Recurrent idiopathic polymorphic ventricular tachycardia/ventricular fibrillation successfully treated by cardiac sympathetic denervation

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Introduction

Idiopathic polymorphic ventricular tachycardia (PVT) or ventricular fibrillation (VF) triggered by short-coupled premature ventricular contractions (PVC) is a well-recognized and rare cause of sudden death in patients with structurally normal hearts.[1] Although implantable cardioverter-defibrillators (ICD) are helpful in preventing sudden death, frequent ICD shocks may significantly affect quality of life. Antiarrhythmic medications are only marginally effective at preventing recurrent arrhythmias. An innovative approach, pioneered by Haissaguerre and colleagues,[2] involves ablation of PVCs triggering PVT/VF.[2,3] It has been shown that in a subset of patients with PVT/VF triggers originating primarily from the Purkinje system, successful elimination of the triggers may lead to long-term freedom from recurrent arrhythmia.[3] However, this approach is commonly limited by the absence of culprit PVCs during the ablation procedure.

We report a case of PVC-triggered PMT/VF successfully managed by cardiac sympathetic denervation (CSD).

Case report

The patient is a 39-year-old man who first presented to a local emergency room with an episode of syncope in 2008. His admission electrocardiogram at that time revealed frequent monomorphic short-coupled PVCs of a left bundle branch block/superior axis morphology consistent with right ventricular (RV) inflow tract origin (Figure 1A). There were multiple monitored runs of PVC-triggered PVT and 1 episode of VF requiring defibrillation. He had no family history of sudden death or arrhythmia. The arrhythmia was apparently controlled with intravenous amiodarone. His initial transthoracic echocardiogram performed soon after resuscitation reportedly showed global hypokinesis of the left ventricle with an estimated ejection fraction of 30%. An echocardiogram obtained the next day after the event was interpreted as normal, with complete recovery of the

KEY TEACHING POINTS

- Idiopathic polymorphic ventricular tachycardia (PVT) or ventricular fibrillation (VF) triggered by short-coupled premature ventricular contractions (PVC) is a rare cause of sudden death in patients with structurally normal hearts.
- Although an implantable cardioverter-defibrillator (ICD) is indicated to prevent sudden death, many patients require adjuvant antiarrhythmic drugs or ablation of PVCs initiating PVT/VF because of recurrent arrhythmia triggering ICD shocks. Although highly effective, the ablation approach is commonly limited by the absence of culprit PVCs during the procedure.
- Cardiac sympathetic denervation (CSD) using a video-assisted thoracoscopic approach is currently a well-established therapeutic option in patients with drug-refractory catecholaminergic PVT (CPVT) and congenital long QT syndrome (LQTS). Experience with the use of CSD in patients with other forms of life-threatening ventricular arrhythmias is limited, and the role of the procedure outside CPVT and LQTS indications continues to evolve.
- Our report suggests that CSD may be considered as an alternative therapeutic option in patients with drug-refractory recurrent idiopathic PVT/VF induced by short-coupled PVCs in whom ablation of culprit ectopy is not feasible or is unsuccessful.

KEYWORDS Arrhythmia; Cardiac sympathetic denervation; Idiopathic ventricular fibrillation; Polymorphic ventricular tachycardia; Short-coupled premature ventricular contractions; Torsades de pointes

