Short-coupled premature ventricular beats leading to ventricular fibrillation in a young patient: A Sudden Arrhythmia Death Syndrome case report and literature review

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Introduction

Short-coupled premature ventricular contractions (scPVCs) leading to ventricular fibrillation (VF) have been described as a rare etiology of cardiac arrest in patients without structural heart disease.[1–3] The arrhythmia is characterized by a PVC coupling interval of <300 ms, a relatively short QRS duration, and a normal QT interval. This report describes a 15-year-old male patient presenting following loss of consciousness with documented scPVCs and sustained and nonsustained VF.

Case report

A 15-year-old male athlete who was previously healthy had sudden onset of syncope while sitting in class. He was reported to have complete loss of consciousness and presumed seizure activity, which resolved after 10 minutes. He denied any prodromal symptoms. Emergency medical services transported the patient to an outside hospital emergency department where monomorphic PVCs were noted with the subsequent development of nonsustained polymorphic ventricular tachycardia (VT), followed by sustained VF (Figure 1). The patient was emergently defibrillated to sinus rhythm and an amiodarone infusion was initiated. Upon transfer to our institution, the patient continued to have single PVCs and nonsustained VF. He complained of no symptoms during PVCs and had mild nausea during more prolonged runs of VF. The baseline electrocardiogram demonstrated a borderline right axis deviation, mild terminal conduction delay, and no QT prolongation, Brugada pattern, or epsilon waves. The PVC morphology revealed a right bundle branch block pattern with a QRS duration of 136 ms and a coupling interval of 250 ms (Figure 2).

The patient was continued on amiodarone (0.5 mg/min) and a lidocaine infusion (40 mcg/kg/min) was initiated with continued, though significantly reduced, ectopy burden. No ectopy was noted with heart rates greater than 100 beats per minute (bpm). An echocardiogram, cardiac magnetic resonance imaging, and signal-averaged electrocardiogram were normal. The past medical history was notable only for a single syncopal episode that occurred following a rapid position change from supine to standing. There was no family history for cardiac rhythm disorders. Following a discussion with the Sudden Arrhythmia Death Syndromes (SADS) Foundation Scientific Advisory Council, amiodarone and lidocaine infusions were discontinued as the patient was

KEY TEACHING POINTS

- Short-coupled premature ventricular contractions (scPVCs) leading to ventricular fibrillation (VF) is an uncommon etiology of cardiac arrest in patients without structural heart disease.
- The arrhythmia is characterized by a PVC coupling interval of <300 ms, a relatively short QRS duration, and a normal QT interval.
- Genetic and electrophysiologic testing have increasingly implicated the Purkinje system as the source of scPVCs.
- Verapamil and quinidine have demonstrated efficacy in reducing the arrhythmogenic burden, with catheter ablation having additional long-term success.

KEYWORDS Cardiac arrest; Pediatric; Premature ventricular contractions; Short coupled; Ventricular fibrillation
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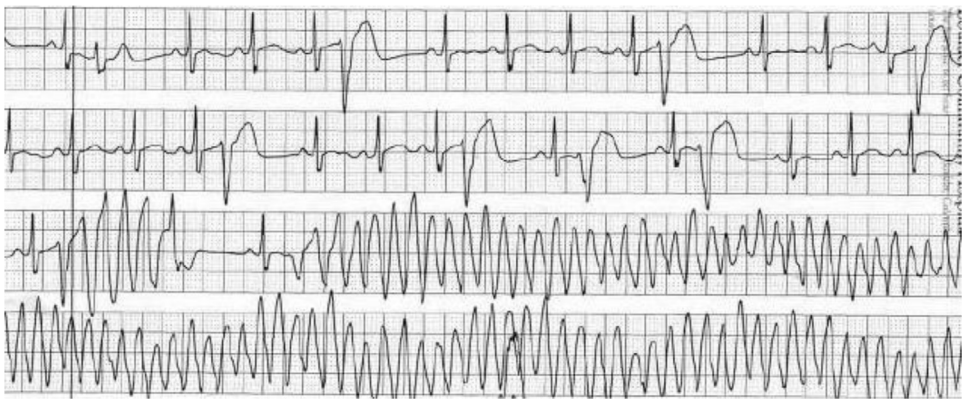

Figure 1 Short-coupled and monomorphic premature ventricular contractions initiating nonsustained polymorphic ventricular tachycardia and torsades de pointes.

transitioned to oral flecainide at 75 mg twice a day. The flecainide was later titrated to 100 mg twice a day with single and monomorphic PVCs only noted at heart rates <60 bpm. A dual-chamber transvenous implantable cardioverter-defibrillator was placed with a lower paced rate of 60 bpm.

One month following hospital discharge, an exercise stress test revealed no ventricular ectopy despite a maximal effort. Genetic testing with whole genome sequencing was negative. His 2 siblings were screened with Holter monitors and they were negative for PVCs. In a follow-up period of 30 months, the patient continues in high school and plays on the varsity lacrosse team. He is maintained on flecainide therapy and has not had syncope or any device discharges (no appropriate or inappropriate shocks).

