. The CHB presents as fetal bradycardia and cardiac failure, i.e., pericardial effusion and hydrops, after 16 to 24 weeks of gestation.

The recurrence rate of CHB ranges from 16 to 20 % in different series, and the prognosis is poor. About 31 % of involved children die and 71 % of deaths occur in the first

month of life because of heart failure. Sixty-seven percent of cases require pacemakers. The most important treatment is preventive, involving steroids, immunosuppressants, intravenous immunoglobulin (IVIG) and plasmapheresis during pregnancy before the critical period of cardiac development. Treatment response of established cases is poor, and the reversal of established heart block is rare. Other treatments are mostly symptomatic, including digitalis, beta-adrenergic agonists and inotropic agents. They are bridges to pacemaker treatment after birth and essential for the baby's survival.

Case Report

Mrs. X, 26 years old, G2P1L0, diagnosed as having systemic lupus erythematosus (SLE), attended our unit at 7 weeks of gestation with anti-Ro and anti-La positive. Her previous pregnancy ended with intrauterine fetal death due to cardiomegaly, complete heart block and pericardial effusion, and placental histopathology showed placental insufficiency. Unfortunately, she did not receive any advice from rheumatologist in her previous pregnancy. In present pregnancy, she was advised to take IV immunoglobulin once in every 3 weeks by the rheumatologist. Her initial evaluation of renal, thyroid and liver function was within normal limits. She had vitamin D deficiency and the same was corrected. Her first trimester screening was at low risk for T21, 18 and 13. Her thrombophilia profile was normal. She was started on low molecular weight heparin and Tab Ecosprin in view of previous placental insufficiency. Her blood pressure was within normal limits throughout the pregnancy. She had no skin lesion related to autoimmunity. She took IV immunoglobulin at 12, 15, 18, 21 and 24 weeks of gestation. Placental growth factor (PLGF) was 13.3 pg/ml. Anatomy scan and fetal echo at 21 weeks was normal. Doppler studies from 24 weeks of gestation onwards were abnormal with high resistance flow in both uterine and umbilical arteries. She was closely monitored with Doppler flow and growth. Steroids were given at 26 weeks for fetal lung maturity. Emergency LSCS was done at 31 weeks of gestation due to abnormal Doppler. She delivered a live female baby weighing 960 g, and cord gases were normal. Microscopic examination of the placenta showed congestion and focal calcification. Baby was in NICU and discharged when the baby gained weight and was 1.8 kg [1–4].

Discussion

CHB is the most severe manifestation of NLS and is associated with high morbidity and mortality. The frequency of CHB in a primigravida with positive antibodies

is 1–7.5 %; however, the recurrence rate is about 2–3 times higher, i.e., around 20 %. Risk factors for recurrence other than a previous child affected with CHB are positive anti-52-kd SSA/Ro and/or anti-SSB/La antibodies, and the presence of human leukocyte antigen-DR3 in the mother. Fifty-three percent of CHB is diagnosed between 16 and 24 weeks of gestation, and 24 % between 25 and 30 weeks. The fetus at risk should be closely followed with echocardiograms starting at 16–24 weeks of gestation and continuing thereafter, because this is the most prevalent period for detection of fetal bradyrhythmia. Incomplete heart block can be detected earlier by measuring the electrocardiogram equivalent of the PR interval by echocardiography. Myocarditis may be followed by CHB. Therefore, the detection of a pericardial effusion, decreased systolic ejection fraction, and biphasic Doppler flow in the inferior vena cava, suggesting probable myocarditis, may be deemed as early signs of CHB. The pathogenic mechanisms of CHB remain unclear. Maternal IgG is present in fetal circulation after 6–11 weeks of gestation, but the fetal concentration of total IgG remains low until week 17. It increases steadily to fourfold by 24 weeks of gestation and around eightfold by 32 weeks as the placental transfer becomes more efficient. The fetal heart reaches its functional maturity by 16 weeks of gestation. Most CHB is diagnosed after 16–24 weeks of gestation, and the earliest documented case of CHB in the absence of structural defects was diagnosed at 16 weeks of gestation. Therefore, the timing of fetal injury does not appear to be random, but rather occurs during a defined gestational period, after the fetus passively acquires maternal anti-SSA/Ro and/or anti-SSB/La antibodies.

There are probably two mechanisms by which these autoantibodies react with the fetal heart. First, direct interaction with cardiac ion channels due to crossreactivity is suggested by an inhibitory effect of anti-52-kd SSA/Ro antibodies on calcium fluxes across cell membranes. Second, the fetal intracellular antigens are translocated to the cell surface by physiologic apoptosis. In this manner, cognate maternal antibodies bind to these antigens (Ro/La) and inadvertently program an inflammatory response by macrophages. Repeated inflammation results in fibrosis. Therefore, the rationales for management are: to decrease maternal autoantibodies and then to decrease the placental transfer of these antibodies, and (2) to decrease the inflammation once it occurs and as early as possible before it leads to permanent fibrosis and irreversible CHB. The maternal autoantibodies are effectively decreased by IVIG and plasmapheresis. As in our case, cesarean section was performed at 31 weeks of gestation due to abnormal Doppler findings and growth restriction. IVIG has been used to decrease the transfer of maternal antibodies to the fetus. If the level of these pathogenic autoantibodies can be

decreased before or during the critical period of heart development, it may prevent the development of CHB. The recurrence rate of CHB is 1 in eight mothers treated with IVIG between 14 and 18 weeks of gestation. However, the 95 % confidence interval of the recurrence rate of CHB ranges from 0.3 to 53 %, which includes the possible recurrence rate of 15–20 %. Although the effectiveness of prevention cannot be demonstrated by few cases, short-term IVIG administration during the critical period of cardiac development may still provide the best chance to prevent the development of CHB.

In summary, our patient with lupus had previous pregnancy with CHB. Her subsequent pregnancy was treated with IVIG, and she delivered a healthy female baby without CHB. Although the risk of CHB in mothers with anti-SSA/Ro and anti-SSB/La antibodies is low, the recurrence rate is about three times higher. Whether CHB can be successfully prevented by IVIG remains to be determined. Nevertheless, IVIG administration is easy, convenient and well tolerated by the patient, and it may therefore be appropriate for high-risk patients. Frequent surveillance between 16 and 20 weeks of gestation and thereafter is required for at-risk pregnancies, as it may offer

a chance for early diagnosis and early treatment of CHB, and may improve the outcome of the fetus.

Compliance with Ethical Standards

Conflict of interest All authors declare no conflict of interest.

Ethical Statement This article does not contain any studies with human participants performed by any of the authors.

References

1. Askanase AD, Friedman DM, Copel J, et al. Spectrum and progression of conduction abnormalities in infants born to mothers with anti-SSA/Ro-SSB/La antibodies. *Lupus*. 2002;11:145–51.
2. Brucato A, Doria A, Frassi M, et al. Pregnancy outcome in 100 women with autoimmune diseases and anti-Ro/SSA antibodies: a prospective controlled study. *Lupus*. 2002;11:716–21.
3. Congenital Fetal Heart Block: a potential therapeutic role for intravenous immunoglobulin Brucato, Antonio; Ramoni, Véronique; Gerosa, Maria; More. *Obstet Gynecol*. 117(1):177 (2011).
4. David AL, Ataullah I, Yates R, et al. Congenital fetal heart block: a potential therapeutic role for intravenous immunoglobulin. *Obstet Gynecol*. 2010;116(Suppl. 2):543–7. doi:[10.1097/AOG.0b013e3181e75a4a](https://doi.org/10.1097/AOG.0b013e3181e75a4a).