Transient Fetal Atrioventricular Block: A Series of Four Cases and Approach to Management

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Abstract

Fetal atrioventricular block (AVB) is a failure of conduction from atria to ventricles. Immune- and non-immune-mediated forms occur, especially in association with congenital heart disease. Second-degree (2°) AVB may be reversible with dexamethasone and IVIG in immune-mediated disease. However, once third-degree AVB develops, it is deemed irreversible with need for a pacemaker and risk for cardiomyopathy. Rarely, 2° AVB is a transient, benign phenomenon in the immature conduction system. Few case series of transient AVB have been reported, but a management approach has not been defined. We report four patients with self-resolving, non-immune fetal AVB and outline a management strategy.

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Abstract :

Fetal atrioventricular block (AVB) is a failure of conduction from atria to ventricles. Immune- and non-immune-mediated forms occur, especially in association with congenital heart disease. Second-degree (2°) AVB may be reversible with dexamethasone and IVIG in immune-mediated disease. However, once third-degree AVB develops, it is deemed irreversible with need for a pacemaker and risk for cardiomyopathy. Rarely, 2° AVB is a transient, benign phenomenon in the immature conduction system. Few case series of transient AVB have been reported, but a management approach has not been defined. We report four patients with self-resolving, non-immune fetal AVB and outline a management strategy.

Key Words: Fetal atrioventricular block, Fetal heart block, Fetal second-degree atrioventricular block, Long QT syndrome

Introduction :

Fetal atrioventricular block (AVB) is estimated to occur in ˜ 1: 20,000 live births[1]. It occurs in immune- and non-immune-mediated forms[1-6]. Immune-mediated block develops from transplacental passage of maternal anti-Ro/SSA autoantibodies that, beginning in the second trimester, damage the fetal AV node[1]. Complete (third-degree) immune-mediated AVB is considered irreversible and has significant associated mortality (15-30%) and morbidity, with about two-thirds of infants requiring permanent pacing postnatally[2-4]. Non-immune AVB most often occurs in the setting of complex structural heart disease, such as left atrial isomerism (LAI) and congenitally-corrected transposition of the great arteries (ccTGA), in which discontinuity of the AV node and ventricular tissue causes complete heart block[5, 6].

There are a few case reports of non-immune-mediated fetal AVB without structural heart disease, with variable outcomes. Some reports describe hydrops or permanent pacing in most patients[7]. Other reports describe transient AVB without significant long-term complications[8-11]. We describe four patients, evaluated in the Vanderbilt University Medical Center fetal cardiology clinic from 2016-2020, with benign, self-resolving, non-immune-mediated, second-degree (2°) fetal AVB and outline a management approach.

Case Presentations (Table 1):

Patient A was initially evaluated by pediatric cardiology at 20 1/7 weeks gestational age (wga) for fetal bradycardia noted that same day on 20-wga anatomy scan, with persistent heart rates of 72-78 beats per minute (bpm). The fetal heart rate was 163 bpm on a 12 wga ultrasound. Fetal echocardiogram (echo) demonstrated regular atrial rates of 146-152 bpm and ventricular rates of 75-80 bpm in a pattern consistent with 2:1 2° AVB. The echo was otherwise normal. Due to concerns for immune-mediated heart block, we initiated dexamethasone but discontinued this therapy when maternal anti-Ro/SSA and anti-La/SSB antibodies were negative; of note, this treatment strategy was used for all the cases reported in this series. Follow-up ultrasound at 21 6/7 wga demonstrated a normal heart rate and rhythm of 163 bpm. Weekly ultrasounds until 25 wga and then every few weeks through the remainder of pregnancy confirmed normal rate and rhythm. A female infant was delivered at 39 2/7 wga via emergency c-section for prolonged heart rate deceleration and maternal chorioamnionitis; Apgar scores were 2, 4, 8. Postnatal EKG demonstrated sinus rhythm with a normal QTc interval; telemetry monitoring demonstrated intact AV conduction. Postnatal echo confirmed a structurally normal heart.

