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CASE REPORT
Rare arrhythmias

31-year old man with short QT syndrome (RCD code: V-1A.3)

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Abstract

Short QT (SQTS) syndrome is a rare inherited autosomal dominant cardiac channelopathy associated with malignant ventricular and atrial arrhythmias. It is the severest form of the major channelopathies, with cardiac arrest or sudden cardiac death (SCD) as the most common presentation. We report a case of a young patient in whom ventricular fibrillation was the first manifestation of the disease.
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Key words: rare disease, channelopathy, electrocardiography, implantable cardioverter-defibrillator

Introduction

Short QT (SQTS) syndrome is a rare inherited autosomal dominant cardiac channelopathy associated with malignant ventricular and atrial arrhythmias. It was first described in 2000 year. It is the severest form of the major channelopathies, with cardiac arrest or sudden cardiac death (SCD) as the most common presentation. SQTS is a result of gain of function mutations in three potassium (K+) channel genes causing three syndromes: SQTS1 caused by mutations in gene hERG, SQTS2 caused by mutations in KCNQ1 gene and SQTS3 caused by mutations in KCNJ2 [1,2]. To date, also some loss-of function mutation in CACNA1C and CACNB2b genes, encoding L-type calcium channel have been identified which are linked with pathogenesis of short QT syndrome. Dysfunction of ion channels leads to the increase of dispersion of repolarization, which in combination with reduced ventricular refractory period, constitute the potential substrate for reentry and thus life-threatening ventricular tachyarrhythmia [3].

In short QT syndrome characteristic changes are observe in ECG. Crucially and in opposite to the more common long QT syndrome, very short and uniform QT/QTc intervals (QTc interval ≤330 ms with the exception of the calcium-dependent variants 4 and 5) are observed. Moreover, some minor ECG abnormalities, such as:

- absent or minimal ST segments,
- interval from J point to T wave peak (Jp-Tp) measured in the precordial lead with the T wave of greatest amplitude <120 ms,
- possible tall T waves with narrow base similar to the T wave found in hyperkalemia ("desert tent T waves"),
- early repolarization pattern [5],
- prolongation of T_{peak}-T_{end} interval,
- presence of prominent U waves,
- and very frequent paroxysmal AF [4].

Additionally, ECG response to exercise is characterized by a discrete QT interval reduction with increases in heart rate. Affected patients may complain about irregular palpitations due to frequent episodes of paroxysmal atrial fibrillation or dizziness. In substantial number of patients, sudden cardiac death (SCD) may be the first manifestation of the disease. Events can occur during rest, sleep or on exertion [1]. The therapy of choice for patients with SQTS is the implantation of cardioverter defibrillator [7,8]. Some data confirm that Quinidine, which prolongs QT interval and normalized the effective refractory periods of the atrium and ventricle, may have a beneficial effect in patients with short QT-1 syndrome [6].

Case report

We report the case of 31-year old male who was referred to our Department for a second opinion. Young and so far healthy patient, with normal physical activity, untreated for any diseases had a sudden cardiac arrest due to first-ever ventricular fibrillation and underwent effective out-of-hospital resuscitation. Afterwards,

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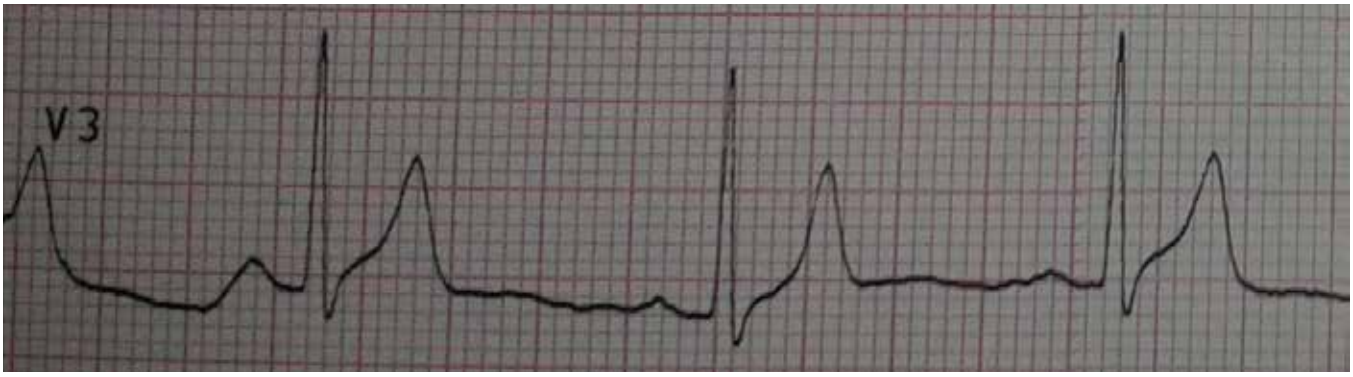

