Journal of Cardiology Cases 19 (2019) 36–39

Contents lists available at ScienceDirect

Journal of Cardiology Cases

journal homepage: www.elsevier.com/locate/jccase

Case Report

Radiofrequency catheter ablation for drug-refractory atrial tachyarrhythmias in a patient with catecholaminergic polymorphic ventricular tachycardia: A case report

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ARTICLE INFO

Article history:
Received 20 July 2018
Received in revised form 4 September 2018
Accepted 30 September 2018

Keywords:
Catecholaminergic polymorphic ventricular tachycardia
Atrial tachycardia
Atrial fibrillation
Pulmonary vein isolation

ABSTRACT

Patients with catecholaminergic polymorphic ventricular tachycardia (CPVT) frequently have atrial arrhythmias, such as atrial tachycardia (AT) and fibrillation (AF), in addition to the ventricular tachyarrhythmias. The development of AT/AF in patients with CPVT is associated with adverse outcomes, and its management is still challenging.

A 43-year-old woman with CPVT underwent radiofrequency catheter ablation (RFCA) for drug-refractory AT/AF. Pulmonary vein isolation (PVI) was carried out prior to AT ablation. Repetitive rapid firing from the left superior PV occurred frequently during PVI. After completion of PVI, the firing disappeared, but both polymorphic VT and multifocal ATs were induced by infusion of isoproterenol (ISP) (0.5 mcg/min). The origins of the two ATs were in the right atrium (RA) posterior septum [cycle length (CL), 285 ms] and ostium of the coronary sinus (CS) (CL, 235 ms). Electrophysiologic evaluation revealed that the earliest activation occurred at the RA posterior septum and CS ostium, preceding the onset of P waves by 52 ms and 84 ms, respectively. Application of radiofrequency energy at the site terminated ATs. After RFCA of the two ATs and PVI, no atrial tachyarrhythmias were induced by continuous ISP administration (0.5 mcg/min).

<**Learning objective:** A 43-year-old woman with catecholaminergic polymorphic ventricular tachycardia (CPVT) underwent radiofrequency catheter ablation (RFCA) for drug-refractory atrial tachyarrhythmias (AT/AF). Catecholamine hypersensitivities were observed in the right atrium and pulmonary veins (PVs) as well as the ventricle. Multiple ATs originating from not only a PV but also non-PVs should be considered for elimination of AT/AF in CPVT patients.>

Introduction

Catecholaminergic polymorphic ventricular tachycardia (CPVT) is a rare inherited arrhythmia disease with an estimated prevalence of 1 in 10,000 [1]. The diagnosis of CPVT is based on the occurrence of adrenergic stress-induced polymorphic ventricular tachycardia (pVT) characterized by bi-directional QRS alternans in the absence of structural heart disease [2]. Patients with CPVT frequently have atrial arrhythmias, such as atrial tachycardia (AT), flutter (AFL), and fibrillation (AF), in addition to the ventricular tachyarrhythmias [3]. Atrial tachyarrhythmias provoke rapid ventricular responses and can cause ischemic stroke. However, the management of atrial tachyarrhythmia in patients with CPVT has not been evaluated in detail.

Case report

A 43-year-old woman presented with paroxysmal AF/AT and underwent catheter ablation for pulmonary vein isolation (PVI) and AT. She initially experienced syncope at the age of 7 years while she was running at school, and she experienced several episodes of exercise-induced syncope until she was a high school