Patient B was initially seen at 19 1/7 wga for bradycardia noted on routine obstetrical evaluation at 19 wga. Fetal echo confirmed a structurally normal heart and 2:1 2° AVB with atrial rates of 145-162 bpm and ventricular rates of 72-75 bpm. The pregnancy was also notable for selective reduction of a twin with trisomy 21. Follow-up echo at 21 1/7 wga demonstrated atrial and ventricular rates of 146-155 bpm with a normal mechanical PR interval. Weekly obstetrical fetal heart rate assessments were normal through 25 4/7 wga, at which time a follow-up echo also confirmed normal rate and rhythm. The mother was returned to routine obstetrical monitoring. A female infant was delivered at term (37 5/7wga) at another hospital; a postnatal EKG was recommended.

Patient C (**Figure 2)** was diagnosed with multiple fetal anomalies (open neural tube defect with hydrocephalus, horseshoe kidney, echogenic bowel, anorectal malformation, 2-vessel umbilical cord) at 25 1/7 wga and referred to pediatric cardiology for right > left ventricular size discrepancy and ventricular septal defect. The initial fetal echo demonstrated a left superior vena cava to coronary sinus and suspected coarctation of the aorta; the fetal heart rate was 138 bpm with a normal mechanical PR interval. However, during an ultrasound in the Maternal Fetal Medicine Center 2 hours later, fetal AVB was suspected. An urgent, repeat fetal echo confirmed 2° AVB with atrial rates of 130-140 bpm and ventricular rates of 65-70 bpm. There was also a brief period of sinus bradycardia (92 bpm) with first-degree AVB (mechanical PR interval 160-180 msec). A follow-up fetal heart rate/rhythm check the next day was normal (137 bpm). A repeat echo at 25 4/7 wga confirmed atrial and ventricular rates of 129-141 bpm with a normal mechanical PR interval. Weekly

fetal heart rate checks for 4-6 weeks and follow-up echos at 31 1/7 wga and 35 1/7 wga demonstrated normal rate and rhythm. A male infant was born at 37 wga via c-section for spontaneous rupture of membranes with an open neural tube defect; he was confirmed to have a large lumbar meningomyelocele and CHARGE syndrome. Postnatal echo confirmed bilateral superior vena cavae, bicuspid aortic valve, and long-segment coarctation of the aorta, for which he underwent aortic arch augmentation at 1 month of age. Although his post-operative course was complicated by an accelerated junctional rhythm, his EKGs and telemetry monitoring otherwise demonstrated sinus rhythm and normal QTc intervals.

Patient D was found to have bradycardia on obstetrical anatomy ultrasound at 18 6/7 wga. Fetal echo the following day (19 wga) confirmed 2° AVB with atrial rates of 150-158 bpm and ventricular rates of 73-77 bpm. Follow-up obstetrical ultrasound at 21 wga demonstrated atrial and ventricular rates of 144 bpm; fetal rate and rhythm remained normal for the duration of pregnancy. A female infant was born at term (40 1/7wga) via an uncomplicated vaginal delivery. Postnatal EKGs demonstrated sinus rhythm with normal QTc intervals.

Discussion :

Fetal immune-mediated AVB is well understood and is known to be associated with maternal anti-Ro/SSA antibodies that can irreversibly damage the developing AV node and injure the myocardium[1-4]. However, AVB is often diagnosed in women who do not know they have anti-Ro/SSA antibodies[12]. Disease onset mostly commonly occurs between 16 and 26 wga; diagnosis after 28 wga is rare[1]. The transition between sinus rhythm and complete AVB may be as short as 12 hours[13]. Children with third-degree AVB require lifelong cardiac pacing; there is also risk for developing cardiomyopathy with need for heart transplantation[1-4]. However, anti-Ro/SSA-mediated 2° AVB treated rapidly with dexamethasone and intravenous immunoglobulin (IVIG) has been shown to be reversible[13].

Differentiating transient, non-immune mediated AVB from anti-Ro/SSA-mediated AVB is critical, as the therapeutic window for anti-Ro/SSA-mediated 2° AVB is short[13]. The differential diagnosis also includes AVB from LQTS, myocarditis, ccTGA or LAI and blocked atrial bigeminy[14-20].

