

## CASE REPORT

# Flipping syncope: The case of an adolescent athlete with syncopal episodes ultimately diagnosed with catecholaminergic polymorphic ventricular tachycardia

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## Abstract

Catecholaminergic polymorphic ventricular tachycardia (CPVT) is a channelopathy which can lead to fatal ventricular arrhythmias. The diagnosis can be challenging due to a wide variety of clinical presentations. In this case, we describe the unusual presentation and subsequent workup of a young patient who was ultimately diagnosed with CPVT.

## KEYWORDS

arrhythmia, catecholaminergic polymorphic ventricular tachycardia, channelopathy, RYR2 mutation, ventricular fibrillation

## 1 | INTRODUCTION

Catecholaminergic polymorphic ventricular tachycardia (CPVT) is a channelopathy affecting children and adults with structurally normal hearts. A high degree of suspicion is needed to make the diagnosis as clinical presentations vary significantly, ranging from asymptomatic patients identified via familial screening to others who suffer from sudden cardiac death secondary to ventricular fibrillation (VF). The diagnosis is typically made by treadmill stress test, but isoproterenol infusion is often used as an alternative in patients who are unable to undergo treadmill testing. In the current study, we describe the case of an adolescent who was ultimately diagnosed with CPVT despite unremarkable initial workup including negative isoproterenol infusion.

## 2 | CASE HISTORY

At age 12, a female gymnast began experiencing sudden syncopal events associated with seizure-like activity and bladder/

bowel incontinence during gymnastics. Most events seemed to be triggered shortly after the peak of exertion, as the patient landed the dismount. When evaluated at outside emergency rooms immediately following these events, no cardiac etiology was found. She had five such episodes between 12 and 13 years of age, always returning to her baseline state within 5-10 minutes. Her family history was negative for sudden cardiac death or arrhythmia at a young age.

Following an event during competition, she underwent a pediatric neurology evaluation at an outside institution which reported two normal electroencephalograms (EEGs) and brain magnetic resonance imaging (MRI), significantly diminishing suspicion for a seizure disorder. Her neurologist concluded that she was most likely suffering from neurocardiogenic syncope. She was then referred to a pediatric cardiologist at an outside institution who performed multiple electrocardiograms (EKGs), a 48-hour Holter, a tilt-table test, and basic laboratories which were all unremarkable. She was again hypothesized to have neurocardiogenic syncope. However, due to the atypical nature of some of her episodes including loss of consciousness for up to three minutes with

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one minute of tonic-clonic movements, she was offered a loop recorder. Her family elected for watchful waiting instead of loop recorder implantation.

At age 14, she had gone approximately one year without any seizure-like activity before again suffering another event. As before, this event began just after dismounting from a gymnastics maneuver. The 45-second event was witnessed by a trauma nurse and physician at the scene who reported “difficulty finding a pulse and some period of apnea.” She was taken to a local emergency department where she was found to be in stable condition and a brief workup was negative. Following this event, she was referred by her primary care provider to our pediatric cardiology electrophysiology team for a second opinion.

### 3 | ADDITIONAL WORKUP AND TREATMENT

On evaluation, her physical examination, EKG, and echocardiogram were all unremarkable. A treadmill stress test was recommended; however, the patient had recently sustained a hamstring injury and was unable to run. Therefore, she underwent an electrophysiology study. Isoproterenol infusion was titrated up to 0.08 mcg/kg/min to achieve the desired heart rate response. There were no atrioventricular node echoes or inducible arrhythmias noted. Atrial burst pacing also failed to induce any arrhythmias. While still in the catheterization laboratory, an implantable loop recorder was placed.

