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Case Report

Efficacy of bilateral thoracoscopic sympathectomy in a patient with catecholaminergic polymorphic ventricular tachycardia

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ABSTRACT

A 27-year-old woman with frequent implantable cardioverter defibrillator (ICD) shocks related to catecholaminergic polymorphic ventricular tachycardia (VT) experienced aborted sudden death due to incessant polymorphic VT despite the administration of beta-blockers, verapamil, and flecainide. Catheter ablation failed to suppress the polymorphic VT. Based on the temporary efficacy of the local anesthetic administered at the left and right cervical sympathetic nerves to suppress VT under an isoproterenol infusion, stepwise, bilateral thoracoscopic sympathectomy was performed. Postoperatively, no further VT or syncopal episodes were documented under ICD telemetry. Bilateral thoracoscopic sympathectomy may be an alternative for patients with drug-refractory catecholaminergic polymorphic VT.

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1. Introduction

Catecholaminergic polymorphic ventricular tachycardia (CPVT) was first reported in 1975 and is characterized by exercise- or emotional stress-induced polymorphic ventricular tachyarrhythmias, syncope, or sudden cardiac death [1,2]. Although β-blockers, verapamil, and Na-channel blockers have been used to suppress VT in these patients, their symptoms persist and prognosis remains poor [3]. We describe a case of aborted sudden death due to catecholaminergic polymorphic VT in a patient who had received treatment with antiarrhythmic agents and an implantable cardioverter defibrillator (ICD) in whom VT could be successfully suppressed after bilateral thoracoscopic sympathectomy.

2. Case report

A 27-year-old woman diagnosed with CPVT, who did not have a family history of sudden cardiac death, and was implanted with a dual chamber ICD at another institution 11 years previously for recurrent syncopal episodes during exercise and emotional stress was followed up by our hospital. She had experienced frequent (nearly 5 times per year) ICD shocks (Secura™, Medtronic, Minneapolis, USA) related to ventricular fibrillation or atrial tachycardia (AT) with a rapid ventricular response under the oral administration of antiarrhythmic agents, including bisoprolol 5 mg/day, verapamil 240 mg/day, and flecainide 150 mg/day (3 mg/kg), which were her maximally tolerable doses because of general fatigue due to hypotension. During the follow-up, she was resuscitated from aborted sudden death due to incessant polymorphic VT documented on electrocardiography. Deep sedation with intratracheal intubation was effective in suppressing VT, and fortunately, no brain damage occurred after hypothermia therapy. The initial premature ventricular contractions (PVCs), which triggered the polymorphic VT, were confirmed to have mainly two morphologies: left bundle branch block with a superior axis (PVC1) and right bundle branch block with an inferior axis (PVC2) under an isoproterenol infusion (ISP) at 1.5 μg/min. We confirmed that the maximum beat runs of VT could be suppressed to only couplets of PVCs by a left stellate ganglion blockade using lidocaine as the local anesthesic, under the same dose of the ISP

