Classic and atypical Wenckebach periodicity in a late gestation fetus with maternal anti-Ro/SSA antibodies

Melanie R.F. Gropler, MD,* Johannes von Alvensleben, MD,* D. Woodrow Benson, MD, PhD, † Bettina F. Cuneo, MD*

From the *Division of Cardiology, Department of Pediatrics, Children’s Hospital Colorado, University of Colorado School of Medicine, Aurora, Colorado, and †Medical College of Wisconsin, Milwaukee, Wisconsin.

Introduction

Atrioventricular (AV) block occurring between 18 and 25 weeks of gestation is the most common expression of maternal anti-Ro/SSA antibody–mediated fetal cardiac disease. Over 90% of affected fetuses present with irreversible third-degree AV block and normal QRS duration and require lifelong cardiac pacing. However, anecdotal reports identify progression from first- to second- to third-degree AV block over several hours to several days. Other prenatal arrhythmias have been reported, including ventricular ectopy, junctional ectopic tachycardia, sinus bradycardia, and atrial flutter. The clinical variability of anti-Ro/SSA antibody–mediated cardiac disease is reflected in the histopathology, which can demonstrate varying degrees of inflammation and fibrosis not only of the AV node, but also of the sinoatrial node, the right and left bundle branches, and the atrial and ventricular endocardium.

When observed as a manifestation of anti-Ro/SSA antibody–mediated fetal cardiac disease, second-degree AV block can present with bradycardia (type 2 second-degree AV block) and/or irregular rhythm (type 1 second-degree AV block). Irregular rhythm resulting from progressive prolongation of the PR interval prior to a nonconducted atrial beat is deemed classic Wenckebach periodicity. On the other hand, atypical Wenckebach periodicity, characterized by irregular sequential changes in the PR interval including both increments and decrements prior to the blocked beat, occurs more frequently after birth.

We report the unusual case of a fetus of an anti-Ro/SSA antibody–positive pregnancy who presented late in the third trimester with prolonged QRS duration and varied manifestations of AV block. The late gestational age at presentation and the detailed features of the conduction abnormality of this case expand the spectrum of anti-Ro/SSA antibody–mediated fetal conduction system disease.

Case report

A 29-year-old G3P1011 healthy and asymptomatic African American woman in the 36 5/7th week of an uncomplicated...
pregnancy presented with an irregular fetal heart rhythm. There was no known family history of congenital heart disease, inherited arrhythmia syndrome, or rheumatologic disease. The woman’s first pregnancy ended in miscarriage and the second resulted in a healthy liveborn.

The fetal echocardiogram at 36 5/7 weeks showed a structurally normal heart with an atypical Wenckebach periodicity (type 1 second-degree AV block), characterized by the AV interval prolonging over 2 beats, shortening with the third beat, and ending with a nonconducted atrial beat (Figure 1). The ventricular rate was 130–144 beats per minute (bpm). An infectious etiology was considered, but polymerase chain reaction of maternal serum for enterovirus, cytomegalovirus, parvovirus, Epstein-Barr, Toxoplasma and human herpesvirus 6 were negative.

One week later, at 37 5/7 weeks, the atypical Wenckebach periodicity was still intermittently present, but the majority of the time, the fetal heart rhythm was type 2 second-degree AV block with 3:1 conduction and a ventricular rate of 51 bpm (Figure 2). Although biventricular systolic function was subjectively normal and endocardial fibroelastosis was absent, mild-to-moderate tricuspid regurgitation and right atrial and ventricular dilation had developed. Maternal anti-Ro/SSA 52 and 60 antibodies were positive at, respectively, 175 AU/mL and 58 AU/mL (negative range < 29 AU/mL; ARUP Laboratories, Salt Lake City, UT).

