Long QT syndrome diagnosed in the postpartum period (RCD code: VII-V-1A.2)

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Abstract

We report a case of 22 years old woman with long QT syndrome type with the first cardiac incidents in the post partum period. We discuss the actual treatment recommendation in the long QT syndrome with special attention on indications for implantation of defibrillator-cardioverter. JRCD 2014; 1 (6): 15–20

Key words: long QT syndrome, ICD, risk stratification, β-blocker

Case presentation

The present patient had been a subject of a preliminary report published elsewhere [1]. A 22-year-old woman, after delivery of her first child 6 months earlier, was transferred to our department by an emergency ambulance following syncope with involuntary micturition at home (blood pressure measured at home, 60/40 mm Hg). On admission, the patient's mentation was good and she reported feeling weak; on examination, tachycardia of 100 beats/min was noted; blood pressure on admission was 90/60 mm Hg. The results of laboratory tests were normal, with the exception of low serum magnesium level (0.56 mmol/L). A resting electrocardiogram (ECG) demonstrated sinus tachycardia of 110 beats per minute (bpm) with an isolated ventricular arrhythmia of dual morphology. Treatment included intravenous fluid and magnesium supplementation. ECG on the following day demonstrated normal heart rate of up to 76 bpm, an elongated QT interval of up to 460 ms, and a QTc interval of 517 ms. Other findings included atypical T wave morphology in leads V2 through V4 (a camel hump, biphasic T wave) (Figure 1). A suspicion of long QT syndrome (LQTS) was raised. On a resting ECG, a pronounced morphology of terminal T wave phase in leads V2 through V4 (Figure 2). On the following days, the QT interval measured by standard ECG in the morning ranged from 520 to 540 ms and after QTc correction it ranged from 536 to 547 ms. Findings in Holter ECG monitoring included a mean sinus rhythm rate of 67 bpm

(with a maximum of 145 bpm, minimum of 45 bpm), an isolated premature ventricular contraction (PVC) with dual morphology (340 PVC s/d), a circadian T wave polymorphism (5 morphological types of the T wave) (Figure 3). The QT interval ranged from 412 to 583 ms and the QTc from 425 to 618 ms. Mean QT and QTc were 516 ms and 538 ms, respectively. The so called postextrasystolic T wave changes were observed with increased T wave amplitude and significant QT interval elongation in sinus beats directly following the premature ventricular beats when com pared with the sinus beats preceding the PVCs (Figure 2).

A treadmill exercise stress test demonstrated initially exacerbated ventricular arrhythmia (including bigeminy, Figure 4), while at >135 bpm, it subsided and reappeared in the resting phase. An ECG performed directly after completion of the exercise stress test demonstrated a shortened QT interval of 440 ms and a QTc of 419 ms. The QT interval/QTc response at peak of exercise load and throughout the stress test could not be assessed because of numerous ventricular arrhythmias.

Due to variable T wave morphology (camel-hump T wave), we suggested of initial diagnosis of LQTS type 2. The patient scored 5 point in the Schwartz scale, e.g., high likelihood of LQTS. She supplied an ECG trace performed 1 year earlier during a routine health check, demonstrating a QTc of 480 ms. An echocardiogram was carried out and no structural pathology of the heart was detected. A family history reveled no sudden cardiac death (SCD); however, the patient`s mother sustained an ischemic stroke at the age of 45 years, which was attributed to aortic insufficiency.
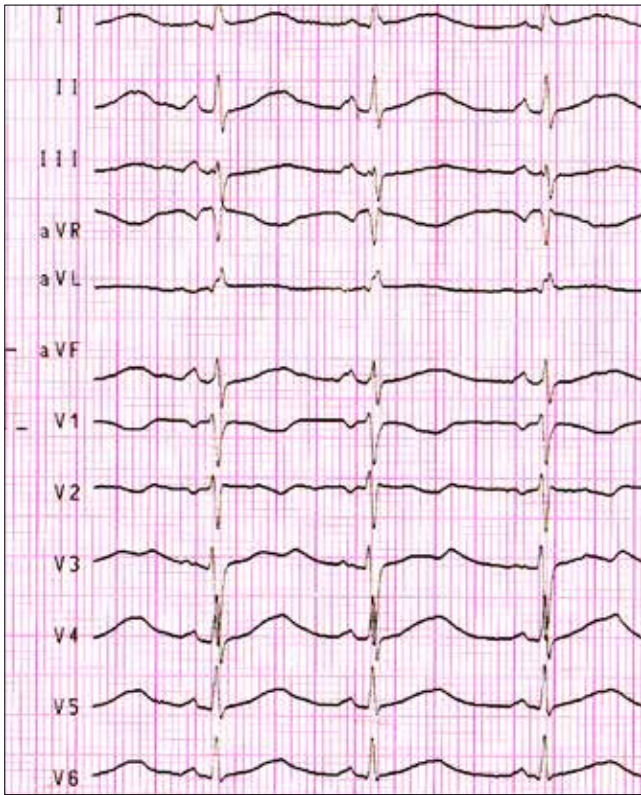
Figure 1. 12-lead ECG on admission after the first syncope episode. Heart rate, 76 beats/min; QT interval 460 ms, QTc interval – 517 ms. Biphasic T wave, campel-hump like T wave in leads V3, V4. *Reprint of with permission of the Editorial Committee of Kardiologia Polska and the Via Medica Publishing Company, Gdańsk, Poland*

