

# Atrial flutter with flecainide-induced 1:1 conduction at a rate <200 b.p.m. at rest: a case report

Sotirios Dardas \* and Asif Khan

Department of Cardiology, King's Mill Hospital, Sherwood Forest Hospitals NHS Foundation Trust, Mansfield Rd, Sutton-in-Ashfield, Nottinghamshire NG17 4JL, UK

Received 25 May 2021; first decision 15 June 2021; accepted 28 September 2021; online publish-ahead-of-print 1 October 2021

## Background

Class IC antiarrhythmic drug flecainide is commonly used in the management of atrial arrhythmias and in particular atrial fibrillation (AF). Although previously reported as a potential complication, atrial flutter (AFL) with 1:1 atrioventricular (AV) conduction is rare, with only few cases reported so far, most of which related to physical activity. In all previous reported cases, 1:1 conduction resulted in ventricular rates of >200 b.p.m.

## Case summary

We report the case of a 60-year-old woman, who presented to our local emergency department with palpitations related to acute onset AF. The patient developed symptomatic 1:1 AFL with a rate of 192 b.p.m., shortly after administration of intravenous flecainide, which spontaneously converted back to AF and subsequently to sinus rhythm, with further administration of amiodarone and beta-blocker.

## Discussion

The case raises awareness of this rare but potentially life-threatening complication to those using flecainide for pharmacological cardioversion of AF. QRS complex widening can be seen in the context of very rapid ventricular rates, posing additional diagnostic challenge, especially with rates of <200 b.p.m. Prescribing an AV nodal blocking agent, such as a beta-blocker, together with flecainide reduces significantly the risk of 1:1 conduction and should always be considered.

## Keywords

Atrial fibrillation • Atrial flutter • 1:1 atrial flutter • Flecainide • Case report

## Learning points

- Flecainide can rarely induce atrial flutter with 1:1 atrioventricular (AV) block, which can be life-threatening.
- Recognition can pose a diagnostic challenge, especially with rates <200 b.p.m. and broad QRS complexes.
- Concomitant use of flecainide with an AV nodal blocking agent, such as a beta-blocker, reduces significantly the risk of 1:1 conduction and should always be considered

## Introduction

Class IC antiarrhythmic drug flecainide is among the most commonly used in the UK for the management of patients with atrial fibrillation (AF), both for the acute pharmacological cardioversion of recent-onset AF as well as the prevention of recurrent episodes.<sup>1</sup> Although the possibility to cause pro-arrhythmic effects has been well established, it is generally regarded as a safe drug in patients without structural heart disease.<sup>2</sup>

\* Corresponding author. Tel: +44 7784303622, Email: [sotdardas@gmail.com](mailto:sotdardas@gmail.com)

Handling Editor: Robert Schönbauer

Peer-reviewers: Christoph Sinning and Peregrine Green

Compliance Editor: Carlos Minguito Carazo

Supplementary Material Editor: Deepti Rangnathan

© The Author(s) 2021. Published by Oxford University Press on behalf of the European Society of Cardiology.

This is an Open Access article distributed under the terms of the Creative Commons Attribution-NonCommercial License (<https://creativecommons.org/licenses/by-nc/4.0/>), which permits non-commercial re-use, distribution, and reproduction in any medium, provided the original work is properly cited. For commercial re-use, please contact [journals.permissions@oup.com](mailto:journals.permissions@oup.com)

Atrial flutter (AFL) with 1:1 atrioventricular (AV) conduction is an additional arrhythmia-related safety issue associated with flecainide. However, it is regarded rare and there is little awareness of this potentially lethal—should it degenerates into ventricular fibrillation complication.<sup>2,3</sup> Interestingly, in the majority of the reported cases, AFL with 1:1 conduction occurred during physical activity, possibly due to increased sympathetic tone.<sup>3</sup> In all those cases, the heart rate was >200 b.p.m.

1:1 AFL induced by flecainide at rest has only been reported twice in the past<sup>1,3</sup> and to the best of our knowledge, it has never been reported with a rate of <200 b.p.m.