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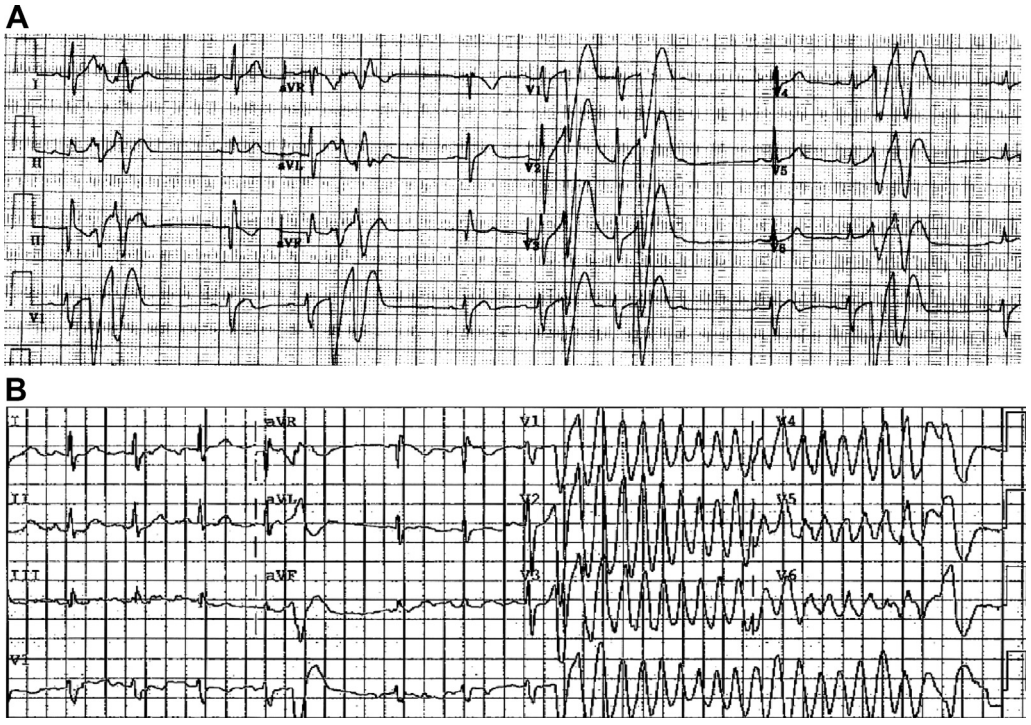

Figure 1 **A:** Twelve-lead electrocardiogram (ECG) shows frequent short-coupled ventricular ectopy with left bundle branch block/superior axis morphology consistent with a right ventricular inflow tract origin. **B:** Twelve lead ECG shows an episode of polymorphic ventricular tachycardia triggered by a short-coupled premature ventricular depolarization. It is important to note that the triggering premature ventricular depolarizations are consistently of the same morphology: left bundle branch block/superior axis.

left ventricular systolic function. A coronary angiogram revealed normal coronary arteries. He subsequently underwent placement of an ICD and was discharged home on amiodarone and carvedilol. Over the ensuing years, he has had multiple admissions for PVT/VF storms and ICD shocks despite therapy with amiodarone up to 400 mg a day in combination with mexiletine, ranolazine, and different beta-blockers (Figures 1B and 2). During these episodes of PVT/VF storms, he usually had frequent monomorphic PVCs of the same morphology as well as multiple runs of PVT. Because of refractory ventricular arrhythmias, he was referred for consideration for a heart transplant in 2016. At that time, he underwent coronary angiography and right heart catheterization. These revealed normal coronary arteries as well as normal filling pressures and cardiac output. His candidacy for a heart transplant was declined.

The patient presented to our hospital in September 2017 after receiving 8 ICD shocks for recurrent PVC-triggered PVT/VF. His antiarrhythmic regimen on admission included amiodarone, mexiletine, and metoprolol. An echocardiogram was unremarkable. Cardiac magnetic resonance imaging (MRI) was not performed because of a non-MRI-conditional ICD. Telemetry showed very rare PVCs. A treadmill exercise test failed to uncover inducible arrhythmia. The patient was discharged home with a 30-day event monitor to assess PVC burden and morphology. No ventricular ectopy was noted during the monitoring period. His genetic testing (Invitae Corporation, San Francisco, CA), including a comprehensive panel of 39 genes (*ABCC9*, *ACTN2*, *ANK2*, *CACNA1C*, *CACNB2*, *CALM1*, *CALM2*, *CALM3*, *CASQ2*, *CAV3*, *DES*, *DSC2*, *DSG2*, *DSP*, *EMD*, *FLNC*, *GPD1L*, *HCN4*, *JUP*, *KCNA5*, *KCNE1*, *KCNE2*, *KCNH2*, *KCNJ2*, *KCNQ1*, *LMNA*, *MYL4*, *NKX2-5*, *PKP2*, *PLN*, *PRKAG2*, *RBM20*, *RYR2*, *SCN5A*, *TMEM43*, *TNNI3*, *TNNT2*, *TRDN*, *TTN*), was negative for pathogenic sequence variants or deletions/duplications.

