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【 CASE REPORT 】

Ventricular Fibrillation Induced by Takotsubo Syndrome with Congenital Long QT Syndrome

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Abstract:

We herein report a case of congenital long QT syndrome (LQTS) in which the QT interval was prolonged by Takotsubo syndrome (TTS), inducing ventricular fibrillation (VF). The patient was a 55-year-old woman who had been diagnosed with LQTS. Cardiopulmonary arrest occurred while coughing during sleep. VF was observed, and her heartbeat returned after two defibrillations. An electrocardiogram showed marked QT prolongation and large negative T waves. Echocardiography demonstrated hyperkinesis at the base of the left ventricle and akinesis at the apex. As there was no significant stenosis in the coronary artery, she was diagnosed with TTS.

Key words: congenital long QT syndrome, Takotsubo syndrome, ventricular fibrillation

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Introduction

Congenital long QT syndrome (LQTS) is an inherited disease that causes polymorphic ventricular tachycardia, similar to Torsades de pointes (TdP) and ventricular fibrillation (VF), leading to syncope and cardiac arrest. Takotsubo syndrome (TTS) causes marked QT prolongation and ventricular tachycardia (VT)/VF (1). This is the first report of a patient with LQTS who developed TTS and VF.

Case Report

A 55-year-old woman had fainted several times around the age of 20. At the age of 35, her daughter was found to have an abnormal electrocardiogram (ECG). Genetic testing revealed a novel splicing mutation in KCNH2, and her daughter was diagnosed with LQTS (type 2). She was also diagnosed with LQTS (type 2), but she declined β-blockers because of bronchial asthma. She was the director of a nursery school and had recently been experiencing trouble on the job. Quinolone antibiotics were prescribed for her bronchitis, and she developed diarrhea seven days before being admitted to our hospital for cardiopulmonary arrest (CPA).

On the day of the admission, CPA occurred while she was coughing during sleep. Her husband sleeping next to her called the ambulance. When the rescue unit arrived, VF was observed using the automatic external defibrillator. Spontaneous circulation was restored after two defibrillations.

Upon admission, her vital signs were as follows: consciousness, JCS III-100; pulse, 100 bpm; blood pressure, 94/70 mmHg; body temperature, 36.5℃; arterial oxygen saturation on pulse oximetry, 99% on 100% oxygen-assisted ventilation; and respiratory rate, 20/min.

She was not responsive on arrival to the hospital, and her breathing was weak and unstable. Ventilation management was required. As shown in the Table, an increased NTproBNP level (3,192 pg/mL), hypokalemia (2.9 mEq/L), and hypomagnesemia (2.1 mg/dL) were observed. Electrocardiography demonstrated a sinus rhythm of 100/min, T wave elevation in V2-4 leads, and QTc interval of 538 ms (Fig. 1). On echocardiography, we confirmed hypercontraction at the base of the left ventricle and no contraction at the apex (Fig. 2). We suspected TTS or acute anterior myocardial infarction, but no significant stenosis in the left or right coronary arteries was found on coronary angiography (Fig. 3). Therefore, we diagnosed her with TTS. At the

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Table. **Laboratory Data on Admission.**

WBC	9,310 /uL	AST	101 IU/L	CK	267 IU/L
RBC	432×10⁴ /uL	ALT	53 IU/L	CK-MB	41 IU/L
Hb	12.8 g/dL	LDH	317 IU/L	TnT	0.019 ng/mL
Hct	38.8 %	TP	6.0 g/dL	NTproBNP	3,192 pg/mL
Plt	35×10⁴ /uL	Alb	3.0 g/dL	Glu	136 mg/dL
		BUN	22 mg/dL	CRP	0.70 mg/dL
		Cr	0.81 mg/dL	TSH	0.58 μlU/mL
		Na	139 mEq/L	FT3	3.15 pg/mL
		K	2.9 mEq/L	FT4	1.69 ng/mL
		Cl	106 mEq/L		
		Mg	2.1 mg/dL		

