CASE REPORT
Catecholaminergic polymorphic ventricular tachycardia: a rare cause of recurrent syncope
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Abstract
Catecholaminergic polymorphic ventricular tachycardia (CPVT) is an inherited arrhythmia characterized by adrenergically induced polymorphic or bidirectional ventricular tachycardia (VT). Although a rare disease, its recognition is important because of its high mortality rate when left untreated. We report an index case of a 32-year-old woman who presented with recurrent syncope. The diagnosis was confirmed by exercise-induced polymorphic ventricular premature beats and episodes of non-sustained VT, in the absence of structural heart abnormalities. She remained event free with beta-blocker therapy. CPVT is a potentially life-threatening disease and should be considered in the case of recurrent syncope, in young individuals. Diagnosis is based on clinical history and exercise testing, which is the gold standard. Therapy is mandatory in all diagnosed individuals. Exercise testing in first-degree relatives is recommended, even in the case of a mutation-negative index patient.

INTRODUCTION
Catecholaminergic polymorphic ventricular tachycardia (CPVT) is a rare inheritable arrhythmogenic disorder, characterized by adrenergically induced polymorphic ventricular tachycardia (VT), in the absence of structural heart disease [1–4]. Presentation includes syncope or sudden cardiac death (SCD) in young patients [2–4]. A high clinical suspicion is necessary and exercise testing is the gold standard for the diagnosis [3, 4].

We present a case of CPVT in an adult woman with a history of recurrent syncope.

CASE REPORT
A 32-year-old woman presented with syncope. Working as a seamstress, she felt dizzy, with blurred vision and had loss of consciousness for a few seconds. She was not anxious and had been working all day.

There was a history of several episodes of complete and transient loss of consciousness, with spontaneous recovery after <2 min, without sequelae. She had dizziness preceding syncope, but no other symptoms. Syncope occurred at least yearly from 14 to 21 years old and ceased at 32 years. There was no family history of syncope or SCD.

Physical examination was unremarkable. Electrocardiogram (ECG) showed sinus rhythm, with polymorphic ventricular premature beats (VPBs) and normal QTc (Fig. 1). Echocardiogram was normal. She started bisoprolol (2.5 mg/day) and was referred to Cardiology consultation.

Syncope did not recur thereafter. Cardiac magnetic resonance was normal. Exercise testing on treadmill showed more frequent polymorphic VPBs and episodes of non-sustained VT with an increase during exercise and a decrease in the recovery phase.
Figure 1: Electrocardiogram.

Figure 2: Exercise testing (Bruce protocol), after 3 months with beta-blocker therapy. (A–D) Stages 1, 2, 3 and recovery.
Figure 3: Exercise testing (Bruce protocol), after 1 year with beta-blocker therapy. (A–D) Stages 1, 2, 3, and 4.

Figure 4: Holter tracing during sleep.
Holter monitoring was performed, revealing very frequent VPBs during daytime (mean 710 VPBs/h) and less frequent during sleep (mean 116 VPBs/h). VPBs were more frequent by the time she woke up and prepared herself to go to work and decreased during lunch and dinner time. Episodes of non-sustained VT were more frequent during daytime and decreased during sleep. No mutations in ryanodine receptor gene (RYR2) or in the gene-encoding calsequestrine (CASQ2) were found.

At 1-year follow-up, exercise testing was repeated. Compared with the first exercise testing, non-sustained VT episodes were shorter and less frequent during exercise and disappeared in the recovery phase (Fig. 3). Holter monitoring was also repeated, revealing a higher frequency of VPBs during daytime (mean 670 VPBs/h) compared with the sleeping time (mean 260 VPBs/h; Fig. 4). There were irregular, polymorphic, large complex tachycardia episodes, ranging from 3 to 15 complexes, with a maximum rate of 142 bpm (Fig. 5). Bidirectional tachycardia was recorded (Fig. 6).

