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CASE REPORT

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Marked prolongation of QRS duration after initiation of dronedarone therapy

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ABSTRACT

Dronedarone is a relatively new antiarrhythmic drug and is held to be less proarrhythmic than comparable compounds, although its proarrhythmia potential in humans has not been sufficiently evaluated. We describe a so far unreported dronedarone effect, namely a significant alteration of both the morphology and the duration of the QRS complex on the electro cardiogram in a 41-year old patient with symptomatic paroxysmal atrial fibrillation.

Keywords: Adverse drug events, Antiarrhythmic drugs, Atrial fibrillation, Dronedarone.

Introduction

Dronedarone is a relatively new antiarrhythmic drug and is held to be less proarrhythmic than comparable compounds, although its proarrhythmia potential in humans has not been sufficiently evaluated. We describe a so far unreported dronedarone effect, namely a significant alteration of both the morphology and the duration of the QRS complex on electrocardiogram (ECG) in a 41-year old patient with symptomatic paroxysmal atrial fibrillation.

Dronedarone is a derivate of the potent antiarrhythmic drug amiodarone that was designed to have less toxic side effects (1). Although dronedarone was approved following reports of an improved safety profile, more recent studies have cast doubt on its safety (1-3). However, dronedarone is still held to be less proarrhythmic than comparable compounds, although its proarrhythmia potential in humans has not been sufficiently evaluated (1). We describe a hitherto unreported dronedarone effect, namely a significant alteration of both the morphology and the duration of the QRS complex on ECG.

Case Report

A 41-year old patient was admitted to our emergency unit because of a highly symptomatic attack of paroxysmal atrial fibrillation (AF) that a few hours later spontaneously converted into sinus rhythm. Atrial fibrillation had been first diagnosed in this patent in 2008 and the AF episodes had been becoming more frequent in the months immediately preceding hospital admission. On admission, the standard ECG showed tachycardic atrial fibrillation with a narrow QRS complex. It should be noted that, during sinus rhythm, the ECG was normal showing an unremarkable QRS morphology and a QRS duration of 85 msec (Fig. 1).

Clinically, the patient was in a good state of health. His risk profile consisted of grade 1 obesity (body mass index 30.9 kg/m^2) and arterial hypertension that was well controlled by a combination therapy of an ACE-inhibitor and a beta-blocker. Routine blood tests, including kidney, liver and thyroid function analysis, were all within normal values. Coronary artery disease had been previously excluded by coronary angiography in 2011, and a recently performed transthoracic echocardiography revealed a structurally normal heart exhibiting normal systolic and diastolic function. After giving informed consent, the patient was reluctant to undergo an invasive approach and preferred pharmacological rhythm management with dronedarone.

According to our standard approach for AF patients admitted to our institution, the initiation of antiarrhythmic therapy, regardless of the antiarrhythmic drug, is always performed in the hospital setting. During the hospital stay, the patients are not restricted to bed rest but are allowed to be ambulant while being continuously monitored using ECG telemetry. In addition, 12-lead standard ECG is registered in each patient on a daily basis.

In the index patient, after two doses of dronedarone (400 mg each), a marked prolongation of QRS duration with a left bundle branch block pattern was documented on the 12-lead ECG (Fig. 2). Telemetric surveillance did not show any other ECG abnormalities. Dronedarone therapy was stopped immediately. Renewed laboratory tests and echocardiography showed normal findings. On the following day, the QRS complexes again showed a normal morphology and a normal duration of 90 msec (Fig. 3). A subsequent exercise stress test

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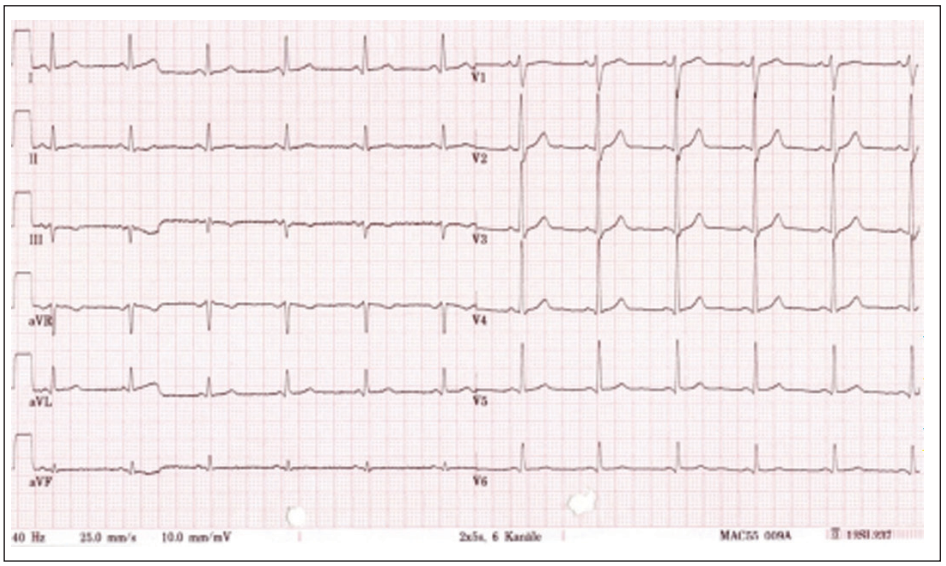

Fig. 1 - Twelve-lead standard electrocardiogram before administration of dronedarone.