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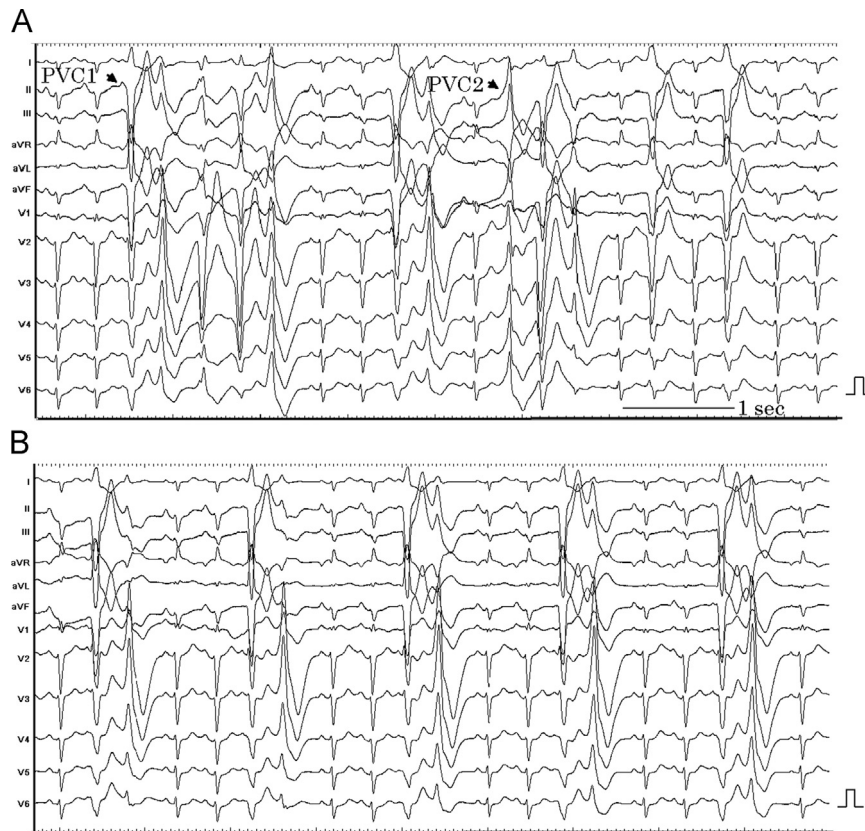E-mail address: kokajima@hbhc.jp (K. Okajima).

Fig. 1. (A) Polymorphic VT (maximally five beat runs) was frequently induced by an ISP infusion (1.5 μg/min). The heart rate (P–P interval during sinus rhythm) was 134 bpm. We immediately discontinued the ISP infusion because we were concerned about the occurrence of life-threatening sustained polymorphic VT. (B) VT could be suppressed up to only couplets of PVCs after the local left stellate ganglion blockade under the same dose of ISP infusion. The heart rate was similar to that mentioned above.

infusion (Fig. 1). First, we attempted catheter ablation targeting those initial PVCs. The right ventricular inferior wall under the tricuspid valve (PVC1: the local bipolar ventricular potential preceded the onset of the PVC by 20 ms without any discrete pre-potentials, and a good pacemap of the QRS configuration was obtained) and left ventricular outflow tract immediately under the aortic valve of the left coronary cusp (PVC2: a good pacemap of the QRS configuration was obtained) were considered as the origins of the PVCs, and ablation at those sites with 25–30 W suppressed the PVCs under the same ISP infusion dose of 1.5 μg/min. However, ablation at the above sites was ineffective under an infusion of ISP of 3.0 μg/min because a maximum of 8 beat runs of a non-sustained polymorphic VT (NSPVT) with an average cycle length of 237 ms was induced. In addition, treadmill exercise testing (10.2 Mets) after the ablation revealed the occurrence of bidirectional polymorphic VPCs. Those PVCs were mainly of two types, such as a left bundle branch block with a superior axis and an inferior axis type, and the morphologies were different from those before the ablation. Although VT did not recur clinically, the catheter ablation was considered insufficient to prevent any future VT recurrence. Therefore, after written informed consent was obtained, the patient underwent left thoracoscopic sympathectomy from the lower one-third of the left stellate ganglion to the Th4 level under general anesthesia (Fig. 2) based on the effectiveness of the left stellate ganglion local blockade and according to a previous report [4]. After that operation, VT was no longer inducible until 10.2 Mets of exercise via treadmill exercise testing, but was easily induced over 11.2 Mets of exercise. We next evaluated the efficacy of the local right stellate ganglion blockade, and found that this dramatically suppressed the polymorphic VT under an ISP 3.0 μg/min infusion. Based on this result, she underwent an additional right thoracoscopic sympathectomy from the

