Congenital long QT syndrome: A challenging diagnosis by fetal echocardiography

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ABSTRACT

The diagnosis of long QT syndrome (LQTS) *in utero* presents many challenges for clinicians, and there is high risk for intrauterine fetal demise as life-threatening arrhythmias develop secondary to QT prolongation. We describe a challenging case of a fetus presenting with sinus bradycardia and second-degree atrioventricular block with episodes of ventricular tachycardia. A prenatal diagnosis of LQTS was suspected given the fetal echocardiographic findings of a short ventricular relaxation time, due to extremely prolonged refractory period. The patient was delivered emergently due to Torsade's with hydrops, with ongoing arrhythmia despite medical management requiring implantation of pacemaker and sympathectomy. Early recognition of LQTS is important to optimize fetal survival with prompt medical management.

Keywords: Channelopathy, echocardiography, fetal arrhythmia, prenatal diagnosis

INTRODUCTION

Congenital long QT syndrome (LQTS) is a relatively rare but important clinical disorder, with a prevalence of approximately 1 in 2500 live births.[1] It is most often inherited in an autosomal dominant pattern and associated with increased risk of cardiac arrhythmias.[2] Mutations in cardiac potassium and sodium ion channels result in prolongation of the QTc interval on electrocardiogram, subsequently leading to life-threatening arrhythmias. Over 75% of cases described occur due to mutations in three major genes, involving potassium (KCNQ1 and KCNH2) and sodium ion channels (SCN5A).[3] Identifying the genetic etiology of LQTS allows for risk stratification and tailored therapy regimen.[3] This is particularly important as LQTS, when untreated can often lead to sudden cardiac death.[1]

The prenatal diagnosis of LQTS is particularly challenging and often delayed as findings on routine evaluation with ultrasound are often subtle. Nevertheless, abnormalities in fetal heart rate, in particular, fetal bradycardia, should prompt a more comprehensive evaluation by pediatric cardiologist as these can indicate underlying cardiac pathology.[4] Congenital LQTS should be suspected when there is echocardiographic evidence of intermittent episodes of ventricular tachycardia and prolonged myocardial contraction. Careful planning should be done for close follow-up to manage any intrauterine arrhythmias that could lead to fetal demise.

CASE REPORT

A healthy 35-year-old female with good prenatal care had presented to routine prenatal visit at 14 weeks gestation and was found to have incidental fetal bradycardia on evaluation. Close monitoring of fetal heart rate was continued by her primary physician with serial ultrasounds. Repeat ultrasound at 18 weeks' gestation showed fetal heart rate in the low range of normal at 110 beats/min (bpm). Given persistent bradycardia, she was referred to pediatric cardiology for evaluation with fetal echocardiogram. Initial fetal echocardiogram at 22 weeks

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and 6 days' gestation showed normal-chamber dimensions and good ventricular function and noted episodes of sinus bradycardia, with heart rates ranging between 108 and 120 bpm. On follow-up, routine evaluation by primary physician at 31 weeks and 6 days' gestation ultrasound revealed episodes of heart rate variability between 207 and 298 as well as a 3-mm pericardial effusion and right ventricular hypertrophy. Given fetal cardiac concerns, she was referred for repeat fetal echocardiogram.

At 32 weeks and 2 days' gestation, fetal echocardiogram showed a heart rate variability between 40–260 bpm with intermittent periods of ventricular tachycardia and premature ventricular contractions (PVCs) [Figures 1 and 2]. Segmental fetal cardiac anatomy was normal, and a small anterior pericardial effusion was noted. Given fetal cardiac findings suggestive of prolonged QTc with Torsade's, the working diagnosis of congenital LQTS was established. She was referred to a tertiary center for management and intervention with a referring diagnosis of ventricular tachycardia and atrioventricular (A-V) block. At 32 weeks and 4 days' gestation, fetal 2:1 heart block with intermittent Torsade's developed. Intravenous magnesium was started for fetal arrhythmia. Fetal echocardiogram showed progressive hydrops, and due to concerns for fetal demise, the patient was delivered emergently via cesarean section.