## Timeline

Time	Events
Day 0 (10:00)	Sudden onset of palpitations
Day 0 (12:30)	Arrival at the emergency department
Day 0 (12:40)	Electrocardiogram (ECG) confirmed atrial fibrillation (AF) at 156 b.p.m. Bloods collected
Day 0 (13:00)	Administration of 150 mg of intravenous (IV) flecainide over 10 min
Day 0 (13:15)	Sudden onset worsening palpitations and chest pain. ECG confirmed 1:1 atrial flutter at 192 b.p.m.
Day 0 (13:25)	Spontaneous conversion back to fast AF (160–170 b.p.m.), while preparing for emergency electrical cardioversion
Day 0 (13:40)	Administration of 300 mg of IV amiodarone over 30 min and 5 mg of IV metoprolol
Day 0 (14:15)	Ongoing fast AF (120–130 b.p.m.). Administration of further 300 mg of IV amiodarone and further 5 mg IV metoprolol, as well as 2 g of IV magnesium sulphate
Day 0 (15:00)	Conversion of AF into normal sinus rhythm
Day 0 (15:30)	Transfer of the patient to the coronary care unit for cardiac monitoring
Day 1 (10:00)	Patient discharged home with small dose of regular flecainide 50 mg b.i.d., bisoprolol 1.25 mg o.d., and edoxaban 60 mg o.d.
Day 30	Patient remains well and asymptomatic

## Case presentation

A 60-year-old woman presented to our local emergency department (ED) with a few hours history of palpitations. She had paroxysmal AF for the last 5 years and had been treated in the past with regular flecainide, following previous treatments with intravenous (IV) flecainide in ED. A pill in the pocket approach had been adopted more recently. Additional past medical history included hypothyroidism, anxiety, and gastro-oesophageal reflux disease. There was no history of ischaemic heart disease or angina. Her regular medications

included levothyroxine, mirtazapine, and omeprazole. Prior to initiation of flecainide, the electrocardiogram (ECG) demonstrated normal QRS and QTc intervals (Figure 1), which remained normal throughout the course of treatment. Transthoracic echocardiogram ruled out any structural heart disease, being completely normal.

At presentation, the initial ECG demonstrated AF at a rate of 156 b.p.m. (Figure 2). Clinical examination findings were normal and the patient was haemodynamically stable, with blood pressure (BP) of 146/104 mmHg. Blood tests, including full blood count, electrolytes, renal function, C-reactive protein, and coagulation were normal. Thyroid-stimulating hormone was slightly raised with normal free thyroxine (T4). Given the patient had tolerated flecainide well in the past, the emergency physician decided to try pharmacological cardioversion with IV flecainide. Weight was 107 kg, therefore, 150 mg over 10 min were administered (no oral flecainide had been taken). A therapeutic dose of subcutaneous enoxaparin (1.5 mg/kg) was also administered, as she was not anticoagulated (CHA2DS2-VASc score was only 1 for being female). Shortly after the flecainide infusion had finished and with the patient at rest, she developed worsening palpitations associated with chest pain. The cardiac monitor demonstrated a regular tachycardia of 192 b.p.m. with broad QRS complexes and the ECG demonstrated a pattern of 1:1 AFL with QRS complexes of 120 ms (Figure 3). She remained haemodynamically stable with BP of 128/88 mmHg. While emergency electrical cardioversion was being prepared, the rhythm spontaneously converted into AF at a rate of 160–170 b.p.m. The total duration of 1:1 AFL was 10 min.