lower one-third of the right stellate ganglion to the Th5 level. After the operation, VT could no longer be induced for up to 11.2 Mets of exercise (Table 1: each number after NSPVT indicates maximum beat runs). The heart rate was lower (93 bpm vs. 103 bpm) during the same 10.2 Mets of exercise, and AT inducibility was suppressed to a greater extent during the exercise (11.2 Mets vs. 12.9 Mets) after right thoracoscopic sympathectomy than after left thoracoscopic sympathectomy alone. Complications such as left ptosis and decreased sweating of the left hand (Horner's syndrome) persisted during the follow-up after left thoracoscopic sympathectomy, but the symptoms could be well tolerated without any complaints of severity. The patient was discharged from our hospital under the oral administration of bisoprolol 5 mg/day and verapamil 240 mg/day. Nine months after bilateral sympathectomy, she felt an ICD shock immediately after bathing but did not experience any syncope. ICD telemetry revealed an inappropriate shock for an AT with a rapid ventricular response and some PVCs without any polymorphic VT (Fig. 3B), but no ICD shocks have been recorded after that last event up to the 12 months of follow-up.

3. Discussion

CPVT is an inherited arrhythmia syndrome, characterized by polymorphic ventricular tachycardia induced by adrenergic stress and caused by mutations of the cardiac ryanodine receptors or calsequestrin gene without any structural heart disease. Beta blockers are currently a class I indication for the treatment of clinically diagnosed patients [5]. Watanabe et al. discovered that flecainide prevents arrhythmias in a mouse model of CPVT by inhibiting the cardiac ryanodine receptor-mediated Ca^{2+} release and directly targets the underlying molecular defect. In addition,
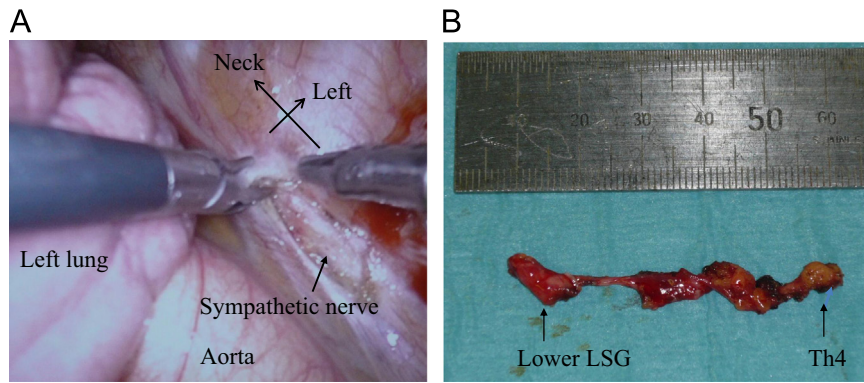
Fig. 2. Demonstration of left thoracoscopic sympathectomy. (A) Thoracoscopic view during the operation. (B) The resected ganglions between the lower one-third of the left stellate ganglion and the Th4 level.

Table 1
Isoproterenol and treadmill exercise testing.

	ISP 1.5 μg/min	ISP 3.0 μg/min	TET 10.2 Mets	TET 11.2 Mets	TET 12.9 Mets
Control	NSPVT 5[#1] SR 134 bpm				
LSG block	PVC couplet SR 134 bpm				
Postablation	PVC (−) SR 134 bpm	NSPVT 8[#2] AT 250 bpm	PVC SR 111 bpm		
PostLSG1/3-Th4 resection			PVC (−) SR 103 bpm	NSPVT 6[#3] AT 135 bpm	
RSG block	PVC (−) SR 120 bpm	PVC couplet SR 140 bpm			
PostRSG1/3-Th5 resection			PVC (−) SR 93 bpm	PVC (−) SR 97 bpm	PVC AT 107 bpm

ISP: isoproterenol; TET: treadmill exercise testing; LSG: left stellate ganglion; RSG: right stellate ganglion; NSPVT: maximum beat runs of non-sustained polymorphic ventricular tachycardia; SR: heart rate during sinus rhythm; AT: heart rate during AT; # indicates the average cycle length of the NSPVT: [#1]=312 ms, [#2]=237 ms, [#3]=400 ms.
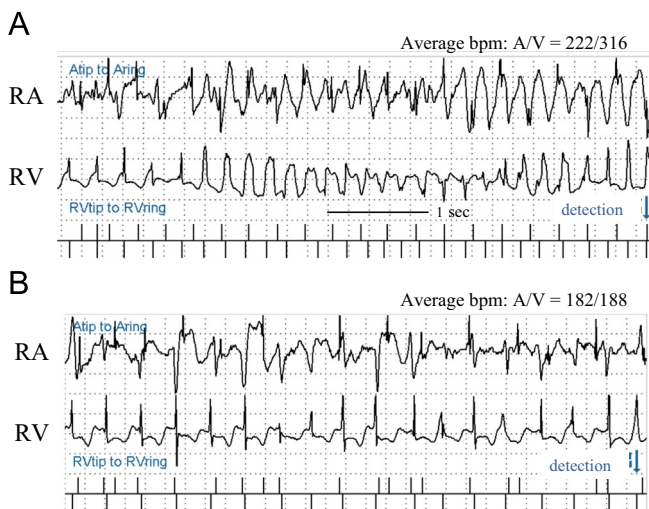