Delivery was uncomplicated and APGAR scores were 8 and 9 at 1 and 5 min, respectively. Birth weight was 2495 g. The patient was breathing comfortably on room air and noted to be intermittently bradycardic to 70 bpm with frequent PVCs. Postnatal echocardiogram showed depressed cardiac function. Electrocardiography (ECG) was notable for extremely prolonged QTc to 653, functional 2:1 heart block, frequent ectopy, and intermittent ventricular tachycardia. A lidocaine bolus was given resulting in brief normalization of arrhythmias and resulted in a 1:1

A-V block. The patient was then noted to have recurrent episodes of polymorphic ventricular tachycardia. She was treated with a magnesium bolus, an additional lidocaine bolus and started on lidocaine 25 µg/kg/min and esmolol 25 µg/kg/min; however, the patient developed recurrent bradycardia and 2:1 A-V block. A decision was then made to take the patient to the operating room for placement of dual-chamber epicardial pacemaker and bilateral sympathectomy, with resolution of arrhythmia following the procedure [Figure 3]. Surgery was uneventful and followed by 2 days of monitoring in the cardiovascular intensive care unit (ICU). The patient was started on lidocaine, esmolol, vasopressin, calcium infusion, and phenylephrine infusion for 2 days. On postoperative day 7, the patient was transferred to the neonatal ICU. Serial ECG throughout hospitalization showed QTc ranging from 437 to 617. She was transitioned to a medication regimen with 8 mg of mexiletine three times per day and 2 mg of propranolol four times per day. Arrhythmia gene panel confirmed the final diagnosis of pathogenic variant identified in KCNH2 gene p.Gly628Ser (c.1882G>A) associated with autosomal dominant LQTS type 2. Mexiletine was increased to 9 mg four times per day with plans to slowly wean off, and she was continued on propranolol 2.3 mg every 6 h as main therapy. The patient was discharged home on day of life 28 with close follow-up by pediatric cardiology.

DISCUSSION

Fetal echocardiography is a noninvasive, cost-effective, and readily available method of assessing fetal cardiac function and diagnosing cardiac disease antenatally. This imaging modality has shown to be a useful tool in the early diagnosis of congenital LQTS, as well as in minimizing prenatal complications by allowing for prompt management and intervention.[5]
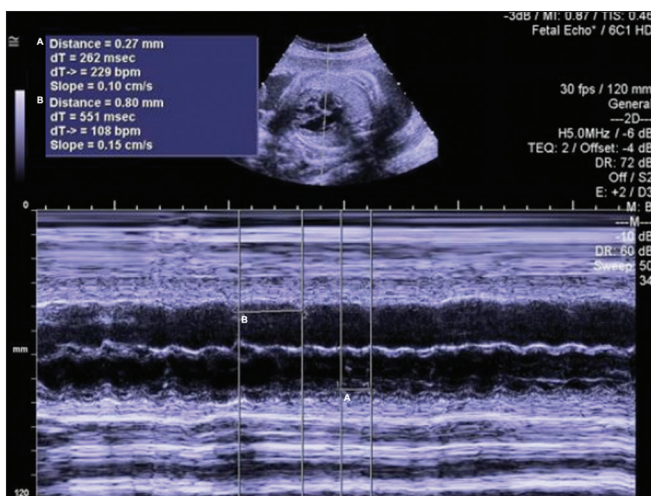

Figure 1: M-mode measurement of R-R interval showing 2:1 ventricular to atrial rate with a ventricular rate of 229 bpm (A), and an atrial rate of 108 bpm (B)
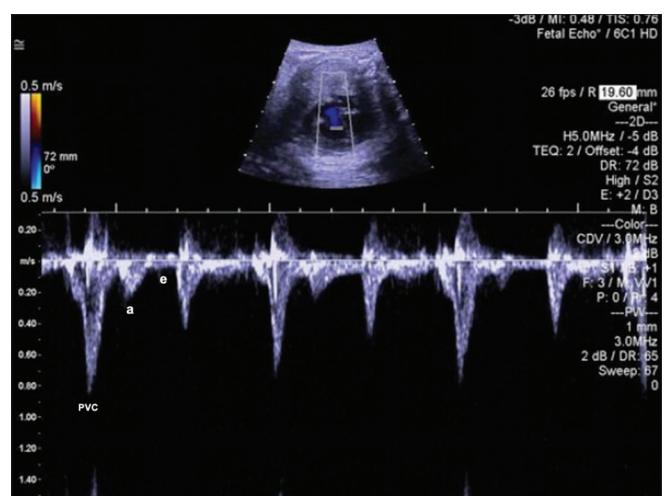

