ARRHYTHMOGENIC EFFECT OF PROPAFENONE ADMINISTERED FOR A "WRONG" CLINICAL DIAGNOSIS

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Dear Editor,

We have read with great interest the work by Pintarić *et al.*[1] about the administration of propafenone in terminating atrioventricular nodal reentrant tachycardia and atrioventricular reentrant tachycardia, where propafenone is presented as a safe and efficient antiarrhythmic drug. That inspired us to present an interesting case which demonstrates how propafenone, if administered in a "wrong" clinical indication, is a potentially extremely harmful medication.

Propafenone is an IC class antiarrhythmic agent which acts by blocking Na^+ channels and partially blocking ß-adrenergic receptors and Ca^{2+} channels. Propafenone thus acts as a stabilizer of ion permeability of cardiac muscle cell membrane in cardiac pathologic conditions such as arrhythmias. Propafenone prolongs both PR interval and QRS complex on electrocardiograms, while it has no effect on QT interval[2,3]. It is metabolized in the liver through cytochrome P-450 2D6. Patients are distinguished as "slow" and "fast" metabolizers. In "slow" metabolizers, better prophylactic effect of propafenone was observed in preventing atrial fibrillation, but not in conversion to sinus rhythm. "Fast" metabolizers have less ß-adrenergic blocking effect. Maximum blood level of propafenone is achieved in 2-3 hours after its application. The main clinical indications for administration of propafenone are supraventricular tachycardias, including the ones occurring in WPW syndrome and atrial fibrillation in patients without structural heart disease. In general, propafenone is not administered in cases of ventricular rhythm disturbances, particularly in patients with preexisting structural heart disease. If given to patients with these cardiac pathologies, propafenone can induce proarrhythmic rather than antiarrhythmic effects with potentially detrimental consequences[4,5].

An 80-year-old patient was admitted to the intensive care unit due to electrocardiographically recorded atrial fibrillation with slow ventricular rate of up to 20 beats *per* minute with RR pauses of up to 3.2 seconds (Fig. 1), accompanied by dizziness and acute heart failure. The patient had a history of heart disease; he had survived two myocardial infarctions (fifteen and four years before) that consequentially led to the development of ischemic cardiomyopathy with reduced systolic function of the left ventricle (EF 40% 2D Simpson's biplane analysis) and moderate mitral regurgitation. Thirteen years before, the patient underwent CABG x 3 (LAD, RCA, OM1-VSM). Recoronarography performed in 2002 showed occluded bypasses on RCA and OM1. Consequently, PCI of LAD-VSM bypass was performed and one stent was implanted. The results of recoronarography performed two years before showed the bypass on LAD to be passable. In addition to the above cardiac pathologies, the patient also had long term arterial hypertension, dyslipidemia and second stage chronic renal failure (GF ~70 mL/min/1.73 m^2). Patient liver function was normal, his weight was 82 kg. His regular medication treatment consisted of bisoprolol 2.5 mg *per* day plus lisinopril, amlodipine, atorvastatin, acetylsalicylic acid, isosorbide mononitrate, and he was in sinus rhythm. Several days prior