Patient's management and follow-up

A β-blocker, metoprolol, was started at a dose of 75 mg/d and the treatment resulted in QT interval reduction from 520 ms to 460 ms. Metoprolol was gradually increased in one-week intervals from 25 mg/d to 200 mg/d under ECG and Holter monitoring. The patient's family members were also screened with ECG: the father, mother, sister, and 6-month-old son of the patient had no features of LQTS. A follow-up Holter ECG trace revealed episodes of ventricular bigeminy and ventricular pairs. No episodes of complex ventricular arrhythmia were observed. The patient took metoprolol regularly at 200 mg/d. After 2 years and 3 months after delivery the second child, the patient had an episode of complete syncope. At that time, she was using metoprolol at 50 mg/d. the patient reduced beta-blocker on her own because of frequent hypotensive episodes and poor tolerance of high metoprolol doses (exceeding 100 mg/d). On admission, the ECG demonstrated ventricular bigeminy. Two consecutive 24-hour Holter monitoring, despite increased the beta-blocker dosage, revealed episodes of polymorphic torsade de pointes (TDP) ventricular tachycardia – 4 episodes lasting up to 7 seconds (Figure 5). A cardioverter-defibrillator was implanted. Over 15-months follow-up, no appropriate device interventions were observed.

Discussion and literature review

LQTS is associated with elongated QT, variable T wave morphology, and typical clinical symptoms(loss of consciousness, presyncope, palpitations, cardiac arrest, or incidents of malignant ven-
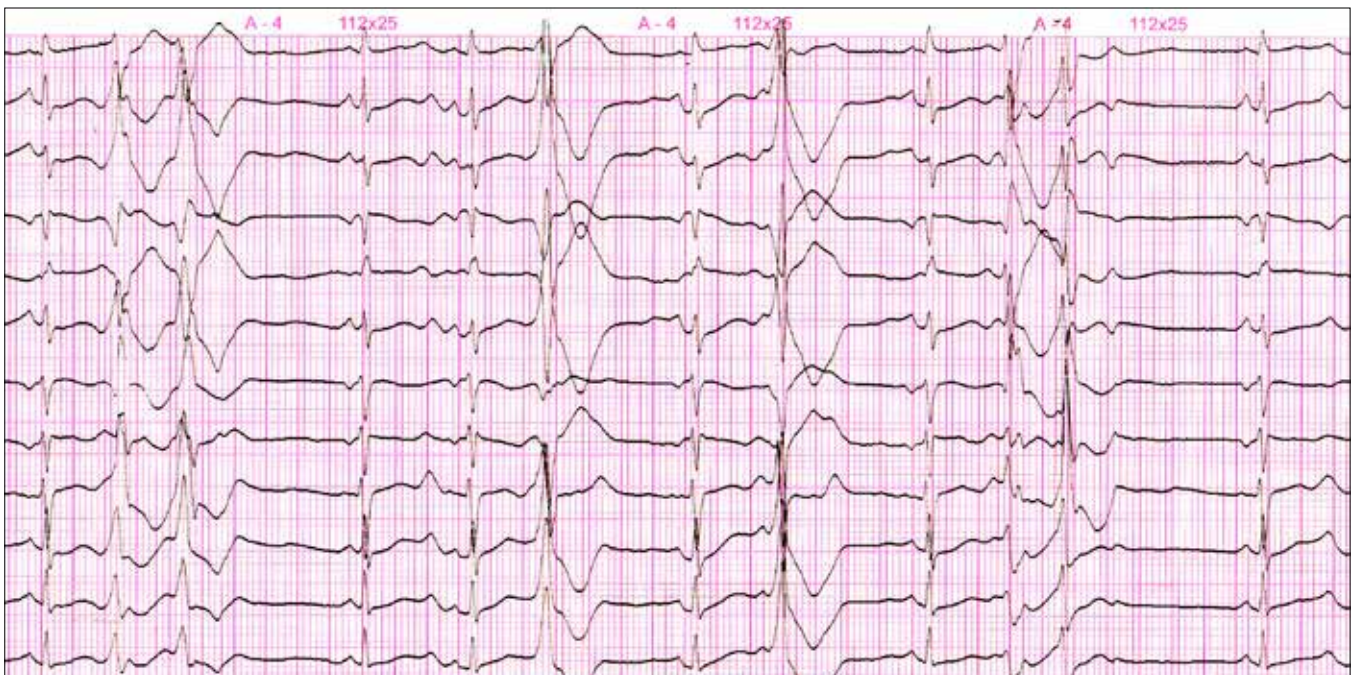

