Case Report

Aborted Sudden Cardiac Death Associated with Short QT Syndrome

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A 43-year-old male was transferred to our institute. His heart rhythm on admission was ventricular fibrillation (VF) which was successfully defibrillated with a direct current shock (DC). A diagnosis of short QT syndrome (SQTS) was made on the basis of an abnormally short QT interval of 280 ms during the sinus rhythm. During treatment for mild total hypothermia, VF recurred repeatedly necessitating DCs. Nifekalant at a dose of 0.3 mg/kg was intravenously administered, the QT interval was prolonged from 280 to 370 ms and VF no longer recurred. Subsequently the patient underwent implantation of an implantable cardioverter defibrillator.
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Key words: Short QT syndrome, Ventricular fibrillation, Implantable devices, Antiarrhythmic agent

Case Report

A 43-year-old male suddenly passed out while working at his desk, and bystanders who witnessed it immediately performed cardiopulmonary resuscitation on him. Despite their efforts, he did not regain consciousness, and they then called for an ambulance. The ambulance transferred him to the emergency room of our institute. His cardiac rhythm upon arrival was VF, and direct current shock (DC) was immediately delivered, resulting in the resumption of sinus rhythm (SR). Serum potassium and calcium concentrations were 3.9 and 9.2 mEq/L, respectively, and arterial blood pH was 6.947. He then underwent treatment for total mild hypothermia to improve his cerebral status which had suffered from brain damage caused by the cardiac arrest. The patient had no history of cardiovascular disease except for the paroxysmal atrial fibrillation. There was no history of sudden death in his family. He had been undergoing treatment for pure red cell aplasia for the past 10 years, and had received many blood transfusions for his anemia. During the total mild hypothermia (34 °C), he had experienced repeated VF attacks which necessitated DCs to regain SR. In order to suppress the incidence of VF, nifekalant, a pure Ikr blocker, was intravenously administered to prolong his QT interval. Continuous intravenous

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nifekalant was started at a dose of 0.2 mg/kg and then increased to 0.4 mg/kg. A routine 12-lead electrocardiogram revealed SR with a significant prolongation of the QT interval from 280 to 370 ms (Bazett-corrected QT interval of 320–410 ms). The QT interval was measured from the onset of the Q wave to the terminal portion of the T wave. The configuration of the QRS complex was similar to an "Osborn wave", and may have been associated with the total hypothermia. Further, the slurring and notching of the terminal portion of the QRS complex might have been a manifestation of the transmural electrical inhomogeneity leading to the serious arrhythmias[1] (**Figure 1**) and peaked T waves that were observed as the nifekalant dose was increased to 0.4 mg/kg/hour. As the QT interval became prolonged by the intravenous nifekalant, the incidence of VF was significantly suppressed (**Figure 2**). The serum potassium concentration was maintained within normal limits and ranged from 4.1 to 5.5 μmol/l throughout his clinical course. Nifekalant was withdrawn when the QT interval significantly prolonged to a value of at least 350 ms, and frequent occurrence of VF was concomitantly and completely suppressed. The QT interval was maintained at approximately 370 ms even after the withdrawal of the nifekalant. After the total mild hypothermia, his consciousness recovered to a normal level. He underwent coronary angiography, ventriculography, and a myocardial biopsy for further examination of the etiology of his pathological status. The biopsy specimen was obtained from the right ventricular septum.

There was no evidence of abnormal coronary arteries or left ventricular function. An electrophysiological study (EPS) was also performed in the clinic to assess his VF 21 days after the cessation of the intravenous nifekalant. The effective refractory period (ERP) of the ventricles was 160 ms at a basic cycle length of 600 ms, which was measured through the electrode catheter positioned at the right ventricular apex. EPS was not performed at any other ventricular location. VF was easily and repeatedly induced by double ventricular extrastimuli (VPE) at a basic cycle length of 600 ms (**Figure 3**). EPS for the assessment of the effects of the antiarrhythmic agents was not performed. Because the ERP of his ventricles was too short, the coupling intervals of the double VPE, which were able to provoke VF, were 170 and 160 ms, respectively. He underwent implantation of an implantable cardioverter defibrillator (ICD). The diagnosis suggested by the myocardial biopsy was myocardial hemochromatosis and was characterized by deposits of hemosiderin in

