

A Congenital Deadly Association: Dilated Cardiomyopathy and Long QT Syndrome

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ABSTRACT

Long QT syndrome is one of the most feared entities in hospitalized patients due to the potential risk for ventricular tachycardia and sudden death. Association between channelopathies and congenital cardiomyopathy is a new entity that has been studied recently. We report an interesting case of this association that maybe related to a genetic mutation.

KEYWORDS: Long QT Syndrome; Cardiomyopathies; Genetic diseases; Ventricular tachycardia; Channelopathies.

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LEARNING OBJECTIVE

Congenital long QT syndrome and congenital cardiomyopathy can be both associated to SCN5A mutations. Despite the fact that this is a rare association, it is important for physicians to be aware of it due to the potential high risk of ventricular arrhythmias and sudden death, especially in young patients.

INTRODUCTION

Long QT syndrome (LQTS) is one of the most feared entities in hospitalized patients due to the potential risk for ventricular tachycardia (VT) and sudden death, happening sometimes in completely asymptomatic patients. Clinicians are usually cautious with QT interval prolongation as many common hospital drugs and electrolytes abnormalities can prolong QT and trigger VT¹.

Since described in 1957, LQTS has been intensively studied, but the association between channelopathies and congenital cardiomyopathy is a relatively new association². This report presents an interesting case with this association and correlates with the current medical literature.

CASE REPORT

A 45-year-old man with a medical history of mild hypertension presented with progressive dyspnea and anasarca. Family history was not contributory. Jugular venous distension, pedal edema and pulmonary rales were observed. No history of alcohol or drug abuse.

Electrocardiogram (EKG) revealed sinus rhythm, left ventricular hypertrophy and a QTc of 440 ms (Fig. 1a). Echocardiogram showed severe left atrial and ventricular dilatation with an ejection fraction of 20%. Started on guideline-based therapy for heart failure with bisoprolol, furosemide, losartan and spironolactone.

At the 5th day of hospitalization, he was diagnosed with a respiratory infection and moxifloxacin was initiated. At the 8th day, he had an episode of ventricular fibrillation followed by two episodes of pulseless polymorphic ventricular tachycardia and monomorphic ventricular tachycardia. Post arrest EKG showed QTc of 550 ms (Fig. 1b).

The antibiotic was discontinued and potassium and magnesium were replaced. Coronary arteries had no lesions. Patient discharged for outpatient follow up after stabilization with a diagnosis of iatrogenic acquired LQTS. Electrocardiogram at discharge QTc was 450 ms (Fig. 1c).

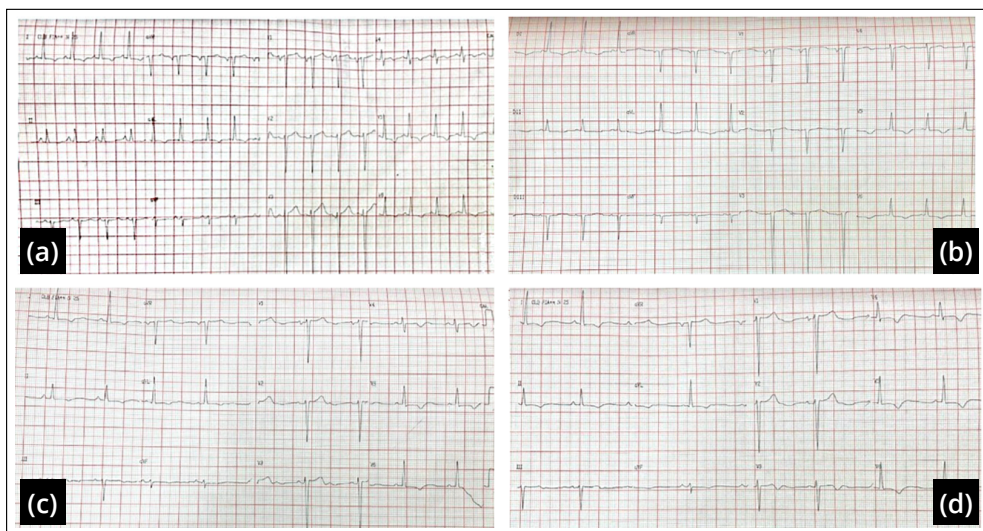


Figure 1. Twelve-lead electrocardiogram showing different QT intervals. (a) admission QTc 440 ms. (b) after cardiac arrest, QTc 550 ms. (c) at the discharge 450 ms. (d) one month after discharge 440 ms.