Owing to the rapid decrease in ventricular rate from 130–144 to 51 bpm, findings of cardiac dysfunction, and near-term gestation (37 5/7 weeks), the decision was made to proceed with a cesarean delivery that day. A vigorous 3.17 kg female infant was delivered with Apgar scores of 7 and 7 and a heart rate of 60–100 bpm. The initial electrocardiogram demonstrated type 2 second-degree AV block with 3:1 conduction, a prolonged QRS duration, and a ventricular rate of 55 bpm (Figure 3A). Taken together, these electrocardiogram findings were consistent with both AV node and distal conduction system disease. The QT interval was also prolonged (509 ms), probably owing to the abnormal depolarization. A postnatal echocardiogram showed mild biventricular dilation and dysfunction and mild-to-moderate mitral insufficiency.

Because of the cardiac dysfunction and maternal anti-Ro/SSA antibodies, the infant received intravenous immunoglobulin, 1 g/kg, and intravenous methylprednisolone (30 mg/kg). In addition, a low-dose epinephrine infusion (0.03 μg/kg/min) was given. On epinephrine, the ventricular rate increased from 55 to 95 bpm, and the rhythm reverted to that seen at 36 5/7 weeks of gestation: type 1 second-degree AV block with atypical and classic Wenckebach periodicity (Figure 3B and 3C). However, in both patterns, the first PR interval was the shortest. Like the rhythm tracing in Figure 3A, the QRS duration was prolonged, suggestive of a block between the atrioventricular node and bundle of His.
of static distal conduction system disease. However, unlike Figure 3A, the morphology of the QRS complex in Figure 3D was variable, suggesting additional His-Purkinje conduction abnormalities. Besides prolonged and varying QRS morphology, Figure 3D also shows another example of atypical Wenckebach periodicity.

Although the epinephrine infusion initially improved left ventricle systolic function and decreased mitral insufficiency, systemic perfusion worsened and lactic acidemia developed on day 2 of life. The ventricular rates decreased from 95 to 40–50 bpm and the rhythm reverted to sustained type 2 second-degree AV block with 3:1 to 4:1 AV conduction.
Despite an isoproterenol infusion, the ventricular rate remained <50 bpm and the lactic acidemia did not improve, so the infant was taken to the operating room and a dual-chamber epicardial bipolar pacemaker was implanted. With dual-chamber pacing, ventricular function had normalized by the end of postoperative day 1. The infant did well and was discharged to home at 12 days of life. An ophthalmologic examination did not identify pigmentary retinopathy and genetic testing eliminated the possibility of the mitochondrial disorder Kearns-Sayre syndrome.

**Discussion**

The global incidence of anti-Ro/SSA antibody–mediated AV block is estimated to be 1 in 20,000–30,000 live births. Most cases, >80%, are immutable third-degree AV block with a normal QRS duration. In comparison, second-degree AV block is transient, and detection is uncommon. For example only 10% of affected fetuses in the registry for neonatal lupus were born with second-degree AV block; type 1 and type 2 second-degree AV block were not distinguished. In our case, the presentation with second-degree AV block at almost 37 weeks of gestation and the failure of second-degree AV block to progress to third-degree AV block were both unusual features. About 80% of fetuses with anti-Ro/SSA antibody–related AV block present before 30 weeks of gestation, while only 2% present at term or as neonates. In the absence of a fetal echocardiogram performed before 36 weeks of gestation, we cannot exclude the possibility that first-degree AV block was present before that time, as first-degree AV block presents as a regular rhythm with normal fetal heart rate.

Another unusual feature of this case is the presentation with atypical Wenckebach periodicity. Type 1 second-degree AV block, or “classic” Wenckebach periodicity, is defined as a single, nonconducted sinus P wave following progressive PR prolongation and is easily recognized by Doppler echocardiography. “Atypical” Wenckebach, characterized by irregular sequential behavior of the PR interval, has not, to the authors’ knowledge, been previously reported in the fetus. Atypical Wenckebach includes cases with variable PR interval increments or decrements where the PR interval may shorten in the middle of the classic-type sequence or even at the end just prior to the blocked beat. In either the classic or atypical form, the PR interval after the blocked beat should always shorten, as it did in the current case. This finding helps to differentiate atypical Wenckebach type 1 second-degree AV block from other fetal arrhythmias.