Figure 1. Electrocardiogram. Lead V3: QT interval-310ms, QTc-323 ms, tall T waves, U wave

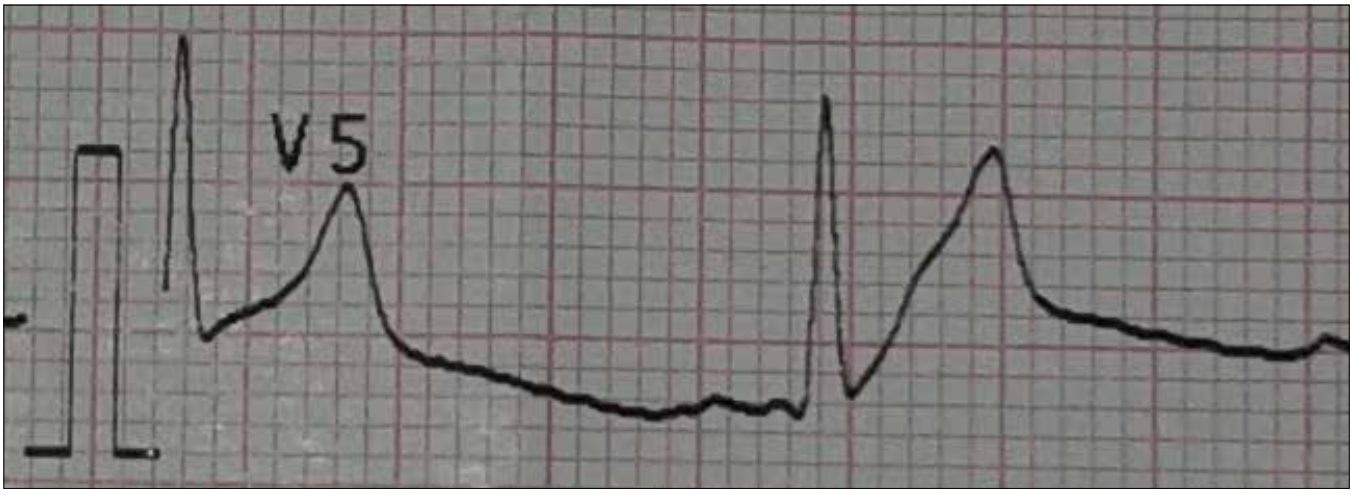

Figure 2. Electrocardiogram. Lead V5: minimal ST segment, tall T waves

he was in coma for a week and stayed in the Intensive Care Unit. During the hospitalization he had detailed diagnostic work-up, including biochemical parameters, presence of drugs in blood, imaging examinations, such as CT scan of the head and cardiac MR. Analyzed blood samples revealed normal level of electrolytes (potassium, sodium, chloride and magnesium ions) and did not contain any drugs or other toxic substances. Imaging examinations did not reveal any abnormalities that could be responsible for sudden cardiac arrest. After several weeks of hospitalization and rehabilitation he fully recovered without any neurological deficits. Despite, having not found the reason for the event, he had cardioverter-defibrillator implanted as a secondary prevention of SCD.

At the presentation, he was mildly obese (BMI 33,4 kg/m^2), works as crane navigator and has regular physical activity. Patient was diagnosed with mild hypertension a few months before and ACE inhibitor was started. His family history was unremarkable. He denied syncope, heart palpitations or dizziness. Physical examination revealed regular heart rate of 60 bpm, blood pressure of 120/70 mm Hg, on-air oxygen saturation was 98%. His respiratory rate was 12/min and alveolar murmur on lungs auscultation was heard. His basic biochemical parameters were within normal and presented as follow: Hb 15,5 g/dl [N 14,0–18,0 g/dl]); electrolytes: K+ 4,6 mmol/l [N 3,5–5,1 mmol/l], Na+ 140 mmol/l [N 136–145 mmol/l], Cl- 102 mmol/l [N 98-107 mmol/l], Mg2+ 0,91 mmol/l [N 0,66–1,07 mmol]; liver transaminazes (Aspat 29 U/L [N <40] Alat 37 U/L [N<41] and renal functioning parameters (creatinine 91 umol/l [N 62-106 umol/l, eGFR 96 ml/min [N >60 ml/min] were normal; NT-pro BNP was 100 pg/ml [N <125].

