

Amiodarone-Induced Third Degree Atrioventricular Block and Extreme QT Prolongation Generating Torsade Des Pointes in Paroxysmal Atrial Fibrillation

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Abstract

Amiodarone is still the most potent antiarrhythmic drug in the prevention of life threatening ventricular arrhythmias and demonstrates a very low incidence of torsade de pointes. An unusual case of an 81-year-old woman who developed serious abnormalities of the conduction system of the heart and torsade des pointes during intravenous infusion of amiodarone for the treatment of paroxysmal atrial fibrillation is described. To the best of our knowledge, this is the first case showing an association of intravenous amiodarone-induced third degree atrioventricular block and extreme QT interval prolongation generating torsade des pointes in a patient with paroxysmal atrial fibrillation who required an implantable cardioverter-defibrillator. Currently, amiodarone is still one of the few remaining treatment options for the medical therapeutic management of serious ventricular arrhythmias and to reduce the incidence of atrial fibrillation without increasing mortality or sudden cardiac death rates in heart failure patients like our elderly present patient. Nevertheless, we have to keep in mind that intravenous amiodarone may generate serious abnormalities of the conduction system of the heart and lethal ventricular arrhythmias in certain patients.

Introduction

Lethal ventricular arrhythmias are one of the major causes of death in patients with structural heart disease. Several investigations have demonstrated the usefulness of intravenous amiodarone in the medical treatment of ventricular arrhythmias, and it is now recommended as a first line antiarrhythmic agent for the treatment of ventricular tachycardia (VT).¹⁻⁶ In addition, amiodarone plays a major role in the treatment of atrial fibrillation, especially in heart failure with severely impaired left ventricular function, where class-I antiarrhythmic drugs or dronedarone are contraindicated.^{3,4}

We describe an unusual case of an 81-year-old woman who developed serious abnormalities of the conduction system and torsade des pointes during intravenous infusion of amiodarone during the treatment of paroxysmal atrial fibrillation. To the best

of our knowledge, this is the first case showing an association of intravenous amiodarone-induced third degree atrioventricular block and extreme QT interval prolongation generating torsade des pointes in a patient with paroxysmal atrial fibrillation who required an implantable cardioverter-defibrillator.

Case Report

An 81-year-old woman with arterial hypertension, transient ischemic attack, and paroxysmal atrial fibrillation presented with complaints of progressive dyspnea and inferior limbs edema that began 2 days earlier. She was receiving a daily ambulatory treatment of losartan 50 mg, carvedilol 25mg, atorvastatin 20 mg, amiodarone 200 mg, and acenocumarol. At the time of hospitalization, she was in New York Heart Association (NYHA) functional class III in atrial fibrillation with an irregular heart rate of 142 bpm; her blood pressure was 140/90 mmHg. She had moderate lung congestion, hepatomegaly, and inferior limbs edema was also present. The chest radiograph showed mild cardiomegaly and pulmonary venous congestion. The electrocardiogram (ECG) showed atrial fibrillation with rapid ventricular response, narrow QRS complexes with normal values of QT and QTc intervals (Figure 1). Transthoracic color-flow Doppler echocardiography revealed diffuse hypokinesia of the left ventricle with an ejection fraction of 48%, moderate mitral regurgitation with moderate left atrial enlargement.

She received 40 mg of furosemide, and a loading IV dose of 300 mg of amiodarone was begun with a maintenance IV dose of 900 mg

Key Words:

Amiodarone, Torsade Des Pointes, Paroxysmal Atrial Fibrillation, Third Degree AV Block, QT Interval Prolongation, Implantable Cardioverter-Defibrillator.

Disclosures:

None.

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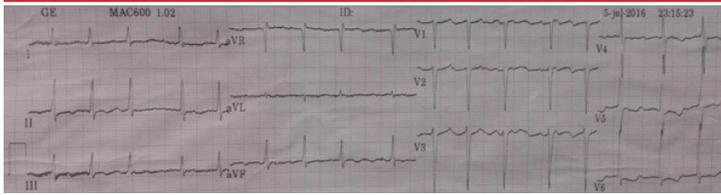


Figure 1: The 12 lead electrocardiogram shows atrial fibrillation with rapid ventricular response, narrow QRS complexes with normal values of QT and QTc intervals

for 24 hs. After 12 hs of amiodarone infusion she developed a sudden third degree atrioventricular block with narrow QRS junction escape and polymorphic premature ventricular contractions with R on T phenomenon (Figure 2). In addition, there was an extreme QT interval prolongation, the QT interval prolonged from 320 ms to 670 ms, and the QTc interval from 416 ms to 685 ms. There was no signs of acute ischemia, neither electrolyte disturbances. Blood tests were within normal limits including cardiac enzymes. There was no hemodynamic alteration. She remained conscious with no symptoms related to the bradycardia. The amiodarone infusion was immediately suspended and a Holter ECG monitoring was