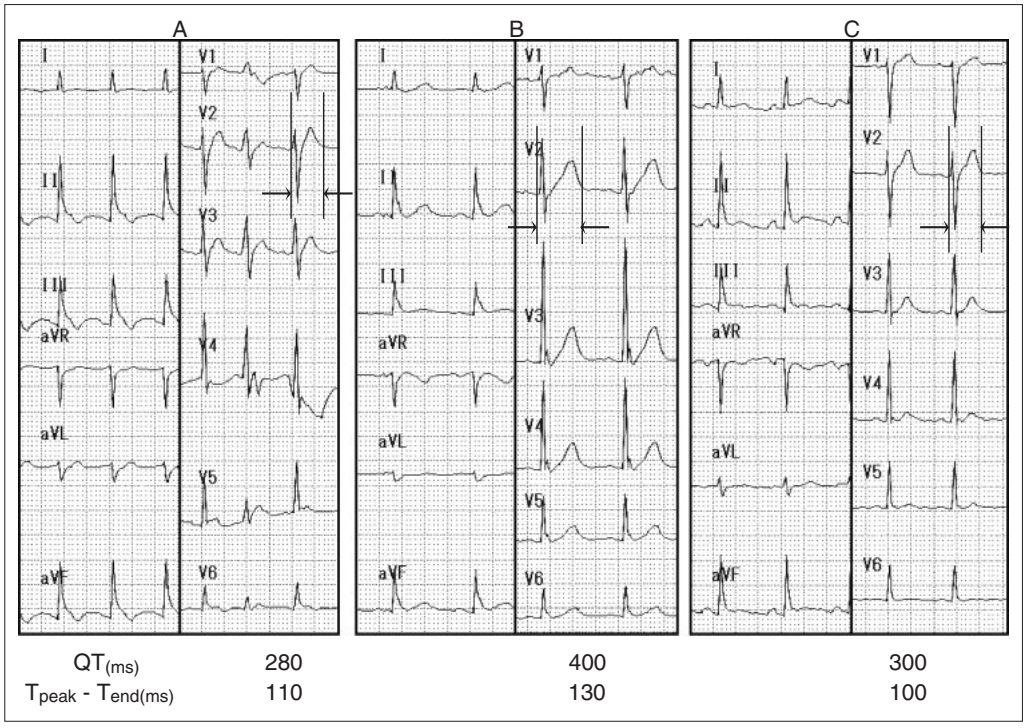

Figure 1 Twelve-lead electrocardiogram.
The QT interval was prolonged from 260 ms (on admission: panel A) to 370 ms (panel B) when intravenous nifekalant was administered, and then shortened back to 300 ms (panel C) when the nifekalant was withdrawn.

