Congenital long QT syndrome: A case report

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ABSTRACT The congenital long QT syndrome (LQTS) is characterized by abnormally prolonged ventricular repolarization due to inherited defects in cardiac sodium and potassium channels, which predispose the patients to syncope, seizure like activity, ventricular arrhythmias, and sudden cardiac death. Early diagnosis and preventive treatment are instrumental in preventing sudden cardiac deaths in patients with the congenital LQTS. The diagnostic criteria for congenital LQTS are based on certain electrocardiographic findings, clinical findings and findings of epinephrine stress test. Recently genotype specific electrocardiographic pattern in the congenital LQTS has also been described. Recent studies suggest feasibility of genotype specific treatment of LQTS and, in near future, mutation specific treatment will probably become a novel approach to this potentially fatal syndrome. We describe one case that fulfilled the electrocardiographic, historical diagnostic criteria and epinephrine stress test suggestive of LQT syndrome.

Key Words: congenital long QT syndrome; cardiac sodium; potassium channels

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Introduction

The Long QT is a rare congenital disorder characterized by QT-interval prolongation and repetitive episodes of syncope and cardiac arrest related to rapid, polymorphic ventricular tachycardia. Genetic linkage mapping defines six types of LQTS (LQT1-LQT6) out of which, LQT1-LQT3 have been well characterized in clinical studies (1). Diagnosis of LQTS is based on clinical and electrocardiographic features (2). These EKG characteristics are useful for selecting which gene to investigate first, while performing genetic analysis. The identification of genotype specific EKG pattern is gaining importance, for its potential use in the management of LQTS, with favorable outcomes (3). Further, epinephrine stress test is important in unrevealing the underlying congenital LQTS.

Case report

A 29 year-old Caucasian male, recently diagnosed with seizure disorder, was brought to emergency room for altered mental status with combative behavior. Patient was having syncopal episodes and sudden seizures with spontaneous resolution in few minutes for the past 4-5 months. Family history was significant for sudden deaths in family in early age.

In ER, the Patient was initially found to be combative but hemodynamically stable. 12 lead EKG showed presence of long corrected QT interval of 710 msec, and presence of U waves correlating with his low potassium levels of 3.1. The urine toxicology screen was positive for cocaine. Patient's mental status rapidly improved and in a span of few hours he was able to provide coherent history. Suddenly, he was found to have a seizure-like activity in the ER. Monitor revealed a wide complex, polymorphic ventricular tachycardia, which reverted to sinus rhythm in a span of few seconds. After the initial episode, patient had 2 more episodes of ventricular tachycardia in the next few minutes, which resolved spontaneously after lasting for a duration of 5-7 seconds.

Patient was initially intubated and transferred to Cardiac Care Unit (CCU). Serial EKG's done in the CCU did reveal a prolonged QTC which gradually decreased to normal duration over a span of 2 days. Given the history of sudden cardiac deaths in the family and seizure like episodes in the patient, diagnosis of Congenital long QT syndrome was entertained and an Epinephrine induced QT stress test was planned.

Initial EKG before the start of epinephrine stress test showed a QTc of 440 msec, patient was started on Epinephrine infusion at rate of 0.25 micrograms/Kg/min for 10 mins under continuous EKG monitoring. QTc at end of this period did show a prolongation to 570 msec after which rate of epinephrine was