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https://doi.org/10.1016/j.jccase.2018.09.004
1878-5409/

student. She had not experienced any noticeable symptoms since that time. She visited a family doctor with palpitation at age of 20 years and oral administration of atenolol (25 mg/day) was started. However, she had remained undiagnosed. When she was 23 years old, an irregular heart rhythm was detected at a medical check-up and she visited our outpatient clinic. She had no family history of sudden cardiac death or syncope. An echocardiogram revealed no structural abnormalities. An exercise test provoked salvos of multifocal and polymorphic VTs and ATs (Fig. 1). She was diagnosed as having CPVT because of characteristic exercise-induced polymorphic VTs and absence of structural heart disease [1]. Gene analysis of the cardiac ryanodine receptor gene (RyR2) did not show any mutations. She did not consent to implantable cardioverter defibrillator implantation and we started oral administration of atenolol (50 mg/day). However, the patient continued to have different ventricular ectopy during exercise despite administration of a β-blocker, and verapamil (240 mg/day) was added to atenolol. Verapamil has been shown to decrease the ventricular rate during AF and prevent rate-dependent triggered ventricular arrhythmias by delayed afterdepolarization. Under this regimen, she did not experience any syncope episodes for 19 years of follow-up. When she was 42 years old, she was hospitalized after suffering right hemiplegia and speaking disturbance. She presented with AF at the emergency unit and a neurologist diagnosed cerebral embolism due to AF. She was treated with a thrombolytic agent and underwent successful thrombolysis. Fortunately, she recovered without aftereffects of the cerebral embolism. However, after discharge from the hospital, an exercise test provoked pVTs and ATs. Administration of atenolol was discontinued and bisoprolol was titrated up to 2.5 mg/day. Finally, flecainide at 100 mg/day was added to the antiarrhythmic medication consisting of bisoprolol at 2.5 mg/day and verapamil at 180 mg/day. After that, an exercise test did not induce polymorphic VT, but a short duration of AT/AF and premature ventricular contractions remained. Because of the residual AT/AF during drug therapy and her anxiety about a recurrent stroke, we decided to perform radiofrequency catheter ablation (RFCA) for the atrial tachyarrhythmias.

A 20-pole catheter was positioned into the coronary sinus (CS) and superior vena cava (SVC) through the right jugular vein. Following the standard Brockenbrough technique, we introduced 20-pole circular mapping catheters and an ablation catheter into the left atrium (LA). Three-dimensional electroanatomical mapping was performed using the Carto 3 system (Biosense Webster, Inc., Diamond Bar, CA, USA). RFCA was applied using an open irrigated-tip catheter (Navister Thermocool, Biosense Webster) with power output up to 30 W close to the PV ostia using an irrigation rate of 20 ml/min (0.9% saline infused with a Cool Flow Pump, Biosense Webster) in order to maintain a tip temperature below 42 °C.

We carried out circumferential PVI prior to AT ablation. Repetitive rapid firing from the left superior PV occurred frequently during PVI (Fig. 2A). The isolation of left PVs eliminated repetitive premature atrial contractions. Complete abolition of all PV potentials was the endpoint and was confirmed by both entrance and exit blocks. After completion of PVI, we induced ATs by infusion of isoproterenol (ISP) (0.5 mcg/min). ISP induced both polymorphic VT and multifocal ATs (Fig. 2B). The origins of the two ATs were in the right atrium (RA) posterior septum [AT1; cycle length (CL), 285 ms] and ostium of the coronary sinus (CS) (AT2; CL, 235 ms). Both ATs were simultaneously present and interfered with each other (Figs. 2B and 3). We tried to perform activation mapping of the ATs using Carto system, but we could not perform the mapping because one focus of the AT moved to the other focus in several atrial beats. The continuous potential was recorded from the distal to proximal electrode of ablation catheter (Fig. 3A and B). Starting with a power of 25 W at the site, a maximum power of 30 W was delivered. The AT terminated in 3 seconds with a

