

Early afterdepolarizations and electrical storm after cardioversion for atrial fibrillation



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Introduction

Prolongation of the QT interval and torsades de pointes (TdP) ventricular tachycardia are potential life-threatening side effects of the use of antiarrhythmic medications with potassium current-blocking properties. Although several antiarrhythmic medications can block the I_{Kr} current (KCNH2 channel) in ventricular muscle cells, their proarrhythmic potential varies. Slow sinus rhythm after cardioversion of previously rapidly conducted atrial fibrillation can potentiate the proarrhythmic effect of I_{Kr} blockers. We report a case of electrical storm post cardioversion of rapidly conducted atrial fibrillation and the use of amiodarone.

Case report

A 60-year-old female patient presented with a 3-month history of progressively worsening shortness of breath. She did not have any chest pain or other cardiac symptoms and she was unaware of palpitations. She noticed that she had been feeling fatigue and her breathlessness had gradually worsened in the last 3 months, leading to her presentation. Her 12-lead electrocardiogram (ECG) in the Emergency Department showed atrial fibrillation with a ventricular rate of approximately 150 beats per minute (bpm) and no repolarization abnormalities (Figure 1a). During her admission to the Coronary Care Unit, she had an echocardiogram, which showed normal left ventricular size but moderate global systolic dysfunction with an ejection fraction of approximately 40%. The left atrium was only mildly dilated and there were no significant valvular abnormalities. She had intravenous amiodarone loading (total of 1200 mg over 24 hours) and subsequently had a transesophageal echocardiogram–

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KEY TEACHING POINTS

- Cardioversion of rapidly conducted atrial fibrillation can be followed by electric instability and repolarization abnormalities leading to torsades de pointes ventricular tachycardia, especially if sinus bradycardia and pauses occur after cardioversion. The mechanism is similar to the torsades de pointes and ventricular fibrillation that can occur early after atrioventricular nodal ablation in the context of previously rapidly contacted atrial fibrillation.
- The reverse use-dependent effect of class III antiarrhythmic drugs also potentiates their proarrhythmic potential and the occurrence of torsades de pointes. Careful monitoring would be prudent when I_{Kr} blockers are used, especially in this situation.
- Temporary acceleration of the heart rate with pacing rather than isoprenaline may be necessary to avoid proarrhythmia and torsades de pointes in similar circumstances.

guided cardioversion, which restored sinus rhythm (single 200 J shock). Despite normal QT interval prior to cardioversion, she developed widespread T-wave inversion with a QTc interval of approximately 460 ms after cardioversion (Figure 1b). She was monitored in hospital for 24 hours after cardioversion and was subsequently discharged with the advice to take amiodarone 200 mg daily.

She re-presented to the Emergency Department the following day after 2 syncopal episodes at home. She denied preceding symptoms such as palpitation or chest pain. ECG done at this presentation showed marked QT prolongation with a brief run of TdP, as shown in Figure 2a. Given the presence of left ventricular systolic dysfunction on her initial echocardiogram and the torsades recorded on telemetry, she underwent coronary angiography, which showed normal coronary arteries. The left ventriculogram showed persistent