Fig. 3. Demonstration of the intra-cardiac electrograms recorded on the ICD telemetry. (A) Before the sympathectomy, dual tachycardias with polymorphic ventricular and atrial tachycardia were frequently recorded. The VT detection interval was > 200 bpm and the VF detection interval was > 250 bpm. (B) Only one event was recorded after the left and right sympathectomies. The VT and VF detection intervals were changed to > 150 bpm and > 200 bpm, respectively, after bilateral sympathectomy to prevent missing any severe VT events. Note that no polymorphic ventricular tachycardia was detected during the atrial tachycardia with a rapid ventricular response.

flecainide completely prevented CPVT in two patients who had remained highly symptomatic with conventional drug therapy [6]. van der Werf also reported that flecainide resulted in either a partial (n=8) or complete (n=14) suppression of exercise-induced ventricular arrhythmias in 22 of 29 patients. In addition, no patients experienced any worsening of their exercise-induced ventricular arrhythmias [7]. However, our case had experienced aborted sudden death due to incessant polymorphic VT under the administration of flecainide. The detection interval of ventricular fibrillation (VF) and VT were more than 250 beats/min and 200–250 beats/min, respectively, at that time, and no VT/VF episodes were recorded in ICD telemetry. An incessant form of VT with a cycle length less than 200 beats/min may be the reason why an ICD shock was not delivered for this event. In this patient, the detection interval for both VT and VF should have been more than 200beats/min to prevent inappropriate ICD shocks for AT with a rapid ventricular response. However, this setting may have been the reason for the under detection of VT combined with a prolonged VT cycle length caused by the flecainide 150 mg/day (3 mg/kg) in this patient. For that reason, we did not increase the dose of flecainide after that severe clinical event. On the other hand, even if the ICD could have detected VT and delivered the shocks, it may have led to catecholamine release, resulting in further electrical storm [8].

The electrocardiographic characteristics and efficacy of catheter ablation of CPVT have been reported. Sumitomo et al. reported that the initiating focus originated from the right ventricular outflow tract in 15 cases, in the right ventricular outflow tract and left ventricular outflow tract in one case, in the right ventricular apex in six cases, in the right ventricular apex and right ventricular outflow tract in three cases, in the left ventricular apex in one case, and in the left ventricular apex and right ventricular outflow tract in one case. The mean CPVT heart rate was 192 beats/min (range, 150–250 beats/min), with most

CPVT cases being nonsustained. Catheter ablation of the initiating focus of the CPVT was attempted in two cases but was unsuccessful [3]. On the other hand, they also reported a case with CPVT in which pulmonary vein isolation was performed for AF. The Holter monitor recordings demonstrated a major decrease in the clinical episodes of AF and VTs in association with a reduced high-frequency (HF) component and ratio of the low-frequency (LF) component power to the HF component (LF/HF) after pulmonary vein isolation [9]. Kaneshiro et al. reported a successful catheter ablation of bidirectional PVCs triggering ventricular fibrillation in CPVT with RyR2 mutation [10]. They could eliminate the PVCs by catheter ablation in the left ventricular inferoseptal area near the posteromedial papillary muscle and the left coronary cusp. Neither episodes of syncope nor ICD therapies occurred during 16-months of follow-up under the administration of bisprorol 2.5 mg QD. We performed mapping and catheter ablation of the PVCs triggering the polymorphic VT. The right ventricular inferior wall under the tricuspid valve and left ventricular outflow tract under the aortic valve of the left coronary cusp were considered as origins of the PVCs, but the efficacy of the ablation was limited. Because PVCs were induced according to the dose of catecholamine administered and polymorphic VTs could be easily induced, activation mapping and ablation of all the PVCs may have been insufficient in our case. Although our patient also simultaneously had AT with a rapid ventricular response and VT, we did not perform pulmonary vein isolation because polymorphic VT is not usually associated with AT (Fig. 1A). As Kaneshiro et al. concluded, more cases and a longer-term observation are mandatory to clarify the effectiveness and safety of catheter ablation for CPVT.