Discussion

Short-coupled PVCs and resultant VF have been described as a rare cause of cardiac arrest in patients[1–3] (Table 1), with a variety of descriptive terms being used. The potential overlap between studies examining short-coupled torsades de pointes (TdP), idiopathic VF, and polymorphic VT creates difficulty in describing the exact incidence. Leenhardt and colleagues[1] first presented a series of patients without structural heart disease and documented TdP, including a 15-year-old male patient, who had a characteristically short coupling interval of the onset of TdP or isolated PVCs. A coupling interval of <300 ms distinguishes this etiology from that seen in congenital or acquired long QT syndrome (600–800 ms). Additionally, the relatively narrow QRS duration suggests an association with the specialized conduction system, particularly the Purkinje network, though myocardial sources have been documented during electrophysiologic study.[4–7]

An accurate incidence is difficult to determine owing in large part to various overlapping descriptions. Idiopathic VF, potentially the most expansive descriptor, accounts for an estimated 5%–10% of all out-of-hospital cardiac arrests,[8,9] although pediatric-specific studies have not identified scPVCs or scTdP.[10,11] In a population of patients presenting for ablation of idiopathic VF, Haissaguerre and colleagues[4] demonstrated that 25% had true scPVCs, with the overwhelming majority having relatively short coupling (297 ± 41 ms). Of particular interest is that cardiac arrest following pediatric scPVCs occurs at rest rather

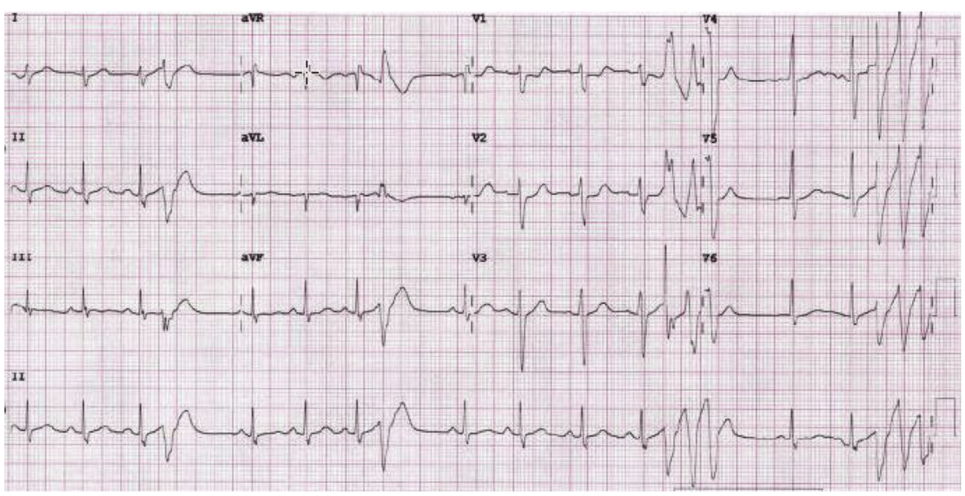

Figure 2 Electrocardiogram demonstrating monomorphic premature ventricular contractions with a right bundle branch block pattern, QRS duration of 136 ms, and a coupling interval of 250 ms. Nonsustained polymorphic ventricular tachycardia is also observed.

Table 1 Patient characteristics and electrocardiographic findings

Article	Age (y)	Sex	Prior symptoms	Documented arrhythmia	PVC cycle length (ms)	Activity at symptoms	Treatment	Follow-up
Leenhardt et al[1]	15	M	Syncope	TdP, VF	240	Rest	Verapamil	Continued VF
Yeh at al[2]	18	M	Syncope	PMVT	220–300	Rest	Diltiazem/ablation	Rare PVCs
Chokr et al[3]	18	F	No symptoms	N/A	300	N/A	Verapamil	Asymptomatic

N/A = not available; PMVT = polymorphic ventricular tachycardia; PVC = premature ventricular contraction; TdP = torsades de pointes; VF = ventricular fibrillation.

than associated with increased adrenergic tone, as is frequently characteristic of generalized pediatric cardiac arrests.[10] This has potential treatment implications for both medication selection and the utility of activity restrictions.

The expansion of genetic testing has helped identify possible underlying molecular mechanisms, with intracellular calcium handling being particularly implicated. Fuji and colleagues[12] and Xiao and colleagues[13] demonstrated the importance of transient outward currents in the Purkinje networks, with loss-of-function mutations in *RyR2* channels resulting in scTdP phenotypes. Interestingly, similar loss-of-function mutations have been described in catecholaminergic polymorphic VT phenotypes despite the primary abnormality in catecholaminergic polymorphic VT being a gain-of-function mutation.[14] Wilde and colleagues[15,16] further implicated abnormalities in the Purkinje network with detailed and population-based screening for a risk haplotype in the *DPP6* gene. Haplotype-positive individuals were at significantly higher risk for sudden cardiac arrest secondary to VF consistently triggered by scPVCs. The mechanism is postulated to be increases in transient outward potassium current in the Purkinje network with subsequent excitement of the surrounding myocardium. Though less well described, mutations in *SCN5A* have also been described in association with scTdP.[17]

The mainstay of treatment for scPVCs resulting in cardiac arrest has been verapamil, with an observed lengthening of the PVC coupling interval and reduction in overall ectopic burden.[1,3] Class Ia antiarrhythmics, with emphasis on quinidine, have demonstrated a reduction in arrhythmogenic events following idiopathic VF,[18,19] with a significant percentage of these likely secondary to scPVCs. Regardless of treatment, however, implantation of an ICD is recommended, as frequent appropriate device discharges remain. Flecainide was utilized in our patient, with significant improvement in the ectopic burden after initiation. More available than quinidine in North America, flecainide was described by Ahn and colleagues[20] in a patient with early repolarization syndrome. Radiofrequency ablation can be successful; Haissaguerre and colleagues[4] and Knecht and colleagues[21] described targeting ventricular ectopy arising from the distal Purkinje fibers and 89% of patients remaining free of VF in follow-up.

Conclusion

Short-coupled PVCs with the development of cardiac arrest is a rare but important cause of cardiac arrest in pediatric patients, potentially distinct from the diagnosis of idiopathic VF. The presentation of cardiac arrest in the absence of structural heart disease or a prolonged QT interval should prompt its consideration. Although medical management and ablation can be considered as adjunctive therapy, implantation of an ICD is important to prevent sudden death.

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