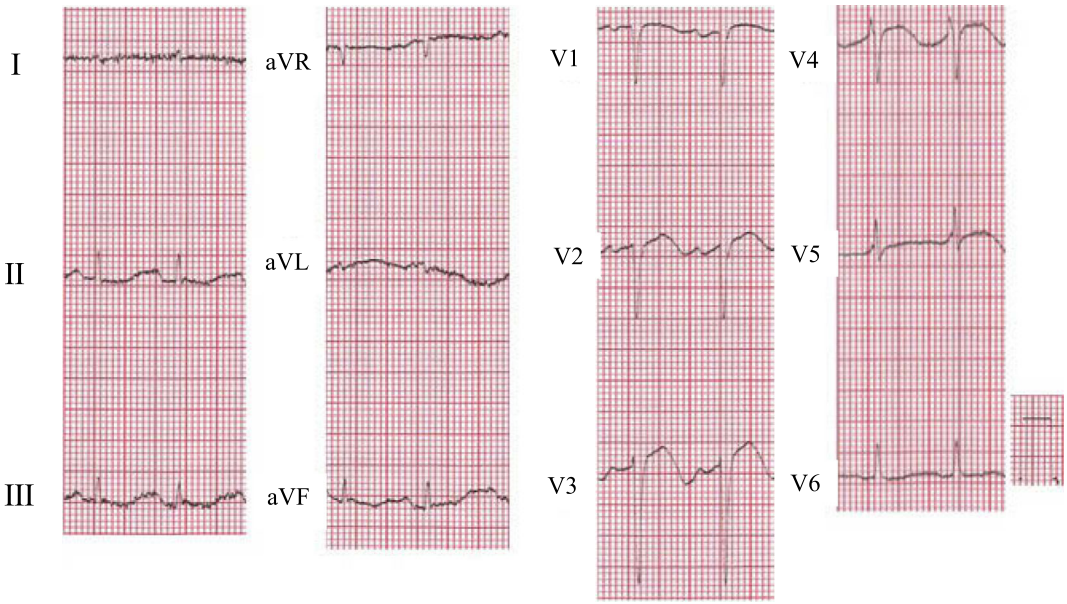

Figure 1. **The electrocardiogram at admission. ST increase in V2-4 leads.**

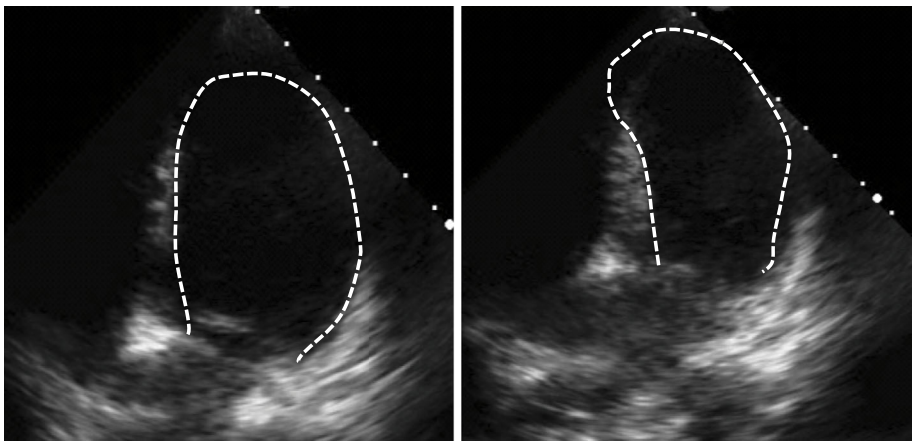

Figure 2. **Echocardiography on arrival. (A=Diastole, B=Systole). Echocardiography in the four-chamber view shows akinesia of the apex with systolic ballooning.**

CCU, we confirmed marked QT prolongation on the monitor. As it was difficult to control the frequent TdP-like polymorphic ventricular tachycardia (Fig. 4), she was deeply sedated under ventilation, and we corrected her electrolyte abnormalities (hypokalemia and hypomagnesemia). Although β-blockers were administered (bisoprolol, 0.03 mg/kg/day)