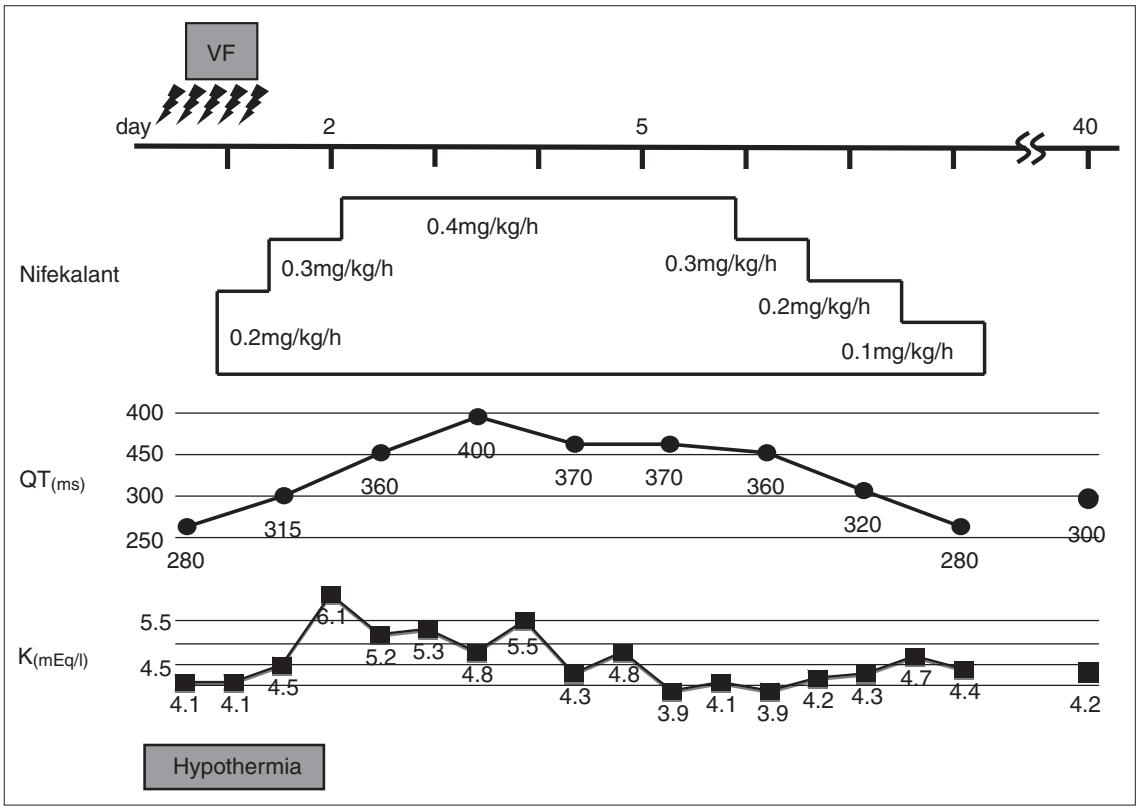

Figure 2 The clinical course in this case.
Since the QT interval was prolonged by the intravenous nifekalant, the incidence of VF significantly decreased.

the myocardium. The ejection fraction of the left ventricle was approximately 57% calculated from transthoracic echocardiography. A genetic screening test was also given. The target genes were KCNH2,[2,3] KCNQ1,[4] KCNJ2,[5] as well as KCNE1 and KCNE2. However, as a result no mutations of those genes were found. Twelve-lead ECG tracings from his parents and children were examined, and no abnormal findings were recognized.

Discussion

Unlike QT prolongation, an abbreviation of the QT interval had not been considered to pose any arrhythmic risk until the publication by Gussak et al.[6] identifying that phenotype as a new clinical entity associated with an arrhythmic burden. In addition, short QT interval is not associated with any electrolyte imbalance or metabolic abnormality just as was seen in the present case. In patients with a prolonged QT interval, the Bazett correction formula is used to assess the risk of a disastrous outcome; however, Extramiana et al. demonstrated that the formula was not appropriate for making a diagnosis of SQTS because that method might induce a false negative diagnosis of SQTS.[7] Dumaine and Wolpert also reported that the rate-adaptation of the QT interval is abnormal in SQTS patients, and the QT interval may appear normal at faster heart rates when Bazett's or other corrections are applied.[8,9]

Gaita et al.[10] tested the therapeutic effects of flecainide, ibutilide, sotalol and quinidine in SQTS patients, and they found that only quinidine produced normalization of the QT interval, T wave morphology and ventricular ERP, which were described as characteristics peculiar to SQTS by Antzelevitch and Giustetto.[11,12] They further suggested that not only the blockade action of Ikr, but also quinidine's other properties were effective for treating SQTS. In our case, nifekalant, a pure Ikr blocker, was effective for dramatically suppressing the electrical storms of VF, although it is possible that the VF in the present case might have been associated with the mild hypothermia provoking a "J wave" in the setting of the SQTS. In addition, we were unable to completely exclude the possibility of VF associated with hemochromatosis.[13,14]

When we are looking for the acute effects of a drug on VF storms in STQS, this drug might be the first option for therapy. In particular, in patients who