Owing to intolerance, the patient was asked to switch from bisoprolol to atenolol (25 mg/day). Symptomatic hypotension (dizziness) stopped up-titration of beta-blocker and addition of flecainide. Since she did not have recurrence of syncope and the second treadmill test showed a reduction in the frequency and complexity of ventricular arrhythmias, no further treatment was initiated.

Patient’s 11-year-old daughter was referred to clinical evaluation and exercise testing.

**DISCUSSION**

CPVT prevalence is 1:10,000 and mortality reaches 50% in untreated individuals [1–4]. This patient fulfills the diagnostic criteria: under 40 years old, normal ECG (besides isolated VPBs), structurally normal heart and exercise-induced polymorphic VPBs and VT [1,2]. Other possible diagnosis criteria include the following:

1. Vasovagal syncope: This is a more frequent cause of syncope [5]. It must be considered as a possible aetiology. She had syncopes since adolescence, with prodrome and related to
emotional stress [2]. However, documentation of episodes of exercise-induced VT is suggestive of arrhythmic syncopes. CPVT is a highly lethal condition and such long history of recurrent syncope is extremely rare. Even considering the possibility of vasovagal syncope, the management would be as described.

(ii) Long-QT syndrome: This is a possible cause of syncope in young ages. The recovery phase of an exercise testing may identify patients with long-QT syndrome with a normal or borderline QTc at rest [2, 3]. However, she did not have QTc abnormalities at rest or during the recovery phase. Also, the exercise-induced VPBs favour the diagnosis of CPVT.

(iii) Short-coupled variant of Torsades de Pointes (TdP): This is a rare cause of polymorphic VT in young patients with syncope which results in ventricular fibrillation (VF). A coupling interval of the first TdP beat is always <300 ms [6]. In this patient, VPB’s preceding VT was not always short-coupled (Fig. 6) and there was no VF. Also, short-coupled TdP is not usually stress-related.

(iv) Andersen–Tawil syndrome: This is associated with mutations in KCNJ2. Ventricular arrhythmias, periodic paralysis and facial and limb dysmorphism are seen. ECG features include QTc prolongation, prominent U waves and frequent VPBs/polymorphic VT. This patient lacks the anatomical and most ECG features [2, 3].

Exercise testing is the gold standard for diagnosis [3, 4]. Typically, the number of VPBs increases and NSVT appears due to exercise. Bidirectional VT is a hallmark of CPVT [3, 4] (Fig. 6). Genetic testing allows identifying asymptomatic first-degree relatives after detection of a mutation in the index case [3, 4]. The absence of pathogenic mutations in the tested genes does not exclude CPVT, since RYR2 and CASQ2 mutations are present in ∼60% of the cases [3, 4].

Risk factors for arrhythmic events remain poorly defined [3, 4]. Cardiac arrest, diagnosis during childhood and no beta-blocker therapy are associated with worse prognosis [2–4]. As we cannot identify patients with a low risk of arrhythmias, all clinically or genetically diagnosed patients should receive treatment [1–4].
The patient was started on beta-blocker and avoided intense exercise and emotional stress. Flecainide and left cardiac sympathetic denervation are options for patients who remain symptomatic [1–4]. Implantable cardioverter defibrillator (ICD) can lead to painful shocks, increasing sympathetic tone and triggering arrhythmias, a vicious and possibly lethal cycle [2–4]. ICD is recommended for patients refractory to medical therapy or in secondary prevention [1–4].

This case highlights the importance of CPVT as a cause of recurrent syncope in young patients. The work-up includes exercise testing. Diagnosis is established with exercise-/emotion-induced bidirectional/polymorphic VT, in the absence of QTc prolongation or structural heart disease. Patients should avoid vigorous exercise and stress and take beta-blockers. Referral to a Cardiology/Arrhythmology consultation should be considered.

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CONFLICT OF INTEREST STATEMENT
None declared.

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