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Case Report

# Brugada pattern exposed with administration of amiodarone during emergent treatment of ventricular tachycardia☆

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ABSTRACT

*Background:* Brugada pattern is a well-known pathological finding on electrocardiogram (ECG) which increases the likelihood of cardiac arrest due to ventricular arrhythmia. These cases generally present in younger patients without evidence of an electrolyte abnormality, structural heart disease, or cardiac ischemia. In many instances, this pattern is either hidden on initial presentation or presents as an incidental finding on an EKG. Often times the Brugada syndrome leads to sudden cardiac death or more rarely can be unmasked with a class 1A or 1C anti-arrhythmic agent. Here, we present a distinctive case in which the pattern was exposed by amiodarone during the emergent treatment of Ventricular Tachycardia (VT).

*Case report:* A 34-year-old female, without significant cardiac history, presented to the Emergency Department after multiple near syncopal episodes at home. Initial ECG showed VT vs. SVT. After a failed trial of adenosine, the patient was treated with 150 mg amiodarone and became hypotensive needing an electrical cardioversion. After becoming bradycardic, the amiodarone drip was discontinued and she was admitted to the MICU. An echocardiogram and left heart catheterization showed no evidence of coronary artery disease or decreased ejection fraction. The patient's ECG now showed a subtle Brugada Type 3 pattern and she received a dual chamber AICD upon discharge.

*Conclusion:* This case emphasizes the awareness needed to seek out this pattern on subsequent ECG's. With the high lethality of Brugada, the emergency physician must recognize that multiple drugs can evoke this pattern after initial presentation.

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## 1. Introduction

In the absence of structural heart disease, cardiac ischemia or electrolyte abnormality, the Brugada pattern predisposes individuals to ventricular arrhythmias and cardiac arrest [1-3]. The typical Brugada electrocardiogram (ECG) pattern is most often veiled until class IA or IC anti-arrhythmic agent, such as flecainide, or procainamide, are used to unmask characteristic features of the well-known ECG phenotypes [4-7]. Reports of drug-induced Brugada pattern from non-class IA and IC agents have been well documented, however, we report a peculiar case of Brugada 'unmasking' during emergent treatment of refractory, stable, wide complex ventricular tachydysrhythmia in the Emergency Department. To our knowledge, there have only been three case reports of Brugada unmasking by amiodarone [4,8]. However, in contrast to the three prior reports, our case is unique as it is the first reported case of Brugada unmasking in a patient treated for VT in both the emergent setting and the emergency literature.

## 2. Case report

A 34-year-old female, without significant past medical history, illicit drug use, nor on any medications presented in stable ventricular tachycardia (VT). She was without provoking factors, prior family history of arrhythmias or sudden cardiac death. Earlier in the day, the patient experienced multiple near-syncopal episodes while mowing her lawn, prompting her emergency room visit. Upon arrival from an outside hospital, the patient was tachycardic, but normotensive and mentating well. Initial ECG (Fig. 1a) showed a wide complex tachycardia at a rate of approximately 150beats/min. The differential at the time included VT and supraventricular tachycardia with aberrancy. Of note, at the outside hospital, her basic metabolic panel was without abnormality. Adenosine was attempted by ACLS standard dosing, and a rhythm change was not detected. Thus, the patient was given an amiodarone bolus of 150 mg, followed by an amiodarone infusion at 1 mg/min. Amiodarone was given per normal ACLS recommendations, and was chosen as it was the most readily available drug. Cardiology was not immediately available for consult. Within 10 min of amiodarone dosing the patient became increasingly hypotensive, and was subsequently electrically cardioverted (Fig. 1b) using fentanyl and etomidate for sedation. The patient was then continued on an amiodarone drip, but developed

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significant bradycardia with a new, atypical Mobitz II second degree heart block, and additional features of Brugada syndrome in the anterior leads (Fig. 1c). The amiodarone drip was immediately discontinued and a single dose of atropine was given for a heart rate in the mid 30's. The patient stabilized and was admitted to the Intensive Care Unit where she continued to have marked bradycardia in the 50's, junctional beats, and a second-degree AV block. Diagnostic Cardiac Ultrasound (ECHO) indicated no significant structural heart disease, except for moderate mitral regurgitation. Left Heart Cardiac Catherization (LHC) illustrated a normal left ventricular ejection fraction and was without any coronary artery disease. However, during programmed ventricular stimulation by the electrophysiologist, the patient was found to have easily inducible ventricular tachycardia, which was refractory to overdrive pacing, and required defibrillation to restore sinus rhythm.