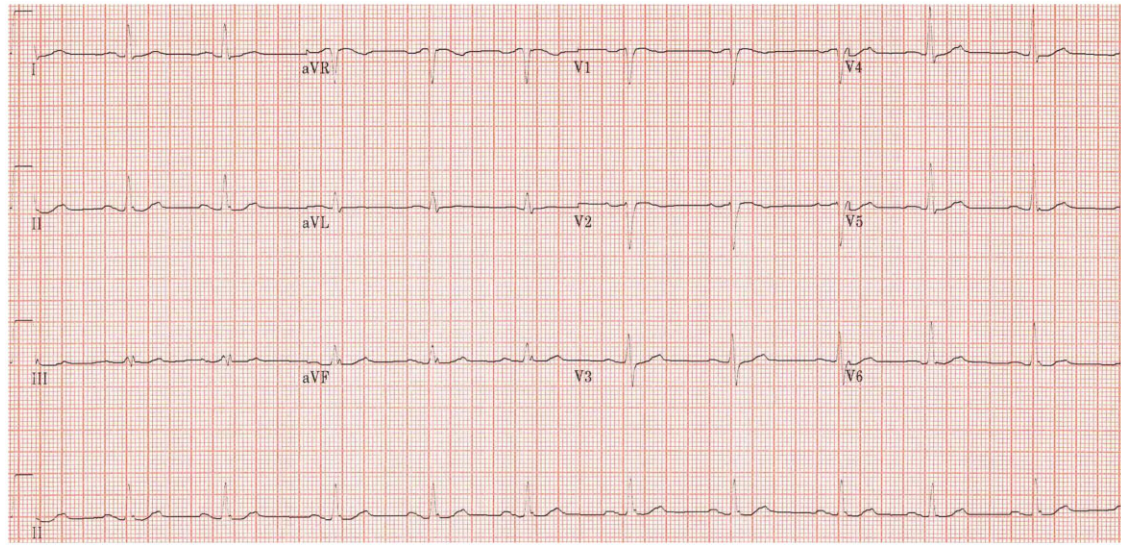
Given the anticipated delays in organizing electrical cardioversion in a haemodynamically stable patient and because the patient's chest pain had completely resolved, clinical decision at the time was to proceed with administration of IV amiodarone, beta-blocker, and magnesium ( $Mg^{2+}$ ), with close monitoring for any further arrhythmias and plan for electrical cardioversion should that failed. The beta-blocker was given to avoid any further 1:1 conduction, by using an AV nodal blocking agent. The use of  $Mg^{2+}$  has been shown to be effective for rate control and modestly for restoration of sinus rhythm in AF, in conjunction with standard care.<sup>4</sup> Following administration of 600 mg of amiodarone and 10 mg of metoprolol together with 2 g of  $Mg^{2+}$ , sinus rhythm was restored and the patient felt a lot better. She moved to the coronary care unit for monitoring and was discharged the next day.

At discharge, a small dose of flecainide 50 mg b.i.d., alongside with 1.25 mg of bisoprolol were initiated. Despite CHA2DS2-VASc score being only 1 due to female sex, given multiple previous episodes of paroxysmal AF and in the absence of any bleeding risks, it was decided to commence regular anticoagulation with 60 mg edoxaban. That would also facilitate electrical cardioversion, should AF recurred.

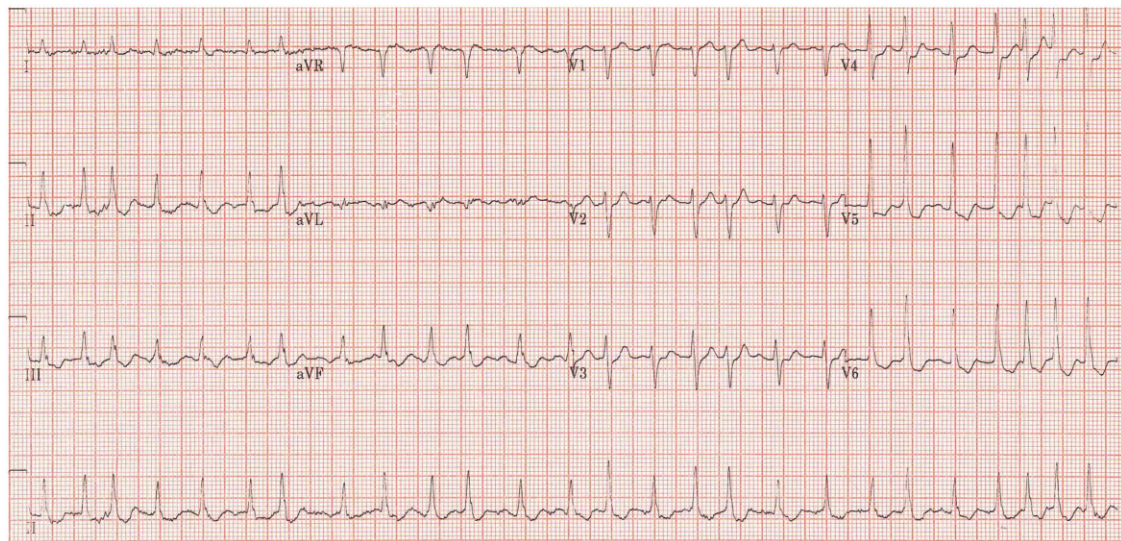
The patient remains asymptomatic at telephonic consultation 1 month after the episode. She will be followed up in clinic, where AF ablation will be discussed, should she remains symptomatic.