Transient, fetal non-immune mediated AVB has rarely been described in the setting of normal intracardiac anatomy and appears to be benign. There have been a few prior case reports of fetal AV block[8-11] that self-resolved in a similar time frame to our reported cases. In our cases, there were no structural cardiac abnormalities that led to malformation of the fetal conduction system.

The mechanism of transient, non-immune fetal AVB remains poorly understood; some suggest it may be a vagally-mediated phenomenon in the immature conduction system, which has a preponderance of parasympathetic tone[8]. All reported cases demonstrate complete and permanent resolution within a couple of weeks[8-11]. In the absence of maternal anti-Ro/SSA antibodies, it is reasonable to monitor fetuses who are otherwise well without intervention. A management approach is detailed below (**Figure 3**).

Careful analysis with fetal echo includes rhythm evaluation and screening for structural heart disease. Simultaneous pulse Doppler assessment of the mitral inflow and aortic outflow, the superior vena cava and aorta, or the pulmonary artery and pulmonary vein can be used to determine the atrial and ventricular relationship and to measure the mechanical PR interval; M-mode and color M-mode can supplement this assessment[14]. Hepatic vein Doppler can be used to determine if there is a regular or irregular atrial rate and to confirm that the rhythm does not represent blocked atrial bigeminy, characterized by a "short-long-short-long" atrial interval and a variable atrial rate[20, 21]. Second-degree AVB is characterized by a regular atrial interval and rate[20]. Structural analysis should exclude ccTGA or LAI[5, 6] and evaluate for other echo signs that may suggest anti-Ro/SSA-mediated disease or myocarditis[12, 22-25]. It is also important to measure the isovolumic relaxation time (IVRT), which is prolonged in LQTS[15], and surveil for other LQTS arrhythmias, including ventricular tachycardia, torsade de pointes, and persistent sinus bradycardia, defined by fetal heart rate below the third percentile for gestational age[17-19].

Upon initial diagnosis of fetal AVB, maternal screening for autoimmune disease includes testing for maternal

anti-Ro/SSA antibodies and careful clinical evaluation for signs/symptoms of autoimmune disease, which is often unrecognized prior to detection of fetal AVB[12]. Dexamethasone should also be considered pending anti-Ro/SSA results given the risks of rapid progression of anti-Ro/SSA-mediated 2° AVB. This can be discontinued if anti-Ro/SSA antibodies are negative. Maternal thyroid studies can also be obtained, as maternal thyroid disease may also impair fetal cardiac conduction[26]. Parental EKGs, as well as inquiries into a family history of long QT syndrome, seizures, syncope, cardiac arrest, or sudden unexplained death encompass a complete screening for LQTS or other inherited channelopathies[17]. Maternal avoidance of QT prolonging medications should also be considered until the fetal diagnosis is made[17].

Once a diagnosis of fetal AVB is made, home fetal heart rate monitoring can be an empowering tool for ongoing fetal assessment[27, 28]. At least weekly fetal heart rate assessment, by the obstetrician or the cardiologist, is recommended until AVB resolves and should be considered for at least four subsequent weeks to exclude recurrence, which is not typical for transient, benign AVB[11]. A follow-up fetal echo in 2-4 weeks can be used to confirm resolution of AVB, with additional fetal echos during the remainder of pregnancy as needed to support obstetrical assessment. In our patients, we chose to repeat a fetal echo at ˜35-36 wga to confirm normal fetal heart rate and rhythm prior to delivery. Fetal magnetocardiography can be considered for more precise determination of fetal cardiac conduction and evaluation for channelopathies; but this currently has limited availability[14-16]. A postnatal EKG completes the assessment.

Conclusion :

Transient, benign 2° AVB is a rare phenomenon that occurs in the second trimester of pregnancy and is a diagnosis of exclusion. Key management approaches include careful screening for anti-Ro/SSA mediated AVB and LQTS, evaluation for structural heart disease, close in utero monitoring for self-resolution, and postnatal EKG.