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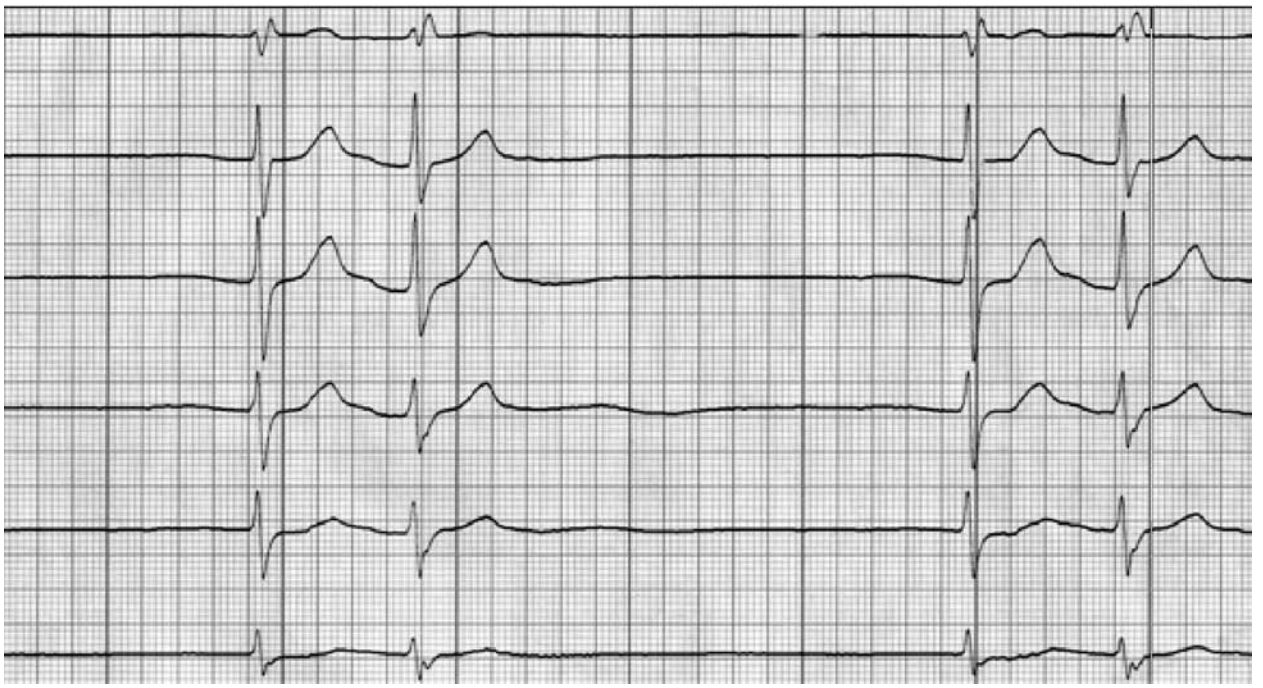

Fig. 1. Atrial fibrillation with slow ventricular rate.

to hospital admission, the patient experienced short-term heart palpitations for which he was prescribed propafenone by his general practitioner. The patient had a history of taking propafenone. Prior to his first heart attack, 15 years before, the patient had been administered propafenone for the same symptoms he was now experiencing and, at that time, the treatment resulted in excellent therapeutic results. This time, several days prior to hospital admission, the patient took propafenone in a dosage of 3x300 mg recommended by his general practitioner. Immediately after hospital admission, temporary cardiac electrostimulator was implanted and the patient was dependent on cardiac electrostimulator for the following 12 hours. Afterwards, along with the patient's sinus rhythm of 60 to 80 beats *per* minute, we observed the occurrence of frequent, non-sustained, hemodynamically irrelevant, asymptomatic, morphologically different wide