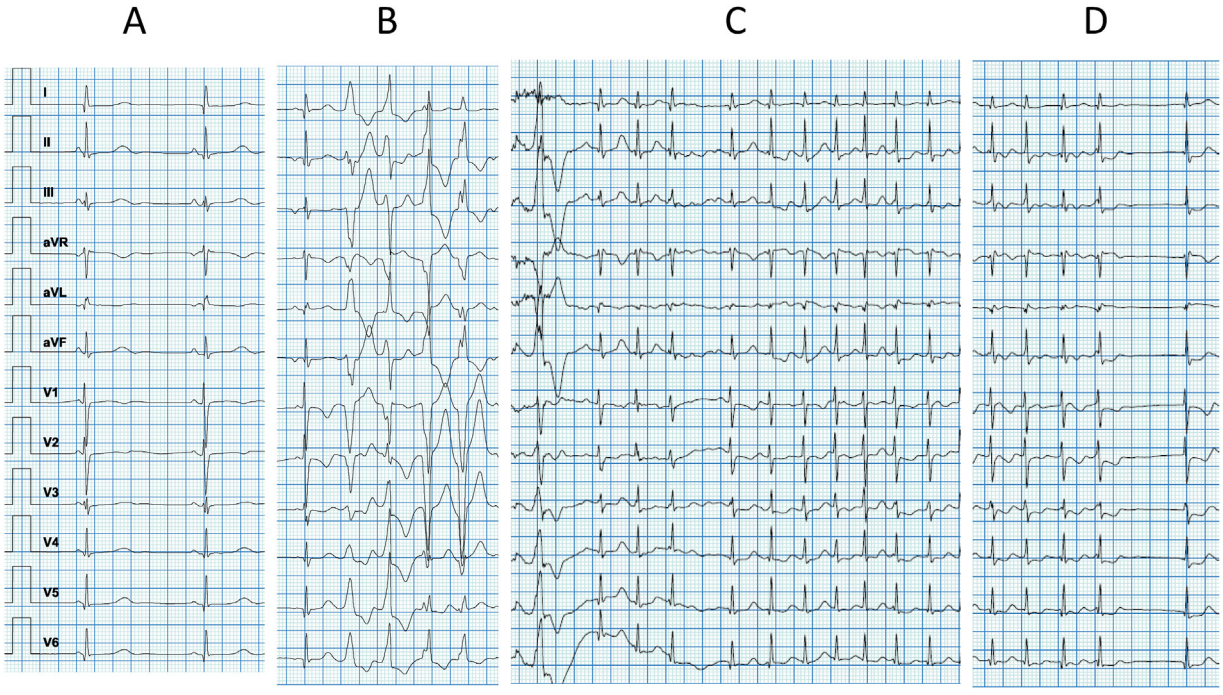

Fig. 1. Twelve-lead electrocardiogram during exercise testing. (A) Junctional rhythm (1st beat) and sinus rhythm (2nd beat) before exercise. (B) Exercise-induced polymorphic ventricular tachycardia (VT). VTs were multifocal and catecholamine-sensitive. (C) An exercise test induced a premature ventricular contraction and atrial fibrillation. (D) Termination of atrial tachycardia after exercise. The cycle length of atrial tachycardia was 384 ms.

