Complex electrocardiographic findings in a neonate with long QT syndrome

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A case of long QT syndrome diagnosed in the early neonatal period is described. A full-term male baby was delivered by cesarean section at 38 weeks of gestation. The indication to cesarean section was sudden marked fetal bradycardia. At birth, he presented the following rhythm disorders: a) an ectopic atrial rhythm with T wave alternans, and b) atrioventricular conduction disorders. Sinus rhythm, with a prolonged QT interval and T wave alternans, was recovered soon after birth, before starting beta-blocker therapy. The family history was negative for the long QT syndrome: sudden unexpected death and/or syncopal episodes and cases of congenital deafness have not been reported. Molecular screening of the five long QT syndrome-related genes did not reveal the presence of any mutation. At 3 years of follow-up, the child is well and he did not present with symptoms or arrhythmias during this period.

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Introduction

The congenital long QT syndrome (LQTS) is a genetic disorder characterized by a long QT interval on the surface ECG and by recurrent syncopal episodes due to "torsades de pointes" that may lead to sudden death[1]. In fetuses and neonates, LQTS may be associated with bradycardia with or without an impaired atrioventricular (AV) conduction[2-8]. In the present report we describe a case of fetal/neonatal LQTS complicated by AV conduction disorders and by an ectopic atrial rhythm. Such a clinical picture has not been previously reported. The clinical, ECG and genetic aspects will be reviewed.

Case report

A male baby was delivered by cesarean section at 38 weeks of gestation in a second level hospital. The indication to cesarean section was a sudden marked bradycardia diagnosed during routine fetal monitoring. Fetal echocardiography showed an irregular ventricular rate of 80-90 b/min and the apparent dissociation of atrial and ventricular contraction raised the suspicion of AV block. No signs of heart failure were demonstrated.

At birth, the Apgar scores were 7 (1st min) and 9 (5th min). The baby's skin was pink, and there were no apparent dysmorphic features. The baby had an irregular heart rate, but the respiratory rate was normal and there were no signs of a low cardiac output. The neonate's blood pressure and oxymetry were normal. The chest X-ray and the echocardiogram showed a normal cardiac anatomy and function. The auditory brain stem evoked potential was normal.

Surface electrocardiogram. At birth, 12-lead ECG showed an ectopic atrial rhythm (160 b/min) (negative P wave in lead I) associated with a prolonged ventricular repolarization wave (QTc 540 ms). The ectopic atrial rhythm was associated with phases of 2:1 AV conduction, alternating with 1:1 AV conduction (Fig. 1). When the AV conduction was 1:1 and the ventricular rate 160 b/min, T wave alternans was observed. Besides an ectopic atrial rhythm, the differential diagnosis could also include an AV nodal reentrant tachycardia or a junctional ectopic tachycardia with transient phases of 2:1 retrograde nodo-atrial block: however, the unusual P wave morphology (i.e., negative in lead I and positive in leads II, III and aVF) was not suggestive of such diagnoses.

Three hours after birth, a sinus rhythm of 160 b/min was recorded with a II degree AV block appreciable on the 12-lead ECG, associated with Wenckebach periodicity

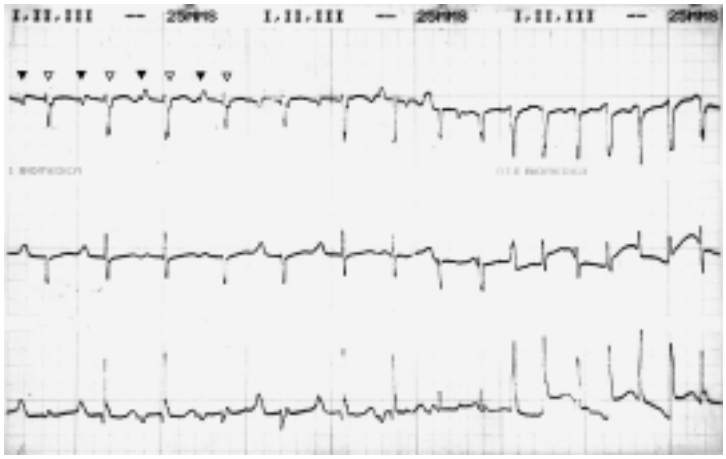

Figure 1. *Surface ECG leads I, II and III recorded at birth. An ectopic atrial rhythm of 160 b/min was recorded with phases of 2:1* (on the left) *alternated to 1:1* (on the right) *atrioventricular conduction. Analysis of the P wave morphology was hampered by its superimposition on the delayed ventricular repolarization* (black arrows) *or on the QRS complex* (white arrows). *In the former condition, the P waves appeared to be of negative polarity in lead I and of positive polarity in leads II and III, suggesting an ectopic origin of the arrhythmogenic focus. T wave alternans was observed.*

(Fig. 2). Finally, a sinus rhythm of 135 b/min with a prolonged QT interval and T wave alternans was recorded 4 hours after birth.

Electrocardiograms of the family members. No QT prolongation was found in the ECGs of the parents and of the brother. Similarly, even the grandparents' ECGs were normal. The family history did not include any episodes of sudden death and/or syncope. Besides, no case of congenital deafness had been reported.

