Delayed diagnosis of short QT syndrome concealed by pacemaker implant due to sick sinus syndrome

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Introduction

Patients with rare diseases unfortunately confront with late or misdiagnosis issues due to unawareness and ignorance of ordinary physicians inexperienced in related subject. Short QT
syndrome (SQTS) is a rare and highly mortal inherited channelopathy. In this case report, we present delayed diagnosis of a SQTS case and underscore red flags to avoid misdiagnosis with sick sinus syndrome (SSS).

**Case Report**

A 26-year-old woman suffering from brief dizziness periods and atypical chest pain was evaluated. A VVI pacemaker was implanted for SSS at the age of 8 years. Atrial fibrillation (AF) was detected when the battery was replaced; on follow-up, she experienced frequent episodes of AF with rapid ventricular response. At the age of 21 years, her pacemaker was upgraded to DDD mode following a successful radiofrequency ablation of AF. Despite amiodarone treatment, AF recurred 18 months later, and electrical cardioversion failed to restore sinus rhythm. On presentation, she was on aspirin and metoprolol, and her physical examination was unremarkable except for a pansystolic murmur at the tricuspid area. Electrocardiography (ECG) indicated AF and pure ventricular pacing (Fig. 1a). Echocardiography displayed normal left ventricular function, mildly dilated left atria, and moderate tricuspid valve regurgitation. Laboratory findings were normal including serum electrolyte levels. Pacemaker interrogation indicated a chronically elevated pacing threshold. Telecardiogram displayed retracted ventricular lead, whereas atrial lead was overlooped and bended toward the tricuspid valve. There was no evidence of significant dysrhythmia or pacemaker malfunction on prolonged Holter monitoring, but QT interval variation between paced and conducted beats was noticed (Fig. 1b). A repeat ECG revealed short QT interval (Fig. 1c) and was confirmed by sinus rhythm tracings found in past medical records (Fig. 1d). Family history was alarming as her father and grandfather had sudden cardiac deaths (SCDs). Her father was also diagnosed with SSS, and a VVI pacemaker was implanted before his SCD. Her father’s available ECG tracing was consistent with AF and paced rhythm with a short QT interval more prominent in conducted beats (Fig. 1e). Therefore, a genetic testing was performed, and p.V141M_KCNQ1 mutation was identified confirming SQTS. Metoprolol was switched to sotalol. In addition, an implantable cardioverter defibrillator (ICD) upgrade procedure was performed involving extraction of the pacemaker leads.

**Discussion**

Diverse presentations of SSS involves chronotropic incompetence, episodic/persistent bradycardia, sinus pause/arrest,
SQTS is a rare disease associated with atrial and ventricular tachyarrhythmias and high risk of SCD (2). From sinus node dysfunction to AF, different aspects of SQTS may manifest in an evolutionary pattern as previously described (3), and short QT interval might be unrecognized such as the presented case. Syncope as initial presentation is not uncommon in SQTS, but generally, its association with SQTS cannot be established, resulting in delayed diagnosis (2). Thus, marked bradycardia or AF in childhood and adolescence should alert physicians to suspect SQTS (2). SQTS is diagnosed (4) if the patient’s corrected QT interval is ≤340 ms. If it is ≤360 ms, one of the following additional criteria is required: (1) confirmed pathogenic mutation, (2) family history of SQTS, (3) family history of SCD before age <40, and (4) survival from a VT/VF episode in the absence of structural heart disease. In our case, short QT interval was confirmed during conducted ventricular beats, but not in paced beats. However, short QT interval in the past ECG tracings was overlooked, and she and her father were both misdiagnosed with SSS. Prolong QT interval during ventricular pacing may obscure the diagnosis, possibly when a purely paced ECG is obtained. Because pacing induced myocardial depolarization conduction wave is slower, hence the repolarization is also longer. Currently, mutations in three potassium (KCNH2, KCNQ1, and KCNJ2) and L-type cardiac calcium channel genes have been defined in association with SQTS (2, 4). In this case a highly pathogenic p.V141M_ KCNQ1 mutation was identified warranting the SQTS diagnosis which is particularly related with cardiomyopathic changes in the left ventricle (5). Her family history supported the diagnosis and poor outcome expectation. There is no validated risk stratification scheme for SQTS, and electrophysiological study has no added value. Theoretically, patients may benefit from antiarrhythmic drugs that prolong QT interval. Hydroquinidine or sotalol is offered in SQTS, and electrophysiological study has no added value. Late follow-up in three unrelated children. Heart Rhythm 2018; 15: 1261-7.

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