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Kawaji, Tetsuma ...[et al]. Early-onset atrial fibrillation in brothers with a huge left atrial appendage. Internal Medicine 2016, 55(9): 1117-1120

ISSUE DATE:
2016

URL:
http://hdl.handle.net/2433/226550

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Early-onset Atrial Fibrillation in Brothers with a Huge Left Atrial Appendage

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Abstract

Having a relative with atrial fibrillation (AF) is one of the risk factors for AF development, especially in young patients, which is known as familial AF. Although familial AF is considered to be associated with inherited factors, its genetic and pathophysiological backgrounds have not been fully identified. We report two young brothers undergoing radiofrequency catheter ablation for AF, who had a huge left atrial appendage (LAA). In both cases, the origins of the main triggers of the AF were not the huge LAA itself, but left pulmonary veins compressed by the LAA. Since catheter ablation including pulmonary vein isolation, the sinus rhythm has been maintained in both patients.

Key words: familial atrial fibrillation, left atrial appendage, radiofrequency catheter ablation

Introduction

Atrial fibrillation (AF) is the most common type of supraventricular arrhythmia with increased morbidity and mortality. Epidemiological studies have shown that AF increases with age and is very rare in those younger than 40 years (1). On the other hand, a high risk of AF among those who have relatives with AF has been reported, which is called familial AF (2). We report two young brothers with AF, who had the same unique morphological features of the left atrium (LA) and the pulmonary veins (PVs).

Case Reports

Case 1

A 35-year-old man with dyslipidemia and diabetes mellitus (body mass index 24.9), whose father had died of a cardiogenic embolic stroke, developed paroxysmal AF and started to take pilsicainide. At 37 years of age, his AF became drug-refractory and he was admitted to our institution for radio frequency catheter ablation (RFCA). A multi-slice CT image revealed that a huge LAA (15.2 mm$^3$) compressed both left superior (LS) and left inferior (LI) PVs (Fig. 1A and B). Left ventricular function was normal and the LA was dilated (48 mm) on transthoracic echocardiography. Transesophageal echocardiography showed a normal LAA flow (74 cm/s on sinus rhythm) and no LAA thrombosis. On LA angiography before RFCA, there was a huge LAA spread over the superior portion of the LA, mimicking LSPV (Fig. 1C and D). A previously acquired CT image of the LA was integrated into the electroanatomical mapping system (CARTO$^\text{TM}$, Biosense Webster, USA) for the navigation of mapping and ablation catheters (CARTOMERGE$^\text{TM}$, Biosense Webster, USA) (Fig. 1E and F). During LPV isolation, AF repeatedly occurred by spontaneous firing from the LPVs (Fig. 2A and B). After LPV isolation, a stable sinus rhythm was maintained. We added right PV (RPV) isolation, superior vena cava isolation and cavotricuspid isthmus linear ablation. Because the intravenous administration of adenosine-triphosphate (ATP) at 20 mg under isoproterenol infusion (1 μg/min) provoked dormant LA-PV conduction on both sides, several RF energy applications were performed until disappearance of the transient LA-PV reconstructions. Coronary angiography after the procedure showed no stenosis. During follow-up, the patient has been symptom-free and AF recurrence has not been documented for three years without antiarrhythmic drugs.
Figure 1. Images of LA and PVs of Case 1. Multi-slice CT image showed LSPV (A) and LIPV (B) compressed by an LAA. Angiography (C) and 3-D CARTO™ image (D) showed a huge LAA mimicking LSPV. Ablation points of PV isolation are shown (E and F). AF: atrial fibrillation, CS: coronary sinus, LA: left atrium, LAA: left atrial appendage, LIPV: left inferior pulmonary vein, LSPV: left superior pulmonary vein.