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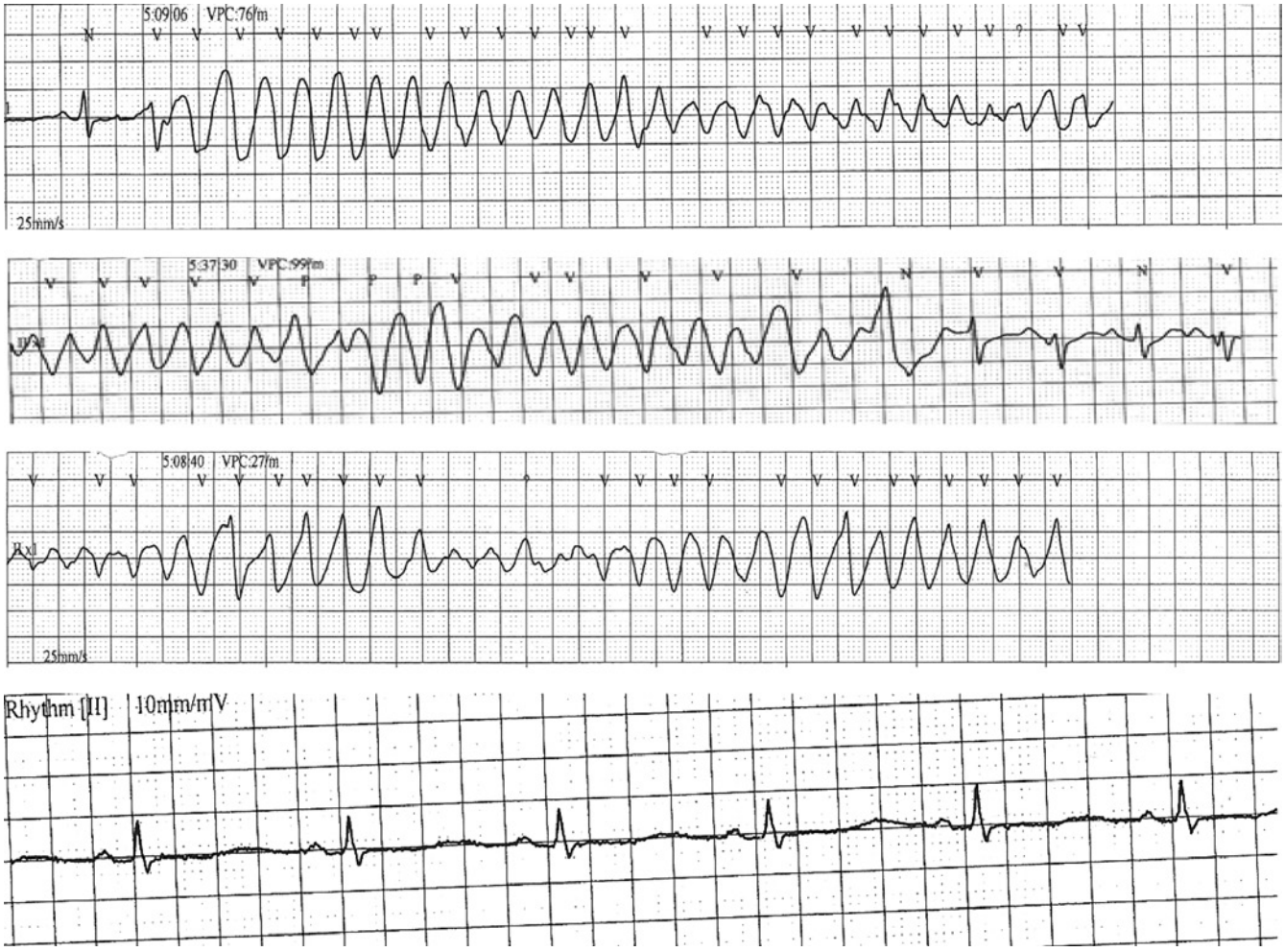


Rhythm strip of II showing QTc of 720 msec at admission

increased to 0.5 mcg/kg/min for another 5 minutes, at end of which QTc prolonged to 600 msec. The test was deemed positive and was stopped at this point of time. Patients QTc rapidly reverted to pre test level after epinephrine was stopped.