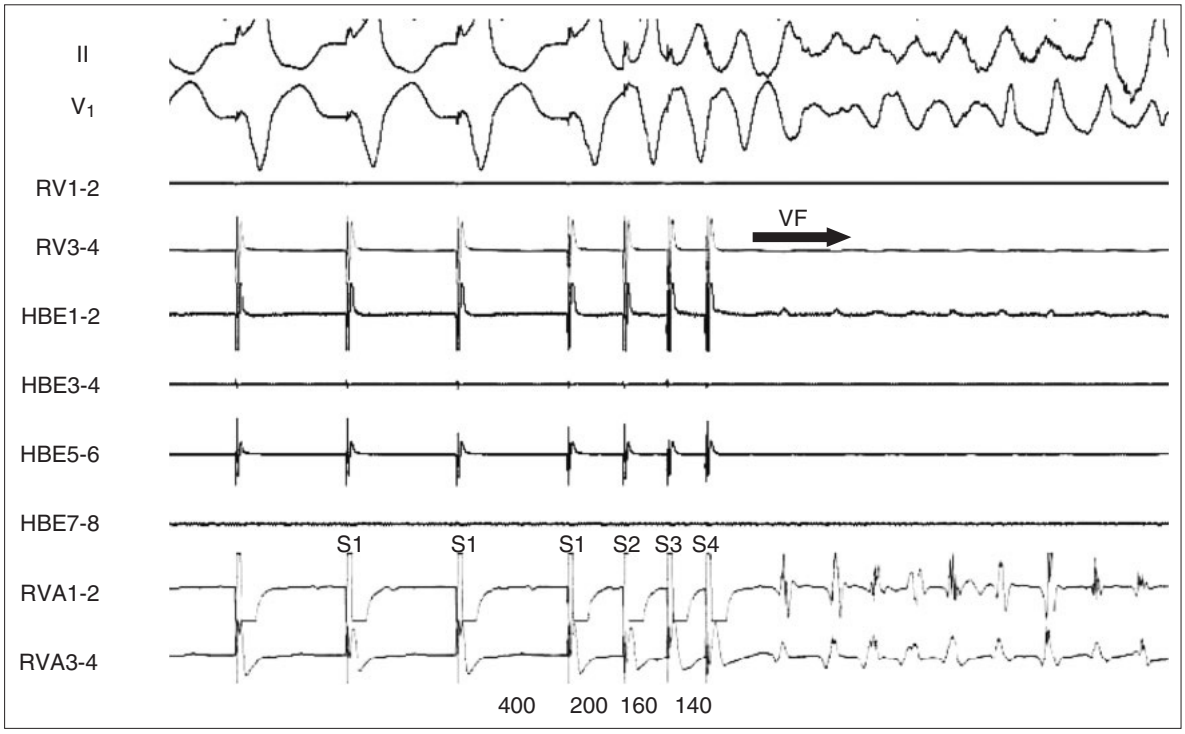

Figure 3 The ERP of the ventricles was very short at 160 ms at a basic cycle length of 600 ms. When double ventricular extra-stimuli were delivered, VF was reproducibly induced as shown in the figure.

are connected to artificial ventilators as in the present case, the intravenous administration of antiarrhythmic agents could be regarded as the sole therapeutic option. Antiarrhythmic Ikr blocker agents such as sotalol and quinidine could also be prescribed for chronic prophylactic treatment for VF.

The diagnosis of hemochromatosis was made according to the results of the myocardial biopsy. However, to our knowledge, there are no reports of a relationship between hemochromatosis and SQTS associated with VF.

We considered the VF in the present case to be unassociated with the electrolyte imbalance and the metabolic acidosis.

In view of the generally insufficient evidence of the protective effects of pharmacological interventions, the possibility of terminating potentially life-threatening episodes of malignant ventricular tachyarrhythmias by electrical shocks delivered from ICDs has become increasingly attractive.[15] Therefore, an appropriate risk stratification provides a rational basis for proposing an ICD implantation with a reasonable risk-benefit ratio. Although the significance of programmed pacing is unclear regarding the risk stratification,[12] we regarded the ease and reproducibility of VF as significant findings. Therefore, we made a decision to implant an ICD in this patient. Atrial fibrillation (AF) may be the first symptom of SQTS, especially in relatively younger patients with lone AF,[16,17] and our patient also had multiple episodes of AF. He was followed up for a year, no shocks have been delivered up to the present without the use of any antiarrhythmic agents. SQTS is a rare, mechanistically heterogeneous and incompletely understood disorder. The primary treatment is an ICD implantation even though this is suboptimal. Despite agreement that effective drug therapy for SQTS is necessary, there are limited opportunities for clinical drug testing in this rare disease. Nifekalant could be regarded as the first line antiarrhythmic agent for acute dysrrhythmic events in short QT syndrome.

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