

Choking-induced cardiac arrest unmasks a diagnosis of catecholaminergic polymorphic ventricular tachycardia



Thomas M. Roston, MD,[†] Leenah AlAhmari,^{*} Andrew D. Krahn, MD, FHRS,[†]
Elizabeth Sherwin, MD,[†] Shubhayan Sanatani, MD, FHRS[†]

From the ^{*}University of British Columbia, Vancouver, Canada, and [†]King Saud University, Riyadh, Saudi Arabia.

Introduction

Catecholaminergic polymorphic ventricular tachycardia (CPVT) is an uncommon cardiac ion channelopathy characterized by polymorphic or bidirectional ventricular tachycardia (VT) during physical or emotional stress.¹ The proband often presents during childhood or early adolescence with syncope, seizure, or cardiac arrest.² In some cases, sudden unexpected death (SUD) can be the first manifestation of CPVT.^{3,4} In 2001, Priori et al⁵ discovered that mutations in the cardiac ryanodine receptor 2 (RyR2), a highly conserved ion channel, underlie most cases of CPVT. The diagnosis is made on the basis of history, exercise stress testing (EST), and genetic testing.⁵

The management of CPVT is challenging. Classically, beta blockers are used to suppress arrhythmia,^{1,2} although nonadherence and treatment failure commonly occur.^{3,4} Flecainide is a promising second-line agent in CPVT.⁶ Patients with refractory arrhythmia or aborted cardiac arrest may be referred for an implantable cardioverter-defibrillator (ICD).⁵ Recently, a multicenter study showed benefit from left cardiac sympathetic denervation (LCSD).⁷ The presented case describes a very young child with a unique trigger for cardiac arrest in CPVT.

Case description

A previously healthy 4-year-old male child had a witnessed cardiac arrest at home. Prior to the event, the boy was eating macaroni and playing with his brother. While trying to climb

onto his brother's back, he suddenly became unresponsive and fell to the floor. Assuming that he had aspirated, his mother administered rescue breaths and called emergency services. Paramedics arrived on scene promptly and found the victim to be in pulseless polymorphic VT. Cardiopulmonary resuscitation, intravenous epinephrine, and several defibrillations were initiated. A piece of macaroni was found lodged inside the boy's trachea during endotracheal intubation. He regained a perfusing rhythm after approximately 10 minutes of resuscitation. He was hemodynamically stable and neurologically intact on arrival to the hospital. Electrocardiography demonstrated frequent multifocal premature ventricular complexes (PVCs). The emergency physician initiated mechanical ventilation and administered intravenous morphine and midazolam for sedation. A single dose of broad-spectrum antibiotic was given for empiric coverage of aspiration. He was cooled to 34°C for 48 hours as per institutional protocol and urgently transferred to the provincial tertiary care pediatric hospital.

That evening, the boy arrived in our pediatric intensive care unit (PICU) with a presumed diagnosis of hypoxia-induced cardiac arrest secondary to aspiration. However, the patient experienced recurrent, unexplained polymorphic VT during the first night of admission (Figure 1). These episodes frequently deteriorated into VF cardiac arrest necessitating amiodarone infusion and external defibrillation on 5 separate occasions. The following day, the patient continued to have runs of bigeminy and polymorphic VT (Figure 2). The consulting cardiac electrophysiologist suspected electrical storm secondary to a catecholamine-sensitive channelopathy and advised against repeated defibrillation. The initiation of intravenous esmolol suppressed the patient's polymorphic VT.

Diagnostic tests performed during PICU admission included normal chest radiographs, transthoracic echocardiography, and cardiac magnetic resonance imaging. Serum troponin level on presentation was mildly elevated in the context of recent cardiac arrest and defibrillation. All other investigations, including electroencephalography, computed tomography scan, and magnetic resonance imaging of the brain, were normal. Subsequent resting electrocardiograms

KEYWORDS Catecholaminergic polymorphic ventricular tachycardia; Sudden death; Child

ABBREVIATIONS CPVT = catecholaminergic polymorphic ventricular tachycardia; ECG = electrocardiogram; EST = exercise stress testing; ICD = implantable cardioverter-defibrillator; LCSD = left cardiac sympathetic denervation; PICU = pediatric intensive care unit; PVC = premature ventricular complex; RYR2 = ryanodine receptor 2; SUD = sudden unexpected death; VT = ventricular tachycardia (Heart Rhythm Case Reports 2015;1:494–497)

Address reprint requests and correspondence: Shubhayan Sanatani, Head, Division of Cardiology, Children's Heart Centre, 1F9, British Columbia's Children's Hospital, 4480 Oak St, Vancouver, BC V6H 3V4, Canada. E-mail address: ssanatani@cw.bc.ca.

