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Ventricular noncompaction and long QT syndrome – A deadly double hit for the foetus

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ABSTRACT

Congenital long QT syndrome [LQTS] is a channelopathy characterized by QT prolongation and polymorphic VT. LQTS however need not be a purely electrical disease. Defects in ion channels may cause myocardial architectural disruption leading to ventricular non compaction [VNC]. It is defined as the presence of prominent ventricular trabeculations and deep intertrabecular recesses within the endomyocardium. We describe the in-utero management of a foetus who was later found to have LQTS with VNC. The detection of ventricular tachycardia and complete heart block in utero should arouse the suspicion of LQTS. It would be wise to avoid QT prolonging antiarrhythmics in this subset of patients.

1. Introduction

Fetal arrhythmias occur in less than 0.6% of all pregnancies. Sustained tachyarrhythmia may be associated with foetal hydrops, neurological morbidity and intrauterine death. Echocardiography is the preferred method to diagnose the aetiology of the foetal tachyarrhythmia. Early recognition, accurate diagnosis, appropriate initiation of therapy and periodic monitoring are crucial for a favourable pregnancy outcome. We describe the management of a foetal tachyarrhythmia in a secondary level hospital.

2. Case presentation

A 21-year-old primigravida presented to us at 31 weeks of gestation. She had her prior antenatal check-ups in a primary care hospital. She had no febrile illness, collagen vascular disease, significant family history of foetal loss or sudden cardiac death.

On ultrasound it was noticed that there was a foetal tachyarrhythmia of 200–220bpm. There were no structural congenital cardiac anomalies and no associated hydrops. Biventricular contractility was sluggish. Placenta was anterior and upper segment in location and the amount of liquor surrounding the foetus was normal. The M mode image (Fig. 1) taken across the atrioventricular [AV] valve suggested AV dissociation. The ventricular wall motion was much faster than the AV valve opening. The ventricular rate being regular and faster than the atrial rate proved ventricular tachycardia [VT].

The prognosis was discussed with the couple and the mother was started on Sotalol 40mg twice a day. She was admitted and underwent daily ultrasound to assess foetal wellbeing and tachyarrhythmia control. The foetal heart rate came down to 110-120bpm the following day. The ECG for the mother was done daily for the first 3 days to ensure that the QT did not prolong. Three days later the foetal heart rate dropped to 70 bpm on clinical examination. The foetal scan suggested the presence of a heart block (Fig. 2) The Sotalol was then stopped for 48 hours and restarted at 20 mg bd. The foetal heart rate remained stable between 120 and 140 bpm with scan confirming sinus rhythm. She was followed up thereafter with twice weekly ultrasound scans to monitor the foetal heart rate and the liquor volume. Biventricular contractility did not improve despite the foetus being in sinus rhythm on follow up.

At 38 weeks the ultrasound showed decreased liquor and so it

Abbreviations: LQTS, Long QT Syndrome; VNC, Ventricular Non compaction; AV, Atrioventricular; VT, Ventricular tachycardia; ICD, Implantable Cardioverter Defibrillator.

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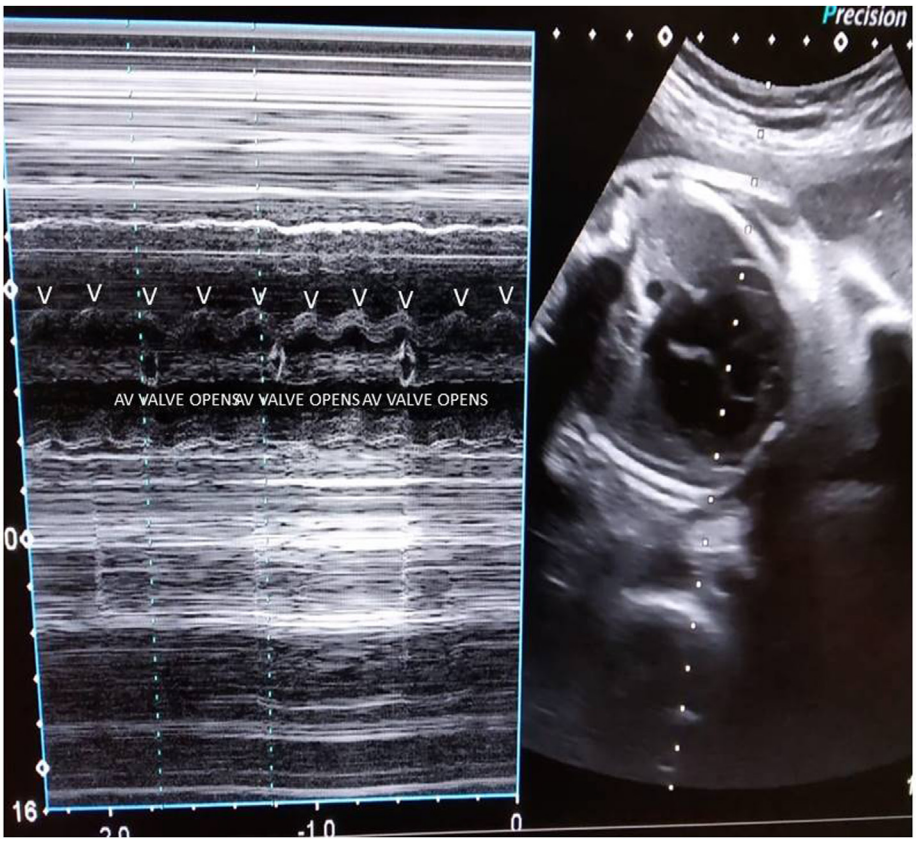