A month later QTc was 440 ms off QT prolonging drugs (Fig. 1d), but a 24-hour Holter showed intermittent QT prolongation up to 530 ms (Fig. 2). Treadmill test showed postexercise complex polymorphic ventricular tachycardia associated with QT prolongation up to 506 ms (Fig. 3). Findings consistent with type 3 long QT syndrome (LQTS-3) associated with dilated cardiomyopathy may related to SCN5A mutation.

Patient declined genetic testing. An implantable cardioverter defibrillator (ICD) was placed and he has been New York Heart Association (NYHA) class II on oral guideline-based heart failure medications.

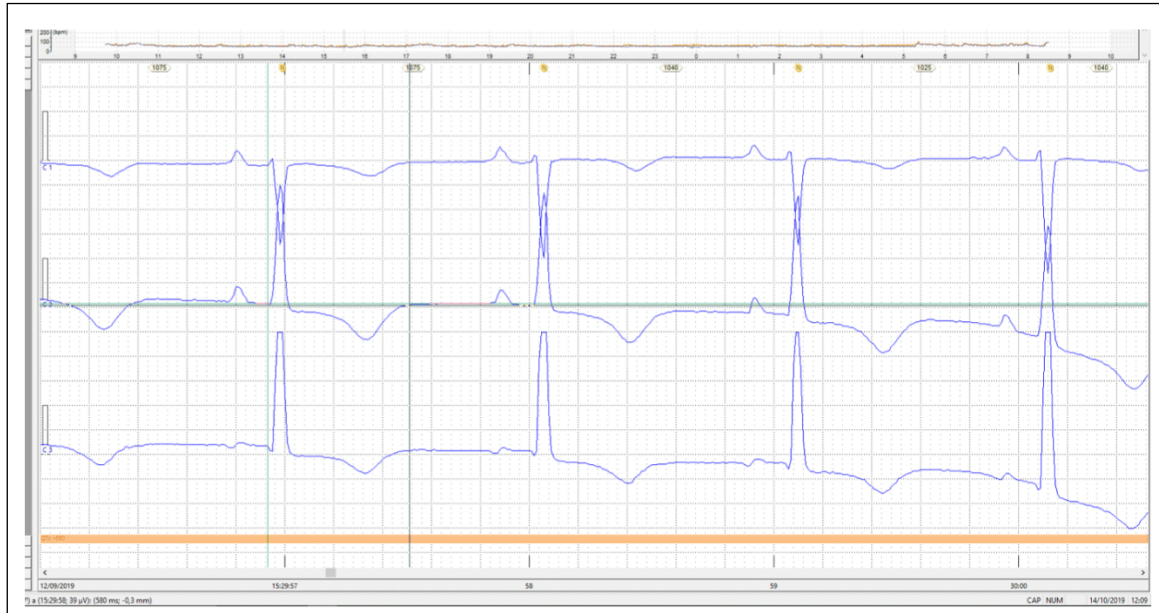


Figure 2. 24-hour Holter showing QTc at 530 ms.

