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Letter to the Editor
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Ventricular Tachycardia in Association with Propafenone Overdose

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Key Words: Intoxication • Propafenone • Ventricular tachycardia

INTRODUCTION

Propafenone is a class IC antiarrhythmic drug used in the treatment of atrial fibrillation and supraventricular tachycardia.[1] It is primarily a potent sodium channel blocker, but is also beta blocker and a calcium channel blocker. Propafenone overdose may cause adverse complications such as hypotension, prolonged QRS complex, atrioventricular block, convulsion, and cardiac arrest. Sustained monomorphic ventricular tachycardia is known to occur with propafenone use; however, only a few case reports have described such events. Recently, we worked on a case of propafenone intoxication with life-threatening arrhythmia, but with a favorable outcome.

CASE REPORTS

The patient was a 54-year-old man who arrived at the emergency department with complaints of palpitations and general weakness. He had a history of paroxysmal atrial fibrillation (AF), prescribed with sustained release (SR) propafenone 325 mg twice daily and bisoprolol 2.5 mg. Sometimes, he was treated with pill in the pocket approach (propafenone 600 mg) for the conversion of paroxysmal atrial fibrillation attack. His vital signs were as follows: body temperature, 36.7 °C; pulse, 140 beats/min; breathing, 25 breaths/min; and blood pressure, 100/60 mmHg. Twelve-lead electrocardiography (ECG) showed wide complex tachycardia with right bundle branch block (RBBB) morphology (Figure 1A). Suspecting idiopathic left ventricular tachycardia, verapamil was given. Tachycardia was terminated after administering 5 mg intravenous verapamil; however, it was followed by cardiac arrest due to extreme junctional bradycardia (Figure 1B). Resuscitation was achieved after less than 3 minutes of advanced life support and atropine administration, and a temporary pacemaker was applied.

The results of the initial blood testing were as follows: white blood cell count, 5,980/mm^3; hemoglobin, 16.3 g/dL; platelets, 218,000/mm^3; aspartate aminotransferase 19.0 U/L, alanine aminotransferase 24.0 U/L, sodium, 137 mmol/L; potassium, 4.4 mmol/L; chlorine, 106 mmol/L; calcium, 9.65 mg/dL and magnesium, 2.48 mg/dL. An arterial blood gas analysis showed a pH of 7.437, pCO_2 of 38.5 mmHg, PO_2 of 96.8 mmHg and HCO_3 of 26.2 mmHg.

Further questioning revealed that he had taken 600 mg propafenone three times in the past 12 hours. He went out for dinner and drunk with his coworkers on the day before. At dinner, he had ingested a substantial amount of alcohol (20 alcohol units). He reported taking propafenone 600 mg twice when he experienced abnormal heart pounding after drinking. In the morning, he received another dose of propafenone 600 mg for his palpitations. However, his symptoms got worse and referred to emergency room.

The possibility of propafenone intoxication was suggested, so a trial of intravenous sodium bicarbonate (1 mEq/kg $NaHCO_3$ bolus, followed by infusion 20 mEq/hour) was administered. Within 12 hours, his intrinsic rhythm was restored and temporary pacer was removed.