Figure 2. 12-lead ECG on the second day. There is an evident increase in the T wave amplitude in sinus beats following the premature ventricular beats (so called postextrasystolic T wave changes). *Reprint of with permission of the Editorial Committee of Kardiologia Polska and the Via Medica Publishing Company, Gdańsk, Poland*

Figure 3. 24 Hour Holter ECG monitoring trace. Different period of the day. The traces demonstrate T wave polymorphism. *Reprint of with permission of the Editorial Committee of Kardiologia Polska and the Via Medica Publishing Company, Gdańsk, Poland*

tricular arrhythmia) [2]. The characteristic arrhythmia pattern is polymorphous TdP ventricular tachycardia initiated with a typical short–long–short sequence. Dangerous ventricular arrhythmias increase the risk of SCD.

Very commonly, congenital LQTS is characterized by paucity of symptoms and the abnormal repolarization period is exacerbated only in pregnancy and the postpartum period, triggering arrhythmia. Pregnancy and the postpartum period result in elevated activity of the sympathetic system, which in the presence of LQTS, is associated with elevated risk of arrhythmia.

In addition, estrogen and progesterone levels are elevated in pregnancy, stimulating the adrenergic receptors. The above hormones affect the protein and potassium channel kinetics. A recent outstandingly well -designed and documented experimental model study conducted by Odening et al.,[3] evidenced an arrhythmogenic effect of estradiol and a protective antiarrhythmic effect of progesterone. In editorial comment to this article to this study in the Heart Rhythm, Arthur Moss stated that the initial analysis of international LQTS registry (not yet published) indicates women using contraceptives experience far fewer cardiac events than women who do not use such drugs [4]. It is possible that contraceptives containing an increased ratio of progesterone to estradiol will be-

come a "new" group of antiarrhythmic drugs targeted for women with LQTS, notably LQTS type 2[5]. In the postpartum period, the heart rate becomes slower, which is associated with increased QT interval. Stress associated with baby care and the altered sleep/rest patterns are associated with elevated sympathetic system activity possibly leading to dangerous ventricular arrhythmias. Rashba et al. [6] have evidenced in the LQTS registry that in a group of 442 patients and relatives the cardiac incidents were especially frequent in the postpartum period (the first 40 weeks following delivery). Almost 10% of the patients experienced their first cardiac incident in the postpartum period. Cardiac incidents were observed before pregnancy in 8% of the patients, and in 9% and in 23% in pregnancy and postpartum period, respectively. β-bloker treatment throughout pregnancy and in the postpartum period was associated with a significant reduction of cardiac incidents. Our patient is a typical example of the initital cardiac incident in the postpartum period. The recommended management includes β-blocker therapy and its continuation throughout pregnancy, breastfeeding, and the postpartum period [6]. According to Priori et al. [7] β-blocker treatment is associated with a significant benefit in LQTS type 1, wheras in types 2 and 3, β-blockers do not significantly reduce the cardiac events. The cardiac events were observed in 10% of pa-