KEY TEACHING POINTS

- Catecholaminergic polymorphic ventricular tachycardia (CPVT) is a rare diagnosis. Key features on clinical history include syncope and aborted cardiac arrest in young patients during times of exertion or extreme emotion. Prompt diagnosis is essential, as life-saving treatments exist, even during acute ventricular arrhythmias at time of presentation.
- Adrenergic triggers of cardiac events typically include competitive sports and sudden extreme emotions. However, other triggers exist, such as swimming, which may be particularly dangerous because drowning may follow a cardiac event. Clinicians need be aware that a variety of triggers may exist in CPVT. Polymorphic ventricular tachycardia in the young should always prompt evaluation for inherited arrhythmia.
- CPVT is often an inherited disorder. Standard family evaluation should include exercise testing in all cases and genetic testing in genotype-positive CPVT, even in the absence of symptoms.

(ECGs) demonstrated normal sinus rhythm with mild QTc prolongation seen transiently in 1 tracing (460 ms). The boy made a full neurologic recovery and was transitioned to oral propranolol (2 mg/kg/day) while on the cardiac ward.

One week after discharge, he was asymptomatic with a normal repeat transthoracic echocardiogram and resting ECG. An outpatient 24-hour Holter monitor revealed frequent PVCs and bidirectional couplets while on propranolol. There was no evidence of supraventricular arrhythmia on any study. He was transitioned to nadolol (1.2 mg/kg/day) as an outpatient. Sequencing of RYR2, calsequestrin 2, and inwardly rectifying potassium channel 2 were performed and a novel variant (A2317T) was identified in *RYR2*, classified as probable disease-causing for CPVT. No other genetic variants were identified.

Family history was negative for syncope, seizures, SUD, unexplained fatal accidents, and drownings. Genetic and exercise testing was unremarkable in both parents. The boy's 12-year-old brother was not genetically screened, as he was considered low risk of the basis of negative parental testing. At 2-year follow-up, the proband described remains asymptomatic on nadolol (1.3 mg/kg/day). No one else in the family has developed a phenotype consistent with CPVT in the interim.

Discussion

CPVT is an important cause of aborted cardiac arrest and SUD in the young. We describe a case involving one of the youngest known symptomatic subjects and demonstrate a unique trigger for cardiac arrest. Classic precipitants of arrhythmia in CPVT are athletics² and emotional circumstances.³ Less-recognized precipitants of arrhythmia include swimming,⁸ inappropriate ICD discharge,⁹ and atrial fibrillation.¹⁰ Life-threatening events in CPVT may even occur



Figure 1 Resting electrocardiogram demonstrating bidirectional ectopy degenerating into polymorphic ventricular tachycardia prior to electrical cardioversion during intensive care unit admission.

