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Case Report

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A case of sinus arrest in atrial fibrillation with pulmonary embolism after flecainide ingestion

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ABSTRACT

A 76-year-old female visited the emergency department with complaining of dizziness and syncope. She had a history of paroxysmal atrial fibrillation (AF) and had been prescribed flecainide 50 mg and apixaban 5 mg 12-hourly in another hospital 1 day before the presentation. Upon admission, her electrocardiogram showed profound bradycardia and extremely long sinus arrest, which required temporary cardiac pacing. Within 24 hours, her intrinsic rhythm was restored, and the temporary pacemaker was removed. Transthoracic and transesophageal echocardiography revealed no structural heart disease or thrombus in the left atrial appendage. Cardiac computed tomography showed no coronary artery stenosis, but a pulmonary thrombus in the right pulmonary artery. She underwent an electrophysiology study, and four pulmonary vein (PV) isolations were attempted to treat the paroxysmal AF. A bidirectional PV conduction block was acquired in all PVs despite spontaneous dissociation of PV potential in the right PV. Programmed stimulation following ablation resulted in sinus node dysfunction. After the procedure, the patient did not complain of dizziness and syncope for 72 hours of telemetry monitoring. She was discharged with anticoagulant and did not show any further symptoms for 6 months. Flecainide acetate is a class Ic antiarrhythmics, and its clinical efficacy has been confirmed in several clinical trials. However, it can unmask sinus node dysfunction in asymptomatic patients with paroxysmal AF. Clinicians should screen candidates for sinus nodal diseases when prescribing flecainide.

Keywords: Atrial Fibrillation; Bradycardia; Drug; Thromboembolism

INTRODUCTION

Flecainide acetate is a class IC antiarrhythmics used to treat atrial fibrillation (AF) [1]. However, based on the Cardiac Arrhythmia Suppression Trial, flecainide should not be used in AF patients with structural heart disease due to its high proarrhythmic risk [2]. Also, flecainide is used cautiously because it prolongs sinus node recovery time in some patients with underlying sinus node dysfunction [3].

Here, we report a case of flecainide with life-threatening arrhythmia but with a favorable outcome. Written informed consent was obtained, and the study was approved by the Institutional Review Board of Chosun University Hospital (CHOSUN 2022-04-030).

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Author Contributions

Conceptualization: Jeong HK, Kim SS, Kim HK, Ki YJ, Park KH, Choi DH; Data curation: Jeong HK, Kim SS, Kim HK, Ki YJ, Park KH, Choi DH; Formal analysis: Jeong HK, Kim SS; Funding acquisition: Kim SS; Investigation: Kim SS; Methodology: Kim SS; Project administration: Kim SS; Resources: Kim SS; Software: Kim SS; Supervision: Kim SS; Validation: Kim SS; Visualization: Kim SS; Writing - original draft: Jeong HK, Kim SS; Writing - review & editing: Kim SS.

CASE REPORT

A 76-year-old female visited the emergency department complaining of dizziness and syncope. She had no family history of arrhythmia and was not taking any medication. However, recently, she experienced chest fluttering and shortness of breath and was diagnosed with AF in a local hospital through 24-hour Holter monitoring, which showed paroxysmal AF with a mean heart rate of 76 bpm (AF burden 18%, sinus pause 2.3 seconds at night, range of 50–138 bpm). Oral flecainide (50 mg) and apixaban (5 mg) 12-hourly were prescribed for the paroxysmal AF. However, she suddenly lost consciousness 1 day later and was brought to the emergency department. Upon admission, she presented with profound bradycardia and extremely long sinus arrest (**Fig. 1**) when she complained of presyncope; thus, a temporary pacemaker was applied. The results of the initial blood testing were as follows: white blood cell count, 8,570/mm^3; hemoglobin, 13.6 g/dL; platelets, 249,000/mm^3; aspartate aminotransferase 25.0 U/L; alanine aminotransferase, 22.0 U/L; sodium, 142 mmol/L; potassium, 4.2 mmol/L; chlorine, 107 mmol/L; calcium, 9.82 mg/dL; and magnesium, 2.07 mg/dL. Arterial blood gas analysis showed a pH of 7.421, carbon dioxide partial pressure of 34.3 mmHg, oxygen partial pressure of 115.0 mmHg and bicarbonate of 23.1 mmHg.