Figure 4. 24 Hour Holter ECG monitoring trace. Ventricular arrhythmia; episode of ventricular bigeminy. *Reprint of with permission of the Editorial Committee of Kardiologia Polska and the Via Medica Publishing Company, Gdańsk, Poland*

tients with LQTS type 1, in 23% of patients with LQTS type 2, and in 32% of patients with LQTS type 3. Furthermore, patients with QTc interval above 500 ms and those who had their first cardiac events before the age of 7 years are specially susceptible to cardiac incidents despite β-blockers therapy. The recent analysis by Priori et al. [7] indicates that the risk of cardiac incident in LQTS patients not receiving treatment is 13% per year. The risk in LQTS type 1 depends primarily on the QTc interval duration. Men with LQTS type 1 and QTc interval above 500 ms are mores susceptible to cardiac events in childhood, while women with QTc duration above 500 ms have unchanging prognosis independent of the age. In LQTS type 2, female sex is a predictor of cardiac events independently of the QTc interval. In LQTS type 3, the prognosis is sex-dependent, males are a high-risk group, especially before the age of 40 years. Khositseth et al. [8] have recently demonstrated that women with LQTS type 2 are specially susceptible to cardiac incidents such as SCD, circulatory arrest, or syncope in the postpartum period. Of all patients followed up with one of the end points, 93% had LQTS type 2. Post partum cardiac incidents were significantly more common in patients with LQTS type 2 when compared with LQTS type 1 (16% vs 1%, respectively). The study by Seth et al. [9] also confirmed the prior observation by Khositseth et al. [8] indicating that pregnancy in women with LQTS is associated with lower risk of cardiac incidents. The postpartum period, notably its first 9 months, is associated with elevated risk, especially in patients with LQTS type 2 [9]. The use of β-blockers is associated with a significant reduc-

tion of cardiac incidents, notably in the high-risk postpartum period. The genetic studies to establish accurate diagnosis and determine the LQTS type (mutation type) are especially important and required for risk assessment and clinical decision making.

Recommended treatment

The following β-blockers and doses are recommended in the treatment of LQTS [10]:
– Metoprolol (1.8 mg/kgmc/d)
– Propranolol (2.9 mg/kg mc/d)
– Nadolol (1.4 mg/kg mc/d)
– Atenolol (1.3 mg/kgmc/d)

The current European Society of Cardiology /American Heart Association / American College of Cardiology 2006 guidelines recommend the following treatment of LQTS [11]:

Class I recommendations

1. Lifestyle modification in patients with clinical and/or molecular LQTS diagnosis (evidence level B).
2. blockers in patients with clinical diagnosis of LQTS (with long QT interval on ECG) (evidence level B).
3. Implantation of an ICD + adrenolytics in patientswith LQTS who previously survived cardiac arrest(evidence level A).
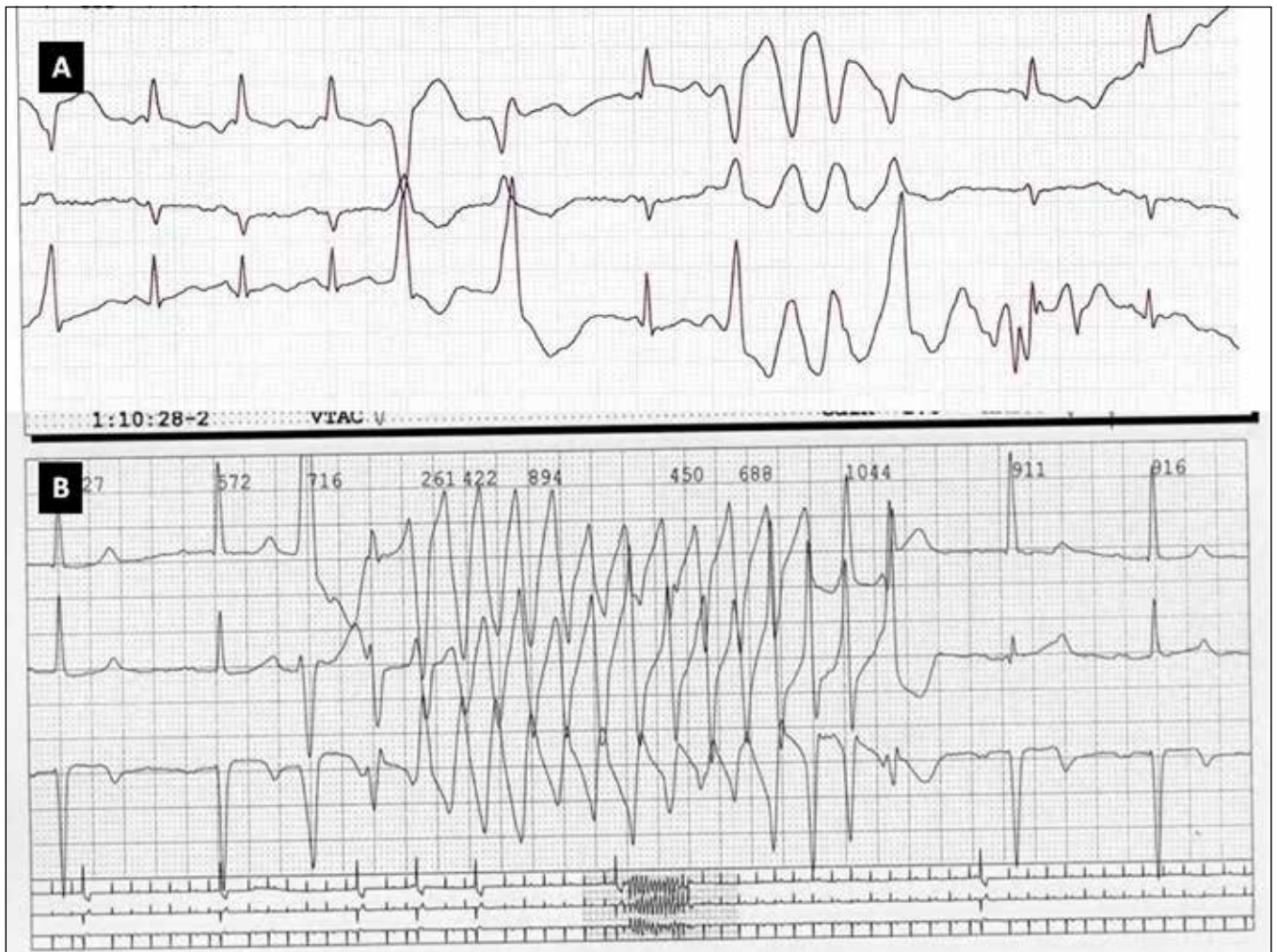
Figure 5. Panels A and B: 24 Hour Holter ECG monitoring trace, two consecutive testes where torsade de pointes episodes were noted. *Reprint of with permission of the Editorial Committee of Kardiologia Polska and the Via Medica Publishing Company, Gdańsk, Poland*