Fig. 1. Ventricular tachycardia with more ventricular systole [V] than atrioventricular [AV] valve opening.

was decided to induce her. She was induced with foleys catheter following which she went into labour. Monitoring during labour was challenging as CTG monitors were unable to consistently sense the foetal heart rate. We hence intermittently used the ultrasound machine. She delivered normally a 2.6 kg baby boy who cried at birth. The baby was shifted to nursery for monitoring and further investigations.

2.1. Investigations

The ECG of the baby showed a prolonged QTc of 620msec (Fig. 3A). Echocardiogram showed biventricular non compaction (Fig. 3B) with severe biventricular systolic and diastolic dysfunction. Holter was done which revealed multiple episodes of ventricular tachycardia [monomorphic (Fig. 3C) and polymorphic with torsade de pointes (Fig. 3D)] and intermittent high grade AV block (Fig. 3E). In view of the prolonged QTc Sotalol was stopped and Propranolol was started. A pacemaker was advised.

2.3. Outcome and follow UP

Unfortunately, despite counselling the parents opted for native medicine and the child expired four weeks later.

3. Discussion

Ultrasound by experienced personnel is crucial in diagnosing foetal cardiac rhythm. M mode and Doppler echocardiography are used to assess the relation between atrial and ventricular activation. Apart from aiding in assessing the foetal cardiac rhythm, foetal ultrasound is a must to exclude coexistent structural heart disease. It may also be used to monitor the foetus during labour when the CTG is unreliable. We were fortunate to have a Cardiologist who was easily reachable and could cross check the findings. This made it possible to manage this case in the secondary hospital setting.

VT is an uncommon arrhythmia in the foetus. VT in the foetus may be associated with structural heart disease or myocardial inflammation [1]. The inflammation may result from a myocarditis or be secondary to a cardiomyopathy. Myocardial hypertrophy secondary to ventriculoarterial valve stenosis can cause hypoxia leading to VT. Electrolyte abnormalities, cardiac tumours like hamartomas and extracardiac tumours adjacent to the heart can also result in foetal VT. Foetal ultrasound in our case showed decreased cardiac contractility which we initially thought was secondary to tachycardiomyopathy. However, its failure to improve after achieving apparent rhythm control in utero makes a cardiomyopathy more likely. The echo done after birth was typical of non-compaction cardiomyopathy.

Ventricular noncompaction [VNC] is an idiopathic rare congenital cardiomyopathy characterized by extremely prominent ventricular trabeculations and deep intertrabecular recesses. This disorder can affect both ventricles and causes ventricular dysfunction, arrhythmias, and systemic embolization. The reason for VNC being arrhythmogenic is still to be fully understood. The inter layer differentiation in VNC leads to a greater dispersion in repolarization [2]. Electrophysiologic studies have found prolonged QT with late potentials. VNC patients with arrhythmia were more likely to have SCN gene mutations which leads to channelopathies [3].

Long QT syndrome [LQTS] is a channelopathy characterized by prolonged ventricular repolarization and malignant arrhythmias. Unfortunately, LQTS cannot be proven in utero except with foetal