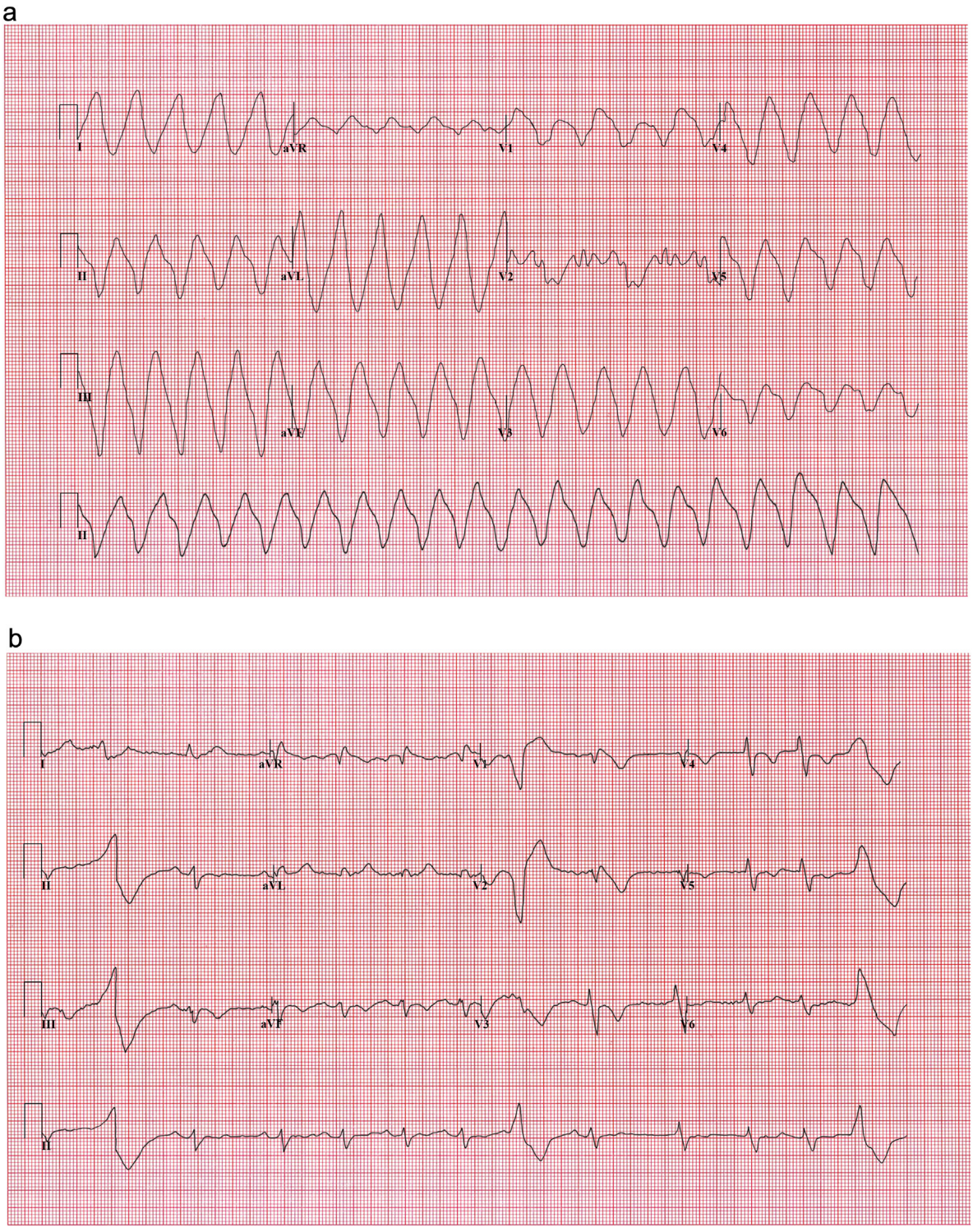


**Fig. 1.** a: Initial presenting ECG. Used with permission by Jason Ausman, MD. b: ECG status-post electrical cardioversion. Used with permission by Jason Ausman, MD. c: ECG status-post amiodarone infusion. Used with permission by Jason Ausman, MD. d: ECG at discharge. Used with permission by Jason Ausman, MD.