He subsequently underwent bilateral CSD using a video-assisted thoracoscopic approach.[4] Amiodarone was discontinued. He remained on mexiletine and beta-blockers. Over the ensuing 11 post-CSD months he had only 1 episode of nonsustained PVT, as compared to 8 episodes of sustained PVT/VF requiring ICD shocks and 13 episodes of nonsustained PVT over 11 pre-CSD months.

Discussion

In this report, we describe a patient with no apparent structural heart disease or electrocardiographic abnormalities known to be associated with arrhythmogenic syndromes (Figure 3) and drug-refractory recurrent PVT/VF initiated by short-coupled monomorphic PVCs who was successfully managed by CSD. However, PVCs related to possibly undiagnosed structural heart abnormalities could not be ruled out because cardiac MRI was not performed.

The exact electrophysiological mechanism of idiopathic PVT/VF is not completely understood and may be heterogeneous. As elegantly summarized in a review by Haissaguerre and colleagues,[5] accumulating clinical and experimental

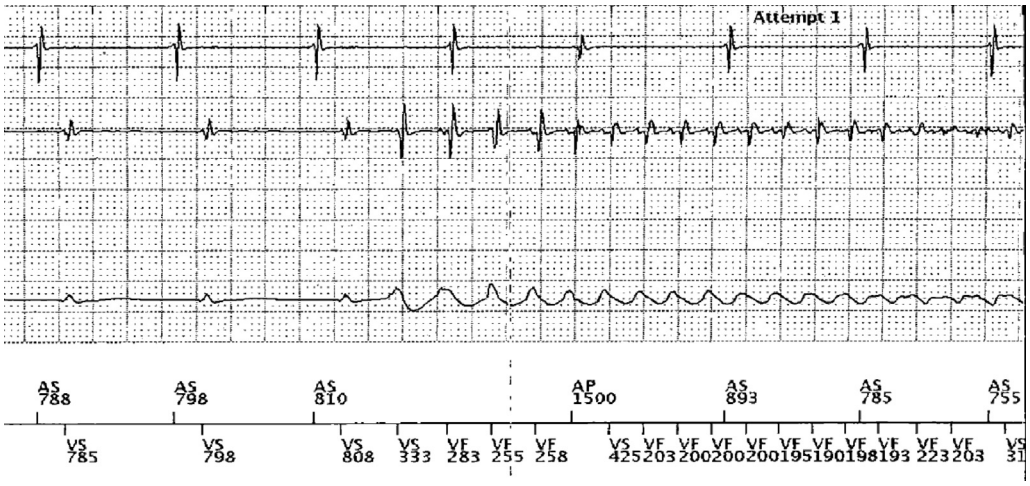

Figure 2 An example of stored implantable cardioverter-defibrillator (ICD) electrogram demonstrating polymorphic ventricular tachycardia triggered by a short-coupled premature ventricular depolarization. The tachycardia degenerated to ventricular fibrillation and was subsequently terminated by an ICD shock.

evidence suggests an important role of the Purkinje tissue in the initiation and maintenance of VF. In the published ablation series, idiopathic PVT/VF was initiated by Purkinje triggers in the majority of patients.[2,3,6] It has been postulated that either triggered activity (early or delayed afterdepolarizations) and/or microreentry in the Purkinje tissue can be potential electrophysiological mechanisms of idiopathic PVT/VF in these patients.[5] The true prevalence of the Purkinje-related mechanism in patients with idiopathic PVT/VF remains unknown, given a potential referral bias in these series. In our patient, PVC morphology (left bundle branch block/superior axis) was consistent with the RV inflow tract origin. Although a very short coupling interval of the PVCs strongly suggests a Purkinje origin, we were not able to determine this definitively, since electrophysiology study and PVC mapping were not performed. Idiopathic PVT/VF triggers arising from the RV Purkinje fibers (including papillary muscles and the moderator band) have been previously reported.[2,3,6,7]