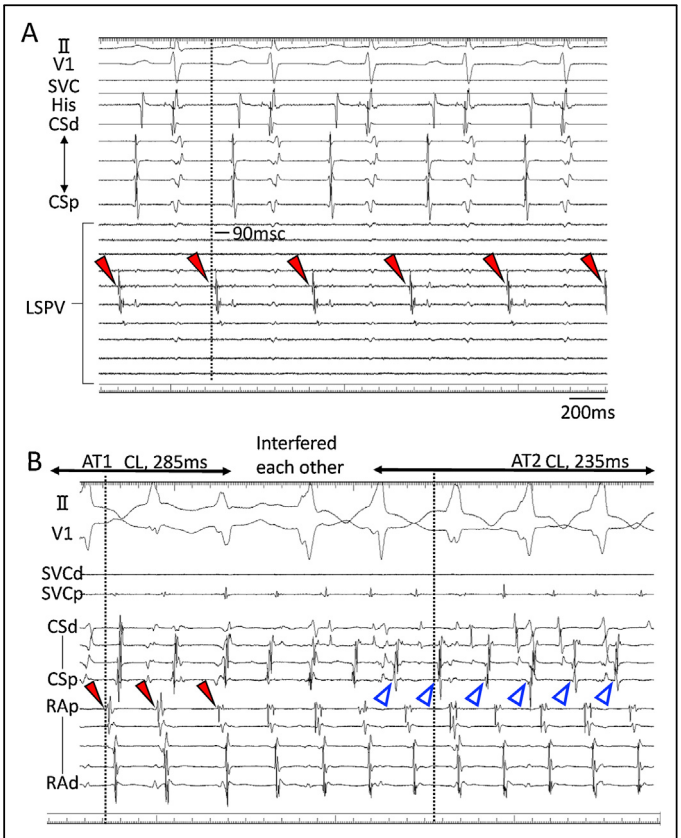

Fig. 2. Isoproterenol-induced atrial tachycardias originated from a pulmonary vein (PV) and the right atrium (RA) after infusion of isoproterenol. (A) PV tachycardia from the left superior PV. Repetitive rapid firing (arrowheads, cycle length: 560 ms) occurred frequently during PV isolation. The earliest activation occurred −90 ms before the onset of a P wave. (B) Migration of the foci of atrial tachycardias (ATs) during isoproterenol infusion. AT arose from the proximal RA in the initial 3 beats (red arrowheads). The earliest activation site of AT moved from the proximal RA to the ostium of the coronary sinus (blue arrowheads) after competition of the two foci. Note that isoproterenol induced polymorphic ventricular tachycardias as well as multifocal ATs in the electrocardiogram.
AT; atrial tachycardia, CL; cycle length, SVC; superior vena cava, CSp; coronary sinus proximal, CSd; coronary sinus distal, LSPV; left superior pulmonary vein, RAp; right atrium proximal, RAd; right atrium distal.

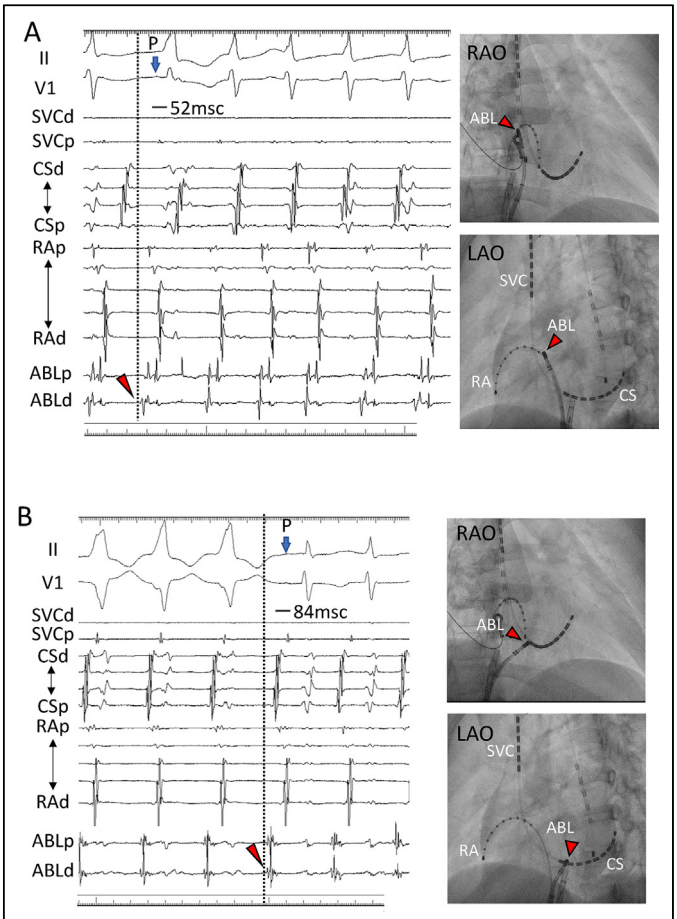

Fig. 3. Electrogram recording and catheter position at a successful ablation site. (A) Successful ablation site and catheter position for AT1. A fractionated potential preceding the surface P wave (arrow in the electrocardiogram) by 52 ms was recorded. (B) Successful ablation site and catheter position for AT2. A fractionated potential preceding the surface P wave (arrow in the electrocardiogram) by 84 ms was recorded.
ABLp; ablation catheter proximal, ABLd; ablation catheter distal, RAO; right anterior oblique, LAO; left anterior oblique.
Other abbreviation as in Fig. 2.

