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CASE REPORT
Electrophysiology

Wide QRS tachycardia in a patient with atrial fibrillation: a case report and approach to diagnosis

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Background Wide QRS complex (QRS) tachycardia in patients with atrial fibrillation (AF) or atrial flutter treated with antiarrhythmic drugs can occur for a variety of reasons and needs careful evaluation for appropriate management of the patient.

Case summary We report a case of wide QRS complex tachycardia in a patient with AF treated with Flecainide who received multiple external cardioversion attempts for a presumed diagnosis of ventricular tachycardia. Intravenous Diltiazem and an oral beta-blocker led to the resolution of wide QRS complex tachycardia.

Discussion Wide QRS tachycardia due to pro-arrhythmic effect or rate-dependency phenomenon of antiarrhythmic agents should be included in the differentials. In this brief report, we discuss the differential diagnosis and outline a practical approach for acute and long-term management of these patients.

Keywords Wide QRS complex tachycardia • Atrial fibrillation • Flecainide • Antiarrhythmic • Use dependency • Aberrancy • Case report

ESC curriculum 5.4 Atrial flutter • 5.3 Atrial fibrillation • 5.5 Supraventricular tachycardia

Learning points

- Flecainide is known to increase QRS duration due to sodium channel blockade.
- This effect is more pronounced at faster heart rates as a result of increased binding of the drug to sodium channels. This rate-related dissociation of drug during slow rates and association during faster rates are referred to as 'use dependency'.
- Patients on Class IC agents may present with wide QRS complex tachycardia during episodes of atrial tachyarrhythmia and rapid ventricular response and can be mistaken for ventricular tachycardia.

Introduction

The differential diagnosis of wide complex tachycardia in patients with atrial fibrillation (AF) and atrial flutter does not differ from those without atrial arrhythmia and include ventricular tachycardia (VT), antidromic re-entrant tachycardia (or pre-excited AF or atrial flutter), and supraventricular tachycardia with aberrancy (or aberrantly conducted AF or atrial flutter). However, special consideration needs to be given to patients who are treated with antiarrhythmic agents, commonly prescribed for the maintenance of the sinus rhythm.

