

Serial Echocardiography to Prevent Major Immune-Mediated Heart Disease in the Fetus: Results of a Risk-Based Prospective Surveillance Strategy

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Background: Exposure of the fetus to maternal autoantibodies (AB) is the main etiology of congenital complete heart block (CHB) and endocardial fibroelastosis (EFE). Because of the perception that these immune-mediated conditions may be preventable if detected and treated at an early disease stage, weekly fetal echocardiographic surveillance during the period of highest fetal risk of complications has been advocated to all mothers with positive anti-Ro/La AB tests. In an earlier study, we found that all mothers of 40 children with immune-mediated CHB had high anti-Ro titers and concluded that serial assessments could be safely limited to women with these high levels. This prospective study examines the utility of this approach.

Methods: Included were referrals ≤ 22 gestational weeks for a positive maternal AB test from 2009-2014. At the baseline fetal echocardiogram, maternal anti-Ro sera titers were measured by ELISA and results graded as equivocal (group 1: anti-Ro < 8 U/ml), low-positive (group 2: 8-49 U/ml), or high-positive (group 3: ≥ 50 U/ml). Weekly echocardiograms to 24 weeks (no previous child with CHB or EFE) or 28 weeks (previously affected offspring) were recommended to group 3 mothers while a neonatal exam including an electrocardiogram was offered to all referrals. Chi-square, Fisher exact tests and the Student *t* test were used for intergroup comparisons.

Results: Of 232 mothers with 241 fetuses, 43 tested anti-Ro equivocal, 62 low-positive, and 127 high-positive. Numbers of fetal exams per patient were significantly less in group 1 and 2 (2; range: 1-7) when compared with group 3 (4; 1-21; $p < 0.001$). Immune-mediated heart disease, including CHB ($n=4$), incomplete heart block ($n=4$) and isolated EFE ($n=1$), was diagnosed in 9 (8%) group 3 fetuses with Ro-titers > 100 U/ml and none of the fetuses exposed to lower Ro-titers (odds ratio: 26.4; $p < 0.001$). Unlike CHB, incomplete block and EFE regressed with perinatal steroid and immunoglobulin therapy.

Conclusions: Restricting fetal echocardiography to women with high anti-Ro AB titers is safe and eliminated the need for ongoing exams in almost half of the referrals. Serial echocardiography allowed the detection of reversible immune-mediated cardiac injury in some but not all of our patients.