progressive prolongation in its CL during RF. After RFCA of the two ATs and PVI, no atrial tachyarrhythmias were induced by continuous ISP administration (0.5 mcg/min). With administration of bisoprolol (5 mg/day) and flecainide (100 mg/day), she remained syncope-free and exercise testing did not provoke polymorphic VT and ATs/AF for 1 year of follow-up.

Discussion

The occurrence of supraventricular tachyarrhythmia is not rare in patients with CPVT, and its incidence has been reported to be 26–38% [3,4]. However, a strategy for management of atrial tachyarrhythmia in patients with CPVT has not been established, and the role of non-pharmacologic therapy such as RFCA of potential arrhythmogenetic foci has not yet been defined [5].

It has been reported that firing originating from the PV is an important initiating source of AF, and PVI has become the standard catheter ablation target [6]. There have been two case reports of PVI to control AT/AF in patients with CPVT [7,8], but a complete dissociation between the PV potential and the LA was not sufficient to suppress all of the ATs. In the present case, multifocal ATs were provoked from the RA septum and CS orifice in addition to ATs from the PV. Several multifocal ATs were simultaneously present and interfered with each other. It was therefore difficult to perform the activation mapping in this case. However, Turbo-map in Ensite or CARTOREPLAY in Carto 3 system now enables mapping of multiple tachycardias with a retrospective review. It could be useful to identify the exact location of the AT origin when trying to map multiple ATs. In this patient, PVI and RFCA of AT foci disclosed by ISP were necessary to achieve satisfactory results.

Ion channel dysfunction is also present in the atrium as well as the ventricle, and leakage of calcium from the sarcoplasmic reticulum related to RyR2 dysfunction in atrial myocytes might play a role in the initiation and/or maintenance of atrial arrhythmia [9]. An experimental study using a mouse model with CPVT mutation showed that abnormal atrial rhythm frequently arose from the RA [10]. Our ablation site ATs originating from the extra PV coincided with the experimental origin of AT in the CPVT model, and these areas should be sensitive to catecholamine to promote focal firing.

After the completion of PVIs and the ablation of ATs, atrial tachyarrhythmias were induced. Although a few premature ventricular contractions were observed, it was difficult to induce ventricular tachyarrhythmias under the condition of low-dose ISP (0.5 mcg/min) administration. Therefore, RFCA eliminates the triggers for AT/AF initiation and may also reduce sympathetic nerve input to the heart, which in turn decreases the incidence of ventricular tachycardia. It was believed that the endpoint had been achieved and the ablation was completed in this case. However, increasing the dose of ISP should promote other extra PV foci. In a clinical setting, completion of PVIs and ablation of ATs that were induced by a low dose of ISP was sufficient to suppress clinical AF and ATs because patients should continue adrenergic blockade to reduce polymorphic VTs. However, the risk of stroke recurrence remains high, and long-term anticoagulation is recommended for patients at a high risk of stroke. With administration of antiarrhythmic drugs, the patient was syncope-free and exercise testing did not provoke polymorphic VT or atrial arrhythmia during 1 year of follow-up.

In conclusion, multiple ATs originating from not only a pulmonary vein but also non-PVs should be considered for elimination of AT/AF in CPVT patients.

Statement of consent

Informed consent was obtained from this patient for publication of this case history and associated images in line with COPE recommendations.

Conflict of interest

Dr Hiroshi Morita is affiliated with the endowed department by Japan Medtronic Inc.

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