영남의대학술지 제28권 제1호
Yeungnam Univ J Med
Vol.28 No.1 p90-93, June 2011

□ 증례 □

Torsade de Pointes Induced by Long-Term Oral Amiodarone Therapy

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－Abstract－

Although amiodarone is generally regarded as safe with a low incidence of associated arrhythmias, torsade de pointes (TdP) has been observed usually in the presence of predisposing factors. We report a case of amiodarone-induced TdP after long-term administration of a low dose of oral amiodarone in the absence of predisposing factors.

Key Words: Torsade de pointes, Amiodarone

Introduction

Amiodarone is a well-known class III antiarrhythmic agent. Despite QT interval prolongation, the drug exhibits a very low torsadogenic activity (<1.0%). The safety of amiodarone is usually associated with homogeneous lengthening of action potential duration and lack of early after depolarizations.[1]

However, it is possible that Torsade de pointes (TdP) may be facilitated in the presence of pre-existing risk factors such as female gender, congestive heart failure, bradycardia, subclinical long-QT syndrome, ion-channel polymorphisms, electrolyte imbalance (hypokalemia, hypomagnesemia, hypocalcemia), hypothyroidism, and starvation.[2,3]

We describe here a case without predisposing factors in whom TdP was induced by long-term low-dose oral amiodarone therapy for the treatment of ventricular tachycardia (VT).

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Case

A 62-year-old man who underwent prosthetic mitral valve (MV) and prosthetic aortic valve (AV) replacement presented with palpitation and dizziness; he had been on furosemide and warfarin. Eight weeks earlier, he had been admitted to the emergency room with chest discomfort and hemodynamically unstable ventricular tachycardia (VT). We had to restore sinus rhythm by DC cardioversion of 150J soon after admission. He was then started on amiodarone at a daily dose 200 mg for VT. At that time, 12-lead ECG revealed sinus bradycardia (50 bpm) with QTc interval of 417 ms (Fig. 1A). On current admission, 12-lead ECG revealed sinus bradycardia (56 bpm) with markedly prolonged QTc interval (627 ms) and broad T-wave inversion in all precordial leads (Fig. 1B). Laboratory findings including serum electrolyte, magnesium, calcium, BUN, and creatinine levels were within normal limits. Transthoracic echocardiography revealed well functioning prosthetic MV & AV, no regional wall motion abnormalities of the left ventricle and an estimated ejection fraction of 55%. A Holter ECG monitoring showed self-limiting TdP, following frequent ventricular ectopic beats (Fig. 1C). A daily dosage of oral amiodarone was reduced to 100 mg & finally withdrawn. Intravenous isoproterenol & magnesium was administered. On the fifth day, the ECG disclosed sinus bradycardia (52 bpm) with QTc interval of 578 ms (Fig. 1D) and TdP was not relapsed.

Discussion

Amiodarone is regarded to have a high safety profile with a low incidence of associated arrhythmias. Compared with other antiarrhythmic agents, it appears to have lower pro-arrhythmic effects.[4]

The reason for the low incidence of pro-arrhythmia with amiodarone remains unclear. Most data suggest that TdP is caused by calcium-dependent early after-depolarizations. Amiodarone has been shown to reduce or abolish early after-deoplarization.[5] This electrophysiologic property may explain the low incidence of TdP associated with amiodarone(1~2 % of chronically treated patients), despite a markedly prolonged repolarization.6 Amiodarone also blocks the slow inward calcium current mediated through the L-calcium channels, besides its blocking effect of the delayed rectifier current (IKr) and fast sodium current. However, in certain conditions, including advanced age (>65 years), bradycardia, hypokalemia, hypomagnesemia, occult or latent congenital Long QT Syndrome (LQTS), and female gender that prolonged QT interval, amiodarone may also produce TdP.[7]