Antiarrhythmic therapy and ablation of PVT/VF triggers are 2 currently used adjuvant approaches in patients with idiopathic PVT/VF and frequent ICD shocks. Although successful elimination of the triggers with ablation is associated with long-term freedom from the arrhythmia recurrences in the majority of patients, this approach is frequently hampered by significant fluctuation in the PVC occurrence. As in our patient, triggering PVCs may only be present for a short period of time during PVT/VF storms. Because of the very low PVC burden in our patient, we felt that ablation would have limited success. While mapping of PVCs is the most useful method for identifying successful ablation target sites, there is no pharmacologic agent or stimulation technique that can reliably and reproducibly elicit short-coupled ventricular ectopy, particularly one originating in the Purkinje tissue.[1,5] Alternatively, pace-mapping technique has limited spatial resolution as compared to activation mapping and usually requires the presence of some culprit PVCs during the procedure for effective template matching.[8] Nevertheless, one of the limitations of our report is that an electrophysiology study was not attempted. Thus, the usefulness of programmed stimulation with and without pharmacologic challenge (including high-dose isoproterenol) for PVC induction in our patient is unknown.

CSD is currently a well-established therapeutic option in patients with drug-refractory catecholaminergic PVT (CPVT) and congenital long QT syndrome (LQTS).[9] In

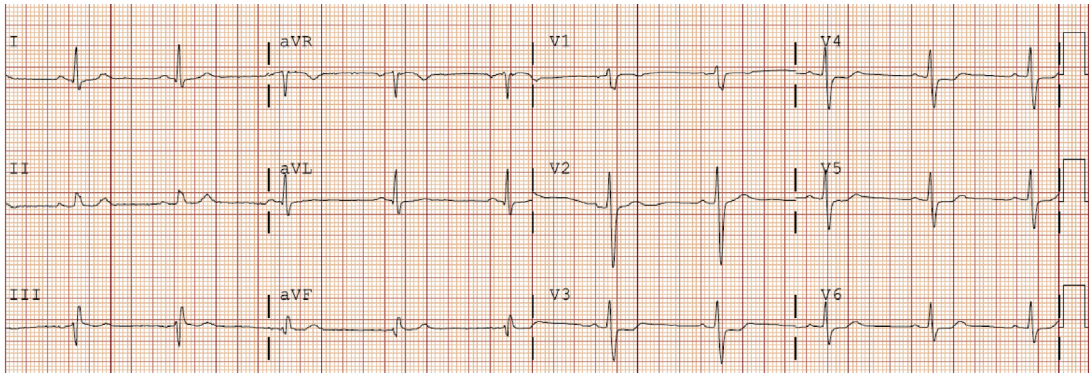

Figure 3 Twelve-lead electrocardiogram shows no abnormalities known to be associated with arrhythmogenic syndromes.

addition, growing evidence indicates a beneficial therapeutic effect of CSD on recurrent monomorphic and polymorphic VT in patients with structural heart disease.[10,11] However, the role of the procedure in this patient population is still evolving. It is plausible to speculate that idiopathic VF may share mechanistic similarity with CPVT and LQTS. Augmented sympathetic stimulation can facilitate induction of early afterdepolarizations and delayed afterdepolarizations. While triggered activity in Purkinje cells is considered to be one of the potential mechanisms of idiopathic PVT/VF induced by short-coupled PVCs, experimental evidence suggests that Purkinje delayed afterdepolarizations and early afterdepolarizations are important triggers of CPVT- and LQTS-related arrhythmias, respectively.[5,12,13] Coleman and colleagues[14] recently reported outcomes of left CSD in a series of 27 patients who underwent the procedure for recurrent ventricular arrhythmias unrelated to LQTS. Four patients in this study carried a diagnosis of idiopathic VF. Following the procedure, 3 of them had no further arrhythmia recurrences and in the remaining patient, the frequency of VF episodes had significantly decreased (only 1 episode over 2.5 years of follow-up). However, no specific details about the diagnosis of idiopathic VF were provided. In a recent series by Richardson and colleagues,[15] 7 patients with different types of recurrent ventricular arrhythmias were successfully treated with CSD, including 1 patient with VF triggered by short-coupled fascicular PVCs in the setting of hypertrophic cardiomyopathy.

Conclusion

Our report suggests that CSD may be considered as an alternative therapeutic option in patients with drug-refractory recurrent idiopathic PVT/VF induced by short-coupled PVCs in whom ablation of culprit ectopy is not feasible or is unsuccessful.

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