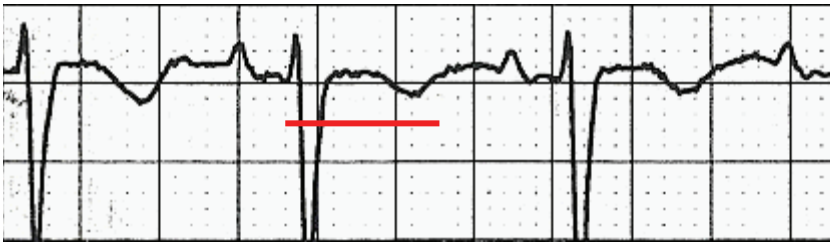
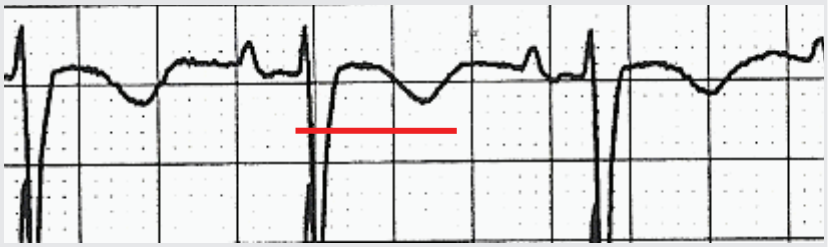
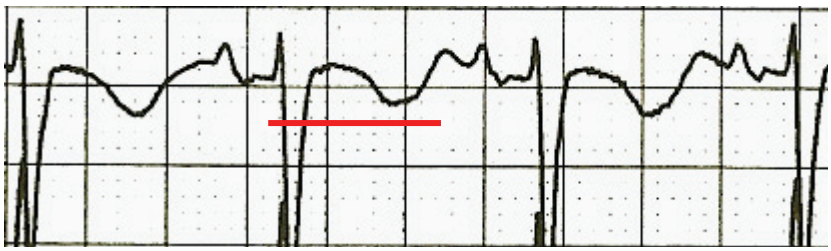
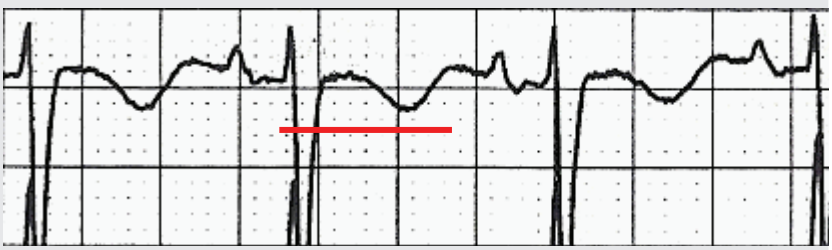
Patient was given an External defibrillator vest and discharged home with close outpatient follow up and plan for repetition of QTc stress test in 2 months time for evaluation of need for AICD.

Discussion

The QT interval is a surface marker of cardiac electrical activity, specifically cellular repolarization. It is generally accepted that the absolute QT interval provides a surface rendering of the underlying cellular action potential durations. Despite overlap of the resting QTc between healthy persons and patients with LQTS, the 12-lead EKG remains one of the principal tools in the LQTS evaluation, and the baseline QTc is still one of the most important diagnostic criteria.

The congenital LQTS is a potentially life threatening condition, caused by mutations in genes encoding cardiac ion channels which result in prolongation of ventricular action potential. Genetic screening of symptomatic patients or their asymptomatic family members may identify patients at risk for life threatening arrhythmias and the type of LQT as it has important implications in the management. Out of the several forms of congenital LQTS, three forms LQT1, LQT2, and LQT3 have been well characterized. These three forms have also been described on the basis of their specific EKG morphology. Recent investigations suggest that even in patients with acquired LQTS (e.g. resulting from intake of QT-prolonging medicines), there are clinically silent gene mutations that lead to overt QT prolongation only with exposure to QT- prolonging medications (4-6).This explains why some patients seem to be more prone than others to have QT prolongation at a given dose of QT-Prolonging drugs, even after adjustment for other factors that could prolong QT-interval.

According to Pfizer Tikosyn program, the QTc should be no more than 500 msec in the presence of ventricular conduction

	QTc (in msec)	V1 @ 20 mm/mv and 25 mm/sec
Base line	440	
10 min of 0.05 mcg/kg/min of epinephrine	570	
5 min of 0.1 mcg/kg/min of epinephrine	600	
10 mins off epi	530	

abnormality (7). This guidance may be used until a standard method is established for the measurement. Treatment with beta-blockers can reduce this risk. The clinical course of the congenital LQTS is influenced largely by the gene affected (8). While cardiac events are more frequent and occur at a younger age in patients with LQT1 and LQT2, they are potentially more fatal in patients with genotype LQT3. Patients with LQT1 and LQT2 genotype typically benefit from high dose beta-blocker therapy (9, 10). However, patients with LQT3 are at higher risk at lower heart rates and potentially may benefit from pace maker therapy. In addition, they shorten their QT-interval more with sodium channel blockers (11).

Provocative tests using catecholamine or exercise testing have long been considered to unmask some forms of congenital LQTS (12). Recent preliminary data by Ackerman et al. have suggested the usefulness of an epinephrine test to unveil concealed LQT1 syndrome (13). An epinephrine provocative test should only be done by cardiologists, under enough preparation of intravenous beta-blockers and direct cardioverter for unintentionally induced ventricular fibrillation.

