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

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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.[1] However, anecdotal reports identify progression from first- to second- to third-degree AV block over several hours to several days.[2,3] Other prenatal arrhythmias have been reported, including ventricular ectopy, junctional ectopic tachycardia, sinus bradycardia, and atrial flutter.[3,4] 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.[5]

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 or decrements prior to the blocked atrial beat, occurs more frequently after birth.[6–8] 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 second-degree 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.

KEY TEACHING POINTS

- Although the most common presentation of fetal anti-Ro/SSA antibody–mediated conduction system disease is bradycardia and third-degree atrioventricular (AV) block detected at 18–25 weeks of gestation, less common forms of AV block can manifest as an irregular rhythm in the third trimester.
- Atypical Wenckebach periodicity, characterized by irregular sequential changes in the PR interval, including both increments and decrements prior to the blocked beat, is an unusual manifestation of fetal anti-Ro/SSA–mediated type 1 second-degree AV block but is common after birth.
- Type 1 second-degree AV block with a wide QRS complex commonly involves infranodal conduction disease. These cases may present with ventricular dysfunction.
- While progression from first-degree to second-degree to third-degree AV block usually occurs over several hours to days, this case failed to progress from second-degree to third-degree block over 1 week and highlights the need to remain suspicious of anti-Ro/SSA–mediated conduction disease in irregular fetal rhythms throughout pregnancy.

Case report

A 29-year-old G3P1011 healthy and asymptomatic African American woman in the 36 5/7th week of an uncomplicated

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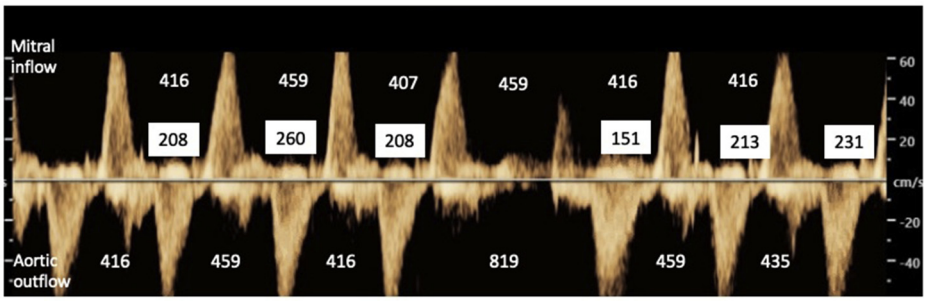

Figure 1 Fetal spectral Doppler showing atypical Wenckebach periodicity in type 1 second-degree atrioventricular (AV) block at 36 5/7 weeks. Mitral inflow (*above baseline*) / aortic outflow (*below baseline*) spectral Doppler. There is fusion of mitral E and A waves. From left to right: The AV interval (*white boxes*) prolongs from 208 to 260 ms, then shortens to 208 ms prior to the nonconducted atrial beat (atypical Wenckebach periodicity). Atrial cycle length (*top row of numbers*) is variable, but the shortest is >80% of the average cycle length, suggesting absence of premature atrial contractions.[14] Ventricular cycle length ranges from 416 to 819 ms (*bottom row of numbers*).

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

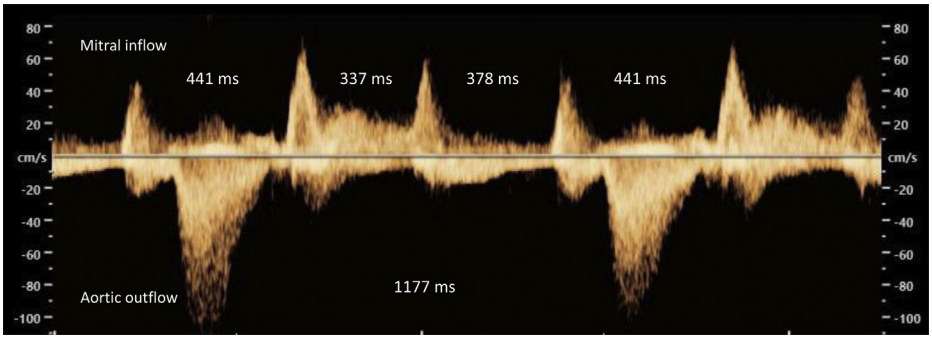

Figure 2 Fetal Doppler showing type 2 second-degree atrioventricular (AV) block with 3:1 AV conduction at 37 5/7 weeks. Spectral Doppler of mitral inflow (*above baseline*) and aortic outflow (*below baseline*). These tracings were 1 week later than those shown in Figure 1. Variability in atrial cycle length (*top row of numbers*) is similar to that shown in Figure 1. Ventricular cycle length is 1177 ms (*bottom row of numbers*).