Case 2

The younger brother of Case 1 without any comorbidities (body mass index 23.4) began to experience palpitations at 27 years old. At 35 years old, AF was documented in a health examination and was considered to be persistent by Holter monitoring. He was admitted to our institution for RFCA at the age of 38. On a multi-slice CT image, his LPVs were also compressed by a huge LAA (14.3 mm³), as in his elder brother (Fig. 3A and B), and there was no coronary stenosis. Echocardiography showed a mildly dilated LA (44 mm) and preserved LAA flow (52 cm/s on AF rhythm) without LAA thrombosis. Following LA angiography, CAR-TOMERGE™ was performed (Fig. 3C-F). Before RF energy applications, cardioversion was performed and sinus rhythm was restored, although bolus injection of ATP at 20 mg under isoproterenol infusion induced electrical firings from LSPV, leading to sustained AF (Fig. 2C). We performed extensive PV isolation under AF and ablated 19 sites with a continuous fractionated atrial electrocardiogram, which prolonged the cycle length of the coronary sinus from 146 to 181 ms. Thereafter, cardioversion was again performed, which successfully restored and maintained the sinus rhythm. No atrial ectopy was observed under isoproterenol infusion. In addition, no dormant LA-PV conduction was induced by the bolus administration of ATP at 20 mg. Since the RFCA, the sinus rhythm has been maintained for three months.

Discussion

Previous studies have reported various types of familial AF (2, 3), which were associated with abnormalities in ion channels, nuclear lamina, developmental programs and cytoskeletal interactions. Mutations of the potassium channel protein KvLQT1 (KCNQ1) and the sodium channel protein NaV1.5 (SCN5A), known as genetic causes of Long-QT and Brugada syndromes, increase the excitability of atrial cells and induce AF. In a previous report of a patient with familial AF who had a gain-of-function mutation in SCN5A, numerous electrical firings from the catheter contact sites in the atrium were documented during RFCA for AF (4). On the other hand, in the present two cases, no such phenomenon was observed, although electrical firings from the LPVs were documented. Given the lack of arrhythmia recurrence following PV isolation, mutations in the ion channels are unlikely to be the causes of AF in the present two cases, although the genetic analyses are still ongoing.

Gene mutations associated with developmental programs, such as GATA4, NKX2-5 and PITX2, are known to induce inherited AF and occasionally complicated with cardiac malformations, such as tetralogy of Fallot, atrial septal defect and LAA aneurysm (2). However, to the best of our knowledge, this is the first report showing familial AF with unique
morphological features of left-sided LA, namely, a huge LAA and compressed LPVs. Although we cannot rule out the possibility that the huge LAA was a secondary phenomenon due to repetitive or persistent AF and/or co-existing morbidities such as diabetes and dyslipidemia, we have never experienced these kinds of unique anatomical features of an LAA and PVs in >1,000 patients undergoing AF ablation at our institution, except for the present two cases.

The arrhythmogenic origins of the electrical firings triggering the AF in the present cases were not the huge LAA itself, but the compressed LPVs. Indeed, most of the triggers causing AF have been reported to be electrical firing from the PVs (5). Although the electrophysiological and pathophysiological mechanisms of PV firing are not fully understood, degeneration of myocardial sleeves within PVs associated with aging and age-related risk factors, such as hypertension, obesity and coronary artery disease, is generally considered to be the underlying cause of PV firing in non-valvular AF (6). In the present two cases, however, given the early onset (<40 years) of AF and the lack of hypertension, obesity and coronary artery disease, the underlying cause of electrical firings from LPVs was strongly suggested to be the compression of LPVs by the huge LAA.

In conclusion, we herein reported two young brothers with AF triggered by electrical firings from LPVs compressed by a huge LAA, which was successfully treated by RFCA including PV isolation.

The authors state that they have no Conflict of Interest (COI).
**Figure 3.** Images of LA and PVs of Case 2. LSPV (A) and LIPV (B) were compressed by a huge LAA in a multi-slice CT image, like in Case 1. Angiography showed dilated LA in a transverse direction (C). Three-dimensional CARTO™ image also showed a huge LAA compressing LPVs (D). Ablation points of extensive PV isolation and continuous fractionated atrial electrocardiogram ablation are shown (E and F). PV: pulmonary vein. Other abbreviations as in Fig. 1.

**References**