Within 24 hours, her intrinsic rhythm was restored, and the temporary pacemaker was removed. Transthoracic and transesophageal echocardiography revealed no structural heart disease or thrombus in the left atrial appendage. Cardiac computed tomography showed no coronary artery stenosis but a pulmonary thrombus in the right lower pulmonary artery (**Fig. 2A**). She underwent an electrophysiological study, and four pulmonary vein (PV) isolations were performed to treat paroxysmal AF. A bidirectional PV conduction block was acquired in all PVs

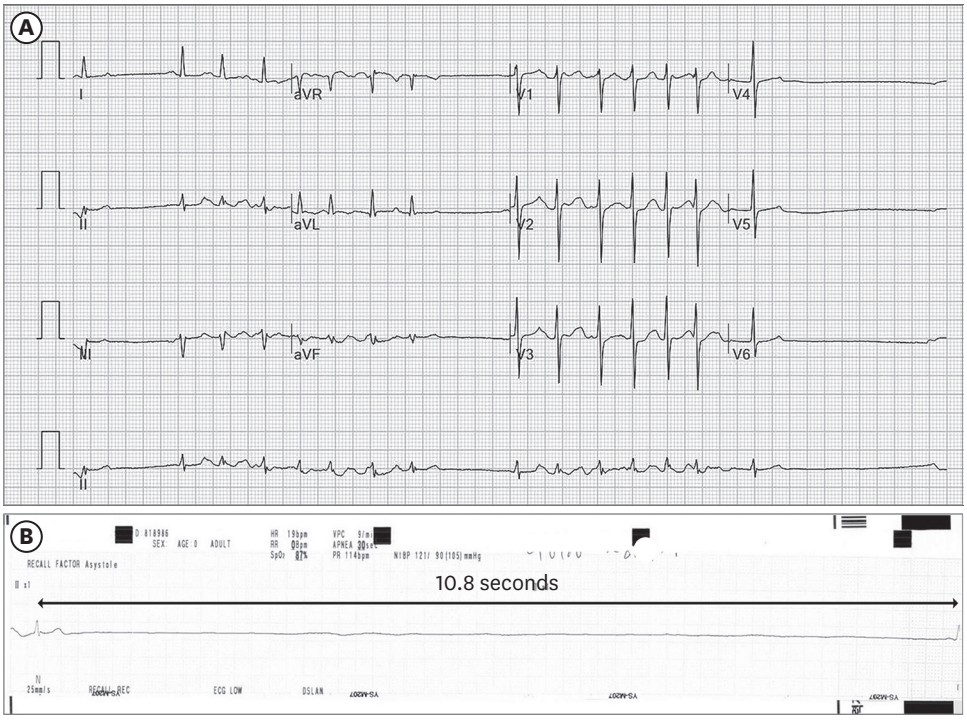

Figure 1. Sinus arrest (A) Twelve-lead ECG showed a rapid, irregularly irregular rhythm followed by a sinus pause. (B) Rhythm strip recording of ECG revealed extremely long sinus arrest (10.8 seconds).
ECG, electrocardiogram.

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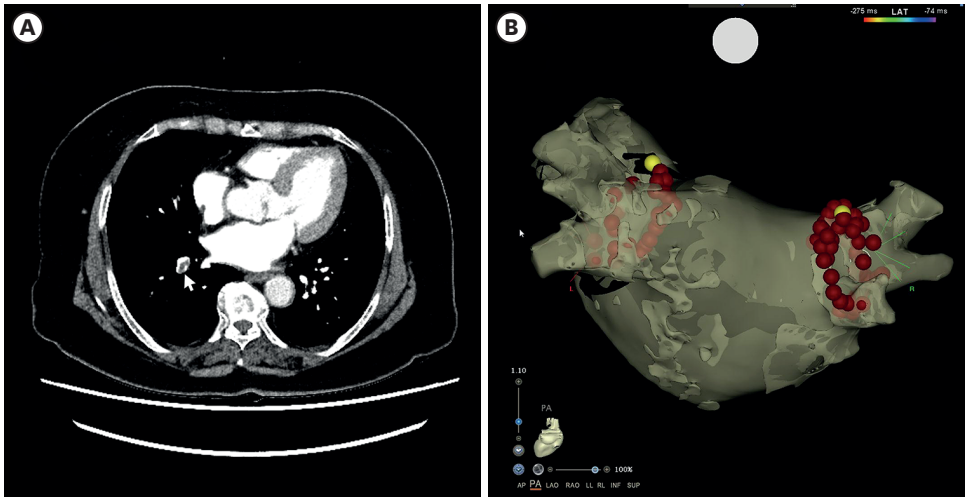

