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CASE REPORT

An unconventional dose of epinephrine for a diagnostic test of catecholaminergic polymorphic ventricular tachycardia: A case report

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Abstract

Catecholaminergic polymorphic ventricular tachycardia (CPVT) is a rare heritable arrhythmogenic disease, and the Mayo Clinic protocol-guided epinephrine test is commonly used for diagnostic purposes. Whether the Mayo Clinic protocol is enough for patients who are insensitive to catecholamine remains an unknown question. Our patient was a19-year-old female who presented with recurrent stress-induced syncope and was saved by cardiopulmonary resuscitation. The initial physical examination and complementary tests (ECG, blood laboratory, cardiac ultrasound, and cranial magnetic resonance angiography) showed no abnormalities on admission. Treadmill exercise testing shows non-sustained and polymorphic tachycardia. A subsequent epinephrine test was performed, and polymorphic ventricular tachycardia was not induced until using a high dose of epinephrine above Mayo Clinic protocol. Therefore, it is suggested that an unconventional dose of epinephrine may be needed fordiagnostic tests of CPVT for some insensitive individuals.

Keywords: Catecholaminergic polymorphic ventricular tachycardia; Syncope; Epinephrine test

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1. Background

Syncope is a transient loss of consciousness, and its differential diagnosis is sometimes difficult. Catecholaminergic polymorphic ventricular tachycardia (CPVT) is a rare heritable arrhythmogenic disease characterized by adrenergic-induced bidirectional or polymorphic VT[1]. The prevalence of CPVT is estimated at 1:10,000; however, the mortality rate is as high as 30% by the age of 30 if untreated. Therefore, early diagnosis of CPVT is of great importance, and epinephrine plays an important role in the standard diagnostic test[2]. Here, we present a special case of CPVT during our diagnostic test using an unconventional dose of epinephrine.

2. Case presentation

A 19-year-old female who had repetitive episodes of syncope induced by physical exertion was referred to our hospital. About 1 year earlier, she suddenly lost consciousness at school during exercise. Paramedics found her pulseless and started cardiopulmonary

resuscitation. After referral to the local hospital, she was intubated, placed on mechanical ventilation in the intensive care unit, and finally successfully discharged. After referral to our center, a 12-lead electrocardiogram (ECG) at rest showed a normal sinus rhythm with a normal QT interval. A detailed history of the patient showed recurrent physical exertion-induced syncope for 4 years without a family history of syncope or sudden cardiac arrest.

Cardiac ultrasound detected no abnormalities, and coronary angiography was also normal. Cranial magnetic resonance angiography and blood laboratory tests, including cardiac troponin I, were normal. The following treadmill exercise testing showed non-sustained and polymorphic tachycardia, suggesting possible CPVT (Figure 1A). Genetic analysis has played an important role in the diagnosis of CPVT[3]; however, genetic analysis was not available in our province; therefore, a subsequent epinephrine test was performed to confirm the precise diagnosis. With continuous ECG monitoring, epinephrine was intravenously infused according to the Mayo Clinic protocol as previously described[4,5] (Figure 1B). Doses of 0.025, 0.050, 0.100, and 0.200μg/kg/min of epinephrine were utilized every 5 min. However, in the beginning, only an increase in heart rate (from ~75 to ~85 bpm) was seen on ECG monitoring. Then, the heart rate further increased to ~96 bpm without any arrhythmia. The heart rate subsequently progressed to sinus tachycardia (~102 bpm) without any other kinds of arrhythmia on ECG. An unusually high dose of 0.40 μg/kg/min was used for diagnostic purposes, but still, no abnormality was detected. Finally, sudden ventricular tachycardia followed by ventricular fibrillation was found on ECG recording at the dosage of ~0.80 μg/kg/min; the patient had sweating, pallor, and convulsion. Ventricular arrhythmia was