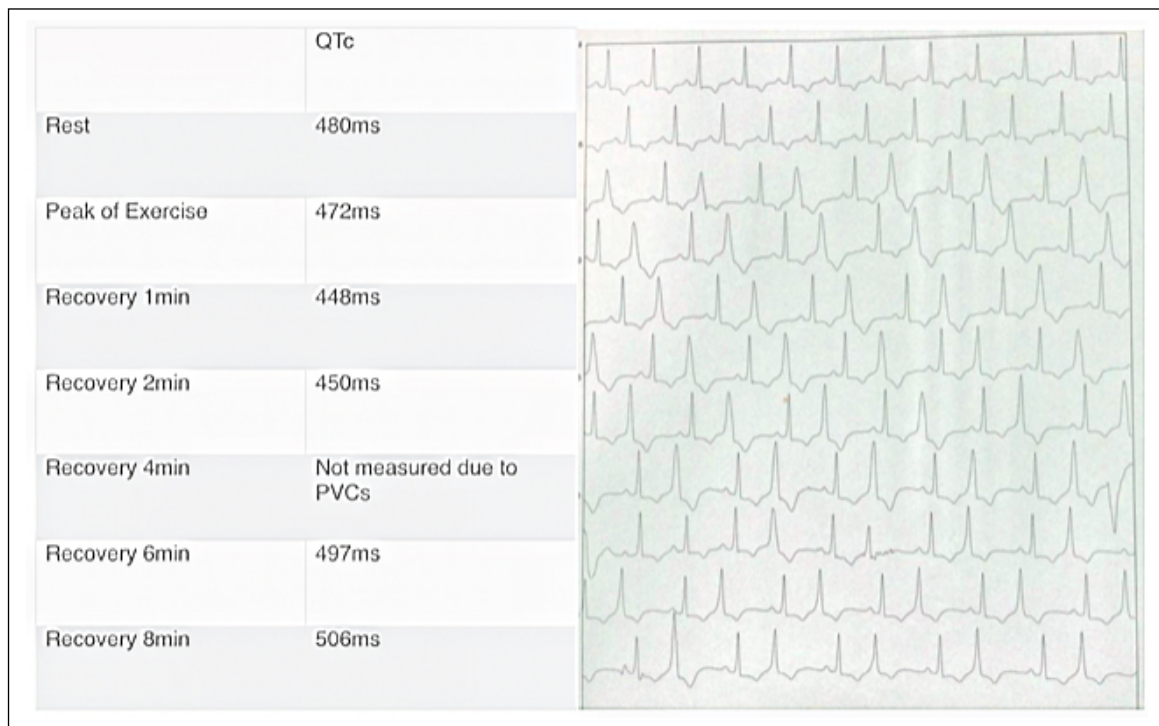


Figure 3. Stress test. Left - QTc by time. Right - polymorphic premature ventricular contractions during recovery time.

DISCUSSION

Acquired LQTS is by far more prevalent than congenital LQTS; however, in the presence of congenital channelopathies, electrolyte abnormalities and drugs can more easily prolong the QT interval and trigger ventricular arrhythmias¹. In this patient, QT interval improved after the discontinuation of the antibiotic, he was initially misdiagnosed with acquired LQTS. Subsequent follow up in the absence of QT prolonging agents showed the presence of intermittent prolonged QT interval.

It is widely known the QT interval can vary due to heart rate, electrolyte level and autonomic changes. An isolated 12-leads EKG might be inappropriate to evaluate patients with LQTS, especially type 2 and 3^{3,4}. In the described patient, a 24-hour Holter after one month showed prolonged QT intervals that were not seen at the discharge. Different strategies to measure the QT variability on 24-hour Holter in LQTS patients have been recently published and should be used in the suspicion for LQTS^{3,4}.

Schwartz's criteria are a widely accepted tool for the diagnosis of congenital LQTS, and the studied patient scored 5 points. It is necessary > 3.5 points to have high probability of LQTS⁴. There are more than 10 different subtypes of congenital LQTS even though genetic analysis is necessary to determine the subtype, EKG changes on treadmill might contribute to the diagnosis. During the peak of exercise QT interval decreases, but during the recovery phase it increases in patients with LQTS type 2 and 3^{5,6}. The EKG also suggests LQTS-3 due to long isoelectric ST segment.

Type 3 long QT syndrome patients present more often with bradycardia, and QT prolongation is more pronounced during slow rate therefore they have more arrhythmic events at rest⁷.

The mutation more associated with LQTS-3 occurs in the SCN5A gene. This gene encodes the pore forming ion-conducting α -subunit of the cardiac sodium channel, which is responsible for the initiation and propagation of action potentials and thereby determines excitability and conduction of the electrical stimuli through the heart. Usually in a patient with LQTS-3, there is a gain of function leading to a pathological increase of sodium influx into cardiomyocytes through aberrant channel gating and causes LQTS⁷.

SCN5A mutations are also associated to other pathologies such as Brugada syndrome and cardiomyopathy. The patient did not have any classical risk factors for heart failure therefore in the setting of LQTS-3 and possible SCN5A mutation the etiology of the cardiomyopathy might be genetic².

SCN5A mutations can cause a proton leak into the cardiomyocyte through the Sodium channel, or increased Na⁺ influx caused by gain-of-function variants, may lead to compensatory activation of the N⁺/H⁺ or the Na⁺/Ca²⁺ exchanger, thus leading to intracellular acidification or calcium overload, respectively, and consequent impaired excitation-contraction coupling and/or myocardial damage with subsequent heart failure^{2,8,9}.

American Heart Association guidelines recommend ICD implantation for patients with LQTS-3 especially in higher risk patients, therefore the ICD was placed¹⁰. He also would meet criteria for ICD placement for being a sudden death survivor in the setting of severe cardiomyopathy¹⁰.

Even though the presented patient refused genetic testing, all clinical and electrocardiographic evidence suggests he has a SCN5A mutation with associated LQTS-3 and cardiomyopathy.

Despite the fact that this is a rare association, it is important for physicians to be aware of it due to the potential high risk of ventricular arrhythmias and sudden death, especially in young patients.

AUTHOR'S CONTRIBUTION

Conceptualization, Lima NA, Andrade AT and Sampaio SMV; Methodology, Lima NA, Andrade AT and Sampaio SMV; Writing – Original Draft; Lima NA, Andrade AT and Sampaio SMV; Writing – Review and Editing; Sampaio SMV and Loehrke M; Supervision, Sampaio SMV and Loehrke M.

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