



Torsades de Pointes associated with QT prolongation after catheter ablation of paroxysmal atrial fibrillation

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ARTICLE INFO

Article history:

Received 10 April 2017

Received in revised form

26 June 2017

Accepted 11 July 2017

Available online 13 July 2017

Keywords:

Torsades de Pointes

QT prolongation

Neural modulation

Atrial fibrillation

ABSTRACT

A 79-year-old woman who underwent catheter ablation for paroxysmal atrial fibrillation presented with Torsades de Pointes (TdP). Aggravation of prolonged QT interval which is most likely due to neural modulation by catheter ablation, played major role in the initiation of TdP. The patient was successfully treated with isoproterenol during acute stage and discharged after stabilization without implantation of permanent pacemaker or implantable cardioverter defibrillator.

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1. Introduction

Ablation of ganglionic plexus (GP) is often performed to reduce vagal innervation and has been shown to confer a better long-term outcome in patients undergoing catheter ablation for AF. Vagal denervation may be anti-arrhythmic in the atria while pro-arrhythmic in the ventricle [1]. We report a case of Torsades de Pointes (TdP) associated with QT prolongation after catheter ablation of the paroxysmal AF.

2. Case report

A 79-year-old female was referred to our electrophysiology laboratory because of repeated episodes of paroxysmal atrial fibrillation (AF) for 15 months. Anti-arrhythmic drug (AAD, flecainide 50mg bid) and anticoagulation therapy (warfarin 2.5mg) was started, because her CHA2DS2-VASc score was 4 (history of hypertension, age ≥ 75, female gender). She had no family history of sudden cardiac death or syncope. She was taking amlodipine 5mg,

losartan 50mg and thiazide 12.5mg for anti-hypertensive medications. Her initial electrocardiography (ECG) during sinus rhythm indicated prolongation of the QT/QTc interval (476/495 ms) and intermittent sinus pause up to 1.8 seconds (Fig. 1A). Echocardiography showed no structural heart disease with normal left ventricular ejection fraction (74%) and left atrial diameter was measured at 51mm. Flecainide 50mg bid was tolerable without aggravation of sinus node dysfunction and QT prolongation; however, paroxysmal AF episodes recurred despite taking AAD for more than three months. Therefore she underwent catheter ablation with uninterrupted strategy of anticoagulation.

Ablation procedure was performed under the guidance of three-dimensional mapping (NavX System, St. Jude Medical Inc., St. Paul, MN, USA). AF triggering focus was found at the left superior pulmonary vein (LSPV) and inside the coronary sinus near the ostium of the vein of Marshall after high dose isoproterenol infusion, therefore, the ablation procedure included four PV isolation and ablation inside the coronary sinus (Fig. 1B). Radiofrequency ablation was delivered at a target temperature of 42 °C and power in the range of 25–30 W using a 4-mm open irrigated-tip catheter (Coolflex, St. Jude Medical, Inc., St. Paul, MN, USA). Significant vagal response, suggesting GP ablation was observed during ablation on the anterior side of LSPV. AF terminated during catheter ablation with a significant sinus pause up to 4.5 seconds. Sinus node function test was performed, which revealed maximal corrected sinus

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Peer review under responsibility of Indian Heart Rhythm Society.