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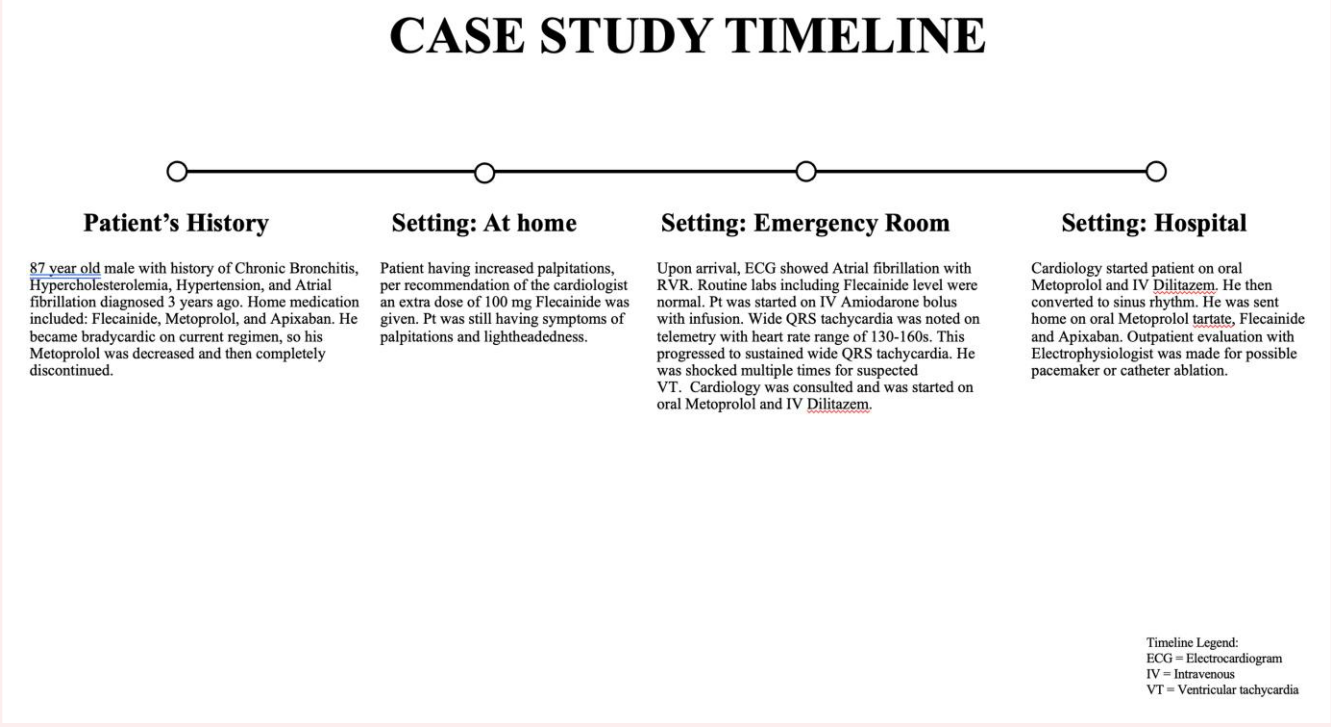
Vaughan-Williams Class IC and III agents are the most common antiarrhythmic agents used for this purpose. These agents can cause wide complex tachycardia either by prolongation of the QT interval (QT) or by use dependency or reverse use dependency phenomenon.[1,2] Prolongation of the QT interval due to Class III agents occurs due to blockade of rapid component of delayed rectifier potassium current (IKr) that predisposes to Torsades de pointes (TdP). Mild prolongation of the QT interval due to Class IC agents occurs due to prolongation of QRS duration but it rarely leads to TdP. Use dependent phenomenon is a property of Class IC agents. Flecainide, like other Vaughan-Williams Class IC antiarrhythmic agents, is known to increase QRS duration due to sodium channel blockade.[1] This effect is more pronounced at faster heart rates, because of increased binding of the drug to sodium channels. This rate-related dissociation of the drug during slow rates and its association during faster rates are referred to as 'use dependency'. This property is used to assess the optimal dosing and risk of toxicity of these agents by exercising the patients on a treadmill. Patients on Class IC agents may present with wide QRS complex tachycardia during episodes of atrial tachyarrhythmia and rapid ventricular response and can be mistaken for VT. We describe a patient who developed wide QRS complex tachycardia from use dependency phenomenon or possible rate-related aberrancy and received multiple external direct current electric shocks for a presumed diagnosis of VT. We discuss the importance of careful rhythm analysis in arriving to a proper diagnosis and summarize the approach in the acute and long-term management of such patients.

Summary figure



Case summary

An 87-year-old man was diagnosed to have paroxysmal AF 3 years ago. At that time, routine laboratory work up including thyroid functions were normal. Echocardiogram showed normal left ventricular wall thickness and systolic function [left ventricular ejection fraction (LVEF) 50–55%] and aortic valve sclerosis without stenosis or regurgitation. Myocardial perfusion imaging was negative for perfusion defects. He was started on Flecainide, Metoprolol, and Apixaban. He developed symptomatic sinus bradycardia necessitating dose reduction and subsequent discontinuation of metoprolol 6 months ago after he declined to have a pacemaker. He presented to emergency room (ER) with palpitations and light-headedness. In addition to scheduled doses of Flecanide 100 mg b.i.d., he took additional 100 mg on recommendation of his physician in the preceding 48 h for symptom control. Past medical history was also significant for hypertension controlled with losartan–hydrochlorothiazide, hypercholesterolaemia treated with atorvastatin, and chronic bronchitis stable on inhaled steroids and beta 2 agonists.