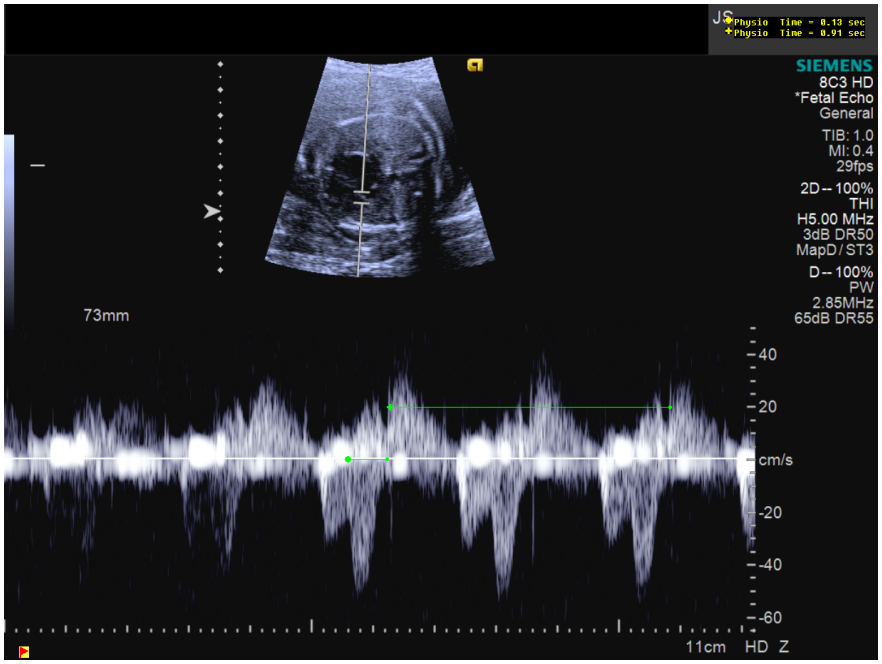
Table 1 . Summary of Cases of Transient Second-Degree Atrioventricular Block

	Patient A	**Patient B**	**Patient C**	**Patient D**
WGA at Diagnosis	20 1/7	18 5/4	25 1/7	18 6/7
WGA at Resolution	21 6/7	21 1/7	25 2/7	21 0/7
Gravida/ Para	G1P0	G3P2	G5P3	G3P2
Maternal age (years)	26	39	37	21
Atrial Rate (bpm)	146-152	145-152	130-140	150-158
Ventricular Rate (bpm)	75-80	72-75	65-70	73-77
Parental ECG	Normal	Normal	Normal	Normal
Maternal Thyroid studies	Normal	Normal	Normal	Normal
Maternal Medications	Prenatal Vitamin	Prenatal Vitamin	Prenatal Vitamin	Prenatal Vitamin
Postnatal EKG	Normal	Normal	Normal	Normal
Other			CHARGE Syndrome	

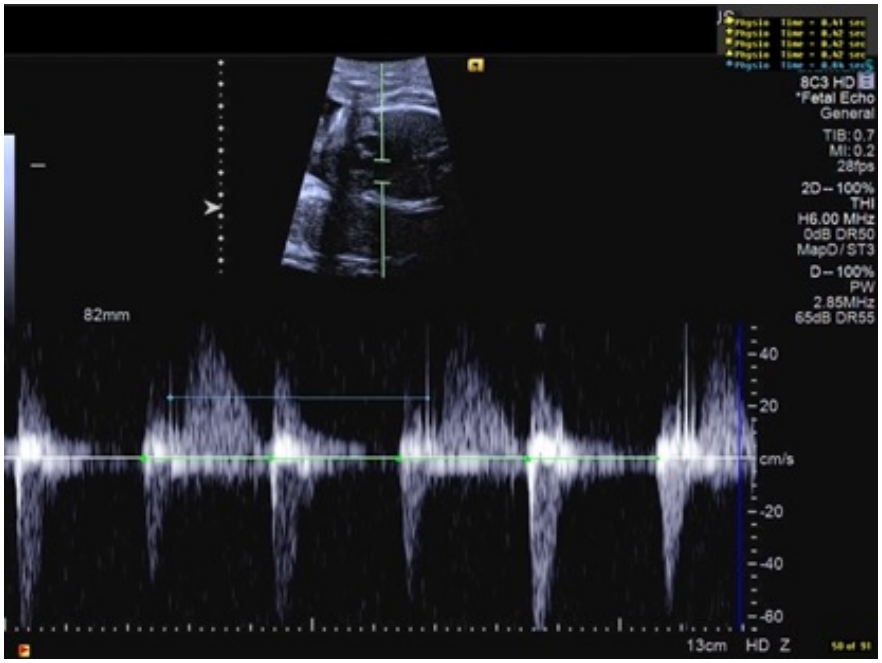
Figure 2 . Fetal echocardiography images from case 3 with Doppler and M-mode showing second-degree atrioventricular block with 2:1 AV conduction. (A) On initial consult for fetal right > left ventricular size discrepancy and probable coarctation of the aorta there was sinus rhythm at 138 bpm with mechanical PR=130 msec (B-D) On follow up, there was 2:1 AV conduction with regular atrial rates of 130-140 bpm