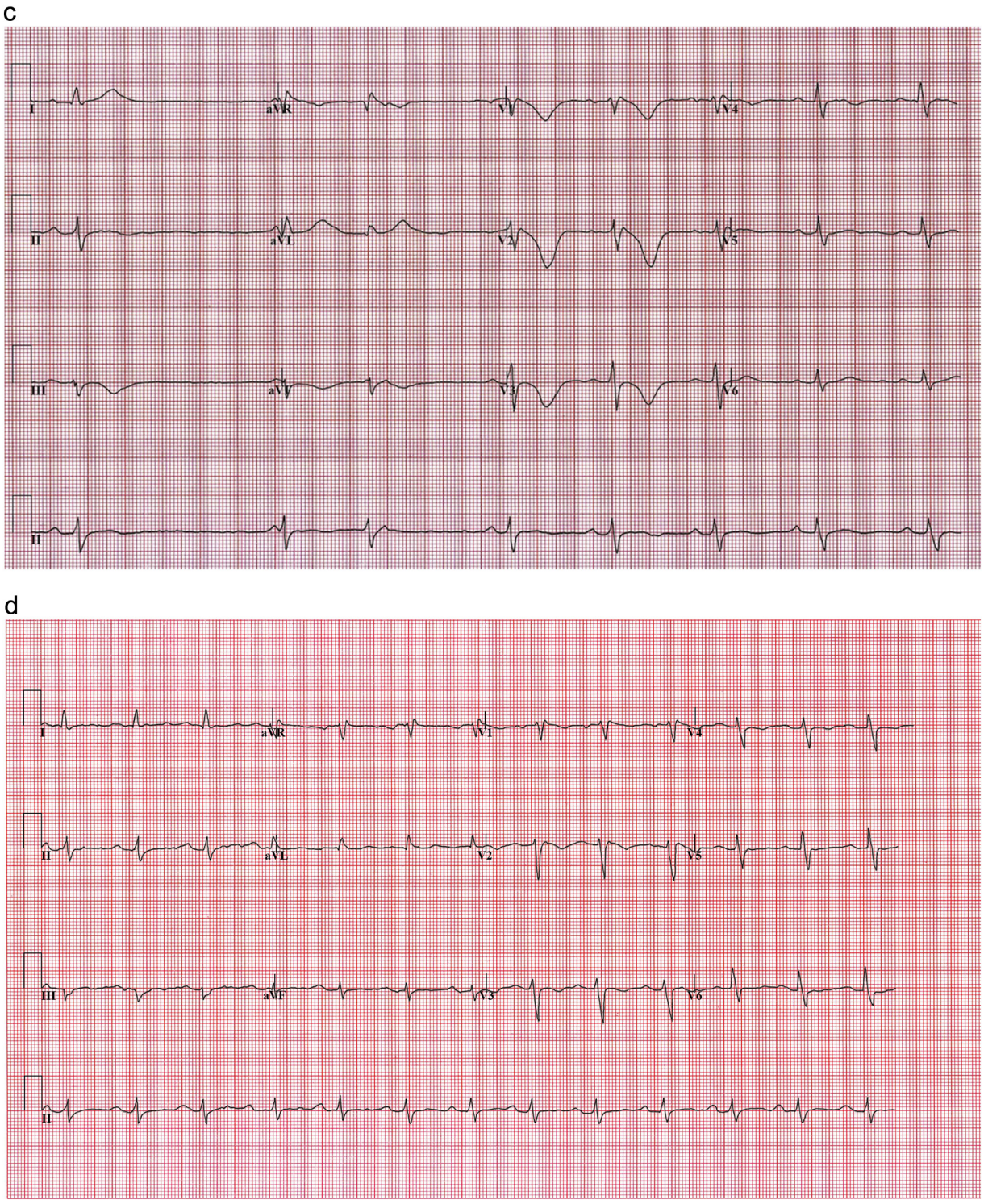


**Fig. 1** (*continued*).

Subsequently, the patient received a dual chamber AICD, and was discharged from the hospital with an EKG demonstrating incomplete right bundle branch pattern, and a subtle type III Brugada phenotype (Fig. 1d).