Upon arrival to the ER, electrocardiogram (ECG) showed AF with rapid ventricular rate (*Figure 1*). The corrected QT interval (QTc) was within normal limits (448 ms). Routine laboratory work up including renal functions, electrolytes, and acid–base analysis were within normal limits. Thyroid function, cardiac biomarkers including Troponin-T, and Pro-B-type natriuretic peptide (BNP) were within reference range. Amiodarone was started intravenously after a bolus dose for rate control as his blood pressure was borderline low (100/70 mm Hg). During observation in the ER, the patient was noted to have frequent runs of wide QRS tachycardia on telemetry with rates varying between 130 and 160 beats per minute (*Figures 2* and *3*) that progressed to sustained wide QRS tachycardia. He reported no new symptoms and was haemodynamically stable. Multiple external synchronized direct current shocks for presumed VT were delivered, which failed to convert the rhythm. Cardiology service was consulted. After careful analysis of the telemetry tracing, 'use dependency' phenomenon related to Flecainide was suspected. Amiodarone was discontinued and intravenous Diltiazem with oral Metoprolol were started, which resolved the electrocardiographic abnormalities after adequate rate control was achieved. Flecainide level was 0.8 μg/mL (reference 0.2–1 μg/mL).

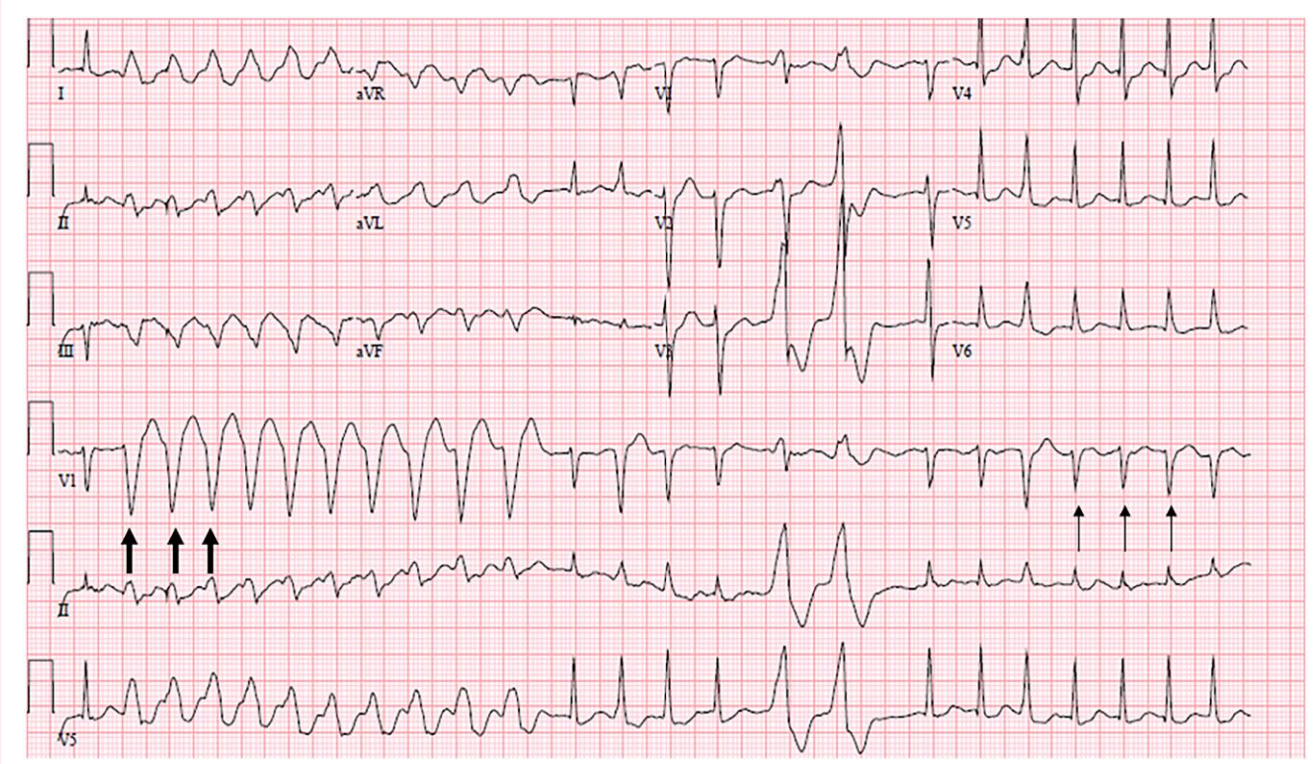


Figure 1 Electrocardiogram at admission showing atrial fibrillation with rapid ventricular response. Also noted are wide QRS complexes during short RR interval (thick arrows) and narrow QRS complexes during long RR interval (thin arrows).

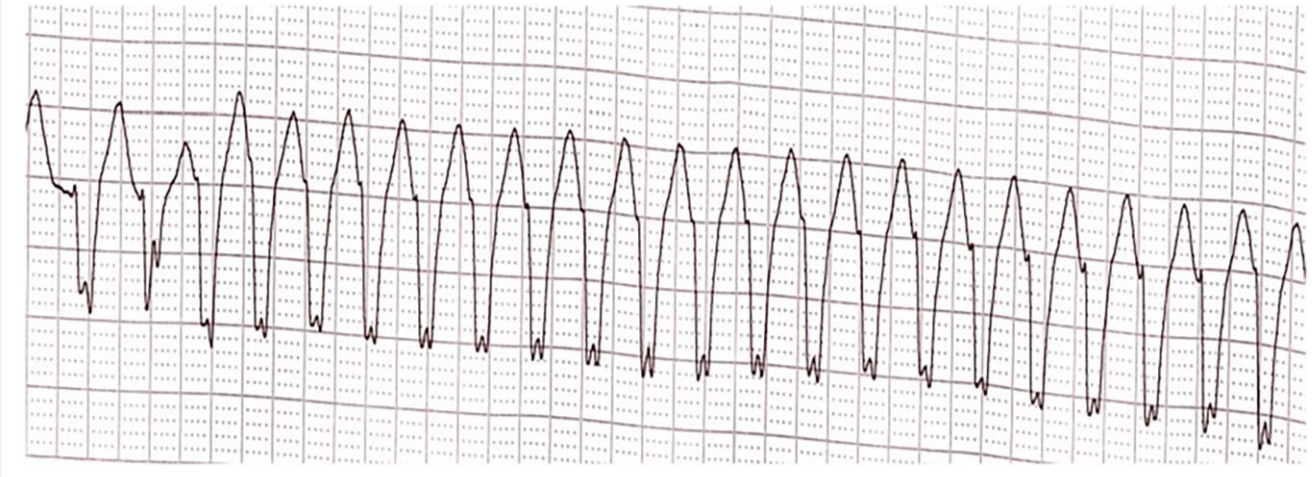


Figure 2 Telemetry tracing showing irregular wide QRS tachycardia.

Bedside echocardiogram showed no new changes compared to his previous study from 3 years ago. The patient subsequently converted to sinus rhythm (*Figure 4*) and was discharged on his usual dose of Flecainide. Metoprolol tartrate was added to his medical regimen and anticoagulation with Apixaban was continued for stroke prevention. Follow up with an electrophysiologist for evaluation of a pacemaker implantation or catheter ablation was scheduled.

Discussion

Class IC agents act by blocking slow sodium channels during phase 0 of action potential in myocardial cells, resulting in prolongation of action potential duration reflected as widening of QRS duration on surface ECG. The binding of these agents to sodium channels is rate dependent, i.e. agents bind to more receptors at faster heart rates, a phenomenon referred to as use dependency.[1–3] This may result in wide QRS