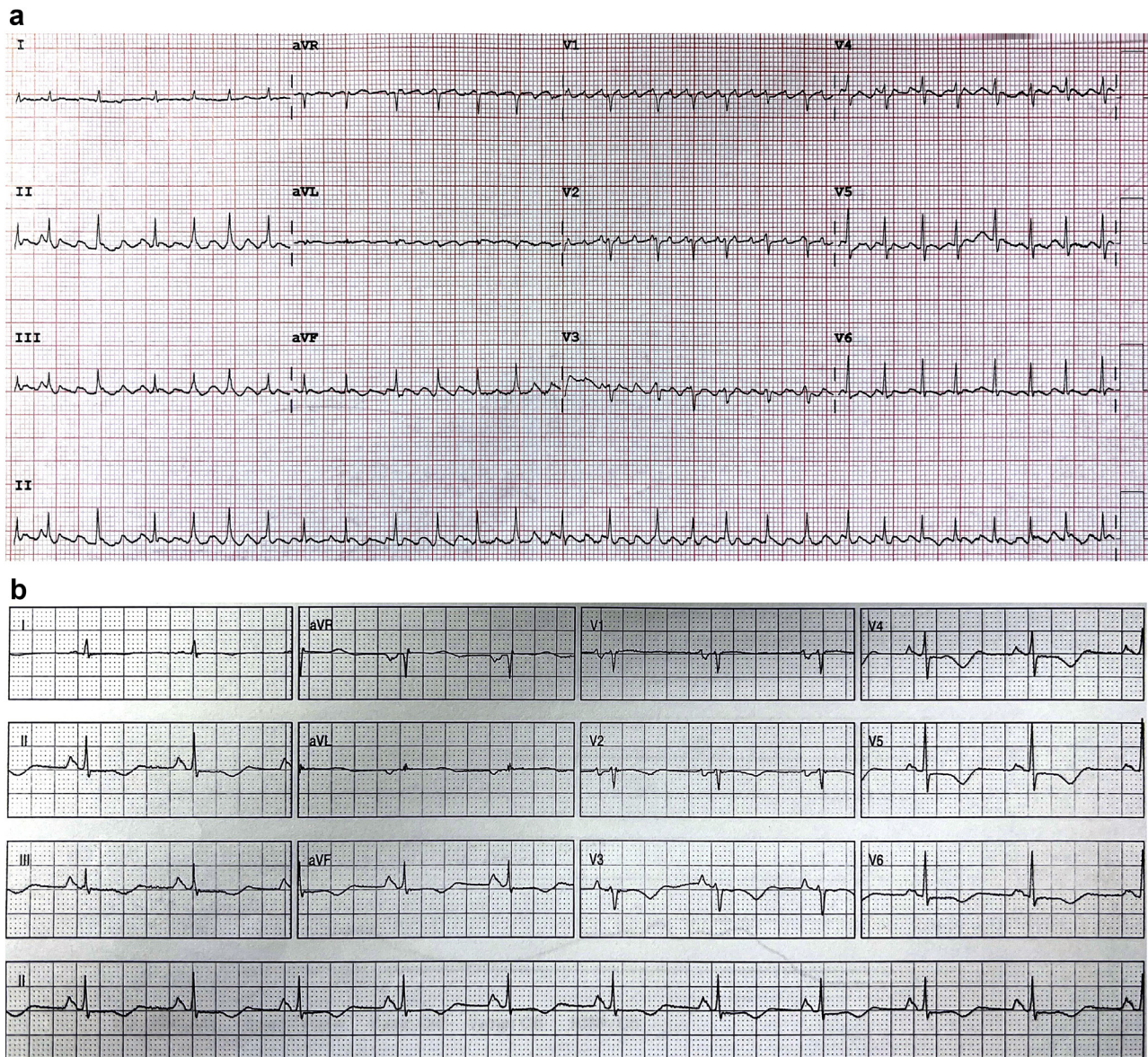


Figure 1 a: Initial electrocardiogram (ECG) showing atrial fibrillation with rapid ventricular response and normal QT interval. b: Postcardioversion ECG showing prolonged QT interval.

moderate systolic dysfunction with an ejection fraction similar to the previous echocardiogram done prior to the cardioversion 2 days before. There was no apical ballooning to suggest takotsubo cardiomyopathy and the NT-proBNP level was 659 ng/L. While in the Coronary Care Unit, she had multiple short runs of torsades on telemetry and 1 sustained episode requiring immediate cardioversion. Her potassium and magnesium levels at this time were normal (4.9 mmol/L and 1.84 mmol/L, respectively); however, additional potassium and magnesium supplements were administered to maintain the levels at the upper end of the normal range. Of note, except for the amiodarone she had not been on any other QTc-prolonging medications. Her weight was 65 kg and she had received a total of 1200 mg intravenously and 800 mg orally of amiodarone since the initial presentation.