and ventricular rates 65-70 bpm, as demonstrated by mitral inflow-aortic outflow Doppler [B], color M-mode [C], and hepatic vein Doppler [D], confirming regular atrial rates. (E) There was also a brief period of sinus bradycardia (92 bpm) with PR prolongation/first-degree AV block (mechanical PR interval 160-180 msec) (F-G) At next clinical follow ups, there was normal fetal heart rate and rhythm of 129-141bpm

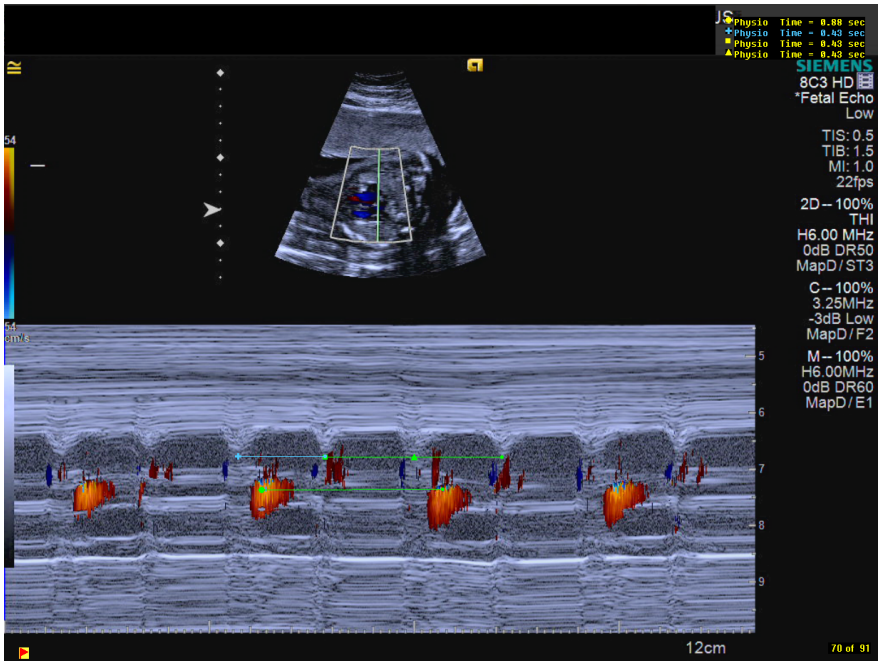
(A)



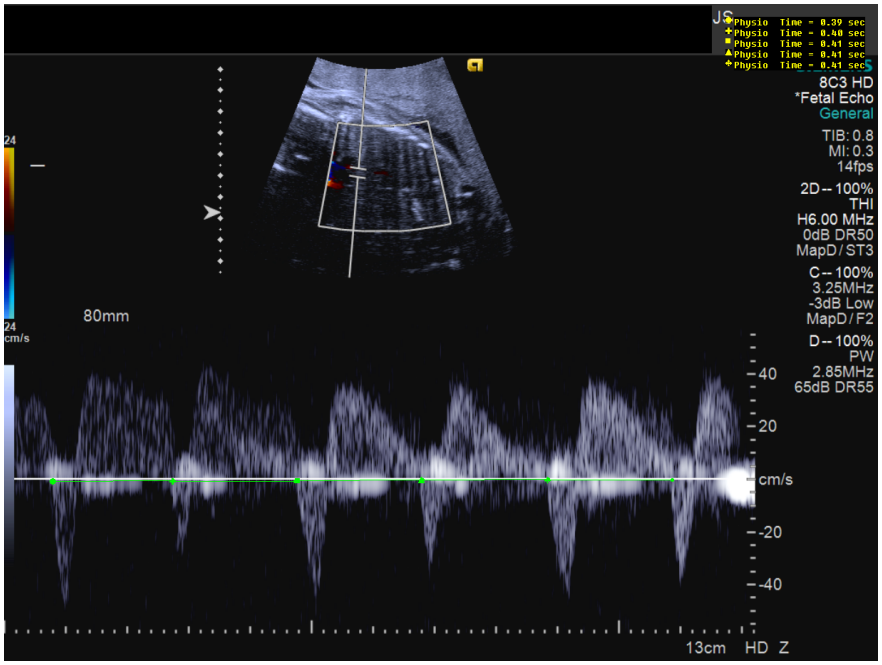
(B)



