Short QT Syndrome in a Pediatric Patient

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CASE REPORT

Short QT Syndrome in a Pediatric Patient

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Abstract Short QT syndrome (SQTS) is a recently described genetic syndrome characterized by abnormally brisk ventricular repolarization. Similar to long QT syndrome, SQTS might result in ventricular arrhythmias, syncope, and sudden death. The clinical diagnosis of SQTS is supported by the finding of an abnormally short QT interval on the resting electrocardiogram in combination with a suggestive clinical or family history. To date, few pediatric cases have been reported and the ideal therapy is unknown. We report a teenage boy who suffered a witnessed ventricular fibrillation arrest and was subsequently diagnosed with SQTS. Additional data from nine other pediatric patients diagnosed with SQTS are presented.

Keywords Channelopathy · Arrhythmia · Sudden death · Syncope

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Introduction

The association between a prolonged QT interval on the resting electrocardiogram (ECG) (long QT syndrome; LQTS) and the risk of sudden death has been known since the 1950s [10, 13, 18]. The recognition of an abnormally short QT interval (short QT syndrome; SQTS) and the risk of cardiac arrhythmias is a relatively recent observation. Both long and short QT syndromes are abnormalities of ventricular repolarization creating electrical instability of the heart, thereby providing the substrate for ventricular arrhythmias that might result in syncope, seizures, and sudden death. SQTS was first described in 2000 when three members of a family were found to have an abnormally short QT interval, with one suffering from atrial fibrillation. An additional patient also had a short QT interval and suffered recurrent ventricular arrhythmias and, finally, sudden cardiac death [9]. To date, genetic evaluation has shown that SQTS is supported by gain-of-function mutations in three different potassium channels [3, 5, 12] and two loss-of-function mutations in the L-type calcium channel [2].

As the name suggests, the diagnosis of SQTS requires an abnormally short QT interval on the resting ECG. There is debate over what constitutes a short QT interval and the lower limit of normal changes with age. In children, a normal QT interval has been reported as 370 ± 30 ms [11] and up to 385 ± 24 ms in adults [7], with a slightly longer

QT interval in postpubescent females. QT intervals in both adults and pediatric patients below 320 ms are rare [1]. As with LQTS, SQTS might be an underrecognized entity. SQTS has been proposed as a potential cause of sudden infant death syndrome (SIDS); however, the postmortem diagnosis of SQTS is very difficult.

Case Report

A 13-year-old previously healthy boy suffered a witnessed cardiac arrest while exercising. Cardiopulmonary resuscitation was initiated immediately and he was resuscitated within minutes by an emergency rescue squad without end-organ damage or neurologic sequelae. His initial heart rhythm recorded by the rescue squad was ventricular fibrillation and he was successfully defibrillated. After transfer to the local emergency room, his ECG showed sinus rhythm at 68 bpm with a QT interval of 300 ms and a heart rate corrected QT interval (QTc) of 319 ms. In addition to the short QT interval, the ECG showed morphologically abnormal T-waves, which were symmetric, tall, and narrow with an absent ST segment (Fig. 1). Diagnostic workup included chest X-ray, electrolytes, and an ECG, which were all normal. A 24-h Holter monitor recording revealed an underlying sinus rhythm with heart rates between 53 to 139 bpm, no ventricular ectopy, and a shortest measured QTc interval of 283 ms. The patient underwent electrophysiology study (EPS) with induction of ventricular fibrillation during ventricular pacing. The atrial and ventricular effective refractory periods were 190 and 200 ms, respectively. Based on these data, the diagnosis of SQTS was made. The patient was started on quinidine and a dual-chamber implantable cardioverter-defibrillator (ICD) was placed. He has been followed for 4 years and has remained asymptomatic without any further dysrhythmias or device discharges. Genetic testing was performed, but, to this date, a gene mutation has not been identified.

There was no family history of seizures, syncope, or sudden unexplained deaths. Family screening with ECGs revealed that the patient's mother and one of two sisters had T-waves that were morphologically identical to his, with tall, symmetric, and peaked T-waves that had no isoelectric ST segment. However, their QT intervals ranged from 360 to 380 ms. They both have been clinically asymptomatic. His remaining sister and father had normal ECGs, with normal appearing T-waves. No ECGs on other family members (grandparents) were available.