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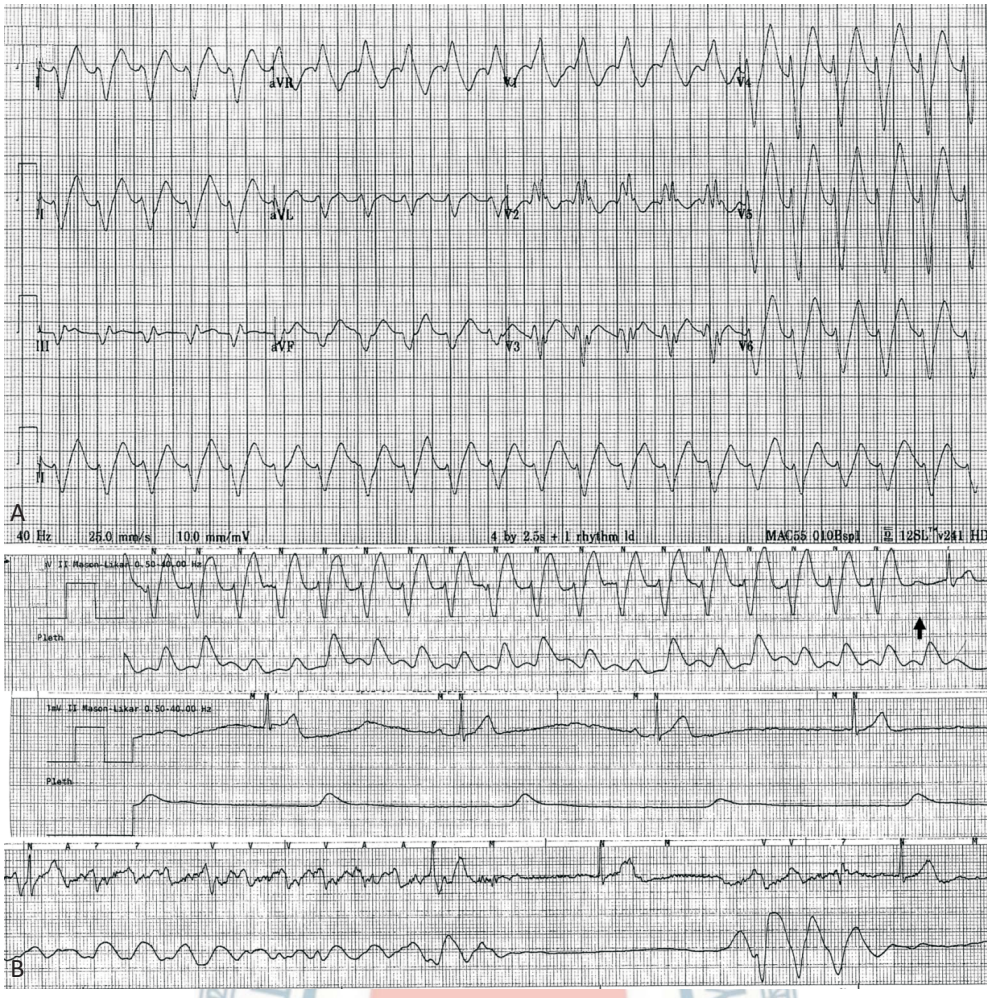

Figure 1. *(A) Twelve-lead electrocardiogram showed a regular wide complex tachycardia with right bundle branch block morphology, RSR' complex with a taller left rabbit ear sign, rS complex in V6 and northwest axis. (B) Initial rhythm strip in the field showing wide regular complex tachycardia. Tachycardia was terminated after administering 5 mg intravenous verapamil; however, it was followed by cardiac arrest due to extreme junctional bradycardia.*

Two-dimensional echocardiography showed no structural heart disease or regional wall motion abnormality. Coronary angiography revealed an anomalous origin of the left coronary artery from the right coronary sinus, but no coronary artery stenosis (Figure 2A-2C). Twenty-four-hour Holter monitoring and 72-hour telemetry did not show clinical arrhythmia nor premature ventricular complex. He underwent an electrophysiological study, in which no ventricular tachyarrhythmia was induced from programmed electrical stimulation. Pulmonary veins isolation was subsequently performed for treating paroxysmal AF (Figure 2D). Following ablation, programmed stimulation and rapid atrial pacing did not induce atrial flutter. On the seventh day, he was discharged with a normal ECG, and did not show any further symptom for three months.