Despite discontinuation of the amiodarone, the episodes of torsades persisted for the following 72 hours. Isoprenaline infusion was commenced to increase the heart rate (the baseline here rate was approximately 55 bpm prior to the isoprenaline initiation) and to overcome the effect of amiodarone. Her heart rate increased to 80–90 bpm, which led to improvement of the duration and the frequency of the torsades episodes. However, it did not make her torsades-free (Figure 2b). The possibility of a temporary pacing wire was considered, but given the presence of left ventricular systolic dysfunction, the decision was made to proceed with a dual-chamber implantable cardioverter-defibrillator insertion that would provide atrial pacing to avoid the same phenomenon in a similar scenario if an I_{Kr} blocker might be used in the future for rhythm control of further episodes of atrial fibrillation.¹

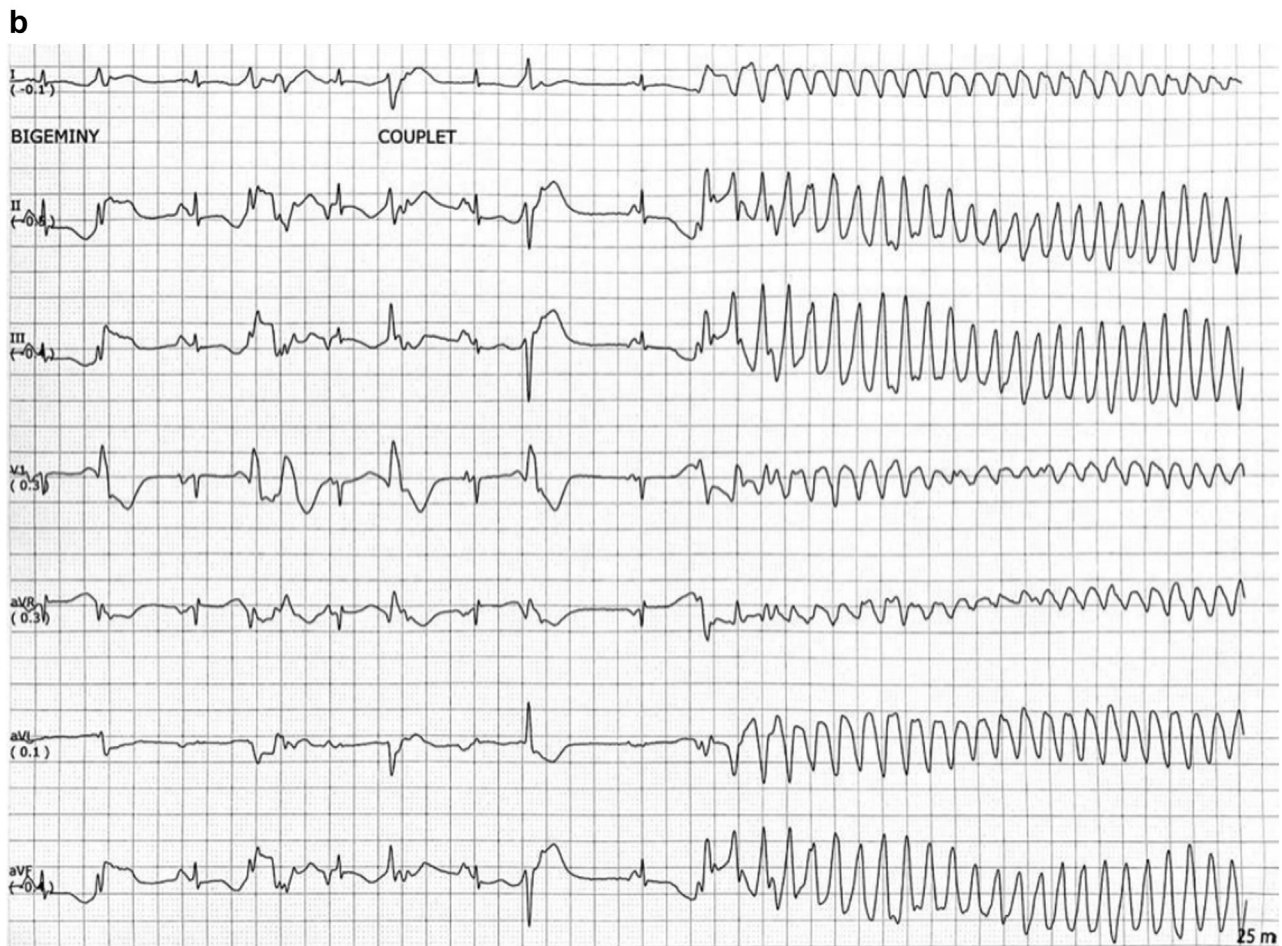
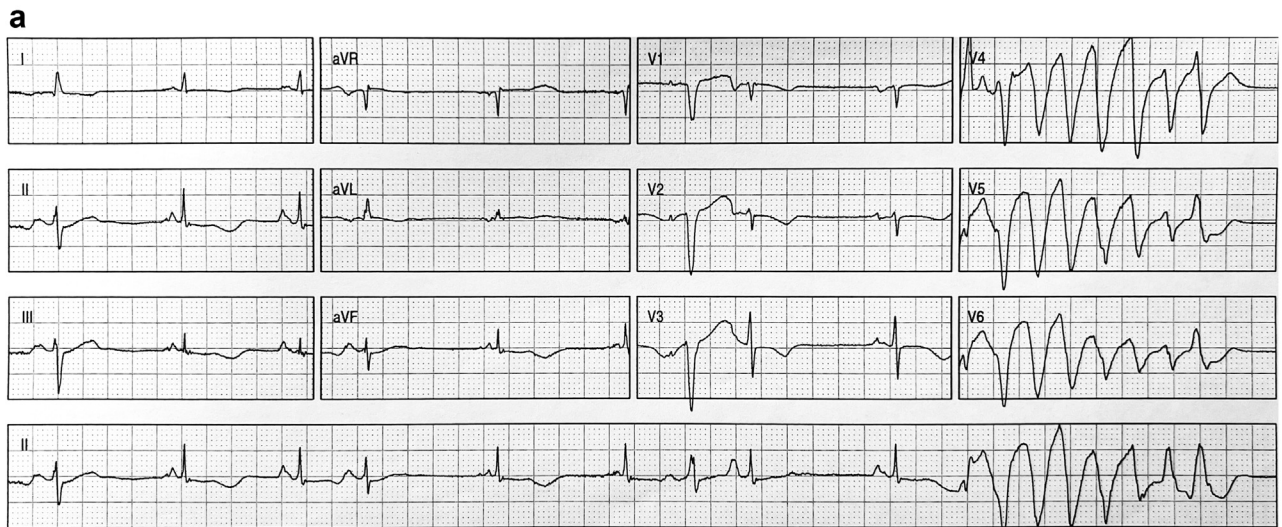


Figure 2 a: Electrocardiogram (ECG) showing initiation of torsades with relative bradycardia. b: ECG showing initiation of torsades at faster heart rate.