Type 1 second-degree AV block with a normal QRS complex typically occurs when inflammation and fibrosis are limited to the AV node. The finding of a wide QRS complex, however, is more consistent with infranodal disease. There is scant literature describing the incidence of infranodal anti-Ro/SSA antibody–mediated disease, but it has been described in both live-born and postmortem studies. We speculate that the development of significant cardiac dysfunction in our case relates to the relatively rapid fall in fetal heart rate from 130–144 to 50 bpm, as well as distal conduction system disease, since cardiac function improved significantly after pacing.

**Conclusion**

While AV block secondary to maternal anti-SSA/Ro antibodies most commonly presents as third-degree AV block with normal QRS duration and develops between 18 and 25 weeks’ gestation, the potential to present with atypical features in the third trimester should be considered. In addition, not all type 1 second-degree AV block follows classic Wenckebach periodicity, and atypical Wenckebach periodicity should not be confused with other fetal rhythms. Lastly, distal conduction system disease may contribute to cardiac dysfunction. Vigilant monitoring of fetal rhythm with detection of even subtle rhythm abnormalities is crucial to identify rapid progression to unstable rhythms.

**References**

1. Izmirly P, Kim M, Friedman DM, et al. Hydroxychloroquine to prevent recurrent congenital heart block in fetuses of anti-SSA/Ro-positive mothers. J Am Coll Cardiol 2020;76:292–302.
2. Saxena A, Izmirly P, Mendez B, Buyon JP, Friedman DM. Prevention and treatment in utero of autoimmune-associated congenital heart block. Cardiol Rev 2014;22:263–267.
3. Zhao H, Cuneo BF, Strasburger JF, Huhta JC, Gotteiner NL, Wakai RT. Electro-physiological characteristics of fetal atrioventricular block. J Am Coll Cardiol 2008;51:77–84.
4. Jaeggi ET, Chitayat D, Taylor G. Atrial standstill associated with loss of atrial myocytes: a rare cause of fetal bradyarrhythmia. Heart Rhythm 2009;6:1370–1372.
5. Ho SY, Escher E, Anderson RH, Michaelsson M. Anatomy of congenital complete heart block and relation to maternal anti-Ro antibodies. Am J Cardiol 1986;58:291–294.
6. Barold SS. Type I Wenckebach second-degree AV block: a matter of definition. Clin Cardiol 2018;41:282–284.
7. Barold SS. Lingering misconceptions about type I second-degree atrioventricular block. Am J Cardiol 2001;88:1018–1020.
8. Denes P, Levy L, Pick A, Rosen KM. The incidence of typical and atypical A-V Wenckebach periodicity. Am Heart J 1975;89:26–31.
9. Brito-Zeron P, Izmirly PM, Ramos-Casals M, Buyon JP, Khamashta MA. The clinical spectrum of autoimmune congenital heart block. Nat Rev Rheumatol 2015;11:301–312.
10. Buyon JP, Hiebert R, Copel J, 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;31:1658–1666.
11. Barold SS, Herweg B. Second-degree atrioventricular block revisited. Herz–chirurgischer Elektrophysiol 2012;13:296–304.
12. Llanos C, Friedman DM, Saxena A, et al. Anatomical and pathological findings in hearts from fetuses and infants with cardiac manifestations of neonatal lupus. Rheumatology (Oxford) 2012;51:1086–1092.
13. Cuneo BF, Strasburger JF, Nitsch A, Ovadia M, Wakai RT. An expanded phenotype of maternal SSA/SSB antibody-associated fetal cardiac disease. J Matern Fetal Neonatal Med 2009;22:231–238.
14. Conen D, Adam M, Roche F, et al. Premature atrial contractions in the general population: frequency and risk factors. Circulation 2012;126:2302–2308.