Drug-induced QT interval prolongation most commoly occurs in a susceptible group

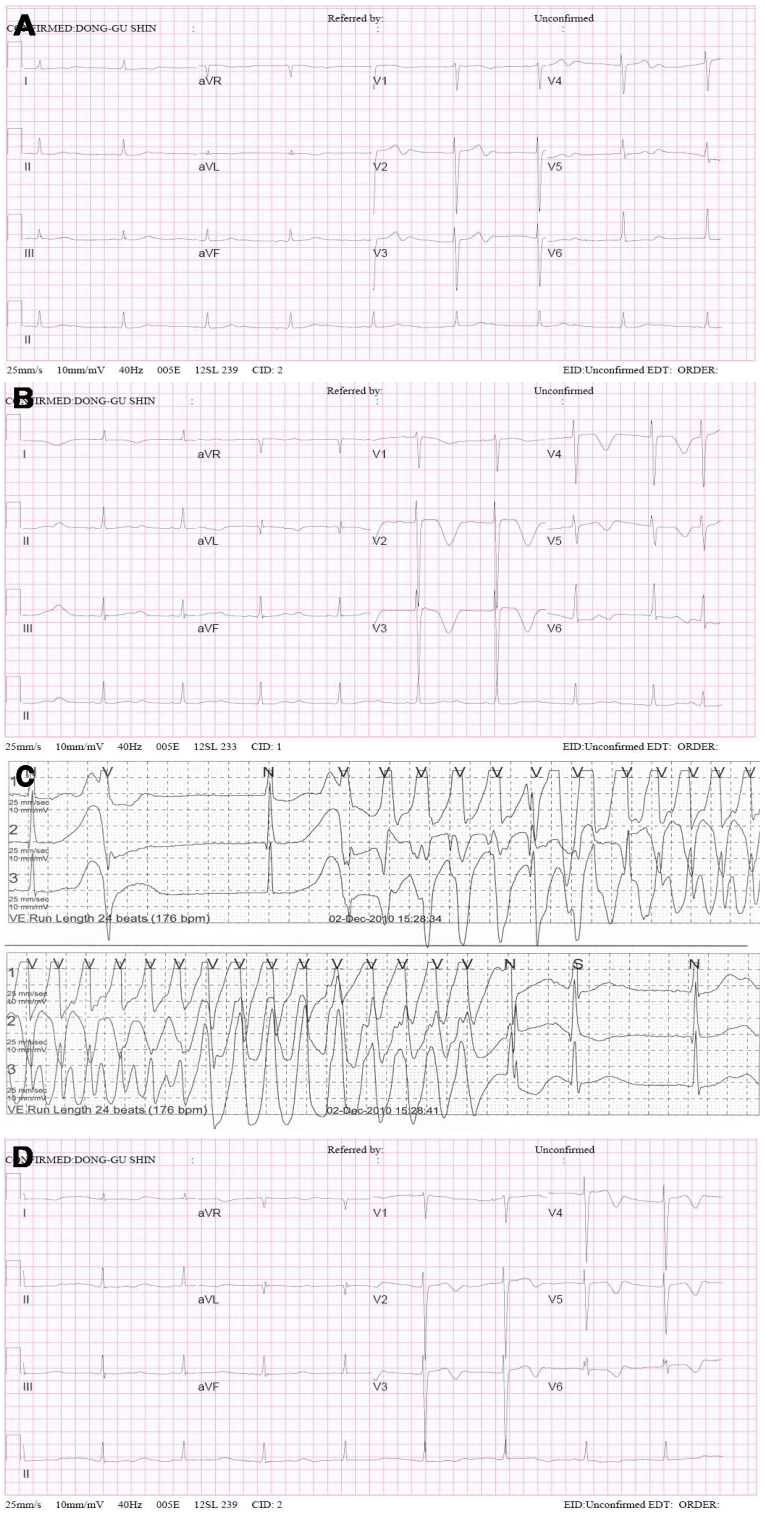

Fig. 1. Electrocardiograms for torsade de pointes induced by long-term oral amiodarone therapy. (A) Following cardioversion, an ECG revealed sinus bradycardia (50 bpm) with a QTc interval of 417 ms. (B) On admission, ECG revealed sinus bradycardia (56 bpm) with a QTc interval of 627 ms. (C) Continuous ECG monitoring showed self-limiting TdP following frequent premature ventricular complexes. (D) The QTc interval was 578 ms after tapering and discontinuing the oral amiodarone.

of patients that carries silent mutations in one of the genes responsible for the congetital long QT syndrome.[8] Although our patient had no family history of congenital long QT syndrome or sudden death by ventricular tachyarrhythmias, and his ECGs revealed decreased values of QTc interval after withdrawal of oral amiodarone, he could belong to the susceptible group of silent mutations in the function of their ion channel, and therefore could to be at high risk of developing TdP if exposed to either cardiac or noncardiovascular drugs that block the potassium channels.

This case of TdP occurring chronically in oral amiodarone therapy at a low dose (200 mg/day) emphasize the importance of careful monitoring during amiodarone therapy.

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