Discussion

This is an example of TdP ventricular tachycardia due to early afterdepolarizations (EADs) precipitated by combination of prolongation of the action potential duration of the ventricular myocardial cells and QT-interval prolongation,

after cardioversion for previously rapidly contacted atrial fibrillation and after administration of an antiarrhythmic medication with I_{K_r} blocking effect.² During repolarization there is an outward current flow of positive charges that increases after the action potential phase 0 and eventually

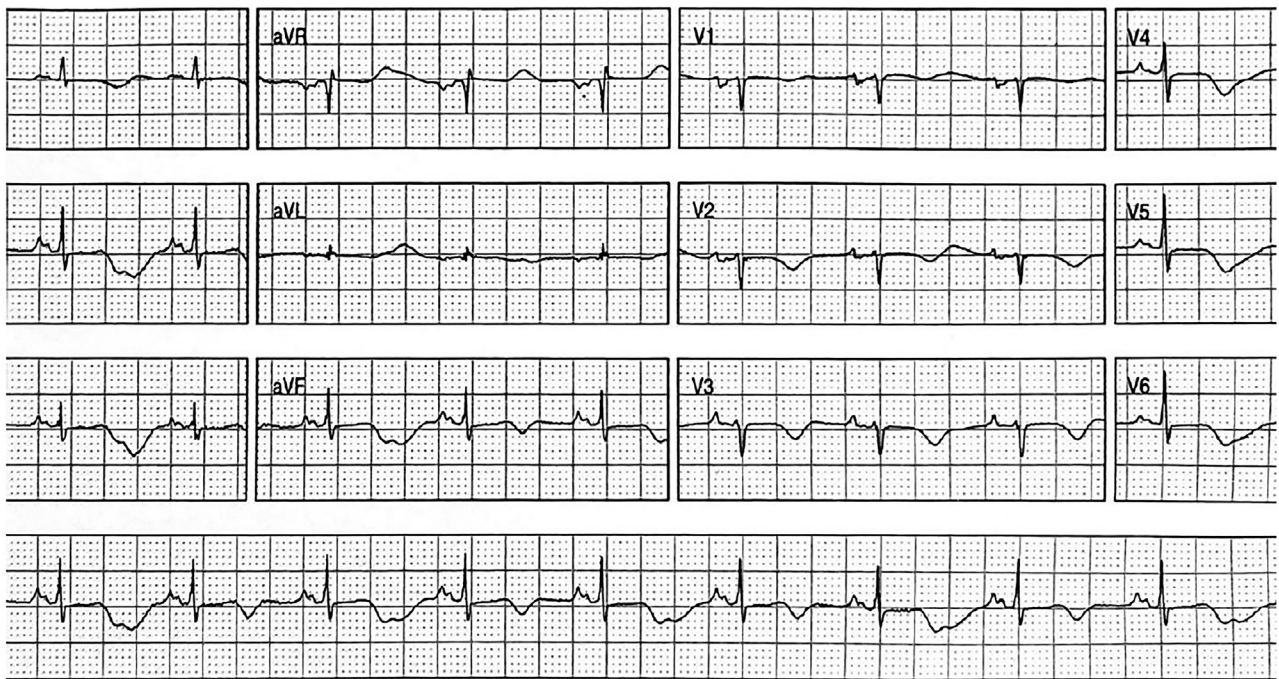


Figure 3 Twelve-lead electrocardiogram findings with U wave alternans in sinus rhythm.

returns the membrane potential to its original diastolic value. This net outward current flow consists of both outward currents (potassium currents like I_{Ks} and I_{Kr}) and inward currents (I_{Na} and I_{CaL}) during phases 1, 2, and 3 of repolarization. A reduction in the outward currents or an increase in the inward currents (or a combination of both) slows repolarization and can lead to the occurrence of the EADs, which are in essence oscillations of the membrane potential that occur during the repolarization phase.³⁻⁵ The EADs are more likely to occur at long cycle lengths, which slow repolarization, prolong the action potential duration, and thus give the opportunity to the inward currents that cause them to become activated.⁶ For the same reason, the EADs disappear at short cycle lengths that have the opposite effect (acceleration of the repolarization phase and shortening of the action potential duration).

