A novel RyR2 mutation in a 2-year-old baby presenting with atrial fibrillation, atrial flutter, and atrial ectopic tachycardia

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Introduction

Catecholaminergic polymorphic ventricular tachycardia (CPVT) is an arrhythmogenic disorder characterized by the development of polymorphic ventricular tachyarrhythmias induced by exercise or emotional stress without any detectable morphologic abnormalities of the heart.[1]

Mutations in genes encoding cardiac ryanodine receptor 2 (*RyR2*) and calsequestrin 2 (*CASQ2*) have been identified in several patients and are recognized as causing the autosomal dominant and recessive forms of CPVT, respectively.[2] In its typical presentation, CPVT is characterized by the occurrence of syncopal episodes triggered by physical exercise or psychological stress; in rare instances sudden cardiac death may be the first manifestation of the disease. The standard ECG is normal, and diagnosis usually is made during an exercise stress test that reproduces a typical pattern of polymorphic or bidirectional ventricular tachycardia.[3]

Although the high prevalence of atrial arrhythmias in CPVT patients is well known, only a limited number of young adults affected by CPVT who also exhibit sinus node dysfunction or episodes of paroxysmal atrial fibrillation (AF) are reported in the current medical literature.[4]

We describe the case of a child with a novel RyR2 gene mutation who presented at a very young age exclusively with atrial tachyarrhythmias and was later diagnosed with CPVT.

Case report

A 2-year-old female healthy baby girl was referred to our institution for an exaggerated heart rate observed by the referring pediatrician during a routine evaluation. There was no history of syncopal attacks or sudden death among her family members. At admittance, the ECG showed AF with mean ventricular response of 220 bpm (Figure 1A). The echocardiogram revealed normal heart structure and mild dilation of the left ventricle with decreased systolic function (ejection fraction 40%). Amiodarone bolus (5 mg/kg over 30 minutes) followed by a continuous endovenous infusion of 15 mg/kg/day was started. The next day, the ECG showed atrial ectopic tachycardia (AET) with a heart rate of 210 bpm (Figure 1B). Amiodarone infusion was continued, and the baby remained asymptomatic and in stable hemodynamic condition. On day 3, the basal ECG showed a typical atrial flutter (AFL) with 2:1 AV ratio alternating with AET (Figure 1C). On the same day, a stable sinus rhythm resumed, and ejection fraction quickly normalized. The patient was discharged on oral amiodarone (5 mg/kg/day) and periodically visited our clinic as an outpatient. During follow-up she was asymptomatic, but on several occasions the basal ECG revealed sinus bradycardia (60–70 bpm). Every 6 months she underwent 24-hour Holter monitoring, which revealed a mean heart rate of 90 bpm, a lower sinus rate of 50 bpm, and rare brief episodes of paroxysmal AET at a rate of 180 bpm. According to her parents, these episodes were never related to physical activity or emotional stress. Amiodarone therapy was withdrawn after 18 months because of thyroid dysfunction and was replaced with the combination of atenolol (1 mg/kg/day) and flecainide (5 mg/kg/day). An attempt at radiofrequency ablation was proposed to the parents but they refused. At the age of 6 years, she performed an exercise treadmill stress test while receiving medical therapy (atenolol 0.5 mg/kg/day and flecainide 3.5 mg/kg/day). After 4 minutes of exercise, at a sinus rate of 120 bpm, she developed monomorphic premature ventricular beats that became progressively more frequent, repetitive, and finally polymorphic at the peak of exercise (Figure 2). After 8 minutes, the test was suspended, and ventricular ectopias gradually reversed with resumption of a stable sinus rhythm after 5 minutes of rest. Diagnosis of CPVT with associated

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ABBREVIATIONS **AET** = atrial ectopic tachycardia; **AF** = atrial fibrillation; **AFL** = atrial flutter; **CASQ2** = calsequestrin 2; **CPVT** = catecholaminergic polymorphic ventricular tachycardia; **JTC** = junctin; **RyR2** = cardiac ryanodine receptor 2; **TRDN** = triadin (Heart Rhythm 2014;11:1480–1483)