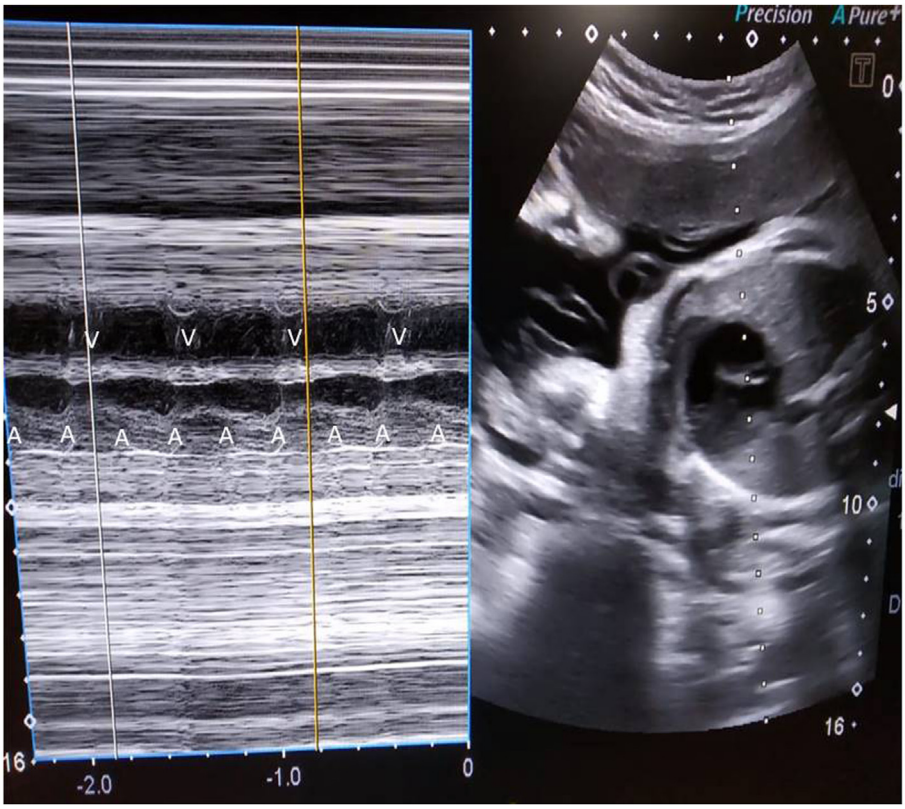

Fig. 2. Complete heart block with dissociation between atria [A] and ventricle [V] with more A than V.

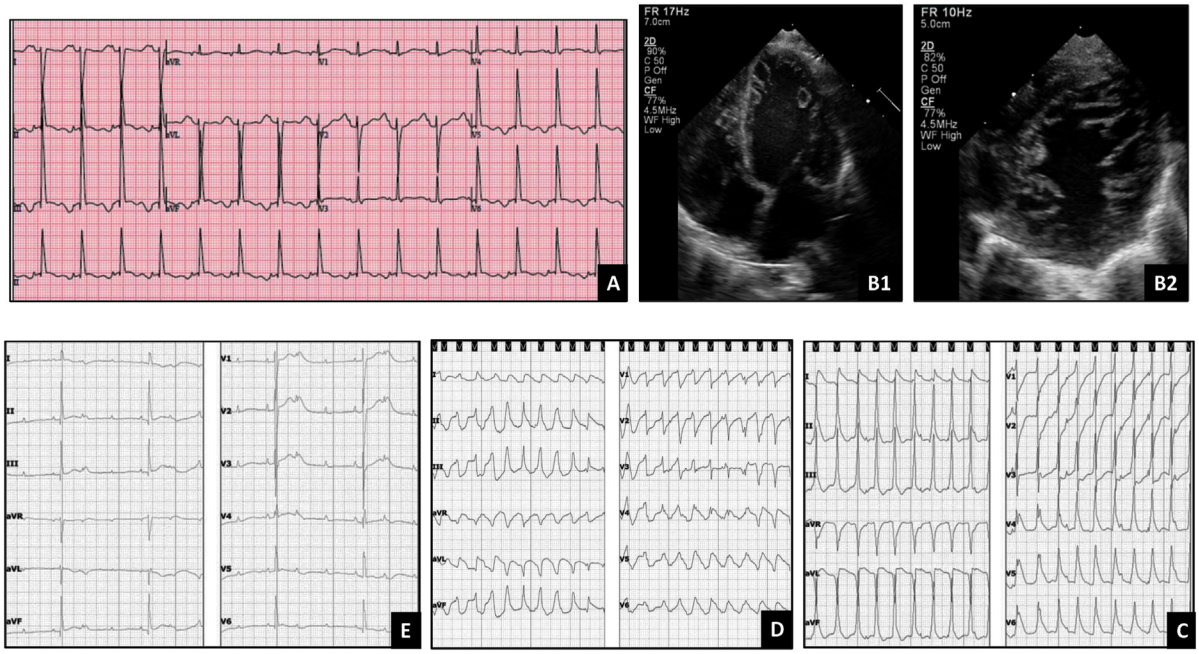

Fig. 3. [clockwise from above].
A – Electrocardiogram showing prolonged QTc of 620
B1 - Apical 4 chamber view showing a hyper-trabeculated Left Ventricle involving mainly the apical and mid segments. The Right Ventricle also appears more trabeculated than usual.
B2 – Short axis view showing obvious non-compaction of the Left Ventricle at the apical level involving all segments.
C – Monomorphic ventricular tachycardia.
D – Polymorphic ventricular tachycardia with torsade de pointes.
E – Electrocardiogram showing complete heart block.