Figure 2. Pulmonary thromboembolism and Pulmonary vein isolation of 3D electroanatomic mapping. (A) Cardiac computed tomography showed a thrombus (white arrow) in the right pulmonary artery. (B) Four PVs isolation for treating paroxysmal AF.
PV, pulmonary vein; AF, atrial fibrillation.

despite the spontaneous dissociation of the PV potential in the right PV (**Fig. 2B**). Following ablation, programmed stimulation and rapid atrial pacing revealed sinus node dysfunction (corrected sinus node recovery time, 2,560 ms; sinoatrial conduction time, 258 ms). After the procedure, the patient did not complain of dizziness and syncope for 72 hours of telemetry monitoring. She was discharged with apixaban 5 mg 12-hourly and did not show any further symptoms for 6 months.

DISCUSSION

Herein, we present a case with paroxysmal AF with pulmonary embolism, who was taking flecainide. She subsequently developed serious cardiac toxicity and experienced multiple sinus arrests that required temporary cardiac pacing. This case reminds us of flecainide's rare but potentially morbid complication in AF patients with sinus node dysfunction.

Flecainide is a class IC antiarrhythmics used in paroxysmal AF [4]. It is administered 12-hourly and is absorbed rapidly without significant interactions with food or antacids [5]. Without renal dysfunction, plasma peak levels are reached after 2–3 hours and steady-state levels within 3–5 days. The recommended starting dose in patients without renal insufficiency and paroxysmal AF is 50 mg 12-hourly and might be increased in increments of 50 mg 12-hourly until efficacy is achieved (maximum recommended dose, 300 mg/day) [6]. Both flecainide and its metabolites are excreted mostly in urine; therefore, renal impairment requires close monitoring and dose reduction. However, in the present case, the patient with normal renal function experienced symptomatic sinus arrest for up to 10 seconds at a 100 mg 24-hourly (50 mg 12-hourly), which required temporary pacing. Flecainide has minimal effects on the normal sinus node but prolongs the sinus node recovery time in some patients with underlying sinus node dysfunction [7]. Thus, flecainide could unmask severe sinus node dysfunction in asymptomatic AF patients, even in small dose.

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Pulmonary thromboembolism (PTE) may also be associated with AF [8]. We could not be certain whether there was an association between PTE and AF or if they only coexisted without any causal relationship [9,10]. However, there is growing evidence of the involvement of AF in PTE. A possible association between AF and PTE is AF arising from an abrupt increase in pulmonary vascular resistance due to the occlusion of the pulmonary vessels. Stretch injuries to the right atrial tissue may facilitate PV arrhythmogenicity, which could trigger the onset of AF. Interestingly, in this patient, after bidirectional PV conduction block could be acquired in all PVs, there was a spontaneous slow dissociated PV potential in the right PV, where the pulmonary thrombus was located. This dissociated potential was not associated with the superior vena cava potential. Another possible mechanism is that AF is associated with a prothrombotic state; thus, thrombus formation in the right atrium has been suggested as a cause of pulmonary thrombus in the context of AF.

This case highlights that flecainide (100 mg) could unmask sinus node dysfunction in asymptomatic patients with paroxysmal AF. Sinus node dysfunction may be associated with underlying structural heart diseases but commonly occurs in the elderly in the absence of apparent accompanying heart diseases. In addition, it may also occur in a familial form with variable mode of inheritance including SCN5A, HCN4 ANK2 [11-13]. Clinicians should obtain the detailed history and screen candidates for sinus and atrioventricular node diseases when prescribing flecainide. It is strongly suggested to test first dose under medical observation. Electrocardiogram monitoring is suggested in case of drug adjustment or concomitant therapy with other antiarrhythmic drugs, particular in the elderly and in patients with hepatic or renal dysfunction. Also, newly diagnosed AF may be triggered by acute precipitants, including pulmonary embolism. Clinicians should be alert to the possibility of pulmonary embolism in patients with AF who complain of chest fluttering and shortness of breath.

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