Idiopathic Short QT Interval: A New Clinical Syndrome?

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Abstract
In this first clinical report of an idiopathic familial persistently short QT interval (QTI), we describe three members of one family (a 17-year-old female, her 21-year-old brother, and their 51-year-old mother) demonstrating this ECG phenomenon, associated in the 17-year-old with several episodes of paroxysmal atrial fibrillation requiring electrical cardioversion. Similar ECG changes seen in an unrelated 37-year-old patient were associated with sudden cardiac death. Our report also describes other manifestations of abnormal shortening of the QTI and considers the possible arrhythmogenic potential of the short QTI.

Introduction
The upper limit of normal for the QT interval (QTI) is well defined and the clinical significance of QTI prolongation is well known. A short QTI is most often encountered clinically in patients with hypercalcemia [1], and is not regarded to be a sign of increased risk for arrhythmias [2]. Other factors, such as increased heart rate [3], catecholamines [4] and acetylcholine (ACh) [5] can shorten QTI. Under such circumstances, the gradual reduction in QTI duration – as a function of the heart rate – is a normal adaptive electrophysiologic response, and its decrement ranges within predictable physiologic limits.

The following report presents two clinical settings in which unexplained very short QTI was associated with serious arrhythmias.

Case Presentation
A 17-year-old Caucasian female patient was hospitalized for laparoscopic cholecystectomy because of symptoms of recurrent cholecystitis and a finding of multiple gallstones on gallbladder ultrasound. She developed intraoperative atrial fibrillation with rapid ventricular response accompanied by pulmonary edema. Her heart rate ranged from 37 to 232 bpm; the longest RR interval was 2,200 ms, and no ventricular ectopics were noted. The patient received intravenous digoxin (0.5 mg) and furosemide (20 mg), and later was successfully direct-current (DC) cardioverted. ECGs taken immediately after cardioversion and on several occasions during follow-up revealed an extremely short QTI (280 ms at a heart rate of 69 bpm) (fig. 1a).

Preliminary data have ben presented at Madrid Arrhythmia Meeting ‘99, Madrid, Spain.
Fig. 1. Familial idiopathic short QTI. a Twelve-lead ECG from 17-year-old patient with a QTI duration of 71% of predictive value. Note: QTI duration 280 ms; heart rate 69 bpm; predictive value of QTI 393 ms; QTc (by Bazzet’s formula) 300 ms; QRS duration 88 ms. b 12-lead ECG from 21-year-old brother with a QTI duration of 66% of predictive value. Note: QTI duration 272 ms; heart rate 58 bpm; predictive value of QTI 415 ms; QTc (by Bazzet’s formula) 267 ms; QRS duration 84 ms (half standard). c 12-lead ECG from 51-year-old mother with a QTI duration of 69% of predictive value. Note: QTI duration 260 ms; heart rate 74 bpm; predictive value of QTI 377 ms; QTc (by Bazzet’s formula) 289 ms; QRS duration 80 ms.

Extensive diagnostic work-up, including serial chest x-rays, electrolytes and acid-base balances, doppler, M-mode, and transesophageal echocardiography, revealed no significant abnormalities to explain such marked shortening of the electrical systole. At discharge, the patient was placed on digoxin (25 mg q.d.), which did not affect the QTI duration. During the 3-month period that followed, the patient had two additional spontaneous episodes of atrial fibrillation requiring DC cardioversion.

Figures 1b, c demonstrate 12-lead ECG from the patient’s 21-year-old brother and 51-year-old mother, respectively. Both ECGs show the same striking abnormally short QTI: 272 ms at a heart rate of 58 bpm in the brother and 260 ms at a heart rate of 74 bpm in the mother. Of note, the mother reported several previous episodes of rhythm irregularities (not documented) unrelated to physical or emotional stress. The patient’s brother was without cardiac complaints.

In the second case, the patient was a 37-year-old Caucasian female without known health-related problems and no family history for sudden death. She presented to a referral hospital for evaluation after two syncopal episodes not related to either exercise or emotional stress. Her ECG (fig. 2) was considered normal except for a strikingly short QTI. Malignant arrhythmias had been suspected as a primary cause of the syncpe. While awaiting a scheduled diagnostic electrophysiologic work-up at a tertiary hospital, the patient died suddenly at home. No autopsy was performed.

Discussion

All QTIs in our subjects were less than 80% of predictive value (QTp) (see below). The 17-year-old patient with paroxysmal atrial fibrillation had a QTI of 280 ms (71% of QTp); her brother had a QTI of 272 ms (66% of the QTp), and her mother had a QTI of 260 ms (69% of QTp). The unrelated 37-year-old female with sudden cardiac death had a QTI of 266 ms (only 62% of the QTp).