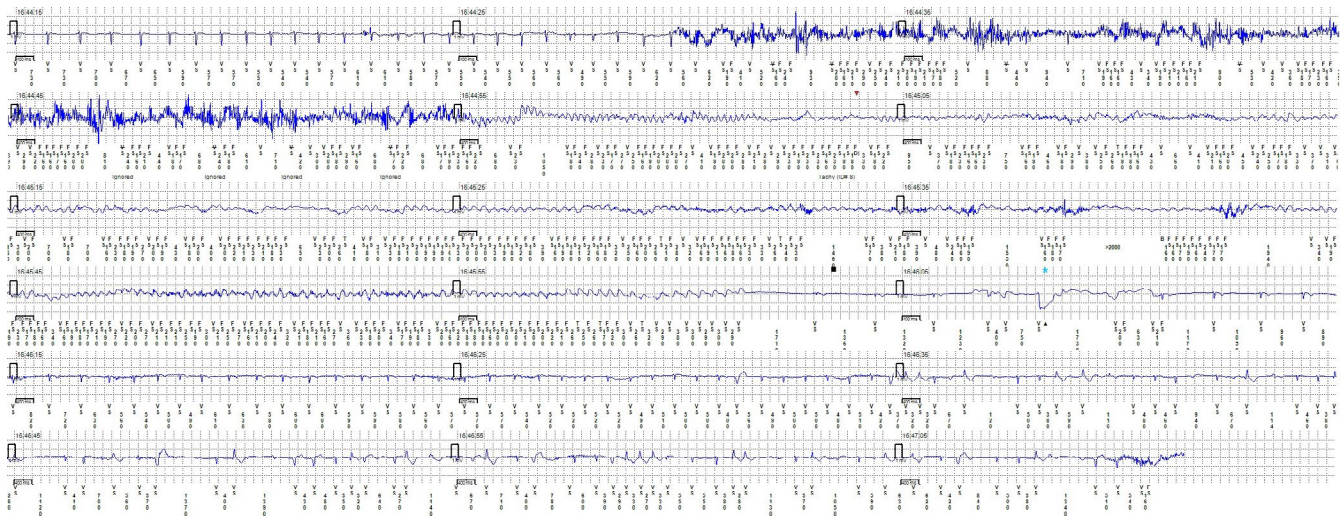
Three weeks later, the patient's mother called stating that the patient had experienced another seizure-like episode while at gymnastics practice. She was reportedly doing

handstands and after dismounting, lost consciousness and began to seize. She woke up spontaneously and quickly returned to her baseline. Her coach manually activated the implantable loop recorder.