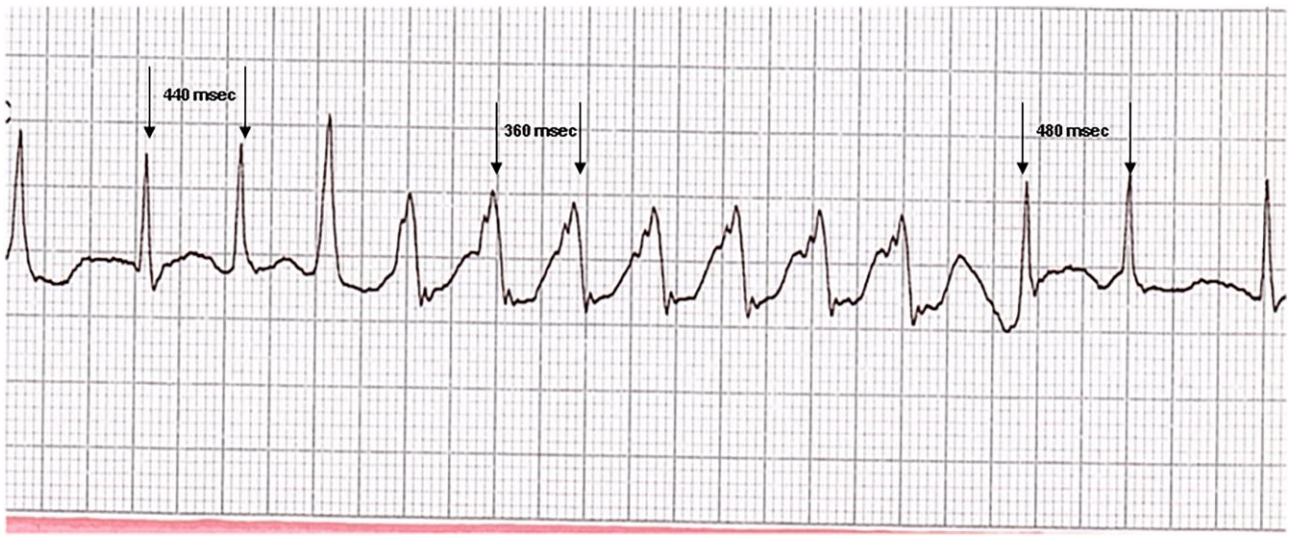


Figure 3 Telemetry tracing showing atrial fibrillation with run of wide QRS tachycardia. Note narrow QRS complexes during long RR interval and wide QRS complexes during short RR interval.

