The ketogenic diet and the QT interval

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ABSTRACT

Long QT syndrome is a disorder of ventricular myocardial repolarization associated with an increased risk of life-threatening cardiac arrhythmias and sudden cardiac death. This report highlights a case of QT prolongation with torsades de pointes in a patient with baseline congenital long QT syndrome, believed to be precipitated by metabolic changes associated with the “ketogenic diet.”

KEYWORDS Electrocardiogram; implantable cardioverter-defibrillator; ketogenic diet; long QT syndrome; nutrition; torsades de pointes

Long QT syndrome (LQTS) may be either congenital or acquired and is characterized chiefly by a prolonged QT interval on an electrocardiogram (ECG). The fatal arrhythmia most commonly associated with LQTS is known as torsades de pointes (TdP), or “twisting of the points.” Clinically, the presentation of LQTS is highly variable; patients range from being entirely asymptomatic to presenting with syncope, presyncope, palpitations, and even sudden cardiac death. Congenital LQTS, as described in the case below, occurs due to genetic mutations in various cardiac ion channels.¹ Arrhythmias in patients with congenital LQTS are traditionally associated with external triggers such as exercise, stress, or startling noises but may also occur at times of rest and sleep. This case describes what we believe was an uncommon trigger (ketogenic diet) for TdP in a patient with baseline LQTS and highlights the importance of completing a detailed history when managing these patients.

CASE DESCRIPTION

A 43-year-old woman who was born in July 1974 with congenital LQTS, specifically long QT syndrome-2 (LQT2), underwent placement of a dual-chamber implantable cardioverter-defibrillator (ICD) after a cardiac arrest in 1999. She had a family history of LQTS, including a sister who died of cardiac arrest. Historically, her condition was more active during times of emotional or physical stress. She recalled that her first ICD shock was in 2003, 1 to 2 months after the delivery of her first child. She was started on atenolol at that

time and while on it remained asymptomatic for 6 years. Given the lack of symptoms, she stopped all antiarrhythmic therapy in 2009. She underwent an ICD generator change in 2014. A single isolated episode of ventricular fibrillation was noted on device follow-up in 2016, for which the patient received an appropriate shock.

In May 2018, the patient started the high-fat, high-protein, low-carbohydrate “ketogenic diet.” While on the diet, she was shocked four times for recurrent TdP over the course of 3 weeks. Interrogation of her ICD confirmed appropriate shocks for four episodes of TdP (with one additional aborted charge) (*Figure 1a*). The shocks occurred predominantly when she was alarmed or stressed. She denied any increased use of alcohol or any new medications. Her serum potassium level was 4.0 mEq/L and magnesium, 2.2 mEq/L. Selenium, ketone bodies, and volatile alcohol levels were all within normal limits. Baseline QTc was 438 ms in an ECG approximately a month prior to admission (*Figure 1b*) but 570 ms upon hospital admission (*Figure 1c*).

The patient was started on nadolol 40 mg daily. She remained arrhythmia free for 48 hours after hospital admission and was discharged with plans for close outpatient follow-up. She was told to stop the ketogenic diet and resume a normal diet. At discharge, she was continued on nadolol 40 mg daily. She was seen in clinic approximately 1 month later. Device interrogation revealed no arrhythmic events, and ECG showed her QTc to be 424 ms. She was continued on nadolol 40 mg daily and had no fibrillation events in the next 6 months.

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Figure 1. Electrocardiogram results from (a) a defibrillation event on June 6, 2018; (b) outpatient testing in May 2018, approximately 1 month prior to hospital admission, with a QTc of 438 ms; and (c) hospital admission, with a QTc of 570 ms.

DISCUSSION

Congenital long QT involves an abnormality in ventricular repolarization, resulting in a prolonged QTc on ECG. If unrecognized, it can ultimately result in fatal arrhythmias and sudden cardiac death in otherwise young and healthy individuals.¹ Patients can experience arrhythmic events in the setting of various external triggers, depending on the subtype of congenital LQTS. They are also more susceptible to acquired QT prolongation from medications and electrolyte disturbances.^{2,3} Symptoms of LQTS include presyncope, syncope, seizures, palpitations, or sudden cardiac death.⁴ Depending on the source, a normal QTc is generally defined

as between 400 and 440 ms. QTc ≥ 450 ms in men and ≥ 460 ms in women is considered prolonged.^{5,6} The Schwartz LQTS score uses QTc, specific ECG findings, symptoms, and family history to predict low, intermediate, or high probability of LQTS.⁷ If the patient falls in the high probability group, there is an 80% chance that he or she will have positive genetic testing. If genetic testing is negative in intermediate-risk individuals, then there is insufficient evidence to diagnose congenital LQTS. Low-probability individuals are often only monitored and generally do not need to undergo further testing.^{8,9} Holter monitors, event monitors, or implantable loop recorders are sometimes used to

help in diagnosis. Facial immersion or catecholamine stress test using epinephrine can be performed.¹⁰ Because there can be variable penetrance, a positive genetic test does not always translate into LQTS. As with all genetically inherited arrhythmic syndromes, it is most helpful to find an abnormality in affected individuals and then do cascade testing of first-degree relatives.¹¹ Consultation with a geneticist knowledgeable about cardiac arrhythmic syndromes can be helpful in navigating potential pitfalls of genetic testing.

The management of congenital LQTS is complex, and treatment is generally tailored around patient symptoms and risk of sudden cardiac arrest. Pending the specific subtype of LQTS, beta-blockers, antiarrhythmics, and cardiac sympathetic denervation are all potential treatment options. ICD placement should be considered in patients with a history of LQTS-associated sudden cardiac arrest or patients with cardiac syncope despite use of a beta-blocker and cardiac sympathetic denervation.¹²

There have been reports, most predominantly in the pediatric literature, regarding QT prolongation in the setting of ketosis.^{13,14} In pediatric patients who presented with diabetic ketoacidosis, 47% had a prolonged QT, which was correlated with ketosis.¹⁴ Moreover, in pediatric patients, prolongation of QT has been positively correlated with low pH,¹⁵ suggesting that QT prolongation may be related to myocardial instability from acidosis. Though the literature appears to support a correlation between ketosis and QT prolongation, further research is required to elucidate the exact mechanism. For our patient, the timing and frequency of her ICD shocks due to TdP upon initiation of the ketogenic diet, the absence of alternate provoking factors, and cessation of arrhythmia upon stopping the diet all led the authors to conclude that metabolic changes from the ketogenic diet were the most likely provoking factor for the patient's increased number of arrhythmia events. Ultimately, clinicians should be cognizant that the increasingly popular ketogenic diet may be a rare cause of QT prolongation and may lead to TdP in susceptible patients, such as those with LQTS.

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