## Discussion

Atrial flutter is categorized into typical and atypical form. Typical AFL is a MACRO-reentry tachycardia. The mechanism is that of a large



**Figure 1** Electrocardiogram in sinus rhythm prior to initiation of flecainide for the first time, showing normal QRS and QTc intervals. Scale: 7.06 cm × 14.65 cm.

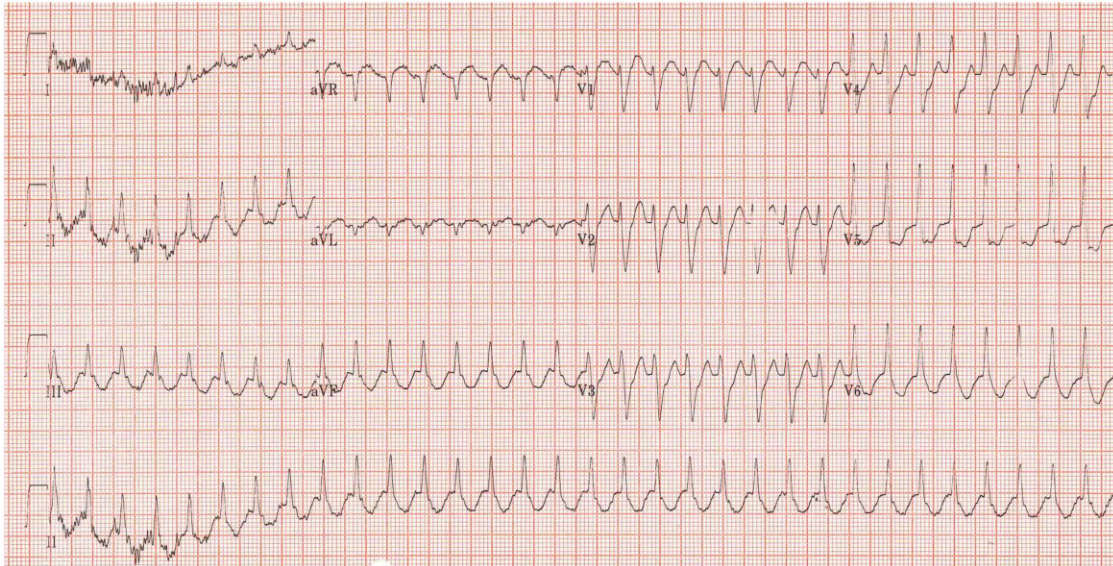


**Figure 2** Initial electrocardiogram at presentation, showing atrial fibrillation at a rate of 156 b.p.m. Scale: 7.02 cm × 14.65 cm.

re-entrant circuit contained in the right atrium (RA), with passive activation of the left atrium. The activation wave front goes downward in the RA free wall, travels through the cavotricuspid isthmus, spreads upward in the septal wall, and crosses the crista terminalis to complete the re-entrant circuit. Depending on the direction of the re-entrant circuit, typical AFL is further sub-divided into counter clockwise (the commonest) and clockwise AFL. The term atypical AFL is used to describe rapid atrial tachycardias with ECG patterns differing from the forms of typical AFL and circuit configuration

different from the typical RA flutter circuit, even if they have an ECG pattern similar to typical flutter. The precise mechanism of atypical flutter can only be determined by electrophysiological studies.<sup>5,6</sup>

The re-entrant circuit present in AFL causes a repeated loop of electrical activity to depolarize the atrium at a rate of 250–350 b.p.m. Atrial flutter usually occurs with some degree of AV block, most commonly 2:1, giving ventricular rates of ~150 b.p.m. However, uncommonly, it occurs without AV block, i.e. with 1:1 AV conduction. This can result in extremely high ventricular rates of up to 320 b.p.m.