Figure 2: Fetal echocardiogram four-chamber view with pulse Doppler evaluation of tricuspid valve inflow showing e-wave, a-wave, and premature ventricular contraction
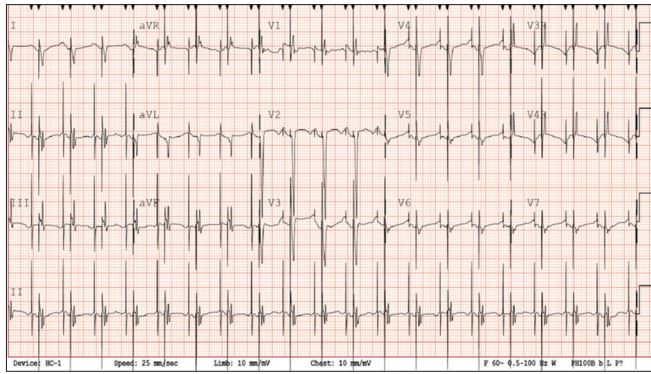
Figure 3: Electrocardiogram following surgical placement of dual-chamber pacemaker showing atrial-ventricular dual paced rhythm at a rate of 120 bpm

In the majority of cases, fetal sinus bradycardia, defined as fetal heart rate <110 bpm (or <3rd percentile for gestational age), is often the only fetal arrhythmia detected *in utero* on routine prenatal ultrasound and should prompt referral to pediatric cardiology for close monitoring with fetal echocardiography.[6,7] Specific markers noted on fetal echocardiogram evaluation can point clinicians toward diagnosing LQTS. In otherwise healthy fetuses with suspected LQTS, the cardiac anatomy is often normal; however, mechanical conduction can become aberrant, and this can be noted on echocardiography. M-mode detects transient episodes of ventricular tachycardia with variable cycle lengths, normal atrial rate and intermittent ventriculoatrial dissociation.[6] A rapid early contraction phase with slow contraction during the late thickening phase has been previously described in patients with LQTS.[8] In addition, tissue Doppler is a well-established and reliable method for cardiac function evaluation and can contribute key evidence to diagnosing congenital LQTS as it allows analyzing cardiac wall motion and myocardial velocities.[5] The characteristic findings for diagnosing congenital LQTS include evidence of a shortened mitral valve deceleration time, marked prolonged left ventricular isovolumetric relaxation time, and overall prolonged myocardial contraction duration.[5] Studies have shown that the duration of myocardial contraction, when compared to a simultaneously recorded fetal electrocardiogram, can be highly specific for LQTS as it strongly correlates to the QT interval on electrocardiogram.[5] These findings should prompt very close monitoring of fetal cardiac development.

The case described highlights the importance of early recognition of LQTS *in utero* as prenatal management of fetal arrhythmias can minimize the risk of life-threatening arrhythmias and sudden cardiac death. Patient outcome is highly correlated with early diagnosis. The first-line therapy for prenatal management of arrhythmias in patients with LQTS is pharmacologic treatment with beta-blocker for rate control. Patients with refractory arrhythmias warrant more invasive methods, which include pacemaker implantation, intra-cardiac defibrillator (ICD), and left cardiac sympathectomy.[9]

Our patient underwent sympathectomy and placement of dual-chamber epicardial pacemaker immediately after birth due to incessant life-threatening tachyarrhythmia, despite optimal pharmacologic management. Cardiac sympathectomy should be considered in patients who are at high risk for life-threatening arrhythmias but are not ideal candidates for an ICD (i.e. premature infants).[9] This procedure allows for a reduction in adrenergic stimulation, thereby reducing the risk of cardiac arrhythmias, and is often indicated in conjunction with the placement of pacing device. Further therapy with beta-blockers, such as propranolol, is often indicated following sympathectomy and pacing, to ensure rate control and optimize management of LQTS.[10]

Conflicts of interest

There are no conflicts of interest.

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