The extreme shortness of the QTI in our patients becomes apparent when examined in the context of a study by Rautaharju et al. [6], who investigated the QTI in 14,379 healthy individuals and established a formula by which the QTI can be predicted: QTp (ms) = 656/(1 + heart rate/100). The prevalence of QTI shorter than 88% of predictive value in that study is 2.5% (360 out of 14,379), whereas QT duration less than 80% is only 0.03% (4 out of 14,379). Since two standard deviations below the mean is 88% of QTp (with only 2.5% of the population having a shorter QTI) [6], this value could reasonably be set as the lower limit of normal QTI.
The presence of an abnormally short QTI in conjunction with an arrhythmia seen very rarely in otherwise healthy subjects (idiopathic paroxysmal atrial fibrillation in the 17-year-old patient; the episodes of rhythm irregularities in her mother, and the sudden and unexpected cardiac death of the 37-year-old otherwise healthy patient with a history of syncope presumably due to malignant tachyarrhythmias) points to a causal relationship. The familial occurrence of a short QTI in our first patient is strong evidence of a hereditary abnormality.

A short QTI is a normal ECG feature in some animals including the rat, mouse, and kangaroo [7, 8] and the kangaroo is also known for a high incidence of sudden cardiac death [8]. Prominent transient outward current (I_{to}) has been attributed to the abbreviated duration of ventricular action potential, and, consequently, to the short QTI in those animals [7, 8]. Other currents that might be responsible for abbreviated action potential and for the short QTI and short refractoriness implicated in arrhythmogenic events are I_{kr} and/or I_{ca}. Although purely speculative, the link between the short QTI, short refractoriness, and electrical instability might explain the proclivity to spontaneous development of atrial and/or ventricular tachyarrhythmias.

Other Forms of the Abnormal QT Interval Shortening

We have recently described a paradoxical ECG phenomenon ‘deceleration-dependent shortening of the QT interval (DDSQTI)’ in a 4-year-old African-American girl with a history of recurrent syncope (fig. 3). Activation of I_{K,ACh} due to unusually high vagal discharge to the heart was proposed as a possible mechanism responsible for the DDSQTI in this young victim of cardiac arrest [9].

Fig. 2. 12-lead ECG obtained from the 37-year-old victim of sudden cardiac death. Note: QTI duration 266 ms; heart rate 52 bpm; predictive value of the QTI 431 ms; QT interval duration of 62% of predictive value; QTc (by Bazett’s formula) 248 ms; QRS duration 86 ms.

Fig. 3. An episode of bradyarrhythmias accompanied by deceleration-dependent shortening of the QTI and liable T wave. 04:34:00: Sinus arrhythmia with normal QTI. 11:20:29: Escape junctional rhythm with progressive shortening of the QTI and tall T wave. 11:22:13: Wandering atrial pacemaker; QTI duration 220 ms; heart rate 54 bpm. 11:23:56: Escape (supraventricular) rhythm with partial (Mobitz II type) atrioventricular block. 11:26:06: Complete atrioventricular block with the shortest QTI duration of 216 ms (third complex). 11:29:06: Atrial arrest with the RR interval of 4,600 ms. 11:38:40: Complete atrioventricular block with acceleration of the ventricular rhythm to 76 bpm and normalization of the QTI duration.

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doxical shortening of the QTI dependent on marked slowing of heart rate has been described in experiments addressing dose-dependent effects of ACh on the heart. Also, in addition to its role in muscarinic modulation of the heart rate, a very high concentration of ACh has been shown to activate IK,ACH, resulting in a marked shortening of the action potential duration [5].

Marked shortening of the QTI immediately after spontaneously terminated ventricular fibrillation has been reported in another patient with a long history of recurrent syncope [10]. Paradoxically shortened QTI after a prolonged pause has been described in 2 patients with a prolonged RR interval; this was interpreted as an abnormal adaptation of repolarization time to an abrupt increase in preceding RR intervals [11]. In each of these cases, DDSQTI was a transient ECG phenomenon, strongly suggesting its extracardiac origin and involvement of the autonomic nervous system. However, neither the clinical significance nor the arrhythmogenic potential of the DDSQTI has been delineated.

After considering the etiology and the pathogenesis of various forms of abnormal shortening of the QTI, experimental models and the possible arrhythmogenic potential of the short QTI, we hypothesized that this hereditary phenomenon probably reflects an abnormality of the cardiac cell membrane related to transmural abbreviation of atrial and/or ventricular action potentials.

Limitations
Electrophysiologic studies were not performed in these patients and might have been helpful. In addition, a more complete investigation of family members, including a genetic evaluation, was refused. Because our information is limited at present, we cannot accurately assess whether or not we are dealing with a new clinical syndrome or simply with an ECG phenomenon of idiopathic short QTI. If additional supporting clinical data become available, we believe that – paralleling the ‘long QT syndrome’ – the combination of short QTI and electrical instability could appropriately be named the ‘short QT interval syndrome’.

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References