Treatment and follow-up. No treatment was started on the first day of life, owing to the fact that no syncopal episodes and/or clinical signs of cardiac failure were observed. Besides, a normal sinus rhythm was spontaneously restored shortly after birth. A few days later, owing to the persistence of a prolonged QT interval, the baby was started on oral propranolol (2 mg/kg/die). The following ECGs, performed at monthly follow-up visits, were all suggestive of a sinus rhythm and narrow QRS complexes with a persistently prolonged QTc interval (QTc 540 ms). Several Holter monitorings revealed 100% sinus rhythm during the 3-year period of follow-up.

Molecular analysis. Mutation analysis was performed on genomic DNA using specific primers pairs on the genes already known to cause the typical inherited forms of LQTS: KvLQT1 and HERG, KCNE1, SCN5A and KCNNE2. The screening of the entire open reading frame of the five LQTS-related genes in the index case was negative for genetic defects.

Discussion

The LQTS may be occasionally diagnosed in the first months of life and at this age may be associated

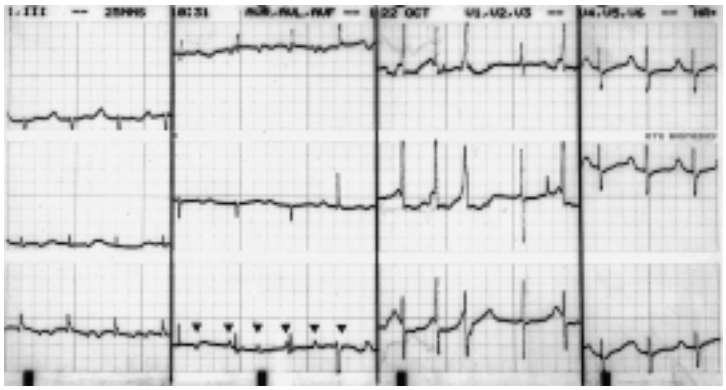

Figure 2. *Twelve-lead ECG recorded 3 hours after birth. Sinus rhythm with Wenckebach periodicity of the atrioventricular conduction was recorded. The phenomenon is best seen in lead aVF; here the P waves are outlined* (arrows). *Note that the P waves of the second, third and fifth beats have an identical morphology, whereas that of the first beat is superimposed on the T wave of the prior beat and that of the fourth beat is fused with the third QRS complex. Also note that, associated with a prolonged PR interval, the fourth QRS complex presents a left anterior deviation pattern.*

with bradycardia and AV conduction disorders. Garson et al.[2] reported a series of several patients who presented with bradycardia *in utero* and Villain et al.[3] reported that 5 of 15 neonates with the LQTS had fetal bradycardia. In these cases, bradycardia is usually due to a 2:1 AV conduction. The P waves are inscribed within the T wave and therefore are likely to occur during the refractory period of the ventricles. Consequently, Rosenbaum and Acunzo[4], owing to the fact that there was no evidence of any intrinsic abnormality of the AV node and/or His fascicle adopted the term of "pseudo AV block". In 1997 Hofbeck et al.[5], in a retrospective study, divided their 9 patients into two groups: 1) neonates presenting with sinus bradycardia, and 2) neonates presenting with functional AV block and ventricular tachycardia. In 1998, Lin et al.[6] described a case of a LQTS manifesting as a fetal ventricular tachycardia and an intermittent AV block. In 1999, Yamada et al.[7] reported the case of a fetus, whose mother had the LQTS, presenting with transient ventricular tachycardia during mid-gestation. In the case described by Gorgels et al.[8], an impaired right and left bundle branch conduction was demonstrated together with sinus pauses and accelerated AV junctional escape beats, almost suggesting the functional involvement of the sinus node and of the distal conduction system. In the present case, we found complex ECG findings in a neonate presenting with a prolonged QT interval: 1) an ectopic atrial rhythm with a 2:1 or 1:1 AV conduction; 2) sinus rhythm with and without second degree AV block. It is interesting to note that T wave alternans was macroscopically visible during the phases of ectopic atrial rhythm at a heart rate of 160 b/min, but also during the phases of sinus rhythm at 135 b/min. So, as shown in the present case, during the neonatal period, T wave alternans may also occur during sinus rhythm phases.

In conclusion, we suggest that the occurrence of bradycardia due to an impaired AV conduction in an otherwise normal fetus, may suggest the presence of a LQTS, even in the absence of a positive family history. However, these phenomena are not so frequent and in the absence of marked bradycardia (due to a 2:1 AV block) and of a neonatal ECG, the LQTS may not be diagnosed until malignant arrhythmias, sometimes triggering sudden death, occur. It has been demonstrated that 14% of LQTS patients die during the first episode of arrhythmia and that 30% of these deaths occur during the first year of life[1].

In a study including more than 33 000 infants who underwent ECG on the third and fourth days of life, it has been found that the presence of a prolonged QTc interval increases the risk of the sudden infant death syndrome by a factor of 41[9]. Recently, an infant who had never been submitted to an ECG, was resuscitated from ventricular fibrillation at 44 days of life. The QTc interval was markedly prolonged; both parents had a normal QT and did not have any genetic mutation responsible for the LQTS. However, a spontaneous *de novo* mutation on the cardiac sodium channel gene was found in the infant's genomic DNA[10]. In the present case we did not find any genetic mutation. However, we cannot exclude a *de novo* mutation on a still unknown gene[11].

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