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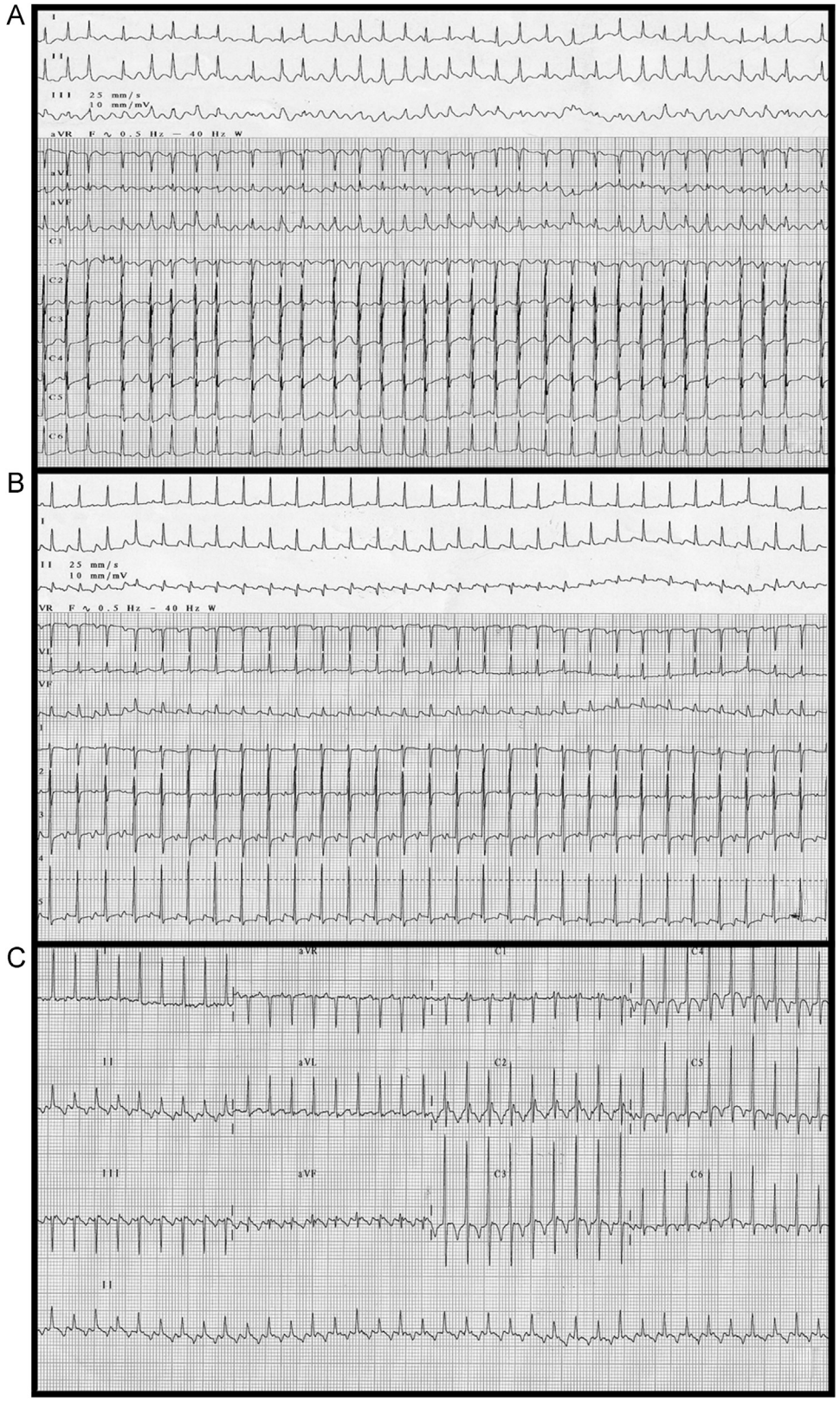

Figure 1 **A:** Day 1 ECG showing atrial fibrillation. **B:** Day 2 ECG showing atrial ectopic tachycardia. **C:** Day 3 ECG showing atrial flutter.

atrial tachyarrhythmias was made. We decided to withdrawn flecainide and to switch the beta-blocker from atenolol to propranolol at a dosage of 3 mg/kg/day. Ten days later, the treadmill test was repeated. After a few minutes of exercise, the patient presented with AET at a rate of 200 bpm alternating with phases of high-rate AF. A stable sinus rhythm resumed after 8 minutes of rest. We then decided to restart flecainide (5 mg/kg/day) in association with