New Insights Into Fetal Atrioventricular Block Using Fetal Magnetocardiography*

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Routine fetal arrhythmia assessment typically involves the use of echocardiographic modalities that demonstrate mechanical events from which electrophysiological events are inferred (1). While M-mode and Doppler-based techniques have been used successfully to diagnose third-degree atrioventricular block (AVB), second-degree AVB, and, more recently, first-degree AVB, our evaluation has been limited to atrial and ventricular rates (2–4), gross P-R interval estimates using atrial-ventricular activity time intervals (5), and rarely detected ventricular ectopy. Although fetal electrocardiogram (ECG) has been shown to be more sensitive than echocardiogram-based techniques in detecting first-degree AVB in anti–Ro-positive pregnancies (6), it has limited use in the evaluation of fetal heart rates out of the normal range, is more difficult to acquire at 28 to 32 weeks, and involves signal averaging, all limiting its clinical application.

Fetal magnetocardiography, the magnetic analog of fetal ECG, is at this time the most effective means of assessing fetal rhythms. Through the work of Zhao et al. (7), it has provided new insight into the electrophysiological characteristics of fetal AVB. Their observations suggest fetal AVB with and without structural heart disease is far more complex than previously appreciated with complex changing rhythms and variable atrioventricular conduction in second-degree AVB, and abnormal QRS waveforms, co-existence of junctional and ventricular ectopy, and atrial and ventricular rate responsivity in third-degree AVB. Fetal magnetocardiography, however, requires a magnetically shielded facility and is available in very few centers. Furthermore, Zhao et al. (7) studied patients for 50 to 100 min at a time, longer duration than is typical of fetal echocardiography. Still, these new observations should prompt a search for perhaps more practical tools to evaluate electrophysiological events in fetal AVB that will ultimately improve the care of affected pregnancies.

In normal pregnancies, fetal heart rate variability and accelerations associated with fetal activity increase with gestation (8,9) coinciding with maturation of the autonomic nervous system. In contrast, reduced fetal heart rate variability and accelerations particularly within lower heart rate ranges (10,11) occur in intrauterine growth restriction and chronic fetal hypoxemia. This has been used clinically to identify the fetus at greatest risk for sudden demise as a consequence of an inability to acutely adapt to changing physiological conditions. That many fetuses with isolated AVB have atrial and ventricular beat-to-beat variability and responsivity (7) suggests similar autonomic control exists, at least at higher ventricular rates. A ventricular rate of <56 beats/min has been previously identified as a perinatal mortality risk factor in fetal third-degree AVB (2,3). Zhao et al. (7) document that while atrial responsivity exists at ventricular rates of <56 beats/min, there is less ventricular beat-to-beat variability, which does not change even when rates increase above 56 beats/min with beta sympathomimetic therapy. This suggests affected fetuses may be less able to adapt to acute physiological demands, which could lead to sudden fetal demise with or without hydrops. Clinically, this should prompt more frequent assessment, perhaps in-patient monitoring and even earlier delivery when the fetus with third-degree AVB and ventricular rates of ≤56 beats/min reaches a viable gestational age.

The outcome of maternal autoantibody-induced AVB has improved over the past 2 decades (12). However, more diffuse myocardial inflammation and fibrosis with decreased myocardial function observed in 15% to 20% of affected fetuses remains an important risk factor for fetal hydrops and perinatal mortality and may evolve postnatally (4,13). While Zhao et al. (7) did not identify any fetus with reduced ventricular function or endocardiofibroelastosis (often underappreciated by echocardiography [13]), the presence of significant ventricular ectopy and wide QRS escape rhythms could be in keeping with more diffuse disease, which may have been ameliorated by corticosteroids (12).

Despite improved outcomes in immune-mediated fetal AVB, the perinatal mortality of third-degree AVB and structural heart disease remains high, particularly for the largest subset of affected fetuses with left atrial isomerism (2,14). Lower ventricular rates (2), severe structural heart disease (15,16), and intrinsic myocardial pathology (16) all contribute to the evolution of hydrops in AVB and left atrial isomerism. Sudden fetal demise without hydrops has also been observed in this subset of fetuses (14). Zhao et al. (7) documented nonreactive, monotonous ventricular rates in all fetuses with structural heart disease and third-degree AVB, which likely contributes to the sudden intrauterine

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deaths. Differences in heart rate variability (7) and response to terbutaline (17) between maternal autoantibody-induced AVB and AVB with structural heart disease suggest a fundamental difference in the nature of the conduction system in these conditions, which is also supported by histological observations (18).

Zhao et al. (7) observed the presence of junctional ectopic tachycardia (JET) in 26% of the fetuses with third-degree AVB with and without structural heart disease, all requiring pacing at birth. While not previously reported in any fetal series, it has been documented postnatally in case reports and small case series (19,20). Villain et al. (19) described patients with third-degree AVB and JET, 5 of whom died suddenly, with autopsy-confirmed focal degeneration of the atrioventricular node. More recently, Dubin et al. (20) described 5 patients with congenital JET and third-degree AVB associated with maternal anti-Ro or anti-La antibodies (1 from Zhao et al. [7]). Junctional ectopic tachycardia and AVB may be a spectrum of injury to the atrioventricular node where partial injury is associated with enhanced automaticity with JET and more complete injury results in third-degree AVB and slower, nonreactive heart rate patterns.

How do the findings of Zhao et al. (7) correlate with prior studies of AVB diagnosed after birth? Earlier investigations on third-degree AVB have focused on minimum, maximum, and average daily heart rates to identify patients at higher risk for sudden death and determine indications for permanent pacing, with no details regarding heart rate variability (21,22). In a recent report evaluating 24-h Holters in patients with congenital third-degree AVB, Vukomanovic et al. (21) showed that low maximum and average daytime heart rates were important risk factors for Adams-Stokes attacks and heart failure. Junctional ectopic tachycardia and significant ventricular ectopy were not documented. Differences found in the prenatal and postnatal series could suggest Zhao et al. (7) has captured a unique window in time in the evolution of AVB. Their observations not only identify important predictors of perinatal outcome, but also offer insight into the dynamic disease process of fetal AVB that may no longer exist later in the disease.

Although we have begun to better understand the complexity of fetal AVB, future work is necessary to fully elucidate its pathogenesis, improve prenatal counseling, identify the pregnancy for which fetal intervention may be indicated, and facilitate development of more appropriate and effective perinatal and neonatal management strategies.

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