Discussion

A short QT interval on the ECG is a rare finding and its importance remains ambiguous [1, 7]. Metabolic and physiologic derangements that can lead to transient shortening of the QT interval include hypercalcemia, hyperkalemia, hyperthermia, acidosis, autonomic dysfunction, sinus tachycardia, acetylcholine administration, catecholamines, and digitalis effect. SQTS has been described in a limited number of patients and is recognized as an abnormality in ion

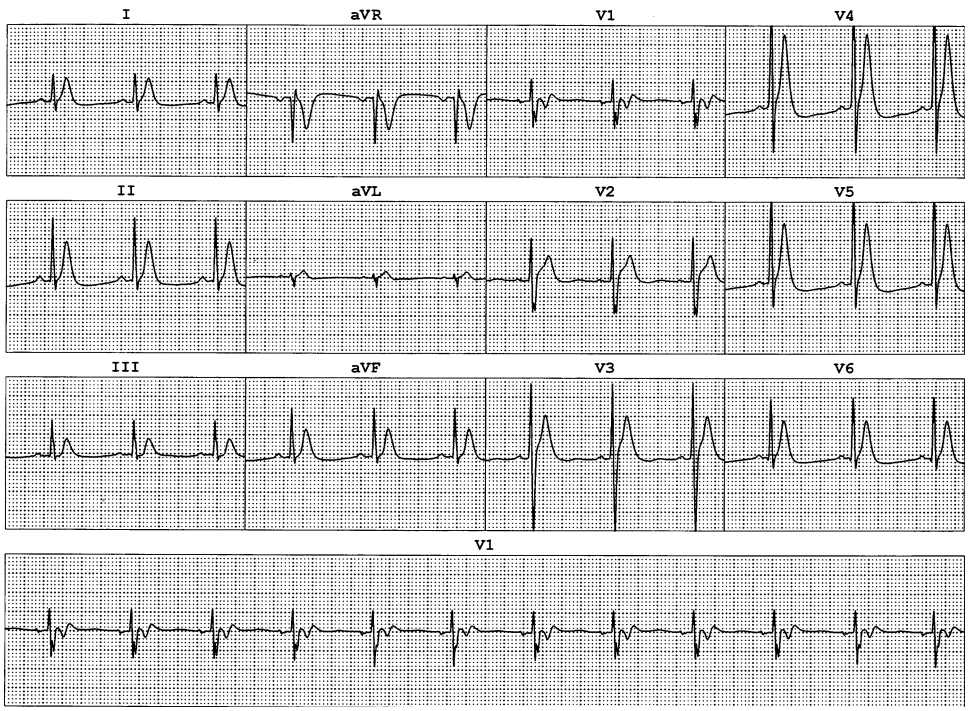

Fig. 1 Resting ECG demonstrating a QT interval of 300 ms and a QTc of 319 ms. Note the tall, peaked, symmetric T-waves with an absence of the ST segment

channels responsible for ventricular repolarization. Five gene defects have been discovered, three leading to a "gain of function" in potassium channels [3, 5, 12] and two resulting in a loss of function of calcium currents [2]. These defects result in accelerated and heterogeneous repolarization of the myocardium and result in a shortening of the QT interval. Typically, patients with SQTS have a QT interval of 320 ms or less and a QTc interval of less than 340 ms. Most SQTS patients have not had a specific mutation identified; thus, SQTS is most likely a genetically heterogeneous syndrome just like the LQTS. Affected patients usually have abnormal rate adaptation of the QT interval and the heart rate corrected QT interval at heart rates above 100 bpm might calculate as normal [20]. SQTS has been associated with atypical syncope, palpitations, atrial fibrillation, ventricular fibrillation, and sudden cardiac death (SCD). In 27% of affected patients, cardiac arrest is the first clinical symptom [8]. In addition to the short QT interval, the T-wave is usually morphologically abnormal, consistently being tall, narrow, and peaked, with almost complete absence of the ST segment in most cases.

There have been few pediatric cases described in the literature. The first clinical report of SQTS described a 17-year-old female with a QT interval of 280 ms, who developed intraoperative atrial fibrillation and pulmonary edema. Upon screening her family, two individuals were identified who had abnormally short QT intervals, one of who also had a history of atrial fibrillation. Atrial fibrillation, which is an extremely rare abnormality in pediatric patients, has been described as a common arrhythmia in patients with SQTS [17].

We have collected data on 10 pediatric patients (all male) from 8 families with SQTS. Their data are presented in Table 1. In six of the symptomatic subjects presented in Table 1, the QT interval was very short, ranging from 248 to 320 ms (QTc ranging from 252 to 320 ms). All of these individuals except one had tall, peaked, and narrow T-waves with an absent ST segment on resting ECG. Of the eight individuals who underwent electrophysiological testing, all had short atrial and ventricular effective refractory periods, which is a measure of the rate of myocardial repolarization. Some of these values are longer than those that have been reported previously in SQTS [4]. There were no significant differences in the atrial and ventricular effective refractory periods between the symptomatic and asymptomatic individuals (AERP: 170 ± 15 vs. 160 ± 20 ms; VERP 160 ± 20 vs. 180 ± 17 m). It is important to note that the population outlined in Table 1 is a biased sampling, as all of the subjects were symptomatic or had a family history of SCD or SQTS.