DISCUSSION

In this case report, we present a patient who was taking propafenone for paroxysmal AF. He subsequently developed serious cardiac toxicity, and experienced cardiac arrest in the hospital. The diagnosis was likely propafenone intoxication; however, we could not be certain because the necessary equipment to measure the serum propafenone level was not available at the hospital. Nonetheless, patient's clinical status upon admission,

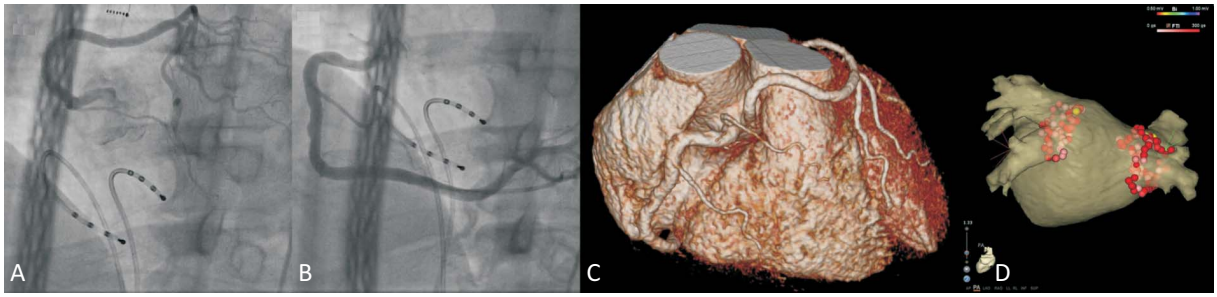

Figure 2. *(A) Coronary angiography and volume rendering image showed anomalous origin of the left coronary artery from the right coronary sinus. (B) Successful radiofrequency ablation of four pulmonary veins for treating paroxysmal atrial fibrillation.*

absence of electrolyte imbalances, ventricular arrhythmia in 72-hour telemetry, ventricular tachycardia induction on electrophysiology study, and non-usage of drugs other than propafenone, led us to concentrate on this diagnosis.

Propafenone is a class IC antiarrhythmic drug, used in the paroxysmal AF and second-line management of other supraventricular and ventricular arrhythmias. It reduces the conduction velocity of the fast-inward sodium channel, resulting in prolongation of conduction and refractoriness in all areas of the myocardium, particularly on the intraventricular conduction. It is metabolized in the liver via the cytochrome P450 2D6 (CYP2D6) pathway. CYP2D6 enzyme is known to have numerous substrates for activation, such as alcohol, which was reportedly consumed by the patient. Peak serum concentration occurs between 2-3 hours after ingestion, during which the most life-threatening ECG changes may occur. Even a therapeutic dose of propafenone may cause cardiac toxicity in poor metabolizers or patients who have consumed drugs that inhibit CYP2D6.[2] Acute toxicity has been reported from therapeutic dosage of 675 mg daily, to one-time ingestion of 8.1 g.[2] In the present case, the patient has ingested a total of 2,450 mg of propafenone (three times 600 mg and twice 325 mg SR) in the past 12 hours. He also consumed a substantial amount of alcohol the day before admission, which could have caused a critical increase in the serum propafenone level.

The mechanism of this proarrhythmic effect is likely due to a delay of conduction in the His-Purkinje system.[3] In particular, a 1:1 conducted atrial flutter to sustained monomorphic ventricular tachycardia has been widely reported in the literature.[4] The differential diagnosis of wide complex tachycardia includes ventricular tachycardia and supraventricular tachycardia with aberrancy. Atrial flutter with 1:1 conduction in the presence of class IC antiarrhythmic agents may present a confusing picture on the ECG with wide QRS complexes. In our case, 12-lead ECG showed regular wide complex tachycardia with a RBBB configuration, RSR' complex with a taller left rabbit ear sign, rS complex in V5-V6, and northwest axis, which is consistent with ventricular tachycardia originating from the left ventricle apex. Propafenone can produce sustained monomorphic ventricular tachycardia, which is characterized by a marked increase in QRS duration and is not associated with QT interval prolongation. The mechanism of this proarrhythmic effect is likely to be due to a delay of conduction in the His-Purkinje system.[5] This effect may encourage reentry by allowing extra time for refractory tissue to recover, thus allowing it to be reexcited. Verapamil could affect the ventricular tachycardia of the fascicular variety, where the mechanism may depend on triggered activity or calcium dependent reentry.[6] Intravenous verapamil might be used for pharmacological termination of hemodynamically stable wide QRS complex tachycardia. However, verapamil termination of wide QRS tachycardia, results extreme junctional bradycardia and cardiac arrest in the propafenone intoxication. Thus, verapamil is not recommended in wide QRS-complex tachycardia cases of unknown etiology.[7]