Both experimental and clinical studies have suggested a differential response of action potential duration (APD) and QT interval to sympathetic stimulation among LQT1, LQT2, and LQT3 (14). Persistent and paradoxical prolongation of APD and QT interval at steady state conditions of catecholamines is reported in LQT1 syndrome. Under normal conditions, beta-adrenergic stimulation is expected to increase net outward repolarizing current, owing to larger increase of outward currents, including Ca-activated slow component of the delayed rectifier potassium current (IKs) and Ca-activated chloride current, than that of an inward current, Na/Ca exchange current (INa-Ca), resulting in an abbreviation of APD and QT interval. A defect in IKs in the LQT1 syndrome could account for failure of beta-adrenergic stimulation to abbreviate APD and QT interval,

resulting in a persistent and paradoxical QT prolongation under sympathetic stimulation (14). In LQT2 syndrome, catecholamines are reported to initially prolong but then abbreviate APD and QT interval, probably because of an initial augmentation of INa-Ca and a subsequent stimulation of IKs. In contrast to the LQT1 and LQT2 syndromes, catecholamines are reported to constantly abbreviate APD and QT interval as a result of a stimulation of IKs in the LQT3 syndrome, because an inward late sodium current (INa) was augmented in this genotype. The epinephrine test may be applied not only for unmasking silent mutation carriers with LQT1 syndrome but also for predicting genotypes.

Facilities for genetic analysis are not easily available. However, in view of the growing importance of genotype specific treatment of this potentially fatal syndrome, one can utilize the ECG criteria and epinephriene QT stress test as a reliable indicator of the underlying genotype and accordingly tailor the management.

References

1. Chiang CE, Roden DM. The long QT syndromes: genetic basis and clinical implications. J Am Coll Cardiol 2000;36:1-12.
2. Scwartz PJ. The long QT syndrome. Circulation 1993;88:782-4.
3. Moss AJ, Zareba W, Kaufman ES. Increased risk of arrhythmic events in long QT syndrome with mutations in the pore region of the human ether-a-a-go-go-related gene potassium channel. Circulation 2002;105:794-9.
4. Priori SG, Napolitano C, Schwartz PJ. Low penetrance in the long QT syndrome: clinical impact. Circulation 1999;99:529- 33.
5. Viskin S. Long QT syndromes and torsades de pointes. Lancet 1999;354:1625-33.
6. Donger C, Denjoy I, Berthet M. KVLQT1 C-terminal missense mutation causes a forme fruste long-QT syndrome. Circulation 1997;96:2778-81.
7. Dofetilide product monograph and confirmation of education. New York, NY: Pfizer Inc; March 2000.
8. Zareba W, Moss AJ, Schwartz PJ, Vincent GM, Robinson JL, Priori SG, et al. Influence of genotype on the clinical course of the long QT-syndrome. International Long QT Syndrome Regisrty Research Group. N Engl J Med 1998;339:960-5.
9. Schwartz PJ, Priori SG, Spazzolini C, Moss AJ, Vincent GM, Napolitano C, et al. Genotype-phenotype correlation in the long-QT syndrome: gene-specific triggers for life-threatening arrhythmias. Circulation 2001;103:89-95.
10. Moss AJ, Zareba W, Hall WJ, Schwartz PJ, Crampton RS, Benhorin J, et al. Effectiveness and limitations of beta-blocker therapy in congenital long-QT syndrome. Circulation 2000;101:616-23.
11. Scwartz PJ, Priori SG, Locati EH, Napolitano C, Cantu F, Towbin JA, et al. Long QT syndrome patients with mutations of the SCN5A and HERG genes have differential responses to Na channel blockade and to increases in heart rate. Implications for gene-specific therapy. Circulation 1995; 92:3381-6.
12. Schechter E, Freeman CC, Lazzara R. After depolarizations as a mechanism for the long QT syndrome: electrophysiologic studies of a case. J Am Coll Cardiol 1984;3:1556-61.
13. Ackerman MJ, Khositseth A, Tester DJ, Hejlik JB, Shen WK, Porter CB. Epinephrine-induced QT interval prolongation: a gene-specific paradoxical response in congenital long QT syndrome. Mayo Clin Proc 2002;77:413-21.
14. Shimizu W, Antzelevitch C. Differential response to beta-adrenergic agonists and antagonists in LQT1, LQT2 and LQT3 models of the long QT syndrome. J Am Coll Cardiol 2000;35:778-86.