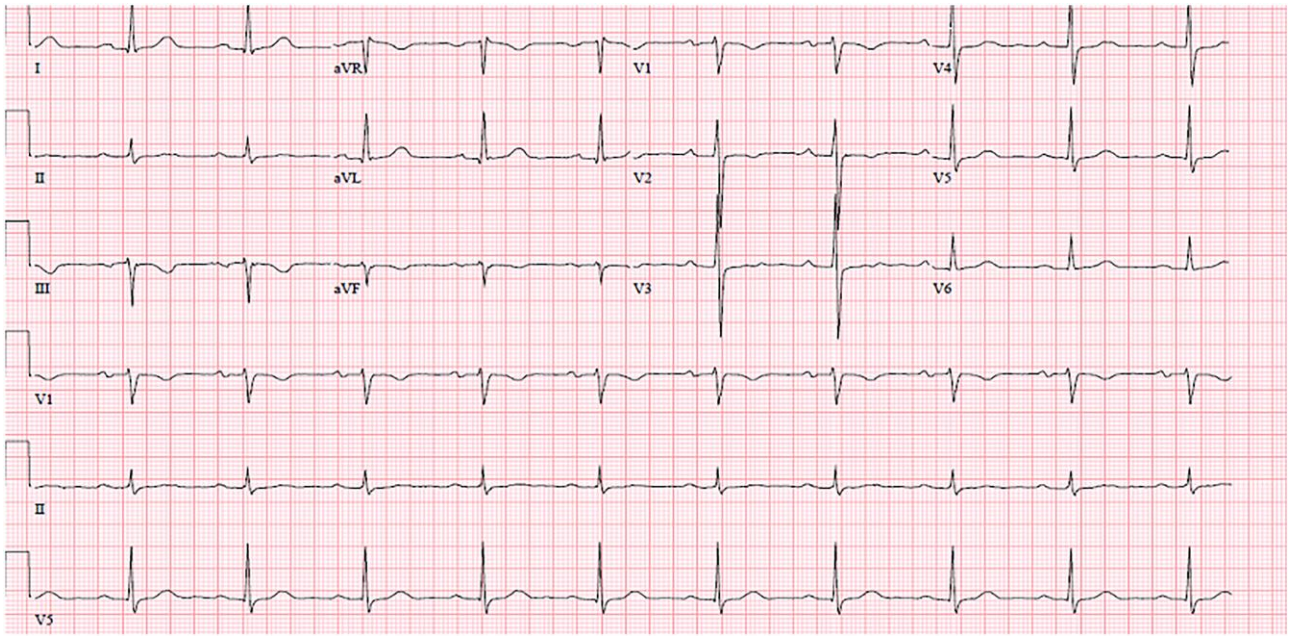


Figure 4 Electrocardiogram showing resolution of arrhythmia and return to sinus rhythm.

tachycardia in patients with atrial arrhythmia and rapid ventricular rates may be mistaken for VT and treated inappropriately. Hence, concurrent use of atrioventricular nodal blocking agent (beta-blocker or calcium channel blocker) is often recommended with the use of these agents, especially in patients with atrial flutter as ventricular rate may rise rapidly during 1:1 atrioventricular conduction and subsequently may result in haemodynamic compromise. It is a common teaching that all wide complex tachycardia should be treated as VT. Hence, there is a very low threshold of externally cardioverting such rhythm, especially when patients are hemodynamically compromised. In our case, the patient was hemodynamically stable, and an awareness of use dependency and careful analysis of telemetry tracing could have prevented unnecessary attempts of cardioversion. The initial ECG (*Figure 1*) showed an irregular rhythm with two different QRS morphologies: an irregular narrow complex tachycardia at a rate of 150 b.p.m. (narrow arrows) and a 10-beat run of regular appearing wide QRS complex