The management of propafenone toxicity consists of hemodynamic and respiratory stabilization together with alkalization of the blood via sodium bicarbonate.[8] Cardiac pacing for symptomatic bradycardia was effective in the case of propafenone toxicity. Sodium bicarbonate therapy has been proposed as a treatment for sodium channel blockade toxicity in conjunction with standard resuscitation. This works by competitive displacement of propafenone from sodium channel binding

sites. Administration of sodium bicarbonate resulted in an immediate reduction in QRS width and improvement in hemodynamics. Maintenance of this therapy, along with hemodynamic support, contributed to the recovery of the patient within hours.

Propafenone is not recommended in patients with structural heart disease, particularly those with left ventricular systolic dysfunction or coronary artery disease. In our case, the left coronary artery originated from the right coronary sinus. The presence of an anomalous coronary artery arising from the opposite sinus is a very rare phenomenon and can be associated with myocardial ischemia because of compression between these vessels.[9] However, in our patient, the left coronary artery was positioned in front of the pulmonary artery, so compression did not occur, thus, it may not have affected myocardial ischemia and propafenone intoxication.

LEARNING POINTS

1. Sustained monomorphic ventricular tachycardia is known to occur with propafenone.
2. In patients with propafenone intoxication, the use of verapamil could be dangerous. Clinicians should be aware that patients presenting to the emergency department with ventricular arrhythmia should be questioned about propafenone intoxication. Obtaining a detailed history is essential for patients admitted to the hospital for ventricular tachycardia.

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CONFLICT OF INTEREST

All the authors declare no conflict of interest.

REFERENCES

1. January CT, Wann LS, Calkins H, et al. 2019 AHA/ACC/HRS focused update of the 2014 AHA/ACC/HRS guideline for the management of patients with atrial fibrillation. *Circulation* 2019; 140:e125-51.
2. Kerns W II, English B, Ford M. Propafenone overdose. *Ann Emerg Med* 1994;24:98-103.
3. Koppel C, Oberdisse U, Heinemeyer G. Clinical course and outcome in class IC antiarrhythmic overdose. *J Toxicol Clin Toxicol* 1990;28:433-44.
4. Bhardwaj B, Lazzara R, Stavrakis S. Wide complex tachycardia in the presence of class I antiarrhythmic agents: a diagnostic challenge. *Ann Noninvasive Electrocardiol* 2014;19:289-92.
5. Femenia F, Palazzolo J, Arce M, et al. Proarrhythmia induced by propafenone: what is the mechanism? *Indian Pacing Electrophysiol J* 2010;10:278-80.
6. Gill JS, Blaszyk K, Ward DE, et al. Verapamil for the suppression of idiopathic ventricular tachycardia of left bundle branch block-like morphology. *Am Heart J* 1993;126:1126-33.
7. Rankin AC, Rae AP, Cobbe SM. Misuse of intravenous verapamil in patients with ventricular tachycardia. *Lancet* 1987;2:472-4.
8. Brubacher J. Bicarbonate therapy for unstable propafenone-induced wide complex tachycardia. *CJEM* 2004;6:349-56.
9. Kragel AH, Roberts WC. Anomalous origin of either the right or left main coronary artery from the aorta with subsequent coursing between aorta and pulmonary trunk: analysis of 32 necropsy cases. *Am J Cardiol* 1988;62:771-7.