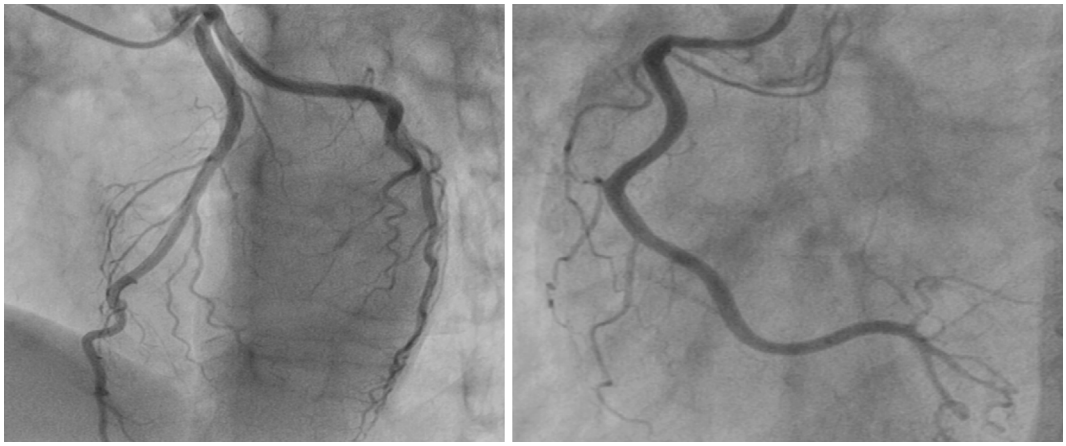

Figure 3. **Coronary angiography. No significant stenosis in the left or right coronary arteries.**

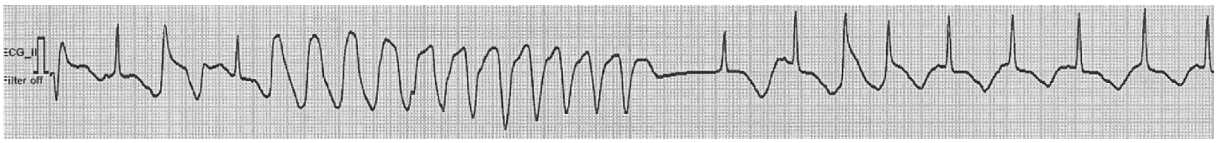

Figure 4. **Monitoring at the CCU. Polymorphic ventricular tachycardia similar to Torsade de pointes.**