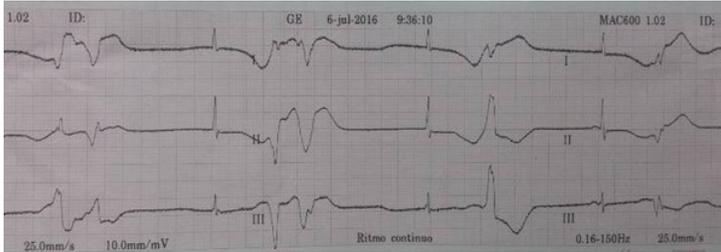


Figure 2: The rhythm trace electrocardiogram shows a sudden third degree atrioventricular block with narrow QRS junction escape and polymorphic premature ventricular contractions with R on T phenomenon. In addition, there is an extreme QT interval prolongation of 670 ms, and the QTc interval is 685 ms

installed. A few hours later she regained sinus rhythm with a low heart rate of 46 bpm, with persistent extreme QT interval prolongation with diffuse repolarization abnormalities (Figure 3). The same day she developed torsade des pointes that began with an R on T phenomenon, and degenerated to ventricular fibrillation which responded well to a DC shock with 200 joules (Figure 4). The Holter ECG monitoring revealed several non-sustained episodes of atrial fibrillation, frequent premature ventricular contractions and several episodes of non-sustained torsade des pointes. A coronary angiogram revealed only irregularities and non-significant stenosis of the left and right coronary arteries. An implantable cardioverter-defibrillator was

installed, and the patient was discharged on optimal medical therapy for her heart failure, but without antiarrhythmic drugs because of persistent QT interval prolongation. One month later, while being in her house she received an appropriate shock due to ventricular fibrillation (Figure 5). A low oral dose of amiodarone was begun and she remains asymptomatic 3 months later in her follow-up visits.

Discussion

Amiodarone, a class-III antiarrhythmic drug, is considered as the most efficient agent for ventricular arrhythmias even in heart failure patients with severe left ventricular systolic dysfunction.⁷ Amiodarone results in a rapid phase-III-repolarization and does not increase dispersion of repolarization. These electrophysiological findings are present in healthy hearts and are preserved in heart failure contributing to its low pro-arrhythmic potential.⁸ Although, intravenous amiodarone is generally regarded as a safe medical treatment, there are several reports on pro-arrhythmia inducing torsade des pointes under certain conditions including electrolyte imbalance.⁹⁻¹² We report this unusual case of an elderly woman who developed serious abnormalities of the conduction system and torsade

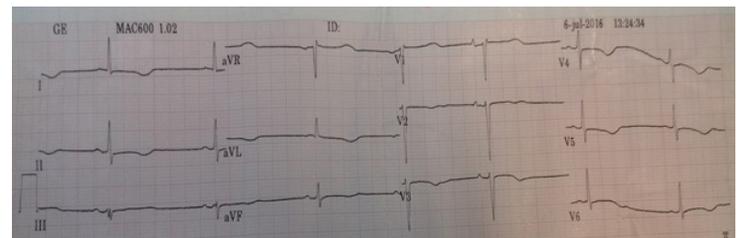


Figure 3: The 12 lead electrocardiogram shows sinus rhythm with a low heart rate of 46 bpm, with persistent extreme QT prolongation with diffuse repolarization abnormalities

des pointes in association with intravenous infusion of amiodarone during the acute treatment of paroxysmal atrial fibrillation. To the best of our knowledge, this is the first case showing intravenous amiodarone-induced third degree atrioventricular block and extreme QT interval prolongation generating torsade des pointes in an elderly patient with paroxysmal atrial fibrillation who required an implantable cardioverter-defibrillator.

Amiodarone is broadly utilized in our emergency department of outpatient clinics, and it is by far the most used antiarrhythmic drug for wide complex tachycardias in our hospital. It is well known that the electrophysiological effect of amiodarone is different when it is administered orally or intravenously.² While being on oral amiodarone, our patient did not have the abnormalities of the

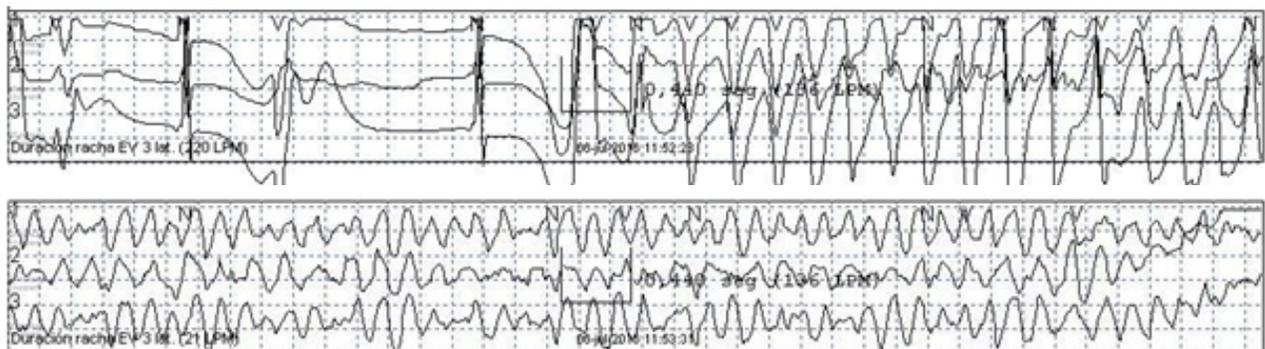


Figure 4:

A: The Holter ECG recording shows the initiation of a sustained episode of Torsade des pointes that began with an R on T phenomenon.
B: The Holter ECG recording shows the sustained episode of Torsade des pointes which begins degeneration to ventricular fibrillation

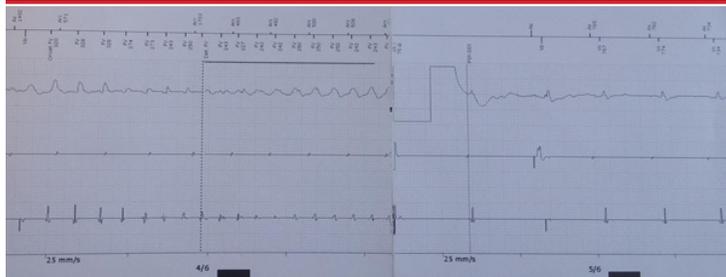


Figure 5:

Representative electrograms obtained upon device interrogation. The device recorded tracings show stored atrial and ventricular intracardiac electrogram signals depicting an episode of ventricular fibrillation which subsides with an appropriate shock

conduction system mentioned earlier, neither the lethal ventricular arrhythmias that she presented in this hospitalization. However, the story was different with intravenous amiodarone. We searched for other causes that could explain this outcome. She did not present signs of acute ischemia, neither electrolyte disturbances, and other blood tests were within normal limits. Since she had diffuse hypokinesia of the left ventricle with an ejection fraction of 48%, a coronary angiogram was performed which revealed only irregularities and non-significant stenosis of the epicardial coronary arteries ruling out ischemic heart disease.

Amiodarone is the most potent antiarrhythmic agent in the prevention of lethal ventricular arrhythmias and demonstrates a very low incidence of torsade de pointes. Several randomized, controlled, clinical trials like, CHF-STAT, CAMIAT, and EMIAT trials showed that amiodarone lacked proarrhythmia and reduced the incidence of VT and arrhythmic death in high-risk patients.¹²⁻¹⁸ It was demonstrated that amiodarone has a low proarrhythmic potential in normal hearts due to a fast phase-III repolarization, a low incidence on dispersion of repolarization, a lower potential to induce early after depolarizations, and a weak effect on reverse-frequency dependence.¹⁸ In addition, amiodarone does not seem to increase the risk of proarrhythmia or sudden cardiac death despite marked QT-prolongation.¹⁶ However, our elderly patient had an organic heart disease, and with the extreme QT prolongation in association with intravenous amiodarone presented an episode of torsade des pointes that required electrical cardioversion. Although proarrhythmic effects of amiodarone are rare, some patients occasionally develop polymorphic VT of torsade de pointes.^{3,4} Although amiodarone blocks multiple ion currents in the heart,¹⁷ the electrophysiological effects by which amiodarone exerts its strong antiarrhythmic action and its low proarrhythmic effects are not well understood. Intravenous amiodarone inhibits sodium channels, inward L-type calcium channels, and has noncompetitive beta-blockade effect. In addition, it also has potassium channel blockade effect which becomes more apparent after long-term oral therapy. The extreme QT interval prolongation can be explained by potassium channel blockade effect of intravenous amiodarone. There is a growing need for antiarrhythmic pharmacological drugs to prevent episodes of ventricular arrhythmias and frequent appropriate discharges of implantable defibrillators. Since amiodarone has been shown to reduce the burden of arrhythmic events and ICD-shocks,² we initiated oral amiodarone in the follow-up visit after documenting an ambulatory ventricular fibrillation and an appropriate ICD shock which saved her life. Although, intravenous amiodarone began all the serious abnormalities of the conduction system and the torsade des

pointes in our patient with paroxysmal AF, we decided to begin low oral dose of amiodarone and she remains asymptomatic 3 months later in her follow-up visits after the appropriate ICD shock.

Conclusions

Currently, amiodarone is still one of the few remaining treatment options for the medical therapeutic management of ventricular arrhythmias and to reduce the incidence of atrial fibrillation without increasing mortality or sudden cardiac death rates in heart failure patients like our elderly present patient.¹ Nevertheless, we have to keep in mind that intravenous amiodarone may generate serious abnormalities of the conduction system and lethal ventricular arrhythmias in certain patients. In conclusion, despite the safe proarrhythmic profile of amiodarone, we described an unusual case showing intravenous amiodarone-induced third degree atrioventricular block and extreme QT interval prolongation generating torsade des pointes in an elderly patient with paroxysmal atrial fibrillation who required an implantable cardioverter-defibrillator.

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