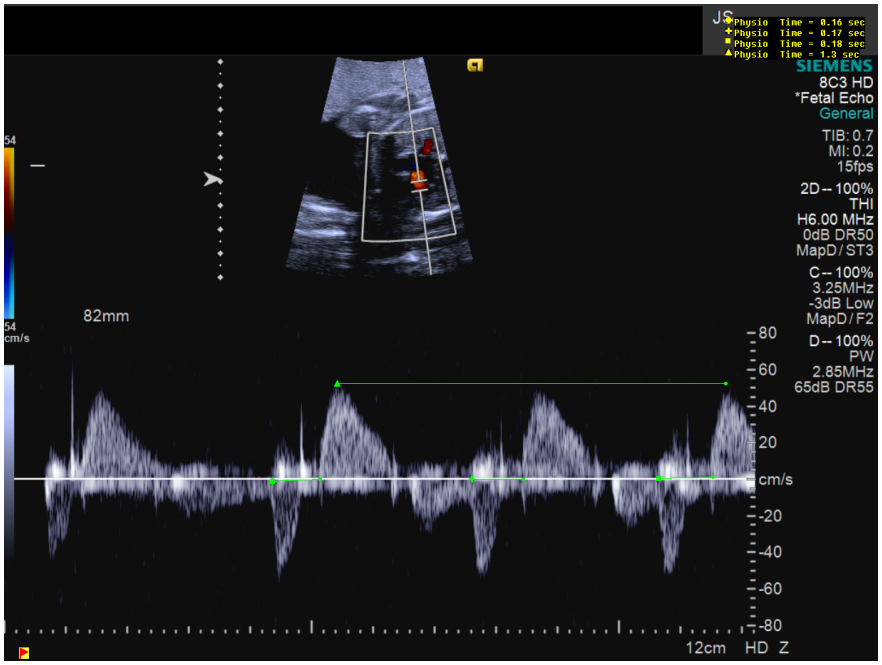
(C)



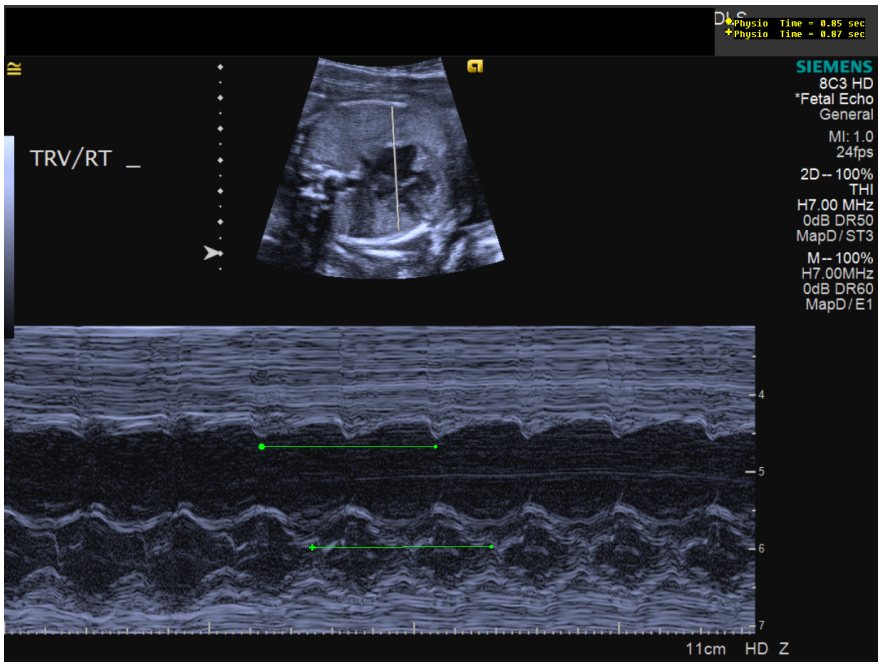
(D)