Both the very fast ventricular rate before the cardioversion and the slow rate postcardioversion played a key role in our patient. A rapid ventricular rate during atrial fibrillation causes excess calcium to enter the ventricular cells through the L-type calcium channels. This excess calcium is then extruded by the Na-Ca exchanger after slowing of the heart rate postcardioversion, leading to an increase in the intracellular Na. When this occurs in the presence of delayed repolarization caused by an I_{Kr} blocker (like sotalol or amiodarone), it contributes further to the genesis of the EADs that lead to torsades.⁷ It is of relevance that the same issue can occur after atrioventricular node ablation in the context of previously rapidly conducted atrial fibrillation. The prolongation of the QT interval and the appearance of U waves (the surface expression of the EADs) are the hallmarks of this condition

(Figure 3). It was somewhat unusual that this occurred in our patient with amiodarone. Not all drugs with an I_{Kr} blocking effect are equally likely to cause TdP ventricular tachycardia. Amiodarone has a much lower incidence of torsades compared to sotalol because in addition to blocking the I_{Kr} current it also blocks both the late sodium current and also the L-type calcium channel, which are necessary for an EAD to trigger action potentials. This likely explains the low overall incidence of torsades with amiodarone even with marked QTc prolongation. Another reason that amiodarone is less likely to cause torsades despite its potent I_{Kr} blocking effect is that it prolongs more uniformly the action potential duration in the endocardium, the epicardium, and the M cells, therefore not causing significant transmural dispersion of repolarization.^{2,8}

It is important to mention that the effects of amiodarone are complex and differ in acute and chronic administration. The acute effects (inhibition of potassium channels but also of inward sodium and calcium currents, which is enhanced in a use- and voltage-dependent manner) result in suppressed excitability and conductivity of myocardium, especially at high frequencies. Amiodarone has no consistent effect on the action potential duration when administered acutely. Chronic administration has been shown to cause a downregulation of Kv1.5 mRNA in an animal model, suggesting a drug-induced modulation of potassium-channel gene expression that results in accumulation of amiodarone and its active metabolite, leading in turn to variable suppression of excitability and conductivity through the direct effects of the compounds retained at the sites of action.⁹ Similarly, dofetilide can cause exaggerated QTc interval prolongation after

restoration of sinus rhythm that cannot be predicted by the QT response from the administration of this medication during atrial fibrillation.¹⁰

It is noteworthy with our patient that the electrical storm occurred within a few days but not shortly after cardioversion. This would urge caution in similar circumstances where I_{Kr} blockers are used postcardioversion, especially in the context of previously rapidly conducted atrial fibrillation. The lack of adequate response of the torsades to the increase in the heart rate with the isoprenaline in our patient is also noteworthy. Sympathetic stimulation accelerates depolarization independent of its effects on the heart rate. It increases the L-type calcium current and thus shortens phase 3 of the action potential. Based on these, sympathetic activation should decrease the repolarization and action potential duration and suppresses any EAD-triggered activity. However, sympathetic activation has also direct effects on the EADs, as it can potentially increase their amplitude via increased intracellular calcium, thus increasing their likelihood to reach the potential threshold to cause triggered activity. Careful attention was paid to the electrolyte levels. Hypokalemia can accelerate the inactivation of the I_{Kr} channel and potentiates the drug blockade of the residual current. Low magnesium levels can also increase the risk of torsades in this setting, likely via potentiation of the L-type calcium current, which participates in the EAD formation. This explains the beneficial effect of intravenous magnesium in the treatment of drug-induced torsades. The benefit of temporary pacing in this situation is that it increases the heart rate and prevents any bradycardia or pause-dependent torsades without the disadvantage of the sympathetic stimulation in the repolarization process. At 3-month follow-up no further episodes of torsades were recorded by the implantable cardioverter-

defibrillator and no therapies were triggered. The patient also had no further episodes of atrial fibrillation during that period and no antiarrhythmic medications were used.

Conclusion

EADs and polymorphic ventricular tachycardia can occur after cardioversion for atrial fibrillation with rapid ventricular response, particularly if I_{Kr} blockers are used. This potentially life-threatening phenomenon may be mitigated with acceleration of the heart rate with pacing.

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