**Figure 3** Electrocardiogram showing 1:1 atrial flutter with broader QRS complexes at a rate of 192 b.p.m. Scale: 7.41 cm × 14.65 cm.

**Table 1** Flecainide indications, adverse effects, and contraindications<sup>2,11,12</sup>

Indications	Potential adverse effects	Contraindications
I. Acute conversion of AF to SR with IV administration	<ul style="list-style-type: none"> <li>Ventricular pro-arrhythmia/sudden cardiac death</li> </ul>	<ul style="list-style-type: none"> <li>Ischaemic heart disease</li> </ul>
II. Acute conversion of AF to SR with 'Pill-in-the-Pocket' approach	<ul style="list-style-type: none"> <li>1:1 AFL</li> <li>Bradycardia, sinus pause, heart block</li> </ul>	<ul style="list-style-type: none"> <li>Left ventricular systolic dysfunction</li> <li>Significant left ventricular hypertrophy</li> </ul>
III. Chronic suppression of AF with regular oral administration	<ul style="list-style-type: none"> <li>Hypotension (negative inotropic action)</li> <li>Worsening of heart failure</li> </ul>	<ul style="list-style-type: none"> <li>CrCl &lt; 35 mL/min/1.783 m<sup>2</sup></li> <li>Significant liver disease</li> <li>Sick sinus syndrome (use with caution)</li> <li>Atrioventricular conduction disturbances (use with caution)</li> <li>Prolonged QTc (&gt;500 ms)</li> <li>Hypotension</li> <li>Pharmacological cardioversion of AFL</li> <li>Brugada syndrome</li> </ul>

AF, atrial fibrillation; AFL, atrial flutter; IV, intravenous; SR, sinus rhythm.

**Table 2** Flecainide dosing, success rate, and important considerations<sup>2,11,12</sup>

Indication	Dosing	Success rate	Important considerations
I. Acute conversion of AF to SR with IV administration	1.5 mg/kg over 10 min (max 150 mg)	Overall: 59–78% (51% at 3 h, 72% at 8 h)	CYP2D6 inhibitors increase concentration QRS widening >25% from baseline or LBBB/any other conduction block >120 ms warrant discontinuation (increased risk of pro-arrhythmia)
II. Acute conversion of AF to SR with 'Pill-in-the-Pocket' approach	200–300 mg		
III. Chronic suppression of AF with regular oral administration	50–200 mg bid or 200 mg od (slow release)		

AF, atrial fibrillation; IV, intravenous; LBBB, left bundle branch abnormality; SR, sinus rhythm.

and although very rare to happen spontaneously, it has the potential to occur more frequently by the use of cardio-depressant drugs, such as flecainide.<sup>7</sup> This has been named in the past ‘Class IC Atrial Flutter’, as it can also be seen with other Class IC antiarrhythmic agents.<sup>8</sup>

Flecainide slows down atrial conduction, reducing the flutter rate by  $\sim 1/3$ .<sup>9</sup> That, together with its infrequent capability of ‘organizing’ AF into AFL can give rise in AFL with 1:1 conduction, resulting in very high ventricular rates, which can potentially degenerate into life-threatening arrhythmias and cause death.<sup>1,3</sup> Thus, 1:1 AFL is a very serious complication of flecainide. The incidence is believed to be 3.5–5.0%, according to some old reports based on small registry data.<sup>10</sup>

Tables 1 and 2 show indications for use of flecainide in AF, together with potential adverse effects, contraindications, dosing, success rate, and other important considerations.<sup>2,11,12</sup>