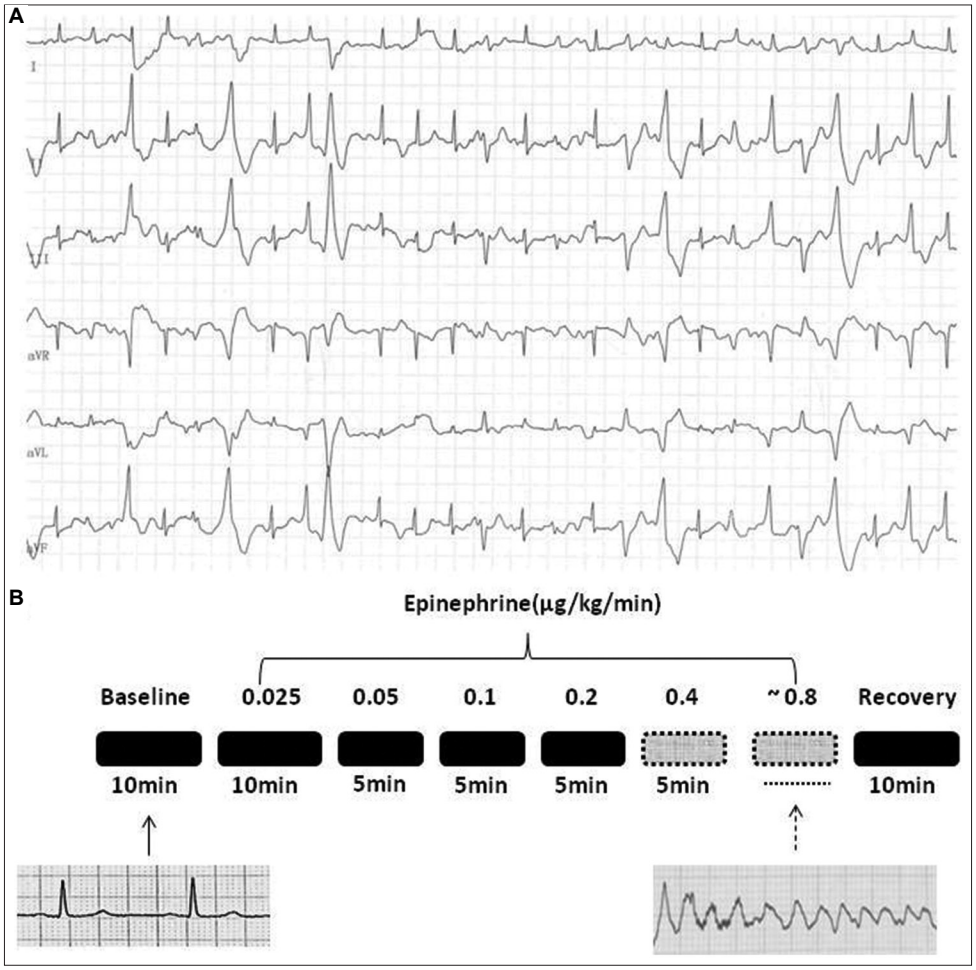

Figure 1. (A) Treadmill exercise testing showed the repetitive physical exertion-induced syncope patient had 3 bidirectional premature ventricular contractions, which was a hint for catecholaminergic polymorphic ventricular tachycardia (CPVT).(B) conventional dose of epinephrine recommended by Mayo Clinic protocol (marked in solid black) caused no arrhythmia, and the unconventional dose (marked in dashed grey) induced ventricular fibrillation, successfully confirming the diagnosis of CPVT.

successfully ceased by 200J electrical shock, returning to sinus rhythm. Since the diagnosis of CPVT was established, β-blocker (metoprolol 23.75 mg/day) was prescribed before discharge.

3. Discussion

CPVT is a potentially life-threatening inherited disease characterized by polymorphic ventricular arrhythmia in the setting of high adrenergic tone[1]. Early diagnosis of CPVT is of great importance since CPVT plays an important role in sudden cardiac death, especially in the young. The patients usually develop syncope or sudden death at an early age in the absence of structural heart disease. In some cases, the resting ECG is normal, and the QT interval can be borderline[6]. Nevertheless, arrhythmia can be reproducibly induced by stress tests as well as epinephrine infusion. The mechanism of CPVT is related to two gene mutations, the cardiac ryanodine receptor gene (RyR2) and calsequestrin 2 gene (CASQ2)[7,8]. These mutations lead to an elevation in intracellular calcium concentration, causing potentially life-threatening ventricular arrhythmias. Current recommendations for therapy of CPVT include β-blocker, implantable cardioverter defibrillator, and verapamil[9]. The efficacy of flecainide has also been confirmed in some studies and could be combined with β-blocker to be administered to highly symptomatic CPVT patients[10].

β-blockers are the key drugs for the treatment of catecholamine-sensitive polymorphic ventricular tachycardia, which belong to Class II antiarrhythmic drugs, and mainly inhibit adrenaline-dependent triggering by reducing heart rate and directly antagonizing catecholamines at the cellular level. It is currently the drug of choice for the treatment of CPVT. It is recommended to use non-selective dosage forms without endogenous sympathomimetic activity and generally choose nadolol, propranolol, metoprolol, and others. Studies have confirmed that β-blockers are effective for most CPVT patients, and the incidence of malignant cardiac events in CPVT decreased significantly after treatment.

Studies have shown that treatment dose is an important factor affecting prognosis. Patients with CPVT need long-term and sufficient use of β-blockers, and whether exercise tests induce arrhythmias is to be used as a tool to evaluate the efficacy of β-blockers and subsequently adjust the drug doses. However, severe bradycardia, atrioventricular block, and increased airway resistance may occur when large doses of β-blockers are used. Therefore, based on our observations during the clinical diagnosis and treatment of this patient, we selected the maximum tolerated dose of 23.75 mg/day.

The most interesting finding was that our case required an unconventional dose of epinephrine before being precisely diagnosed. The upper limit recommended by the Mayo Clinic protocol was 0.20 μg/kg/min, which showed no arrhythmia but only increased heart rate. Taking some insensitive individuals into consideration, we decided to use ~0.80 μg/kg/min dose. Ventricular fibrillation following tachycardia was induced and subsequently stopped by giving an electrical shock. Although the Mayo Clinic protocol was generally regarded as the standard method for diagnosis of CPVT, our patient was not diagnosed until an unconventional dose was selected and administered. Other centers reported some CPVT patients with negative results during regular dose epinephrine infusion who were eventually diagnosed by RyR2 genetic test[3]. It may be due to individual variations in the sensitivities to catecholamine. Some insensitive patients may not respond well to a regular dose of epinephrine (≤0.20 μg/kg/min). Therefore, we believe that our special experience will provide some useful information for the diagnostic test of CPVT.

4. Conclusion

An unconventional dose of epinephrine is needed for a diagnostic test of CPVT for some insensitive individuals.

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Conflict of interest

The authors declare no conflicts of interest.

Author contributions

Conceptualization: Jun Guo
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Writing – original draft: Xianghui Chen
Writing – review & editing: Yongji Lai

Ethics approval and consent to participate

Not Applicable.

Consent for publication

The patient consented the data for publication.

Availability of data

Data are fully available under explicit request to the corresponding author.

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