(E)



(F)



(G)

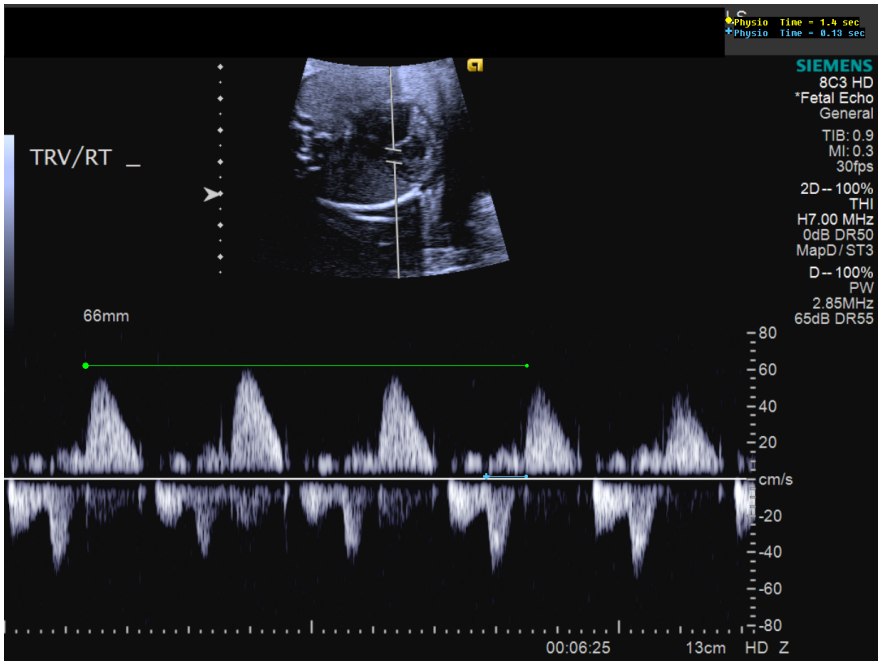


Figure 3. Suggested Management Approach for Fetal Second-Degree Atrioventricular Block

References:

1. Buyon, J.P., et al.,*Autoimmune-associated congenital heart block: demographics, mortality, morbidity and recurrence rates obtained from a national neonatal lupus registry.* J Am Coll Cardiol, 1998. **31** (7): p. 1658-66.

2. Brucato, A., F. Franceschini, and J.P. Buyon, *Neonatal lupus: long-term outcomes of mothers and children and recurrence rate.* Clin Exp Rheumatol, 1997. **15** (5): p. 467-73.

3. Julkunen, H., et al.,*Isolated congenital heart block: fetal and infant outcome and familial incidence of heart block.* Obstet Gynecol, 1993.**82** (1): p. 11-6.

4. McCune, A.B., W.L. Weston, and L.A. Lee, *Maternal and fetal outcome in neonatal lupus erythematosus.*Ann Intern Med, 1987. **106** (4): p. 518-23.

5. Machado, M.V., et al., *Fetal complete heart block.* Br Heart J, 1988. **60** (6): p. 512-5.

6. Gembruch, U., et al., *Fetal complete heart block: antenatal diagnosis, significance and management.*Eur J Obstet Gynecol Reprod Biol, 1989. **31** (1): p. 9-22.

7. Berg, C., et al.,*Atrioventricular block detected in fetal life: associated anomalies and potential prognostic markers.* Ultrasound Obstet Gynecol, 2005. **26** (1): p. 4-15.

8. Newbury, A. and M. Fahey,*Resolution of fetal second-degree atrioventricular block.* J Electrocardiol, 2018. **51** (6): p. 945-947.