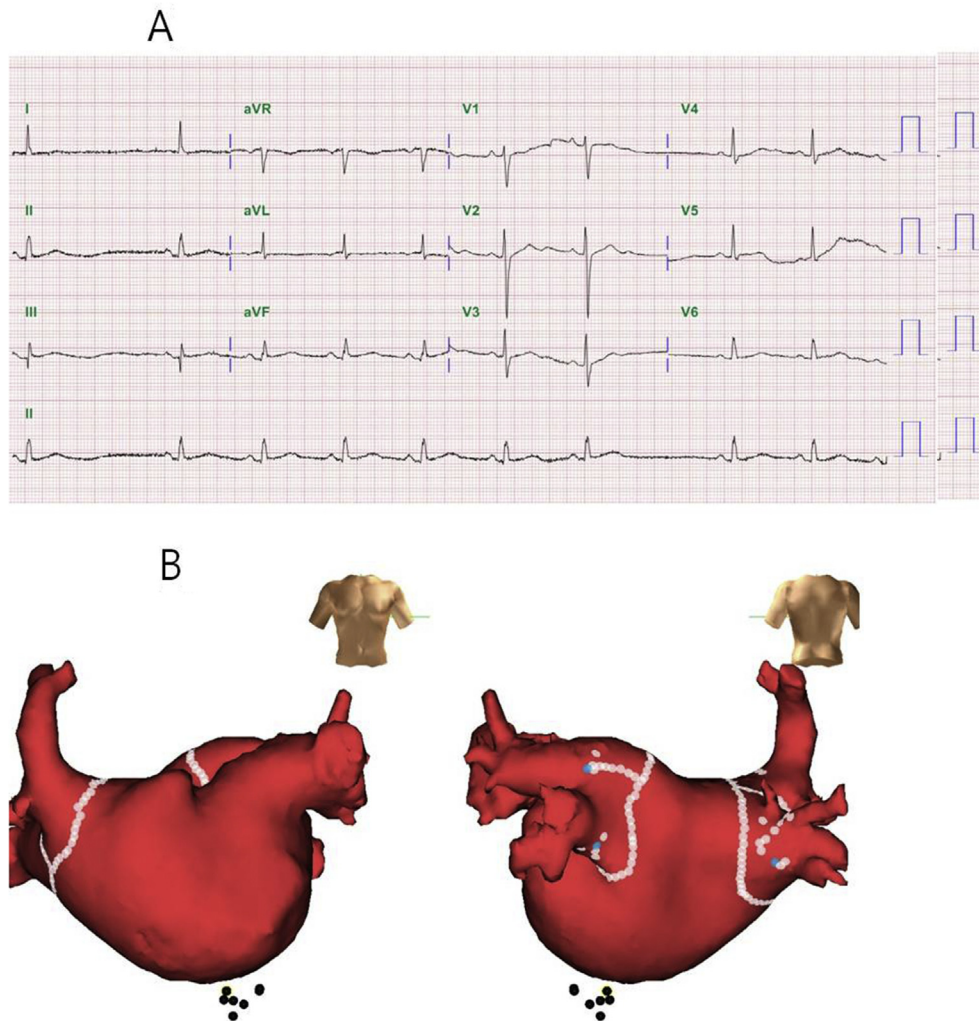


Fig. 1. (A) ECG during sinus rhythm indicated prolongation of the QT/QTc interval (476/495 ms) and intermittent sinus pause up to 1.8 seconds. (B) Three-dimensional image of the Navx system (St Jude Medical Inc., St Paul, MN, USA); ablation procedure included isolation of four pulmonary veins and ablation inside the coronary sinus.
ECG = Electrocardiography.

node recovery time was 4,665 ms. High dose isoproterenol infusion test was repeated after ablation and there was no immediate recurrence of AF. Total ablation time was 51 minutes. There were no procedure-related complications and she was discharged uneventfully 3 days after catheter ablation with resuming the same dose of AAD (flecainide 50mg bid) she had been taking before and warfarin.

She came to the hospital 10 days after the ablation procedure because of palpitation followed by dizziness and presyncope. She was admitted and ECG indicated more prolongation of QT/QTc (580/590 ms) with T inversion at precordial leads (Fig. 2A). Holter monitoring showed repeated episodes of TdP (Fig. 2B) without significant sinus pause or bradycardia. She was not taking any other medication except for cardiology medication. Laboratory testing showed no electrolyte imbalance such as hypokalemia or hypomagnesemia and normal range of cardiac enzyme. Flecainide was stopped and magnesium was injected, which was not effective, therefore, isoproterenol 1 $\mu\text{g}/\text{min}$ was infused targeting heart rate >80 bpm. Her heart rate was maintained higher than 80 bpm and TdP was no longer observed. After careful review of the previous ECG, we found that QT/QTc prolongation (560/592 ms) was already aggravated on the third day after catheter ablation. Isoproterenol

was infused for 11 days and was stopped, because there were no further events of TdP. On serial follow up ECG, QT/QTc interval showed gradual recovery to the baseline on the 25th day of catheter ablation. Later, we considered the possibility of injury of the left circumflex artery during inside coronary sinus ablation despite no chest discomfort. Coronary angiogram was performed, which showed significant stenosis (>80%) at the proximal left anterior descending artery while the left circumflex artery was intact (Fig. 3). Coronary intervention with drug-eluting stent implantation was performed and she was discharged with anti-anginal medications (isosorbide dinitrate) and dual antiplatelet agents (aspirin and clopidogrel).

She was stable for 1 month, therefore, a low dose of flecainide (50mg bid) was resumed for prevention of AF recurrence during the blanking period. Two days after taking flecainide, she returned to the emergency room with repeated non-sustained TdP. ECG showed significant prolongation of QT/QTc with U wave again. Subsequent arrhythmic events were successfully suppressed by administration of isoproterenol. Coronary angiogram was repeated to rule out in-stent restenosis, which showed no significant lesion. After a washout period of flecainide, the U wave disappeared and the QT/QTc interval was recovered to baseline after discontinuation



Fig. 2. (A) ECG indicated more prolongation of QT/QTc (580/590 ms) with T inversion at precordial leads. (B) Holter monitoring showed repeated episodes of TdP. ECG = Electrocardiography; TdP = Torsades de Pointes.