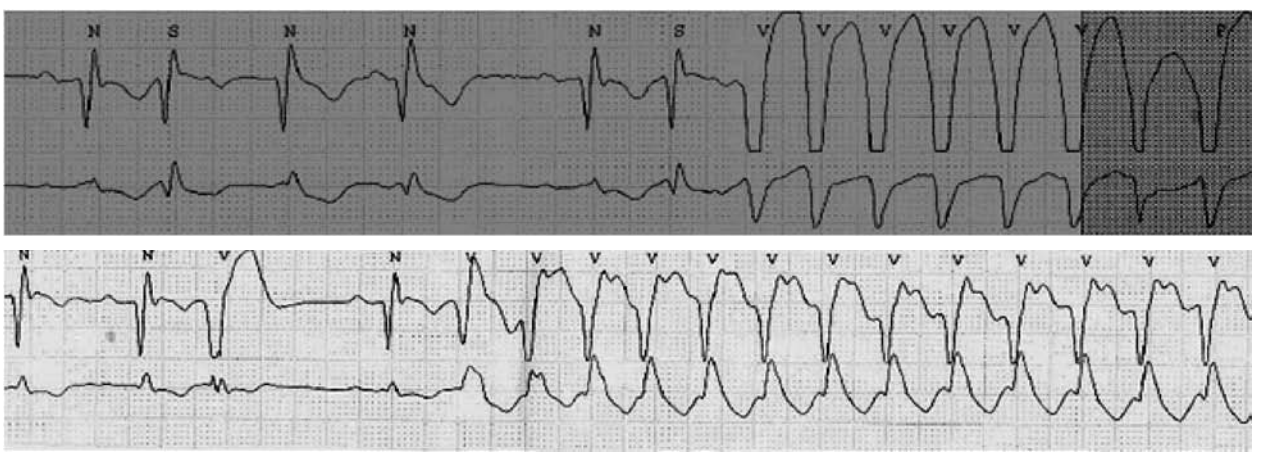

Fig. 2. Different wide QRS complex tachycardias.

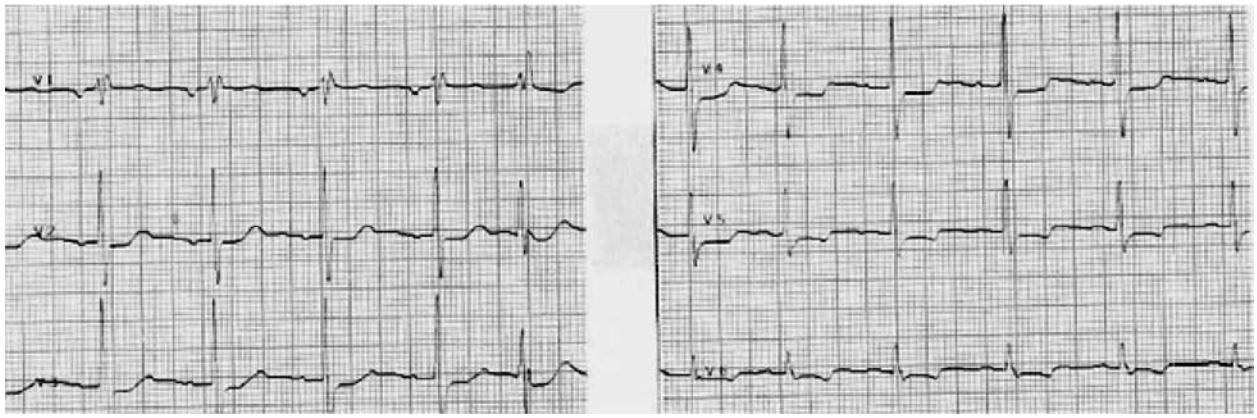

Fig. 3. Stable sinus rhythm at discharge from the hospital.

QRS complex tachycardias with the duration of up to maximum of 10 seconds (Fig. 2). Twelve hours after the onset of tachycardia, the patient was in stable sinus rhythm, without significant arrhythmias and pauses (Fig. 3), thus we considered him clinically fully recovered. We observed no increase of cardioselective enzymes or any signs of acute coronary syndrome development. Consequently, the patient was judged to be in excellent condition and was discharged.

In the case described, the administration of propafenone to a patient with ischemic cardiomyopathy along with significant comorbidity almost resulted in fatal outcome. Fortunately, the patient received appropriate clinical treatment on time. In the case described, propafenone was improperly administered to a patient with structural heart disease and renal failure[1-3]. The improper administration was detected *via* symptomatic atrial fibrillation with slow ventricular rate, followed by propafenone induced arrhythmia[4-6] that was detected by non-sustained tachycardias with wide QRS complexes. The observed tachycardias were asymptomatic and hemodynamically irrelevant. We would like to emphasize that general practitioner prescribed propafenone based on the patient's history of using propafenone with favorable outcome.

In summary, the case we present here is another illustration that the administration of any antiarrhythmic drugs can have serious side effects[5,6], and exceptional caution should be practiced when making a decision to prescribe them. Furthermore, in order to avoid the potentially lethal side effects[2,3], it is necessary to detect arrhythmia/arrhythmias on electrocardiogram and thoroughly evaluate the patient's disease history prior to the administration of any antiarrhythmic drug.

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