It is important to emphasize that concomitant use of flecainide with an AV nodal blocking agent, such as a beta-blocker, reduces significantly the incidence of 1:1 conduction.<sup>2,11,12</sup> Another important point to remember is that given the high ventricular rates, it is common to see a pattern of aberrant ventricular depolarization, which produces a regular broad complex tachycardia and can be mistaken for ventricular tachycardia (VT), further complicating the diagnosis. In our case, the presence of what looked like P waves before each QRS complex directed us towards 1:1 AFL, rather than VT, despite the fact that we would normally expect a ventricular rate of much  $>192$  b.p.m. We believe that flecainide slowed the atrial rate quite significantly and therefore, allowed such a ventricular rate.

In our opinion, our case presents several important learning points to the reader and raises awareness of a rare and under-recognized complication of flecainide, which should be considered by all those using this or other Class IC antiarrhythmic drugs, for the treatment of AF.

## Lead author biography



Dr Sotirios Dardas is a cardiology specialty trainee in the East Midlands Deanery in the UK. His aspiration is a career in interventional cardiology with a special interest in structural interventions.

## Supplementary material

Supplementary material is available at *European Heart Journal - Case Reports* online.

**Slide sets:** A fully edited slide set detailing this case and suitable for local presentation is available online as [Supplementary data](#).

**Consent:** The authors confirm that written consent for submission and publication of this case report including images and associated text has been obtained from the patient in line with COPE guidance.

**Conflict of interest:** None declared.

**Funding:** None declared.

## References

1. Taylor R, Gandhi MM, Lloyd G. Tachycardia due to atrial flutter with rapid 1:1 conduction following treatment of atrial fibrillation with flecainide. *BMJ* 2010; **340**:b4684.
2. Echt DS, Ruskin JN. Use of flecainide for the treatment of atrial fibrillation. *Am J Cardiol* 2020; **125**:1123–1133.
3. Comelli I, Pigna F, Cervellin G. 1:1 atrial flutter induced by flecainide, whilst the patient was at rest. *Am J Emerg Med* 2018; **36**:2131.e3–2131.e5.
4. Ramesh T, Lee PYK, Mitta M, Allencherril J. Intravenous magnesium in the management of rapid atrial fibrillation: a systematic review and meta-analysis. *J Cardiol* 2021; **78**:375–381.
5. Cosío FG. Atrial flutter, typical and atypical: a review. *Arrhythm Electrophysiol Rev* 2017; **6**:55–62.
6. Tai CT, Chen SA. Electrophysiological mechanisms of atrial flutter. *Indian Pacing Electrophysiol J* 2006; **6**:119–132.
7. Marks J. Atrial flutter with 1:1 A-V conduction. *AMA Arch Intern Med* 1957; **100**:989–993.
8. Nabar A, Rodriguez LM, Timmermans C, Smeets JL, Wellens HJ. Radiofrequency ablation of “class IC atrial flutter” in patients with resistant atrial fibrillation. *Am J Cardiol* 1999; **83**:785–7, A10.
9. Heldal M, Orning OM. Atrieflutter med 1:1 AV-overledning under intravenøs flekainidbehandling [Atrial flutter with 1:1 AV conduction during intravenous flecainide treatment]. *Tidsskr nor Lægeforen* 1989; **109**:2309–2310. [in Norwegian].
10. Falk RH. Proarrhythmia in patients treated for atrial fibrillation or flutter. *Ann Intern Med* 1992; **117**:141–150.
11. American College of Cardiology/American Heart Association Task Force on Practice Guidelines. 2014 AHA/ACC/HRS guideline for the management of patients with atrial fibrillation: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines and the Heart Rhythm Society. *J Am Coll Cardiol* 2014; **64**:e1–e76.
12. ESC Scientific Document Group. 2020 ESC Guidelines for the diagnosis and management of atrial fibrillation developed in collaboration with the European Association for Cardio-Thoracic Surgery (EACTS): the Task Force for the diagnosis and management of atrial fibrillation of the European Society of Cardiology (ESC) Developed with the special contribution of the European Heart Rhythm Association (EHRA) of the ESC. *Eur Heart J* 2021; **42**:373–498.