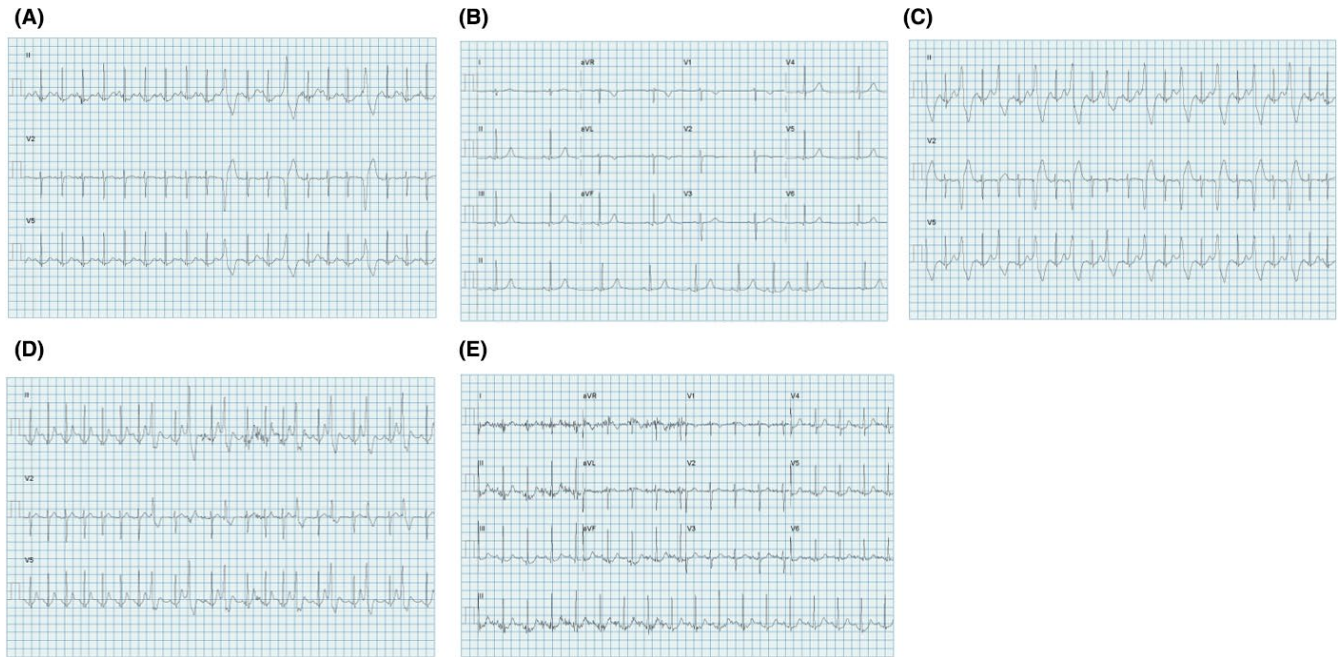
On loop recorder interrogation, the presenting rhythm was 89 beats per minute (bpm). Review of the tracings revealed that the device also autotriggered around the time of the event. The tracing showed sinus rhythm with periods of muscle/motion artifact and occasional premature ventricular complexes (PVCs). A significant amount of what appears to be noise rhythm is consistent with ventricular fibrillation (VF) which lasts approximately 90 seconds and spontaneously breaks into sinus bradycardia with frequent PVCs including couplets and a triplet (Figure 1).

Following documentation of her ventricular arrhythmia, she was instructed to cease all moderate to high exertion activity until cardiology follow-up. Treadmill testing the next day demonstrated polymorphic ventricular ectopy that increased at higher levels of exertion, consistent with the diagnosis of CPVT (Figure 2). She was started on nadolol 20 mg twice daily and restricted from strenuous physical activity. Genetic testing demonstrated a heterozygous variant of unknown significance in the RYR2 gene which has been implicated in the majority of CPVT cases.<sup>1</sup> Both parents subsequently tested negative for any RYR2 mutations.

For the last two years, she has been followed regularly in clinic with treadmill testing as well as remote loop recorder interrogations. Her nadolol has been titrated up to 60 mg AM and 40 mg PM daily with adequate beta blockade demonstrated on routine treadmill testing. During this period, she has been compliant with her medication and activity restrictions. There has been no evidence of breakthrough ventricular arrhythmias.



**FIGURE 1** Presenting rhythm is sinus @ 89 bpm. Patient family called to notify us that the patient had an episode after dismounting from doing handstands and that they activated her loop recorder. Review of the activations shows that the device also autotriggered at this time as well for tachycardia. There is some muscle/motion artifact noted on the tracings, but the initial rhythm appears to be sinus with occasional PVCs, after a significant amount of what appears to be noise rhythm is consistent with VF which lasts approximately 90 s and spontaneously breaks into sinus bradycardia with frequent PVCs including s



**FIGURE 2** Exercise treadmill test ECG. Resting ECG was sinus rhythm (A). With onset of activity, she began to have PVCs which increased with increasing heart rate (B). Ventricular bigeminy was noted starting at a heart rate of 130 bpm (C). Ventricular couplets and triplets were noted around the time of peak exertion (D). All ventricular ectopy extinguished as the heart rate fell below 100 bpm (E)