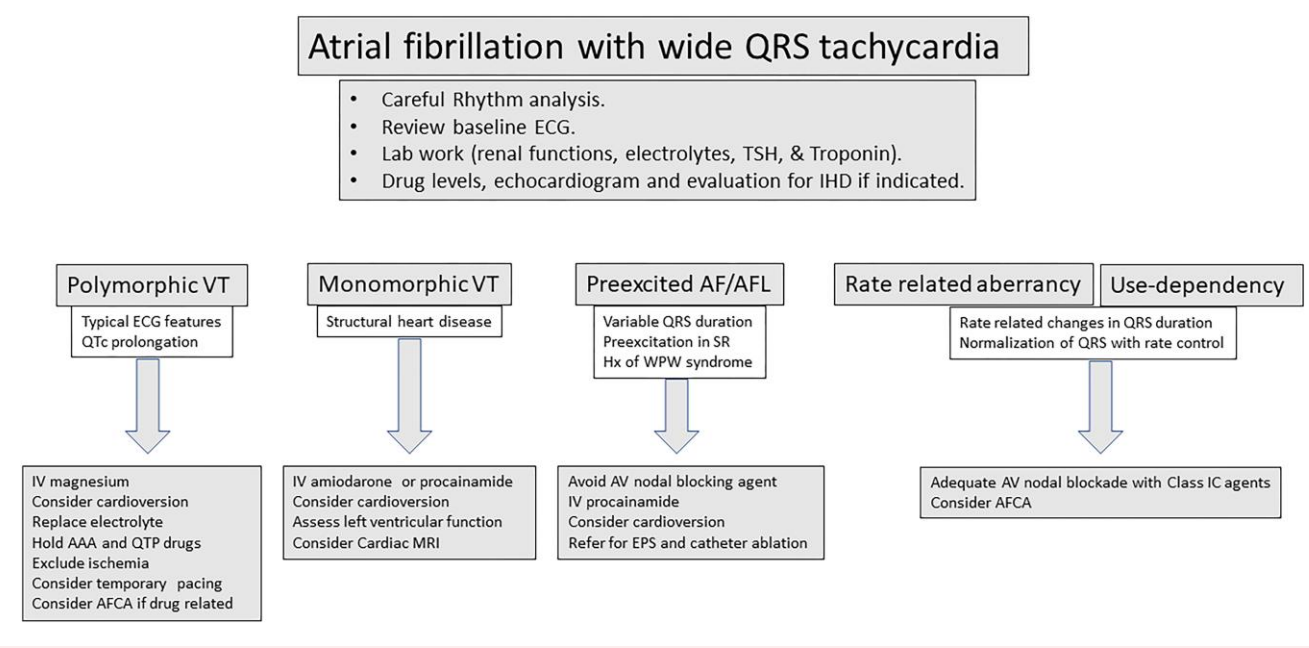


Figure 5 Flow chart summarizing the management of patients with wide QRS tachycardia in patients with atrial fibrillation. IHD, ischaemic heart disease; VT, ventricular tachycardia; AAA, antiarrhythmic agent; AFCA, atrial fibrillation catheter ablation; EPS, electrophysiology study; IV, intravenous; QTP, QR prolongation.

tachycardia at a rate of 186 b.p.m. (wide arrows). In a patient with AF and very rapid ventricular response, the QRS complexes may appear regular and may easily be mistaken for VT, but subtle variability can be appreciated by careful use of callipers. This rate-related variability in QRS duration in our case is best explained by 'use dependency' phenomenon of Flecainide; characterized by higher drug effect at faster heart rates (short cycle length or RR interval [RR]) due to enhanced availability and binding of the drug to the sodium channels. The effect of heart rate (cycle length) on QRS duration is best demonstrated in telemetry tracing (*Figure 3*). During slower heart rates (cycle length 460–480 ms), the QRS is narrow and during rapid heart rates (cycle length 380 ms) the QRS is wide. This effect completely resolved after adequate rate control was achieved with intravenous Diltiazem. Intravenous Amiodarone is a commonly used rate control agent, especially in patients with hypotension or intolerance to calcium channel and beta blockers. However, it may result in more sodium channel blockade, independent of Flecainide. One may argue about rate dependent aberrancy, commonly referred to as Ashman phenomenon, as a possible explanation of wide QRS during faster rates as in our patient. However, Ashman phenomena usually causes right bundle branch pattern, as opposed to the left bundle pattern seen in our patient. The shorter effective period of right bundle makes it more susceptible to conduction block during faster atrial rates and normal atrio-ventricle (AV) nodal conduction. However, that alone does not exclude with certainty the possibility of rate-related left bundle branch block pattern aberrancy in our patient. Administration of atrioventricular nodal blocking agents to decrease the ventricular rate will dissociate the drug from sodium channels in case of use dependency and peel back the refractoriness in the bundle branches in case of aberrancy and normalize QRS duration in both instances. Torsades due to QTc prolongation can easily be diagnosed by characteristic ECG findings. Torsades usually causes haemodynamic compromise and can be fatal. Hence, immediate restoration of rhythm may need cardioversion if intravenous magnesium fails. Discontinuation of antiarrhythmic agents and other drugs known to cause QT prolongation and replacing the electrolyte is the key to successful and sustained suppression of Torsades. Overdose due to antiarrhythmic should always be considered and excluded by checking serum drug levels. The possibility of Flecainide toxicity, although rare but potentially fatal, should always be kept in mind under such situations. This was excluded by normal serum Flecainide level in our case. Flecainide toxicity is associated with a mortality rate of 10%[4] due to profound hypotension from myocardial depression and, less often, malignant ventricular arrhythmias due to QT interval prolongation. Pre-excited AF should be suspected if QRS duration is variable including a normal QRS from intrinsic conduction among the broad QRS complexes. Evidence of pre-excitation on sinus rhythm ECG or known history of Wolf-Parkinson-White syndrome should raise the suspicion. One should be careful using AV nodal blocking agents in such situations, and Procainamide or even cardioversion should be considered to terminate the rhythm. Intermediate QRS morphology complex, a potential fusion beat, and QRS notching during wide QRS tachycardia, best appreciated in *Figure 3*, could be pointers towards VT. But structurally normal heart in our patient, variable RR interval and normalization of QRS with rate control would argue against VT. If the diagnosis of VT is strongly suspected and patient is hemodynamically compromised, immediate synchronized cardioversion should be performed, and appropriate work up started. Antiarrhythmic medications are limited by their moderate efficacy, intolerance, and side effects. Many patients receive a pacemaker for symptomatic bradycardia to facilitate the use of antiarrhythmic medications. Multiple randomized trials have demonstrated superiority of AF catheter ablation over medical therapy in terms of maintenance of sinus rhythm, reducing AF burden and improving symptoms and quality of life.[5] Hence, catheter ablation for AF has received Class I recommendation by both European Society of Cardiology and American Heart Associated/Heart Rhythm Society in patients with paroxysmal AF either as initial therapy or for those who fail antiarrhythmic drugs.[6,7] The management of patients with AF and wide QRS tachycardia is summarized in *Figure 5*.