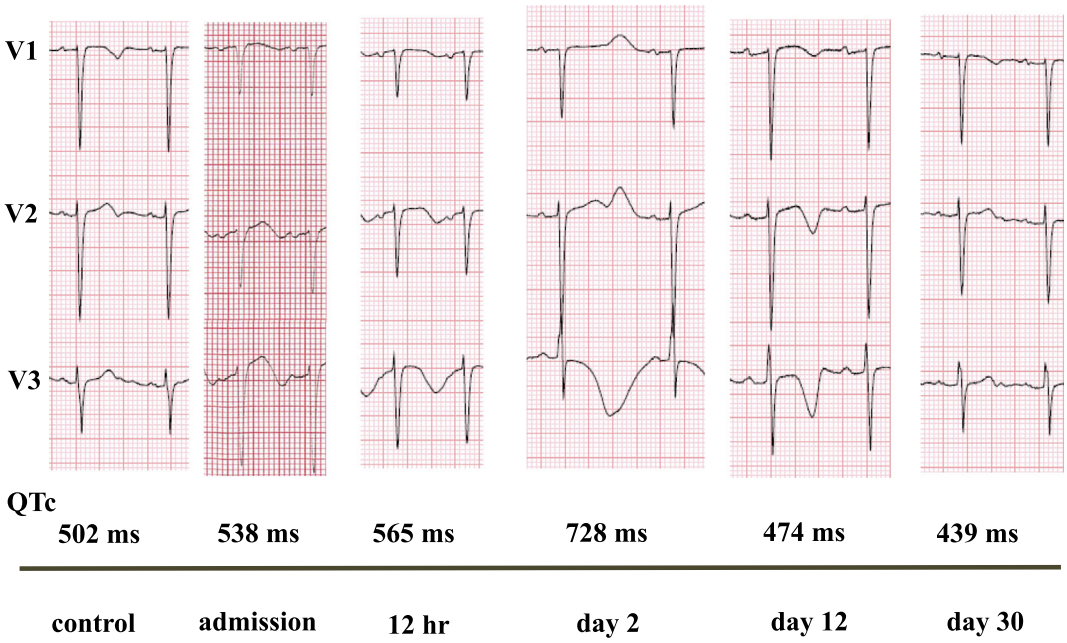

Figure 5. **QTc. Electrocardiographic changes.**

for LQTS, VT recurred. Ventricular arrhythmias were controlled by verapamil at 3 mg/kg/day and mexiletine at 7.5 mg/kg/day. Due to LQTS and TTS, the QTc interval at arrival was 538 msec, but after 12 hours, it increased to 565 msec with negative conversion of T waves. The QTc interval increased to a maximum of 728 msec after 48 hours and then gradually shortened to 474 msec on the 12th day (Fig. 5). On the 15th day, we implanted a cardioverter-defibrillator (ICD) to prevent sudden death. Echocardiography before discharge was normal, which was consistent with the course of TTS.

Discussion

To our knowledge, this is the first report of VF induced by TTS in a patient with LQTS. Electrolyte abnormality (hypokalemia and hypomagnesemia due to diarrhea), quinolone antibiotics, and TTS caused by cold stress and stress due to trouble on the job led to further QTc prolongation in the patient, resulting in VF. Some severe complications of

TTS have been previously reported to cause VT and VF in 3-5% of patients (1, 2), ventricular thrombus in 1.3%, and ventricular rupture in 0.2% (2). QT prolongation was observed in 50% to 100% of TTS patients (3), and it took 97 to 191 days on average for the QTc interval to normalize (4).

The stress of VF induced by further QTc prolongation by electrolyte abnormality (hypokalemia and hypomagnesemia) and quinolone antibiotics in a patient with LQTS might have caused TTS. However, there have been no reports of VF causing TTS. Nevertheless, we feel that it is likely that TTS caused VF because she had a history of developing TTS, such as in response to cold stress and trouble on the job.

In the acute phase, it was difficult to control fatal arrhythmias due to QTc prolongation. β-blockers, such as nadolol and propranolol, as drug treatment for long QT syndrome have been demonstrated to be useful (5). We first used bisoprolol, a β1-selective β-blocker, because of active bronchial asthma, but it was ineffective. We then added a Na channel blocker (mexiletine) and calcium antagonist (verapamil) because bisoprolol alone was insufficient to control the arrhythmias. These agents have been prescribed for LQTS when the β-blocker alone was ineffective, but their effects were limited (6, 7). A QTc exceeding 500 ms in LQTS patients receiving β-blocker therapy was reported to be a significant predictor of cardiac events and cardiac arrest (8). In the present case, the QTc interval normalized with these agents on the 30th day. We therefore considered the dose of these agents for LQTS to be optimal. In contrast, there has been no evidence suggesting any survival benefit with the use of β-blockers for TTS (2). Patients who survived the initial TTS had a second event in approximately 5% of cases, typically 3 weeks to 3.8 years after the first event (9). As the prevalence of recurrent TTS is relatively low and LV dysfunction as well as ECG abnormalities were reversible, an implantable cardioverter-defibrillator (ICD) for secondary prevention was of uncertain value in TTS patients experiencing malignant ventricular arrhythmias (10, 11). In case of excessive prolongation of the QT interval or life-threatening ventricular arrhythmias a wearable defibrillator may be considered (12). As she strongly requested an ICD, it was implanted as the secondary preventative measure for LQTS.

Given that sound stimuli, such as telephones and alarm clocks, often cause fatal arrhythmias (13), the presence of removable triggers must be considered. However, even with these treatments, some cardiac events, such as fainting and fatal arrhythmias, develop in approximately 10% of LQTS patients within 10 years (14). In the present case, the risk of cardiac events was intermediate because there were two risk factors: female gender and LQTS (type 2) (15). It is necessary to optimize treatments according to the individual patient risk.

Conclusion

We treated a patient with congenital LQTS who developed TTS leading to VF. Congenital LQTS patients are often young at the diagnosis and require optimization of treatments according to their individual cardiac event risk.

The authors state that they have no Conflict of Interest (COI).

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