Of the 10 individuals included in this report, 6 had an ICD placed and 1 has received an appropriate device discharge. There have been two individuals who have received inappropriate ICD shocks, both from inappropriate classification

Table 1 Data collected on the 10 pediatric patients from 8 families with SQTS

Parameters	Patient									
	1	2	3	4	5	6	7	8	9	10
Age (years)	13	14	18	17	19	15	19	7	7	10
Sex	M	M	M	M	M	M	M	M	M	M
QT (ms)	300	248	280	320	300	245	295	280	295	300
QTc (ms)	286	252	313	320	312	315	310	262	335	355
Tall & peaked T-waves	Y	Y	Y	N	Y	Y	Y	N	Y	Y
Symmetrical T-waves	Y	Y	Y	Y	N	Y	Y	Y	Y	Y
Absent ST Segment on ECG	Y	Y	Y	N	Y	Y	Y	N	N	N
Symptoms	SCD	Sync, VF	SCD, VF	Sync & palp	Exert sync	SCD, VF	N	N	N	N
Family history	N	SQTS, SCD (father)	SQTS	N	N	SQTS	SQTS	SCD (cousin)	SCD (brother)	SCD (brother)
EPS-AERP	190	150	<180	–	160	170	180	–	140	160
EPS-VERP	200	140	<180	–	200	170	160	–	190	190
EPS-AFIB	N	N	–	–	Y	Y	N	–	Y	Y
EPS-VFIB	Y	N	–	–	N	Y	N	–	N	N
ICD Implant	Y	Y	Y	N	N	Y	Refused	N	Y	Y
FU (months)	47	63	48	44	14	38	35	32	41	41

Sync syncope, *exert sync* postexertional syncope, *VF* ventricular fibrillation, *Palp* palpitations, *SCD* sudden cardiac death, *AERP* atrial effective refractory period, *VERP* ventricular effective refractory period, *ICD* implantable cardioverter-defibrillator

of sinus tachycardia and not from T-wave oversensing, as has previously been described as a frequent problem in patients with SQTS [16].

Optimal therapy remains unclear for patients with SQTS [20]. Some recommend an ICD in all subjects with SQTS and a family history of SCD [8]. Others feel that ICDs should be reserved for symptomatic subjects or those with inducible ventricular fibrillation [6]. Although appropriate ICD discharges have been reported in patients with SQTS [14], their use in this population has been complicated by a high rate of inappropriate ICD discharges [16]. Most of the symptomatic individuals in this report received an ICD, as did two of the asymptomatic patients with a family history of SCD.

Ideal medical therapy for SQTS also remains unknown. Quinidine has been demonstrated to prolong the QT interval and lengthen the ventricular effective refractory period in patients with SQTS [15, 19]. It has not, however, been demonstrated to effectively prevent arrhythmias in this population. Only one of the patients included in this study is receiving quinidine.

As in LQTS, subjects with SQTS vary in their clinical presentation, which could range from asymptomatic to SCD. This appears to be true even in families, with the assumption being that they share the same genetic mutation. Six of the patients detailed in Table 1 had symptoms, including exertional syncope, ventricular fibrillation, and SCD. The other four patients remained asymptomatic. Three of the individuals have a family history of SCD and the fourth one has a sibling with symptomatic SQTS.

The utility of electrophysiological testing in the catheterization laboratory for risk assessment in SQTS has not been established. Electrophysiologic studies performed in eight of the subjects included in this report showed short effective refractory periods, at both the atrial and ventricular level, typical of SQTS. Atrial and/or ventricular fibrillation was induced in five of the eight individuals who underwent EPS. Two of the three asymptomatic individuals who underwent EPS had inducible atrial fibrillation. Interestingly, only two of the five symptomatic individuals had inducible ventricular fibrillation and one had inducible atrial fibrillation. One of the symptomatic individuals (Case No.2) had short atrial and ventricular effective refractory periods but no inducible atrial or ventricular fibrillation. This adolescent had two family members with SCD, underwent implantation of an ICD, and received an appropriate shock for ventricular fibrillation. Thus, noninducibility of ventricular fibrillation during EPS does not exclude future risk of ventricular fibrillation and should not be used as the only factor for risk stratification. The poor negative predictive value of the EPS in our cohort is consistent with a prior report [8].

Conclusions

Short QT syndrome is a recently described heritable abnormality of ventricular repolarization predisposing individuals to syncope and/or sudden death. In addition to the abnormally short QT interval, individuals with SQTS have morphologically abnormal T-waves that are tall and peaked with little to no ST segment between the QRS and T-wave. Affected patients usually have abnormal rate adaptation of the QT interval, leading to undercorrection of the QTc interval (inappropriately long corrected value) at heart rates above 100 bpm, which might lead to a missed diagnosis if a strict QTc cutoff is used. Screening for a short QT interval should be performed using a routine ECG in subjects with atypical syncope, survivors of SCD, and any young patient with lone idiopathic atrial or ventricular fibrillation. It has been suggested that SQTS might be involved in a small percentage of infants with SIDS and older children with unexplained SCD. Optimal medical therapy is evolving and medical therapy directed at prolonging the QT interval might be beneficial. Implantation of an ICD should be considered in subjects with SQTS, although risk stratification is poor at this time.

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