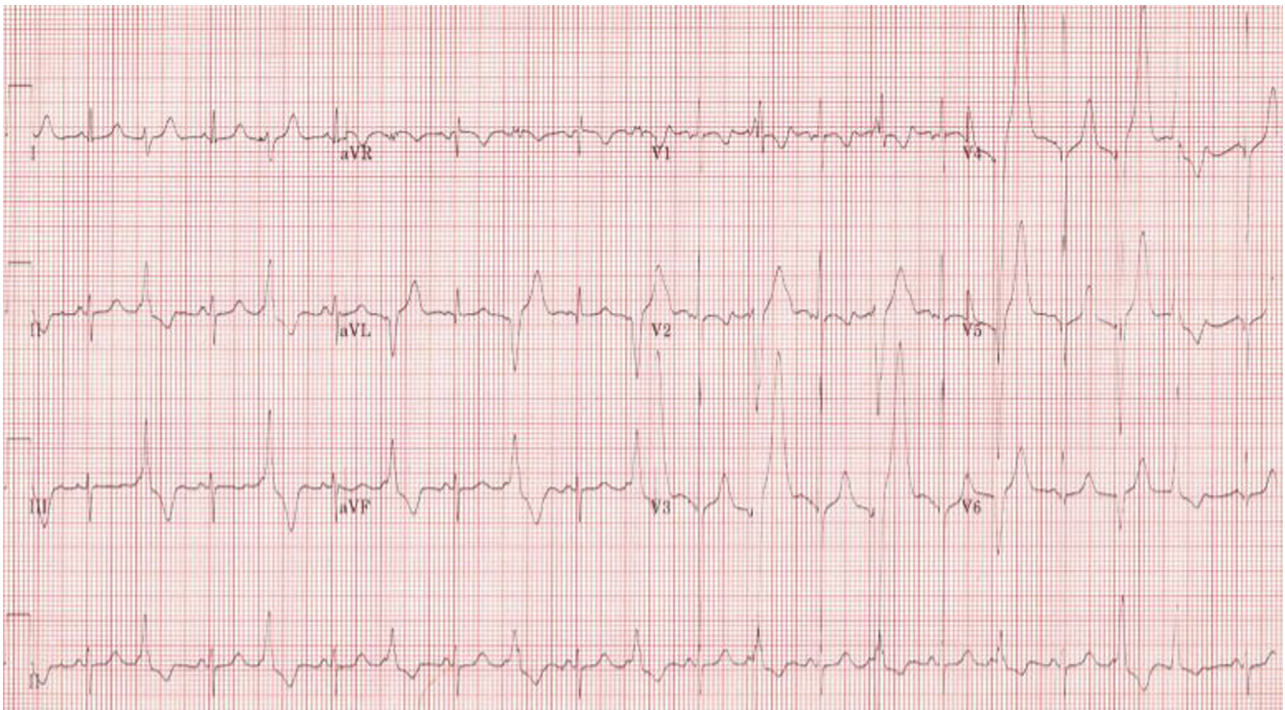


Figure 2 Resting electrocardiogram demonstrating bigeminy during intensive care unit admission.

under normal, resting circumstances.³ We describe a case in which the trigger for cardiac arrest is unique and controversial. Ostensibly, the patient had an aspiration and choking event resulting in a respiratory-induced cardiac arrest. Alternatively, the aspiration event may have caused a catecholamine surge leading to an arrhythmic cardiac arrest, or the patient's polymorphic VT may have been precipitated merely by exertional play, with the foreign body lodged in his trachea being an incidental finding. Regardless, a polymorphic VT arrest in a young patient should prompt the clinician to consider CPVT even if alternative explanations, such as hypoxia, seem more likely.

Iatrogenic triggers must also be considered in every case of CPVT. ICD discharges can heighten catecholamine release and propagate electrical storm.^{3,11} As observed in this case, external defibrillation in the PICU worsened ventricular arrhythmia. The electrophysiologist instead used intravenous esmolol to suppress catecholamine release. Limited evidence has also indicated that intravenous propranolol and verapamil may be effective options under these circumstances.^{12,13} Guidelines suggest ICD placement for secondary prevention as a class I recommendation.⁵ However, the risks of ICD discharges in CPVT are substantial and life-threatening.^{3,11} In this case, we decided against ICD placement after the documented recurrent VF and shocks during the patient's initial course, and the subsequent excellent response to beta blocker therapy. This approach should be considered in all new diagnoses of CPVT. Providers, patients, and their family should be aware of the risks and benefits of ICD implantation unique to CPVT. Initiation of adjunct therapies, such as flecainide and LCSD, are safer, are possibly more effective, and should be

discussed early on.⁵⁻⁷ Recent data support the early adoption of LCSD either before or at the time of ICD surgery.⁷

Our evaluation for suspected CPVT was also atypical. We used Holter monitoring, rather than EST, as young children often lack the coordination required to safely use a treadmill. The Holter monitor demonstrated frequent polymorphic PVCs during exertion, which alone does not meet consensus diagnostic criteria⁵ for CPVT but raises suspicion for arrhythmia substrate. This approach may be useful in patients with equivocal EST, or those unable to exercise owing to deconditioning, comorbidities, or age. Holter monitoring should not be routinely used in lieu of EST, as detection of classic CPVT-associated arrhythmias may be lower in nonexertional testing. Treadmill testing has also been shown to be negative in gene-positive carriers that subsequently developed symptoms.¹⁴

CPVT typically manifests during early adolescence^{2,3,5} and is complicated by substantial diagnostic delay despite life-threatening events,³ in part because the resting ECG is typically normal. There is little data on very young children with CPVT. We demonstrate that arrhythmia related to CPVT can occur early in life, especially under an extreme physiologic stress. To our knowledge, we describe a novel variant in (A2317T) in the Central-forming domain on *RYR2* localizing to the second hotspot on the cytosolic side of the receptor. Numerous mutations underlying CPVT have been described in this area of *RYR2*.¹⁴ As frequently seen in severe childhood diseases like CPVT, this boy also harbored a de novo variant. This evidence, coupled with a pathognomonic phenotype, suggests a high likelihood of pathogenicity. Literature suggests that children presenting early in life and male subjects with *RYR2* mutations may be

at highest risk of life-threatening events and treatment failure.^{2,3}

The family assessment should focus on eliciting clues of CPVT in each pedigree, including syncope, presyncope, seizures, unexplained drownings, or motor vehicle-related deaths. In addition, EST and genetic testing should be performed in both parents whenever possible. This is of paramount importance, as a bimodal age distribution has been described in CPVT.¹⁵ The boy's older brother was not clinically or genetically tested based on negative parental testing.