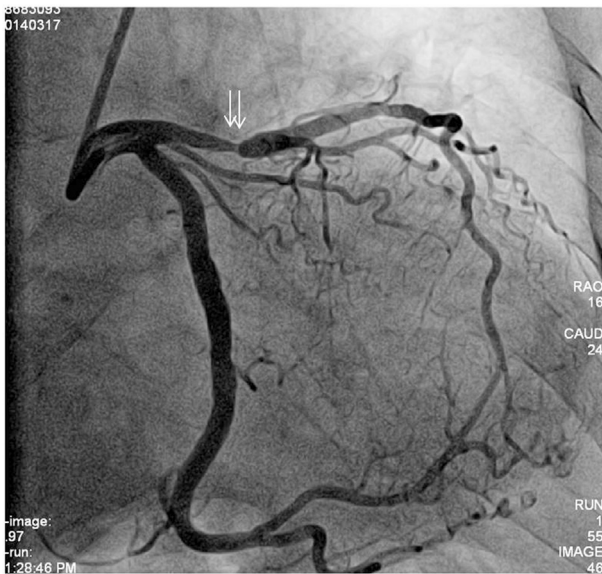


Fig. 3. Coronary angiography showed significant stenosis (>80%) at the proximal left anterior descending artery (white arrows).

of isoproterenol. She was successfully discharged and she had been in sinus rhythm without episodes of ventricular arrhythmias or AF during follow up > 3 years.

3. Discussion

The PV region is richly innervated by the autonomic nervous system and has a high density of GP [2]. Myocardial fibers and nerves adjacent to the vein of Marshall have been implicated as a source of ectopic beats initiating paroxysmal AF, and as a source of arrhythmogenic autonomic innervation [3]. Vagal stimulation has different effects on atrial and ventricular myocytes. In the ventricle, vagal stimulation prolongs the duration of an action potential and

the effective refractory period [1], while reducing the atrial effective refractory period [4], augments spatial electrophysiological heterogeneity [5], and promotes early afterdepolarization toward the end of phase III in the action potential in the atria [6]. Thus vagal denervation may be anti-arrhythmic in the atria while pro-arrhythmic in the ventricle.

In a recent experimental study, GP ablation in normal heart did not change the threshold of ventricular fibrillation despite facilitating the occurrence of action potential duration alternans while GP ablation in acute myocardial infarction significantly promoted the occurrence of ventricular fibrillation [7]. Significant myocardial ischemia might exacerbate transmural dispersion of repolarization and played an additional role in causing our patient to be vulnerable to ventricular arrhythmia. However, QT prolongation was recovered before coronary intervention and TdP occurred again despite coronary intervention, meaning that coronary ischemia was not the sole precipitating factor in this patient.

Flecainide has no significant effect on cardiac repolarization and usually prolongs QT intervals slightly by increasing the duration of an action potential through the selective I_{Kr} channel blocking properties on ventricular myocytes [8]. Thus flecainide induced TdP is rare, generally occurring with the association of other conditions such as electrolyte imbalance or other QT prolonging drugs. A second episode of TdP occurred soon after administration of flecainide in our patient, therefore, prolongation of the QT interval by flecainide appears to be the triggering factor. Then, why did the same dose of flecainide aggravate QT prolongation after AF ablation, which was tolerable before catheter ablation? Inadvertent neural modulation by catheter ablation might be a mechanism of changing susceptibility and vulnerability to flecainide. The findings that PV and inside coronary sinus are the regions richly innervated by the autonomic nervous system and vagal response during radiofrequency application at LSPV can support the inadvertent neural modulation, even though causal relationship cannot be proven definitely.

Isoproterenol infusion was effective after acceleration of the basic heart rate during acute stage. Isoproterenol should only be used when TdP is the result of an acquired long QT syndrome, the

underlying rhythm is slow, and TdP is clearly pause dependent. In animal models, beta-adrenergic stimulation by isoproterenol induces TdP by increasing transmural dispersion of repolarization in congenital long QT syndrome type 1 and type 2 [9]. Genetic testing was not performed and regarding absence of syncope or sudden cardiac death in her and her familial history, it remains unclear whether she is in the diagnosis of congenital long QT syndrome or not.

Permanent pacemaker implantation was considered because of latent sinus node dysfunction, however, sinus node dysfunction itself was not clinically problematic so far and repeated Holter monitoring showed that mean heart rate was higher than 70 bpm and sinus pause more than 2 seconds was never observed. In addition, TdP was no longer observed and recovery of QT/QTc interval to baseline after approximately 1 month of catheter ablation indicated resolution of disturbance of cardiac autonomic function. Usage of flecainide and coronary ischemia were reversible causes. Thus pacemaker or ICD implantation was deferred with careful follow up.

To the best of our knowledge, this is the first case reporting TdP after catheter ablation of AF. Although destruction of the major cardiac parasympathetic elements by GP ablation may cause an increase in sympathetic activity, it may not be arrhythmogenic in the normal heart due to the lack of an appropriate substrate for ventricular arrhythmia. However, it might predispose the heart to ventricular arrhythmia by making the patient more vulnerable to associated conditions. Therefore, we should be aware of the possibility of future ventricular arrhythmia after inadvertent GP modulation during AF ablation, particularly in patients with underlying long QT interval, sinus node dysfunction, coronary ischemia, and flecainide. Further study regarding the long-term effects of autonomic neural modulation by catheter ablation on ventricular arrhythmia is required.

Funding

None.

Conflicts of interest

All authors have no conflicts of interest.

Disclosures

No conflicts to disclose.

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