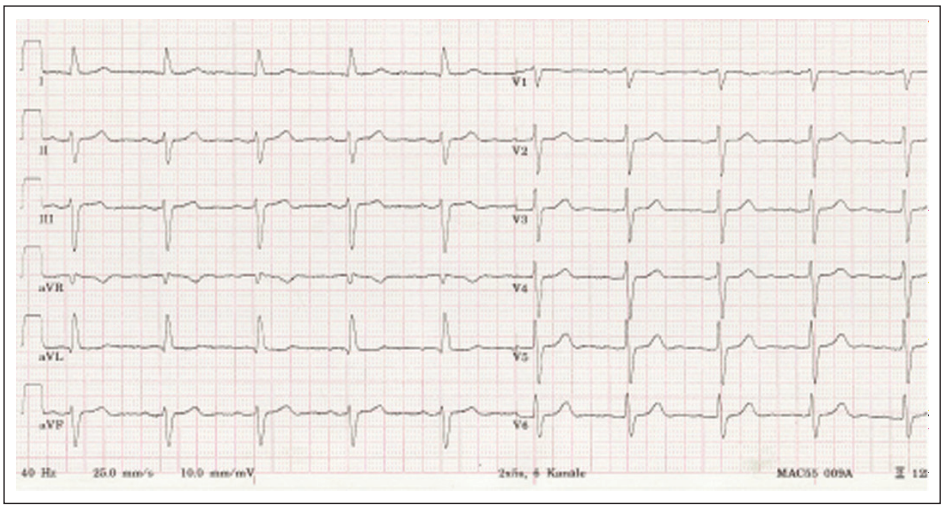

Fig. 2 - Left bundle branch block pattern after two doses of dronedarone.

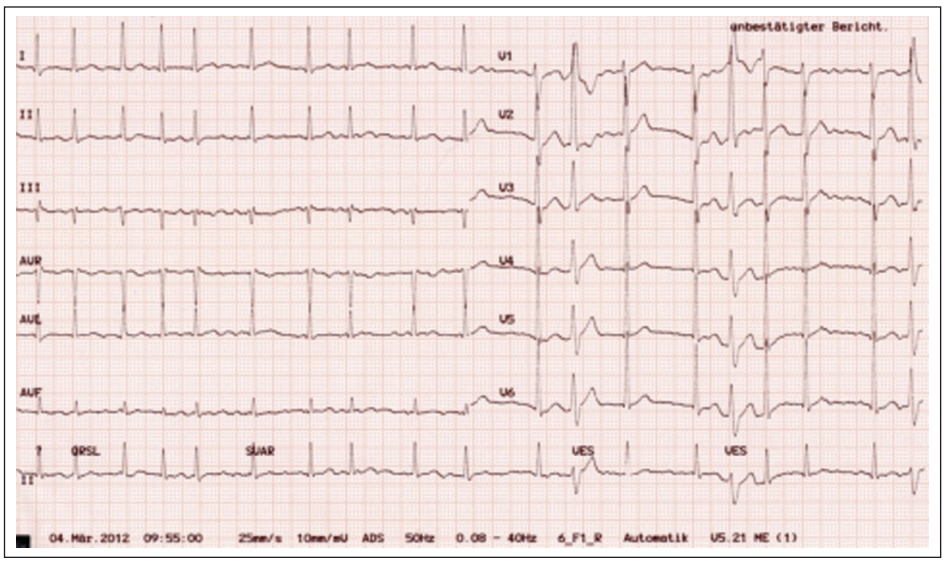

Fig. 3 - Return to normal QRS-width after dronedarone withdrawal and self-limiting episode of atrial fibrillation.

provided no pathological findings. Subsequently, the patient refused further attempts at pharmacological rhythm control, but requested a catheter ablation of atrial fibrillation that had recurred. Therefore, circumferential pulmonary vein isolation was successfully performed.

The patient was discharged in good health. Three months later, at the first follow-up visit in our rhythmology outpatient clinic, the patient was free of AF and continued to show a narrow QRS-complex.

Conclusions

Dronedarone is a multichannel blocker exhibiting all of the 4 Vaughan Williams classes of action (4). Therefore, a wide variety of potential ECG alterations can be expected. In fact, QT-interval prolongation, increased frequency of ventricular premature beats, and episodes of atrial flutter have all been reported as potentially proarrhythmic side effects of dronedarone (2, 3). However, increased QRS duration has not so far been documented. Mechanistically, this phenomenon may be explained by a reduction in the maximum slope of the action potential upstroke due to an increased inhibition of the fast Na(+) inward current by dronedarone (4, 5). Thus, a widened QRS complex may be indicative of slowed impulse conduction in the ventricles and may herald potential proarrhythmia. Therefore, careful telemetry monitoring appears to be mandatory, particularly during the period following the first administration of dronedarone.

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Conflict of interests: The authors declare no potential conflict of interests.

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