This case is reported to demonstrate that unusual triggers for cardiac arrest exist in CPVT. A careful history, clinical evaluation, and molecular testing can improve the substantial delay to diagnosis described in CPVT. Prompt initiation of treatment can be life-saving. Clinicians should be aware that newer therapeutic options for managing CPVT exist.^{4,7} Further studies are needed to better understand phenotype-genotype correlations in children and families with CPVT.

References

1. Leenhardt A, Lucet V, Denjoy I, Grau F, Do Ngoc D, Coumel P. Catecholaminergic polymorphic ventricular tachycardia in children: a 7-year follow-up of 21 patients. *Circulation* 1995;91:1512–1519.
2. Priori S, Napolitano C, Memmi M, et al. Clinical and molecular characterization of patients with catecholaminergic polymorphic ventricular tachycardia. *Circulation* 2002;106:69–74.
3. Roston T, Vinocur J, Maginot K, et al. Catecholaminergic polymorphic ventricular tachycardia in children: an analysis of therapeutic strategies and outcomes from an international multicenter registry. *Circulation* 2015;8(3):633–642.
4. Van der Werf C, Zwinderman A, Wilde A. Therapeutic approach for patients with catecholaminergic polymorphic ventricular tachycardia: state of the art and future developments. *Europace* 2011;14:175–183.
5. Priori SG, Wilde AA, Horie M, et al. HRS/EHRA/APHRs expert consensus statement on the diagnosis and management of patients with inherited primary arrhythmia syndromes: document endorsed by HRS, EHRA, and APHRs in May 2013 and by ACCF, AHA, PACES, and AEPC in June 2013. *Heart Rhythm* 2013;10:1932–1963.
6. van der Werf C, Kannankeril P, Sacher F, et al. Flecainide therapy reduces exercise-induced ventricular arrhythmias in patients with catecholaminergic polymorphic ventricular tachycardia. *J Am Coll Cardiol* 2011;57:2244–2254.
7. De Ferrari G, Dusi V, Spazzolini C, et al. Clinical management of catecholaminergic polymorphic ventricular tachycardia: the role of left cardiac sympathetic denervation. *Circulation* 2015;131(25):2185–2193.
8. Tester D, Spoon D, Waldivia H, Makielski J, Ackerman M. Targeted mutational analysis of the *RyR2*-encoded cardiac ryanodine receptor in sudden unexplained death: a molecular autopsy of 49 medical examiner/coroner's cases. *Mayo Clin Proc* 2004;79(11):1380–1384.
9. Pizzale S, Gollob M, Gow RM, Birnie D. Sudden death in a young man with catecholaminergic polymorphic ventricular tachycardia and paroxysmal atrial fibrillation. *J Cardiovasc Electrophysiol* 2008;19:1319–1321.
10. Lawrenz W, Krogmann O, Wiczeorek M. Complex atrial arrhythmias as first manifestation of catecholaminergic polymorphic ventricular tachycardia: an unusual course in a patient with a new mutation in ryanodine receptor type 2 gene. *Cardiol Young* 2013;24(4):741–744.
11. Miyake C, Webster G, Czosek R, et al. Efficacy of implantable cardioverter defibrillators in young patients with catecholaminergic polymorphic ventricular tachycardia. *Circulation* 2013;6:579–587.
12. De Rosa G, Delogu A, Piastra M, Chiaretti A, Bloise R, Priori S. Catecholaminergic polymorphic ventricular tachycardia: successful emergency treatment with intravenous propranolol. *Pediatr Emerg Care* 2004;20(3):175–177.
13. Swan H, Laitinen P, Kontula K, Toivonen L. Calcium channel antagonism reduces exercise-induced ventricular arrhythmias in catecholaminergic polymorphic ventricular tachycardia patients with *RyR2* mutations. *J Cardiovasc Electrophysiol* 2005;16:162–166.
14. Hayashi M, Denjoy I, Hayashi M, et al. The role of stress test for predicting genetic mutations and future cardiac events in asymptomatic relatives of catecholaminergic polymorphic ventricular tachycardia probands. *Europace* 2012;14:1344–1351.
15. Sy R, Gollob M, Klein G, et al. Arrhythmia characterization and long-term outcomes in catecholaminergic polymorphic ventricular tachycardia. *Heart Rhythm* 2011;8:864–871.