JACC: CASE REPORTS VOL. 2, NO. 4, 2020


EDITORIAL COMMENT

# The Unpaceable Heart

## Flecainide Toxicity?*

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In the paper by Nadel et al. (1) in this issue of *JACC: Case Reports*, the authors describe a case of flecainide toxicity manifested by cardiogenic shock and an "unpaceable heart" in a patient with a prior medical history of iatrogenic complete heart block with a permanent pacemaker in place. They discuss and exclude all potential causes of the unpaceable heart and conclude that flecainide toxicity was the most likely cause. After flecainide had been held and extracorporeal membrane oxygenation support provided, the cardiogenic shock and wide QRS interval, which was presumably ventricular tachycardia, resolved, and the patient's intrinsic narrow QRS junctional rhythm returned with normalization of left ventricular size on echocardiogram.

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The authors discuss the electrophysiological basis for flecainide toxicity (i.e., excessive blockade of the rapid sodium channel of phase 0 of the action potential [upstroke] and inhibition of the slow calcium channels). Flecainide is also known to inhibit ryanodine receptor 2, a major regulator of sarcoplasmic release of stored calcium ions, which may have contributed to myocardial depression of contractility (2). Presumably, despite normal renal function, the significant low cardiac output during the wide QRS interval, which was thought to be ventricular tachycardia, could have resulted in elevated flecainide serum levels. The authors do not mention whether it was ever determined if the patient had taken an overdose of flecainide but do note that the serum flecainide levels were markedly elevated at >3 times the therapeutic levels and had obtained psychiatric evaluation before discharge (3).

In general, as CAST (Cardiac Arrhythmia Suppression Trial) demonstrated, both flecainide and encainide can result in a wide QRS interval and incessant ventricular tachycardias with hemodynamic compromise in patients with depressed left ventricular function (4). In addition, there are multiple reports in the literature of flecainide resulting in ventricular tachycardia, hemodynamic compromise, and elevation of pacing thresholds (5,6). Because these antiarrhythmics have been around since the 1970s, plenty of data on their use exist. Importantly, toxicity associated with flecainide can happen both acutely and with chronic use. In regard to its effect on left ventricular function, Santinelli et al. (7) tested the acute effects of intravenous flecainide in humans and noted a small proportion (2/40 patients) had a marked drop in left ventricular systolic function immediately after receiving flecainide with a drop in left ventricular ejection fraction to 35% and 40% from 65% and 55%, respectively. It is for this reason that when flecainide is prescribed for a patient with a structurally normal heart, exercise treadmill testing is usually done to assess for QRS widening >25% from baseline, given flecainide's heart rate-dependent binding to sodium channels (8).

What is unusual in this case report is that it appears that their patient had normal left ventricular function (i.e., normal left ventricular ejection fraction) and endomyocardial biopsy. However, there is no mention as to whether the patient took an overdose of flecainide and whether the patient had right

*Editorials published in *JACC: Case Reports* reflect the views of the authors and do not necessarily represent the views of *JACC: Case Reports* or the American College of Cardiology.

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The authors attest they are in compliance with human studies committees and animal welfare regulations of the authors' institutions and Food and Drug Administration guidelines, including patient consent where appropriate. For more information, visit the *JACC: Case Reports* author instructions page.

ISSN 2666-0849 https://doi.org/10.1016/j.jaccas.2020.03.003

ventricular pacing-induced cardiomyopathy because the patient's echocardiogram revealed a dilated right ventricle.

The authors deserve credit for their description of the potential causes and mechanisms of flecainide toxicity by their comprehensive exclusion of most other etiologies of this constellation of clinical findings. They also highlight the reversibility of flecainide toxicity by aggressive hemodynamic support of the patient with extracorporeal membrane oxygenation, sodium bicarbonate, and lidocaine (9). The paper also highlights the need to avoid the use of flecainide in any patient with cardiomyopathy and known coronary artery disease.

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**KEY WORDS** cardiogenic shock, flecainide toxicity