Emotional stress as a cause of syncope and \textit{torsade de pointes} in patients with long QT syndrome

Emocionalni stres kao uzrok sinkope i \textit{torsade de pointes} kod bolesnika sa produženim QT intervalom

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Abstract

Introduction. Long QT syndrome (LQTS) is a disorder of myocardial repolarization characterized by the prolongation of QT interval, as well as the high risk propensity of \textit{torsade de pointes} (TdP) that can lead to syncope, cardiac arrest and sudden death. Congenital LQTS is a genetic disease as more than 700 mutations described in 12 genes (LQT 1-12) which tend to be inherited in autosomal dominant fashion.

Case report. A 25-year-old female patient was hospitalized due to syncope that occurred immediately after her solo concert, first time in her life. The patient studied solo singing and after intensive preparations the first solo concert was organized. Electrocardiography (ECG) on admission registered frequent ventricular premature beats (VES), followed by polymorphic ventricular tachycardia – TdP that degenerated into ventricular fibrillation (VF). After immediate cardioversion magnesium and beta-blockers were administered. TdP was registered again several times preceded by VES. The corrected QT interval (QTc) was 516 msec. For secondary prevention of sudden cardiac death, a cardioverter defibrillator was implanted, and beta-blockers continued. After a 1-year follow-up there were no recurrent episodes of TdP, and measured QTc was reduced to 484 msec.

Conclusion. Patients with syncope following intensive emotional stress should be evaluated for malignant arrhythmias in the context of LQTS.

Key words: syncope; stress, psychological; torasades de pointes; drug therapy; electrophysiologic techniques, cardiac.

Apstrakt

Uvod. Sindrom produženog QT intervala (LQTS) je poremećaj repolarizacije miokarda koji se karakteriše prolongacijom QT intervala i sklonosti ka ventrikularnim aritmijama koje mogu dovesti do sinkope, srčanog zastoja i iznenadne smrti. Epizode aritmije mogu biti izazvane različitim stimulima, u zavisnosti od tipa LQTS. Prikaz bolesnika. Bolesnica, stara 25 godina, hospitalizovana je zbog krize svesti koja se javila neposredno nakon solističkog koncerta. Na prijemnom elektrokardiogramu (EKG-u) registrovane su ucestale komorske ekstrasistole (VES), a potom i polimorfna ventrikularna tabihardija – \textit{torsade de pointes} (TdP), koja se degenerisala u ventrikularnu fibrilaciju (VF). Pristupilo se hitnoj električnoj kardioverziji, nakon čega je ordiniran magnezijum i beta-blokatori. U daljem toku, u par navrata, ponovo je registrovana TdP kojoj su prethodile VES. Urađeno je merenje korigovanog QT intervala (QTc) koji je iznosio 516 msec. Zbog sekundarne prevencije iznenadne srčane smrti bolesnici je implantiran kardioverter debrifilator, a nastavljena je i terapija beta-blokatorima. Nakon jednogodišnjeg pračenja nije bilo epizoda ponovnog javljanja TdP, a izmereni QTc redukovan je na 484 msec. Zaključak. Bolesnica sa sinkopom na stalom neposredno nakon intenzivnog emocionalnog stresa, trebalo bi da se ispita zbog mogućeg postojanja maligne aritmije u sklopu LQTS.

Ključne reči: sinkopa; stres, psihički; torsad de puant; lečenje lekovima; elektrostimulator srca.

Introduction

Long QT syndrome (LQTS) is a disorder of myocardial repolarization characterized by the prolongation of QT interval and high risk propensity of \textit{torsade de pointes} (TdP) that can lead to syncpe, cardiac arrest and sudden death. Episodes may be provoked by various stimuli depending on the type of the condition. Case report. A 25-year-old female patient was hospitalized due to syncope that occurred immediately after her solo concert, first time in her life. The patient studied solo singing and after intensive preparations the first solo concert was organized. Electrocardiography (ECG) on admission registered frequent ventricular premature beats (VES), followed by polymorphic ventricular tachycardia – TdP that degenerated into ventricular fibrillation (VF). After immediate cardioversion magnesium and beta-blockers were administered. TdP was registered again several times preceded by VES. The corrected QT interval (QTc) was 516 msec. For secondary prevention of sudden cardiac death, a cardioverter defibrillator was implanted, and beta-blockers continued. After a 1-year follow-up there were no recurrent episodes of TdP, and measured QTc was reduced to 484 msec.

Conclusion. Patients with syncope following intensive emotional stress should be evaluated for malignant arrhythmias in the context of LQTS.

Key words: syncope; stress, psychological; torasades de pointes; drug therapy; electrophysiologic techniques, cardiac.
to prolong the duration of the ventricular action potential, thus lengthening the QT interval. The three most common forms of the disease, which together account for up to 65% are LQT1, LQT 2 and LQT3. Episodes may be provoked by various stimuli depending on the type of the condition. In LQT1 episodes of ventricular arrhythmias predominantly occur during sympathetic stimulation or physical activity, especially during swimming. Triggers for life-threatening arrhythmias in LQT2 are often emotional stress, auditory stimuli and rarely occur during sleeping or physical activity. The greatest risk of ventricular arrhythmias in LQT3 is during sleeping or bradycardia.

The aim of our case report was to indicate that syncope immediately after intense emotional stress should be evaluated in the context of LQTS.

**Case report**

A 25-year-old female patient was hospitalized due to the syncope that occurred immediately after her solo concert, first time in her life. The patient studied solo singing and after intensive preparation the first solo concert was organized. Electrocardiography (ECG) on admission registered frequent ventricular extrasystoles (VES) followed by polymorphic ventricular tachycardia (TdP) that degenerated into VF. After immediate electrical cardioversion, magnesium and beta-blockers were administered. Repetitive TdP was registered several times, preceded by VES. The corrected QT interval (QTc) measured by Bazett’s formula was 516 msec.