magnetocardiography which is not routinely available for clinical use [4]. It was suspected since the baby's ECG a day after birth showed a prolonged QTc of 620msec. This was despite the child not having received any Sotalol since birth and mother having only received 20mg twice daily of the drug which is subtherapeutic. We resorted to this dose since it seemed to keep the VT in check while at the same time prevented complete heart block from happening. For foetal arrhythmias, the recommended maternal dosing is 80–160mg twice daily [5]. The dosage of Sotalol is titrated based on the maternal QT response to the drug [6]. It is highly unlikely for a subtherapeutic dose of Sotalol to cause QT prolongation in the foetus while it had little effect on the mother's ECG. Besides a QTc of 620msec the baby was also documented to have Torsade de pointes on Holter, making a Schwartz score of 5. A score of 4 or more suggests a definite diagnosis of LQTS [7].

The presence of AV block in patients with congenital LQTS is seen with mutations in HERG [LQT2], SCN5a [LQT3], CACNA1 [LQT8] and SCN4B [LQT10] [8]. It portends a poor prognosis [9]. The QT in this subset of patients is markedly prolonged in comparison to those with just LQT. This is seen in 5% of LQTS patients and manifests early as foetal bradycardia, hydrops or ventricular tachycardia [10]. LQTS with 2:1 AV block is often due to prolonged ventricular refractoriness, which inhibits alternate depolarizations. These p waves fail to conduct as they are inscribed within or before the T waves [11]. This pseudo-AV block is functional as proven by 1:1 conduction happening at lower heart rates. True AV conduction abnormalities account for the remaining cases. These patients may have a compromised distal conduction system secondary to fibrosis and probable apoptosis leading to a prolonged HV interval [9,12]. In our case as in Fig. 3E there was a high-grade AV block with p waves failing to conduct despite there being no physiological reason for the ventricle to be refractory.

LQTS however need not be a purely electrical disease. Defects in ion channels may disrupt myocardial protein architecture during development leading to VNC. KCNH2 mutation has been documented in 2 patients with LQT and VNC [13]. During mice embryonic development KCNQ1 channel expression coincides with the time of ventricular compaction [14]. A family with 4 members across 2 generations with LQT and VNC were found to have a pathogenic mutation in KCNQ1 [15].

Milder forms of VNC are associated with a mortality rate of 14% during 5–6 years of follow up, while those with RV involvement have a worse outcome [16]. Needless to say, VNC with LQT has a poor prognosis. If the arrhythmia was sustained there is a greater risk of hemodynamic compromise leading to hydrops fetalis and foetal demise. Since our patient had AV block, LQT and frequent runs of ventricular arrhythmias; treating the child with beta blockers and pacing would have helped reduce the QT and normalise the rhythm. Sometimes however VT that is poorly controlled coupled with a strong family history of sudden cardiac death warrants an implantable cardioverter defibrillator [ICD] [17]. ICD implantation in a neonate is difficult and often best avoided if pacing can suppress the arrhythmia and reduce the QT. However long-term RV pacing causes dyssynchrony and is known to lead to pacing induced cardiomyopathy. This is further hastened by the presence of VNC. Should that occur one has to resort to a biventricular pacing upgrade [18] or try physiological pacing involving the His bundle.

3. Conclusion

Management of foetal arrhythmias can be done in a low resource setting provided there is a Cardiologist who is readily reachable and a nearby tertiary care facility to refer the baby once it is born.

In addition to rhythm abnormalities the foetal scan also provides an opportunity to study the ventricular myocardium and detect VNC early.

Detection of VT and complete heart block at different times on foetal ultrasound should raise the suspicion of LQTS. QT prolonging antiarrhythmics like Amiodarone and Sotalol are best avoided in this setting.

VNC and LQTS can coexist and together portend a poor prognosis. This is further worsened if LQTS is associated with AV block.

Credit author statement

AGC: Clinical management and follow up, writing original draft.
PL: Draft review, clinical follow up.
JK: Draft review, clinical follow up.
JRJ: Clinical management, Draft writing, review and follow up.

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Declaration of competing interest

The authors declare no conflict of interests.

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