

CASE REPORT

Amiodarone and digitalis: An odd couple in a tachycardiomyopathic patient

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Abstract

Amiodarone is one of the most used anti-arrhythmic drug for rate and rhythm control in atrial fibrillation. Unfortunately, it has also well-known pro-arrhythmic properties and it has been reported as a common cause of malignant ventricular tachyarrhythmias, especially torsade de pointes. Proarrhythmic effects of amiodarone are greatly increased by other concomitant factors, such as ventricular dysfunction and concomitant treatment with digitalis. Current evidence shows how amiodarone and digitalis together are associated with torsade de pointes in ischemic patients with heart failure. The present case report describes, for the first time, how amiodarone and digitalis can concur in producing torsade de pointes also in a tachycardiomyopathic patient with no coronary artery disease.

Key words

Atrial fibrillation, Torsade de pointes, Amiodarone, Digitalis, QT interval, Tachycardiomyopathy

1 Introduction

Torsade de pointes (TdP) has been reported in less than 1% ^[1] of patients treated with amiodarone. The association between amiodarone and TdP may be promoted by concomitant electrolytes imbalance, high drug dosages, or left ventricular dysfunction ^[2,3]. Amiodarone and digitalis have already been described as an “odd couple”, producing TdP and other ventricular arrhythmias, especially in chronic heart failure secondary to coronary heart disease ^[4,5]. Hereby, we are presenting the first case in which the proarrhythmic effect of this combination is evident in acute non-ischemic ventricular dysfunction.

2 Case presentation

A 76 years old woman was admitted to the Emergency Department (ED) for shortness of breath and fatigue after mild exertion since the day before. She was taking felodipine 5 mg and ramipril 10 mg daily as antihypertensive therapy, and referred no other cardiovascular risk factors. After the admission to the ED, an ECG revealed atrial fibrillation (AF) with a fast mean ventricular rate. Minimum and maximum QT intervals were equal to 280 and 320 ms, respectively. The corrected minimum and maximum QT (QTc) intervals were equal to 450 and 475 ms, respectively.

Signs of heart failure, such as bibasilar rales, hepatomegaly and jugular turgor, were present at physical examination. A 3/6 apical systolic murmur was found and interpreted as mild mitral regurgitation. Routine laboratory tests were normal. Chest x-rays showed cardiogenic pulmonary venous congestion. The patient was treated with furosemide 20 mg IV and digoxin 0.5 mg IV. As AF apparently started less than 24 hours before, a pharmacological cardioversion was attempted. Amiodarone 300 mg IV bolus was given, followed by a 0.6 mg/minute infusion.



Figure 1. 12-lead ECG showing failure of pharmacological cardioversion

After 12 hours, AF with rapid ventricular response persisted (see Figure 1). Echocardiography showed mild left ventricular dilatation and confirmed the mild mitral regurgitation. Left ventricular ejection fraction (LVEF) was 35%, with no evidence of localized motion abnormalities. Left ventricular diastolic impairment with a restrictive pattern was also present. Since pharmacological cardioversion proved to be ineffective, amiodarone infusion was stopped and direct-current cardioversion was attempted after another 6 hours. After inducing deep sedation with midazolam 5 mg IV, a single 150 J biphasic shock was delivered, restoring sinus rhythm. Sinus rhythm persisted during the following hours, although it was interrupted by frequent premature supraventricular complexes. In order to avoid early AF recurrence, amiodarone infusion (0.6 mg/minute IV) was started again. A few hours later, syncope occurred and the ECG monitoring recorded an episode of TdP preceded by frequent PVCs, probably due to late after-depolarization (see Figure 2). TdP was self-terminating and AF recurred a few minutes later, this time associated with a slow ventricular response (51 bpm).

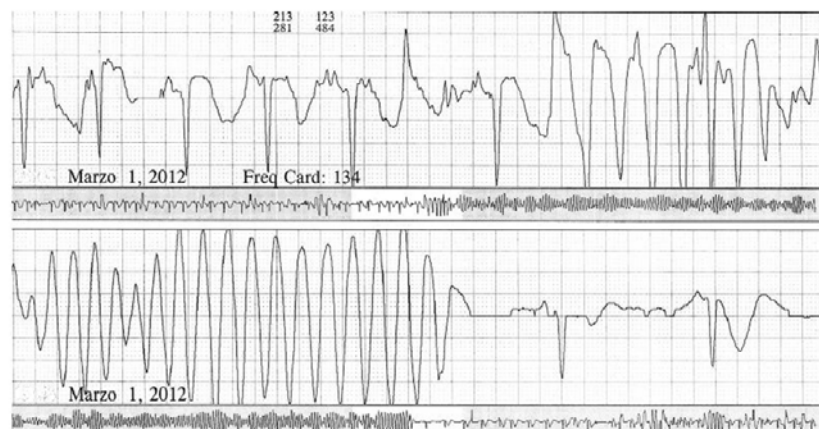


Figure 2. Start and end of TdP

Potassium and sodium levels were 3.7 mEq/l and 134 mEq/l respectively and were promptly supplemented. A temporary pacemaker at 90 bpm was inserted to prevent further bradycardia-related TdP episodes. In the next 7 days, QTc shortened progressively to 420 ms and no further arrhythmic events were recorded. Coronary angiography performed 2 days later did not show any significant coronary lesions. At discharge, the patient's heart rate was normal and stable, thanks to an adequate rate control with beta-blockers, and LVEF improved to 45%.

3 Discussion

Persistent high heart rate associated with AF may cause tachycardiomyopathy^[6]. This condition is usually asymptomatic, especially in the initial hours, and therefore underestimated^[7,8]. However, the acute systolic dysfunction may contribute to a small extent to a QT interval prolongation. Ventricular dysfunction translates at cellular level into abnormal $\text{Na}^+/\text{Ca}^{2+}$ handling, in this case further enhanced by digitalis, which favors Na^+ intracellular accumulation. Amiodarone prolongs QT interval and is associated with rare cases of TdP^[1,2]. The arrhythmogenic potential of this old drug was recently stressed by new evidences. By using an isolated rabbit heart model, amiodarone caused TdP when associated to late INa^+ enhancement^[9]. In our patient, it seems that the combination of tachycardiomyopathy, digitalis and amiodarone may have resulted in triggered activity due to delayed after depolarization and, finally, TdP. This was probably due to intracellular Na^+ accumulation, which in turn could have provoked delayed after-depolarizations.

The present case shows that tachycardiomyopathy could predispose to QT prolongation, making amiodarone not safe enough when given to patients with acute ventricular dysfunction and concomitant digitalis therapy. Proarrhythmic effects of amiodarone and digitalis combination have already been described in case series^[4] and small observational studies^[5] but no large clinical trial has tackled this important issue yet. Moreover, said evidence is mainly related to ischemic cardiomyopathy and our case is the first to report similar proarrhythmic events in acute left ventricular dysfunction due to a reversible tachycardiomyopathy, without any coronary disease. A clinical trial specifically set for hard safety endpoints is mandatory, and, waiting for that, we think that these observations should be taken into consideration in the next atrial fibrillation guidelines, in order to lead clinical practice and avoid serious life-threatening adverse events. It is also presumable that dronedarone, as an amiodarone derivate, could have caused the same proarrhythmic effects in the elderly, decompensated PALLAS^[10] patients treated with digoxin, as suggested by retrospective adverse events reporting^[11]. Further subanalyses of the PALLAS study could support this hypothesis.

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