Laboratory tests did not show abnormalities of electrolytes (Na⁺ 142 mmol/L, K⁺ 4.8 mmol/L, Mg²⁺ 1.02 mmol/L, total Ca²⁺ 2.3 mmol/L), nor of thyroid hormones (TSH 0.70 mlU/L, FT4 12.6 pmol/L, FT3 3.5 pmol/L) and drug induced QT prolongation also was excluded. Ultrasound of the heart showed normal heart size cavities, preserved global systolic function of the left chambers, ejection fraction was estimated at 60%. There was no sudden cardiac death in her family. QTc measurements were performed on her family members, but normal values were obtained. Due to technical limitations genetic mutations analysis was not performed. Cardioverter defibrillator (ICD) was implanted due to high risk of sudden cardiac death. Permanent cardiac pacing with continuously treatment of β-blockers (propranolol 120 mg per day) prevented bradycardia and ‘short-long-short’ cycle length sequence.

**Fig. 1** – Electrocardiography (ECG) on admission registered frequent ventricular extrasystoles (VES) followed by *torsade de pointes*.

**Fig. 2** – *Torsade de pointes* degenerated into ventricular fibrillation.

**Fig. 3** – Corrected QT interval (QTc) measured by the Bazett’s formula was 516 msec.
and reduced QT interval. Recurrent episodes of TdP were not registered during a 1-year follow-up and the measured QTc was reduced to 484 msec (Figure 4). The patient is well now, but stopped singing.

**Discussion**

LQTS is characterized by the corrected QT interval prolongation leading to TdP and sudden cardiac death. The most frequent LQTS phenotype is LQT2, accounting for 35–40% of the LQTS phenotypes and mutations 2,3.

The diagnosis of LQTS is not easy, because 2.5% of the healthy population have the prolonged QT interval and 10–15% of LQTS patients have the normal QT interval7. A commonly used criterion to diagnose LQTS is the Schwartz et al. 8 LQTS "diagnostic score". The current criteria are based on clinical history, family history and ECG findings.

According to these criteria the presented patient had syncope with stress, QTc more than 480 msec, TdP was registered as well as notched T-wave at least 3 leads which indicates the total score of 8 points and leads to the high probability of LQTS. Namely, in the presented patient the low-amplitude and the most prominent notched T-waves were registered in precordial leads, while 12-lead surface ECG at rest showed a prolonged corrected QT (QTc) interval with low T-wave amplitude and a double-notched T-wave morphology indicating LQT2 9. The prolong QTs interval showed no further extension during exercise testing which also could indicate LQT2 type. These facts also support life-threatening ventricular arrhythmias occurring immediately after emotional stress.

Cardiac activity is influenced via autonomic fibers of the sympathetic and parasympathetic nervous system. In patients with congenital long QT syndrome, noradrenaline and adrenaline as predominant mediators of sympathetic action commonly trigger *torsade de pointes* in a so far unknown mechanism. The human ether-a-go-go-related gene (hERG or KCNH2) encodes the α subunit of the channel underlying the rapid components of rectifier potassium current (I,Kr), which is crucial for the repolarization of cardiac action potentials (AP) 10. There is increasing evidence that hERG/I,Kr channels are modulated by various G protein-coupled receptors including α- and β-ARs, which act through the intracellular signaling modulators cAMP, protein kinase A (PKA), and protein kinase C (PKC) 11. Malfunction of slow (I,Ks) and rapid (I,Kr) components of rectifier potassium current (Ik) may play important role in arrhythmias in long QT 12. Namely, the length of the cardiac action potential is largely determined by both I,Ks and I,Kr 12. The rapid component of delayed rectifier potassium current (I,Kr) is modulated by β-adrenergic stimulation, so the high dose of catecholamines due to intense emotional stress leads to the prolongation of QT interval particularly in patients with congenital prolonged QT interval with the consequent induction of TdP 13. Pheochromocytoma as well as another clinical application of high-dose catecholamines like dobutamine-atropine stress echocardiography is often associated with QT prolongation and ventricular arrhythmias like *torsades de pointes* 13, 14.

Beta-blockers, preferably a non-selective beta-blocker such as propranolol or nadolol, are the first line therapy in patients with LQTS for minimizing effects of the adrenergic stimulation 15. These drugs reduce QT hysteresis and decrease dispersion of repolarization and may normalize response of repolarization to adrenergic stimulation 16. Beta blockers also attenuate the beta receptor mediated enhancement of L-type calcium channels and restore balance of cardiac ion channel forces 16. These drugs are not completely protective in preventing cardiac events such as syncope, aborted cardiac arrest and sudden cardiac death particularly in patients with symptoms prior to therapy, younger age, longer baseline QTc (> 500 msec), and a genotype other than LQT1 16.

ICD is the most successful therapy for the prevention of sudden cardiac death. According the to current recommendations, implantation of an ICD along with the use of beta-blockers is recommended for LQTS patients with previous cardiac arrest, so the presented patient was implanted ICD (Class I, Level of Evidence: A) 17.

**Conclusion**

Prolonged QT interval is a problem in clinical practice with increasing attention that should be the area of intensive research. Patients with symptoms during or immediately af-

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ter intense emotional stress should be evaluated for malignant arrhythmias in the context of LQTS. Improving knowledge about genetic mutations gives hope that genetic therapies, as therapy of the future can stabilize repolarization and reduce the possibility of life-threatening arrhythmias and sudden cardiac death.

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