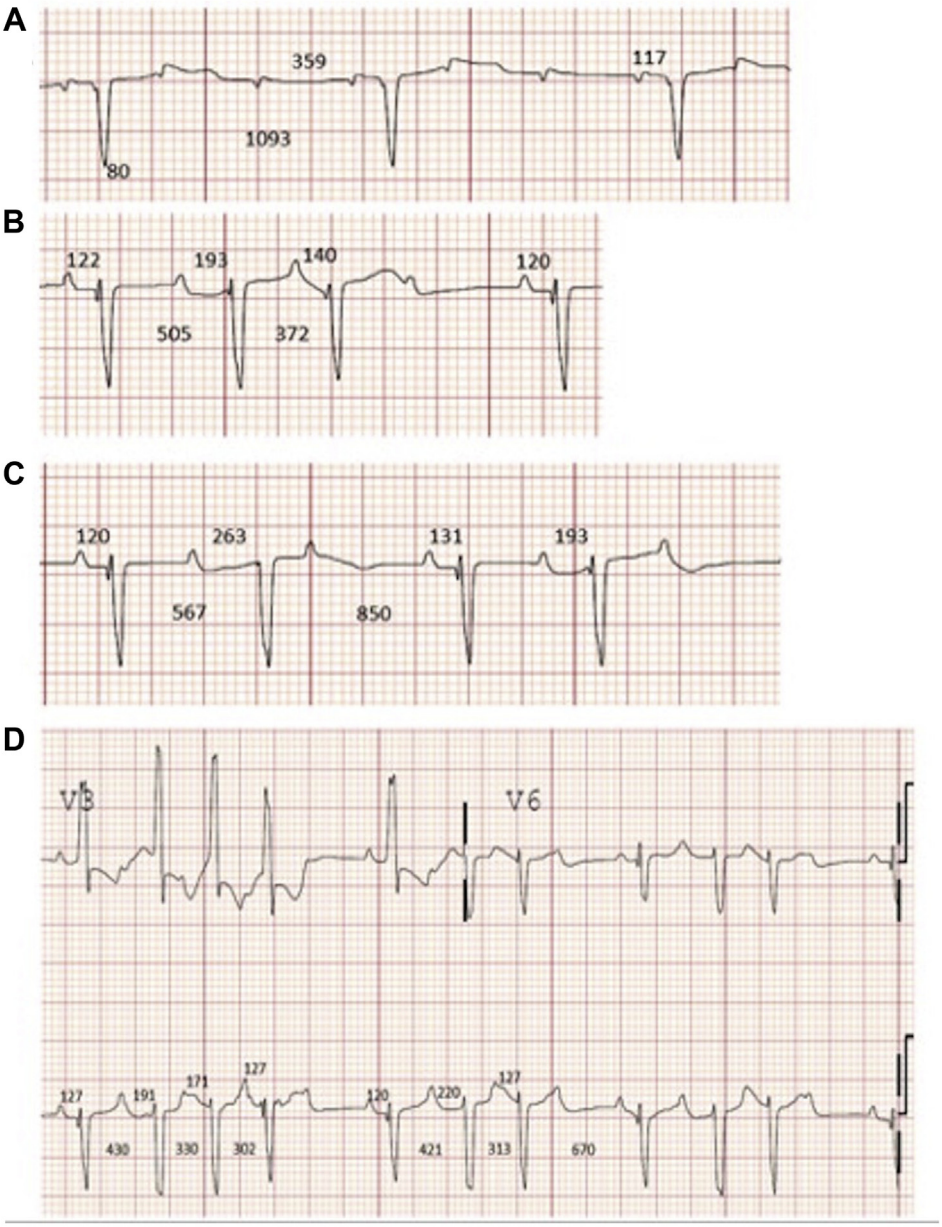

Figure 3 Postnatal rhythm tracings. **A:** Lead II rhythm tracing on day of life 0. Type 2 second-degree atrioventricular block with 3:1 conduction. The QRS is prolonged (80 ms). The PR interval of the conducted beat is 117 ms. The atrial and ventricular cycle lengths are 359 ms and 1093 ms, respectively. This 3:1 conduction pattern was also seen during the fetal echocardiogram (Figure 2). **B:** Lead II rhythm tracing from day of life 1. Atypical Wenckebach periodicity with PR interval (*above baseline*) initially lengthening from 122 to 193 ms, then shortening to 140 ms prior to nonconducted atrial beat. Ventricular cycle lengths are labeled *below baseline*. **C:** Lead II rhythm tracing from day 1 of life. Two episodes of classic Wenckebach periodicity are shown. In the first, the PR interval (*above baseline*) increases from 120 to 263 ms prior to the nonconducted atrial beat. In the second episode, the PR interval prolongs from 131 to 193 ms before the nonconducted atrial beat. In both B and C, the QRS complexes are wide, and the first PR interval of the group is always the shortest PR interval of the grouping. Ventricular cycle lengths are labeled *below baseline*. **D**: Leads V_3, V_6, and II on day of life 1. Atypical Wenckebach periodicity with a prolonged QRS duration are once again noted. The variable QRS morphology is more obvious than in panel C. The atrial cycle length is 350 ms. The PR intervals are labeled *above baseline* and ventricular cycle lengths *below baseline*.

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.[9] 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[10]; 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.[10] 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.[6] 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.[7,11] 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.[12,13] 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.

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