12-leads ECG revealed sinus rhythm 60/min, normal axis, PQ interval 160 ms, QRS 80 ms, QT interval 310 ms. QTc 323 ms, U wave (Figure 1,2).

24-hour Holter-ECG registered sinus rhythm throughout with maximal HR 84 bpm, minimal 48 bpm and average HR 59 bpm, single ventricular extra-systoles (49). Normal circadian twenty–four–hour cycle.

An echocardiogram showed normal sized left ventricle (LVEDd – 55 mm; LVEDs – 36 mm) with mild hypertrophy of the walls (interventricular septum 12 mm, posterior wall 12 mm) and slightly enlarged left atrium (LAA 25 cm^2). Preserved global systolic function of left ventricle with ejection fraction of 60% was observed. Besides normal systolic function of right ventricle (TAPSE 24 mm), trans-valvular gradients and flow spectrum was seen. Diastolic function was slightly impaired with E/A 0,82. There were no signs of pulmonary hypertension (PASP 20 mm Hg).

Discussion

Taking into account fact that a young, healthy man suffered from sudden cardiac arrest forced us to search for a possible cause, which could have been crucial for further management and treatment. In a comprehensive approach to this patient we included patient's medical history, actual functioning state, physical examination and results of additional tests. Based on the results of conducted diagnostic schedule, there was no objective reason found so far responsible for ventricular fibrillation (VF). Patient did not have electrolytes imbalance or he hadn't been under drugs influence. His MRI and echocardiography revealed normal structure and functioning of the heart, there was no signs of pulmonary embolism. 24-hour Holter-ECG monitoring did not register ventricular or supraventricular arrhythmias, neither conduction disturbances. Obviously, should be remembered the fact that idiopathic ventricular fibrillation is not relatively rare and accounts for up to 14% of all VFs [10]. However, in this case basic 12-lead resting electrocardiogram (ECG) draws an attention and directs further reasoning. Firstly, it revealed very short corrected QT interval (Qtc), estimated with Bazett formula, which is definitely ≤330 ms and range as 323 ms (Figure 1). Secondly there is absent or minimal ST segments seen in precordial leads, an interval from J point to T wave peak (Jp-Tp) measured in the precordial lead lasts <120 ms, finally presence of U waves can be seen. That picture of ECG inclined to diagnosed Short QT Syndrome. Furthermore to determine the probability of that diagnosis we used probability scoring proposed by Gollob. Gollob et al. [11] published a systematic review based on a comprehensive analysis in order to develop diagnostic criteria for congenital SQTS to facilitate clinical evaluation of suspected cases [12]. The score was established on the basis of clinical, electrocardiographic, and genetic criteria as follows:

- 2 electrocardiographic criteria:
  - QT interval corrected by Bazett's formula <370 ms (1 point), <350 ms (2 points) and <330 ms (3 points)
  - and J point-T peak interval duration in ms: Jp-Tp, <120 ms (1 point);
- 4 personal clinical history dates:
  - history of sudden cardiac arrest (2 points),
  - documented polymorphic VT or VF (2 points),
  - unexplained syncope (1 point)
  - and/or AF (1 point),
- 3 family history parameters:
  - first-or second-degree relative with high probability of SQTS (2 points),
  - first-or second-degree relative with autopsy negative SCD (1 point),
  - and sudden infant death syndrome (1 point);
- 2 genetic findings:
  - genotype-positive (2 points)
  - mutation of undetermined significance in a culprit gene (1 point).

A score ≥4 points is considered high probability, 3 points intermediate probability and 2 points low probability of SQTS. Taking into consideration above scoring our patient received 7 points: QTc <330 ms (3 points), history of sudden cardiac arrest (2 points), documented VF (2 points), which means a high probability diagnosis of SQTS. Therefore he was given a recommendation to perform the genetic examination of himself and his first-degree relatives. As regards to the treatment of Patients with SQTS the cardioverter defibrillator (ICD) implantation remains the main strategy associated with drugs (Quinidine or Propaphenone) for atrial fibrillation (AF) prophylaxis and for reducing the number of ventricular arrhythmic events [13]. Our Patient had an ICD implantation as an secondary prevention of SCD. Also, an important issue is an appropriate programming of the ICD to prevent an inadequate shocks due to over-sensing the prominent T waves [14]. The Patient and his family remains under regular cardiological control.

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