Sympathetic denervation is considered as one of the alternative treatment options for CPVT. Wilde et al. reported the long-term efficacy of surgical left cardiac sympathetic denervation in three young adults with CPVT, all of whom had symptoms before the procedure and were symptom-free later [11]. They suggested the important advantages of left cardiac sympathetic denervation. Once the procedure is performed, the effects are permanent, because preganglionic denervation precludes reinnervation. Denervation does not result in the limitations that occur with medical therapies such as incomplete compliance, especially among teenagers. Scott et al. reported the successful treatment of CPVT with bilateral thoracoscopic sympathectomy in a young woman with multiple ICD-related complications that finally needed to be explanted due to an ongoing infection. During 4 years of follow-up since the sympathectomy, the patient has been free from any further syncopal episodes without any re-implantation of an ICD [12]. The authors mentioned that sympathectomy may have a useful role as an adjunctive therapy in CPVT, as beta-blockade was not completely effective and long-term ICD use was associated with potential complications. Vaseghi et al. reported the efficacy of left ($n=14$) and bilateral ($n=27$) cardiac sympathetic denervation (CSD) in 41 patients with VT storms. Although both showed beneficial effects with VT suppression, bilateral CSD resulted in greater ICD shock-free survival compared to left CSD alone [13]. In our case, the patient first underwent left thoracoscopic sympathectomy, which was effectively suppressed polymorphic VTs under 10.2 Mets of treadmill exercise testing, but did not suppress these VTs over 11.2 Mets of exercise. Based on the dramatic efficacy of the right stellate ganglion blockade using local anesthesia to suppress the polymorphic VT under an ISP infusion, the patient also underwent right thoracoscopic sympathectomy. After the last procedure, no VT events or syncope was documented for a follow-up of 21 months, except for one inappropriate ICD shock due to AT with a rapid ventricular response nine months after bilateral sympathectomy. Interestingly, dual tachycardias with polymorphic VT and AT were frequently recorded simultaneously before the sympathectomy (Fig. 3A), but no polymorphic VT was detected during the last AT event (Fig. 3B). This phenomenon can be explained in light of the following literature. A number of antiarrhythmic effects after sympathectomy are mediated by a reduction in the amount of intracardiac noradrenaline release. This includes an increase in the threshold for the induction of VF and an increase in ventricular refractoriness [14,15].

We hereby described an initial case of drug- and ablation-refractory CPVT that was successfully suppressed by step-wise, bilateral thoracoscopic sympathectomy in an Asia-Pacific country. Although PVCs occurred under 11.2 Mets of exercise, neither couplets nor polymorphic VTs could be induced, which suggested that the bilateral thoracoscopic sympathectomy in this patient suppressed the maximum beat runs of polymorphic VT. The reason why our patient not only needed left but also right sympathectomy to suppress the CPVT was not clear. The anatomical distribution of cardiac sympathetic nerves and its role in the induction of cardiac arrhythmias may differ between patients. In addition, it would be better to evaluate the efficacy of bilateral thoracoscopic sympathectomy on autonomic nervous activity by heart rate variability. However, this was difficult in our patient because heart rate was dependent almost solely on the atrial pacing rhythm under full medication.

4. Conclusion

Thoracoscopic bilateral sympathectomy may be an alternative therapy for patients with drug-refractory CPVT.

Conflicts of interest

All authors declare no conflict of interest related to this study.

Acknowledgment

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