Conclusion

In conclusion, wide complex tachycardia in patients with atrial arrhythmia should be managed as in those without atrial arrhythmia. Rate-dependency and aberrancy related wide QRS complex tachycardia in patent with AF may be mistaken for VT and treated inappropriately. Careful analysis of the rhythm and challenge with atrioventricular nodal blocking agent are useful tools to diagnose these phenomena. Concurrent use of atrioventricular nodal blocking agents especially in patient with atrial flutter is strongly recommended with Class IC antiarrhythmic agents.

Lead author biography

Dr. Mohammad Shaikh is an internal medicine physician-in-training at Mercy Health—St. Rita's Medical Center (OH, USA).

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Data availability

The data underlying this article are available in PUBMED and other search engines using https://www.ahajournals.org/doi/10.1161/CIR.0000000000001193.

References

1. Nattel S, Zeng FD. Frequency-dependent effects of antiarrhythmic drugs on action potential duration and refractoriness of canine cardiac purkinje fibers. *J Pharmacol Exp Ther* 1984;**229**:283–291.
2. Wang Z, Fermini B, Nattel S. Mechanism of flecainide's rate-dependent actions on action potential duration in canine atrial tissue. *J Pharmacol Exp Ther* 1993;**267**:575–581.
3. Padrini R, Piovan D, Busa M, Al-Bunni M, Maiolino P, Ferrari M. Pharmacodynamic variability of flecainide assessed by QRS changes. *Clin Pharmacol Ther* 1993;**53**:59–64.
4. Koppel C, Oberdisse U, Heinemeyer G. Clinical course and outcome in class 1C antiarrhythmic overdose. *J Toxicol Clin Toxicol* 1990;**28**:433–444.
5. Turagam MK, Musikantow D, Whang W, Koruth JS, Miller MA, Langan M-N, et al. Assessment of catheter ablation or antiarrhythmic drugs for first-line therapy of atrial fibrillation: a meta-analysis of randomized clinical trials. *JAMA Cardiol* 2021;**6**:697–705.
6. Joglar JA, Chung MK, Armbruster AL, Benjamin EJ, Chyou JY, Cronin EM, et al. 2023 ACC/AHA/ACCP/HRS guideline for the diagnosis and management of atrial fibrillation: a report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines. *Circulation* 2024;**149**:e1–e156.
7. Hindricks G, Potpara T, Dagres N, Arbelo E, Bax JJ, Blomström-Lundqvist C, et al. 2020 ESC guidelines for the diagnosis and management of atrial fibrillation developed in collaboration with the European Association for Cardio-Thoracic Surgery (EACTS). *Eur Heart J* 2021;**42**:373–498.