Class II a recommendations

1. blockers in patients with normal QT interval and molecularly confirmed LQTS (evidence level B).
2. ICD implantation + adrenolytics in prevention of SCD in patients with syncope or recorded ventricular tachycardia episodes during treatment with blockers (evidence level B).

Class II b recommendations

1. Ablation of the left stellate ganglion (left sympathetic cardiac denervation, LCSD) can be considered in patients with syncope, TdP tachycardia, or circulatory arrest during treatment with blockers (evidence level B)
2. ICD implantation + treatment with adrenolytics in primary prevention of SCD in probable high risk patients such as LQT2 and LQT3 (evidence level B).

Various treatment and risk stratification schemes have been proposed. Recently, Schwartz et al. [12] suggested the following LQTS patient groups as candidates for ICD implantation:

1. All patients who survived cardiac arrest during blocker treatment.

2. Most patients who survived cardiac arrest without prior blocker treatment
3. Symptomatic patients (syncope) despite full blocker dose, where the LCSD option is unavailable or not accepted by the patient.
4. All patients with 2 mutations who remain symptomatic despite treatment with full blocker dose
5. Exceptionally, asymptomatic patients with significant QTc elongation >550 ms, who present with electrical instability, for example, T wave or very long pauses favoring early afterdepolarizations and consequently TdP.

Despite the numerous risk stratification schemes, the clinical question of which LQTS patients should only receive a blocker and which should additionally be implanted with an ICD is difficult. The current recommendations (2006) for ICD implantation in prevention of SCD in LQTS appear to be defective.

In our case, syncope episodes were always observed in the postpartum period. However, the first episode occurred without blocker treatment when the patient was not yet diagnosed with LQTS. The second episode of complete syncope was observed during blocker treatment. However, the patient was on a suboptimal blocker dose at that time. Furthermore, when hospitalized and with in-

creased blocker dose, the ECG monitoring revealed TdP episodes. The decision of ICD implantation in the young patient is always controversial and difficult. We made the decision of ICD implantation considering the following factors:

1. syncope with documented TdP during blocker treatment
2. significantly elongated QTc interval in Holter ECG monitoring; max QTc – 618 ms
3. maternity and care of two children by our patient and periodic suboptimal blocker dosing because of the tendency for recurrent hypotensive episodes and intolerance of high blocker doses.

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