9. Friedman, D.M., et al.,*Benign fetal bradycardias diagnosed by echocardiography.* Am J Perinatol, 1995. **12** (2): p. 87-90.

10. Breur, J.M., et al.,*Transient non-autoimmune fetal heart block.* Fetal Diagn Ther, 2005. **20** (2): p. 81-5.

11. Chang, Y.L., et al.,*Perinatal outcome of fetus with isolated congenital second degree atrioventricular block without maternal anti-SSA/Ro-SSB/La antibodies.*Eur J Obstet Gynecol Reprod Biol, 2005. **122** (2):

p. 167-71.

12. Wainwright, B., et al.,*Autoimmune-mediated congenital heart block.* Best Pract Res Clin Obstet Gynaecol, 2020. **64** : p. 41-51.

13. Cuneo, B.F., S.E. Ambrose, and W. Tworetzky, *Detection and successful treatment of emergent anti-SSA-mediated fetal atrioventricular block.* Am J Obstet Gynecol, 2016. **215** (4): p. 527-8.

14. Donofrio, M.T., et al.,*Diagnosis and treatment of fetal cardiac disease: a scientific statement from the American Heart Association.* Circulation, 2014.**129** (21): p. 2183-242.

15. Clur, S.B., et al., *Left Ventricular Isovolumetric Relaxation Time Is Prolonged in Fetal Long-QT Syndrome.* Circ Arrhythm Electrophysiol, 2018. **11** (4): p. e005797.

16. Strasburger, J.F., B. Cheulkar, and R.T. Wakai, *Magnetocardiography for fetal arrhythmias.* Heart Rhythm, 2008. **5** (7): p. 1073-6.

17. Cuneo, B.F., J.F. Strasburger, and R.T. Wakai, *The natural history of fetal long QT syndrome.* J Electrocardiol, 2016. **49** (6): p. 807-813.

18. Mitchell, J.L., et al.,*Fetal heart rate predictors of long QT syndrome.* Circulation, 2012. **126** (23): p. 2688-95.

19. Winbo, A., et al., *Third trimester fetal heart rate predicts phenotype and mutation burden in the type 1 long QT syndrome.* Circ Arrhythm Electrophysiol, 2015.**8** (4): p. 806-14.

20. Eliasson, H., M. Wahren-Herlenius, and S.E. Sonesson, *Mechanisms in fetal bradyarrhythmia: 65 cases in a single center analyzed by Doppler flow echocardiographic techniques.* Ultrasound Obstet Gynecol, 2011.**37** (2): p. 172-8.

21. Saemundsson, Y., et al.,*Hepatic venous Doppler in the evaluation of fetal extrasystoles.*Ultrasound Obstet Gynecol, 2011. **37** (2): p. 179-83.

22. Brito-Zeron, P., et al.,*The clinical spectrum of autoimmune congenital heart block.* Nat Rev Rheumatol, 2015. **11** (5): p. 301-12.

23. Hornberger, L.K. and N. Al Rajaa,*Spectrum of cardiac involvement in neonatal lupus.* Scand J Immunol, 2010. **72** (3): p. 189-97.

24. Nield, L.E., et al.,*Maternal anti-Ro and anti-La antibody-associated endocardial fibroelastosis.* Circulation, 2002. **105** (7): p. 843-8.

25. Krishnan, A., et al.,*Outcomes of fetal echocardiographic surveillance in anti-SSA exposed fetuses at a large fetal cardiology center.* Prenat Diagn, 2014.**34** (12): p. 1207-12.

26. Spence, D., et al.,*Increased risk of complete congenital heart block in infants born to women with hypothyroidism and anti-Ro and/or anti-La antibodies.* J Rheumatol, 2006. **33** (1): p. 167-70.

27. Cuneo, B.F., et al., *Home Monitoring for Fetal Heart Rhythm During Anti-Ro Pregnancies.* J Am Coll Cardiol, 2018. **72** (16): p. 1940-1951.

28. Cuneo, B.F., et al., *Heart sounds at home: feasibility of an ambulatory fetal heart rhythm surveillance program for anti-SSA-positive pregnancies.* J Perinatol, 2017. **37** (3): p. 226-230.