## 4 | DISCUSSION

Catecholaminergic polymorphic ventricular tachycardia requires a high index of clinical suspicion to make the diagnosis, as evidenced in the case of this adolescent female. Despite undergoing substantial workups by a pediatric neurologist and pediatric cardiologist including EEGs, EKGs, tilt-table testing, and a brain MRI, her seizure episodes were thought to be secondary to neurocardiogenic syncope, a common pitfall in the diagnosis of CPVT. Syncope associated with exercise should raise the clinical suspicion for a cardiac etiology.<sup>2</sup> When her episodes persisted and had concerning features including prolonged loss of consciousness, bladder/bowel incontinence, apnea, and weak pulses noted by healthcare professionals, her primary care physician wisely referred her for a second pediatric cardiology evaluation. Delays in diagnosis for CPVT can be life-threatening, but unfortunately, these are relatively common. Indeed, it was recently demonstrated that the diagnosis of CPVT was delayed in approximately 15% young patients with sudden cardiac arrest due to exercise stress test either not being performed or not being interpreted correctly.<sup>3</sup> Unfortunately, some patients are physically unable to participate in treadmill testing due to physical limitations (as initially evidenced in this case due to a hamstring injury).

The failure of high-dose isoproterenol infusion to induce underlying ventricular ectopy during an electrophysiology study was notable in this case. It has been demonstrated in

both humans and mouse cardiomyocytes that beta-adrenergic receptor stimulation is a more potent trigger for ventricular arrhythmias than rapid pacing which circumvents adrenergic stimulation to produce rapid heart rates.<sup>4</sup> Case series have also shown the value of epinephrine challenges in pediatric postarrest evaluations subsequently diagnosed with CPVT.<sup>5</sup> Given these findings, it is surprising that isoproterenol, a nonselective pure beta agonist, failed to induce any ventricular ectopy during her electrophysiology evaluation.

It is also worth noting that despite prior negative workups as well as negative chemical stress test, a loop recorder was placed and ultimately captured VF, leading to definitive diagnosis in this case. The use of loop recorders in syncope of uncertain etiology is well described, and the documentation of VF has been reported.<sup>6</sup> Reports of VF lasting greater than one minute which spontaneously self-terminate have been reported, but are exceedingly rare.<sup>7,8</sup> To our knowledge, this is among the longest lasting documented episodes of VF with self-termination. Our group previously published a case series of two young athletes in whom loop recorders proved to be invaluable in determining the etiology of their syncope as being cardiogenic.<sup>9</sup> These cases highlight not only the need for high clinical suspicions for CPVT, but also the value of loop recorders in scenarios when episodes are not reproduced with exercise stress testing or electrophysiology studies.

Finally, this case demonstrates that beta blockade is a safe and effective preventative measure in the setting of CPVT. Along with activity restrictions and close follow-up with exercise stress testing, beta blockade has allowed this patient

to avoid implantable cardiac defibrillator (ICD) placement which is associated with a high burden of complications.<sup>10</sup> This is in accordance with patients falling into the Class I category of the 2013 Heart Rhythm Society Consensus Statement on CPVT.<sup>11</sup>

## 5 | CONCLUSIONS

Despite prior nondiagnostic evaluations by neurology, and cardiology including EKG's, Holter monitors, and chemical stress test with isoproterenol, this patient was ultimately diagnosed with CPVT after VF was captured on an implantable loop recorder. This case highlights the need for a high index of clinical suspicion needed to make the diagnosis of CPVT as well as the value of loop recorders in scenarios when the diagnosis is unclear. It also suggests that exercise stress test may be more sensitive than chemical stress test for making the diagnosis of CPVT. Finally, this case serves as an example of beta blockers providing adequate therapy with the goal of avoiding ICD placement which is associated with a high rate of complications in the CPVT population.

## CONFLICT OF INTEREST

The authors have no conflicts of interest to disclose.

## AUTHOR CONTRIBUTIONS

CK: reviewed the patient medical record, compiled data, and drafted the manuscript for review of all other authors. JM: oversaw the research process, helped compile data, and contributed to manuscript drafts. AK: involved in data collection and then helped provide high-quality images for the manuscript, and contributed to manuscript review. IL: oversaw the patient's care and initial concept for this case report and oversaw manuscript revisions.

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