## 3. Discussion

Brugada syndrome (BS) was originally described by the Spanish cardiologists Pedro and Joseph Brugada in 1992 [3,9]. It is a now well-recognized sodium channelopathy that has a high association with sudden cardiac death (SCD), is found mainly in men with a mean age of 40, and has a higher incidence in southeast Asia [1,10-12]. Although less common, Brugada syndrome is known to present in infants and children, especially in the presence of fever, and has become a consideration in sudden infant death syndrome [13,14].

In those individuals with structurally normal hearts, BS is suggested as a leading cause of SCD, causing approximately 20% of these deaths, and accounting for 4% of all sudden death events [3,13]. Mutations in

the SCN5A gene leading to a loss of function of the cardiac sodium channel has been quoted as the most common genotype found among patients; and subsequently almost 300 mutations in SCN5A have been found to be associated with Brugada syndrome [11,15-17]. Although sodium channelopathy is often quoted in the literature, inward calcium and outward potassium channels have been suggested as culprits. This potentially explains how non sodium channel acting agents unmask the phenotype [18]. Additionally, there have been increasing reports of non-class IA and IC drug-induced Brugada patterns; specifically, with lithium, cocaine, carbamazepine, tricyclic antidepressants, propofol, amiodarone, fluoxetine and valproic acid [19-22].

As in our described case, the typical Brugada ECG phenotype is often concealed in an affected individual [10]. Often, sodium channel blocking pharmacologic agents such as amiodarone or flecainide, are required to uncover the potentially malignant ECG findings [4-7,23]. Although, as in most cases the exact mechanism of Brugada unmasking in this case remains unclear.

Due to the morbidity and mortality associated with this disease process, identifying the presence of Brugada patterns on ECG is of vital importance for the emergency medicine physician. In order to make the diagnosis one should recognize the various ECG phenotypes of Brugada pattern (Fig. 2). Of note, type 1 is the only truly diagnostic ECG pattern, as the type 1 ECG pattern has been shown to have the highest incidence of arrhythmia and mortality in comparison to type 2 or type 3 patterns [22,24]. Once the ECG pattern is recognized and depending on the clinical picture of the patient, treatment and disposition are the emergency medicine physician's next course of action.

It has been documented that the strongest predictor of poor outcome in patients with an ECG diagnostic of Brugada pattern without previous cardiac arrest history, is inducibility during programmed ventricular stimulation [3]. Brugada et al. noted that inducible individuals have 6 times the risk of experiencing sudden death or ventricular fibrillation compared with non-inducible individuals [3]. Unfortunately, this is not information usually available in the acute setting. Other important historical features for risk stratification are those who are asymptomatic, with a type I pattern, and with a positive family history of SCD; as they are higher risk. These individuals are recommended to undergo electrophysiologic studies (EPS), and thus require expert consultation [22,24,25]. Although consultants will vary on their management of the asymptomatic patient, there is strong agreement on current management guidelines for symptomatic patients [26]. All symptomatic type 1 patients should receive EPS and an ICD, a current ESC class I recommendation [25,27]. After Brugada phenotype pattern recognition, the most important aspect for the emergency physician is the acute management of symptomatic patients.

The most well studied treatment for Brugada induced ventricular arrhythmias appears to be quinidine. This drug has been shown to both suppress VF and spontaneous ventricular tachyarrhythmias in Brugada syndrome [2]. Additionally, a large European study has shown that the frequency of ICD shocks in patients with Brugada syndrome with implantable devices is statistically and clinically lower when patients take Quinidine daily [28]. Although these results are procured during outpatient management of this syndrome the data is consistent and this drug represents a likely adjunct for emergent treatment. From the emergency medicine and critical care perspective, there are several reports of quinidine use in the case of electrical storm in a Brugada patient. In these cases, quinidine was combined with a sympathomimetic, such as isoproterenol. The rationale of the addition of a sympathomimetic agent is due to the ability of these agents to normalize the aberrant membrane conductance. A study by Jongman et al. in 2007 demonstrated attenuation of refractory electrical storm in Brugada with an isoproterenol infusion (0.5 μg/min) coupled with oral quinidine sulfate (400 mg TID) [29]. Another case report described similar treatment success in a patient who experienced 63 episodes of ventricular fibrillation refractory to multiple medications and electrical cardioversion during an electrical storm in the emergency department. This patient successfully terminated his electrical storm after isoproterenol infusion (0.5 μg/min) followed by oral quinidine (324 mg Q 8 h) [30]. Although there are few case studies describing the efficacy of IV isoproterenol

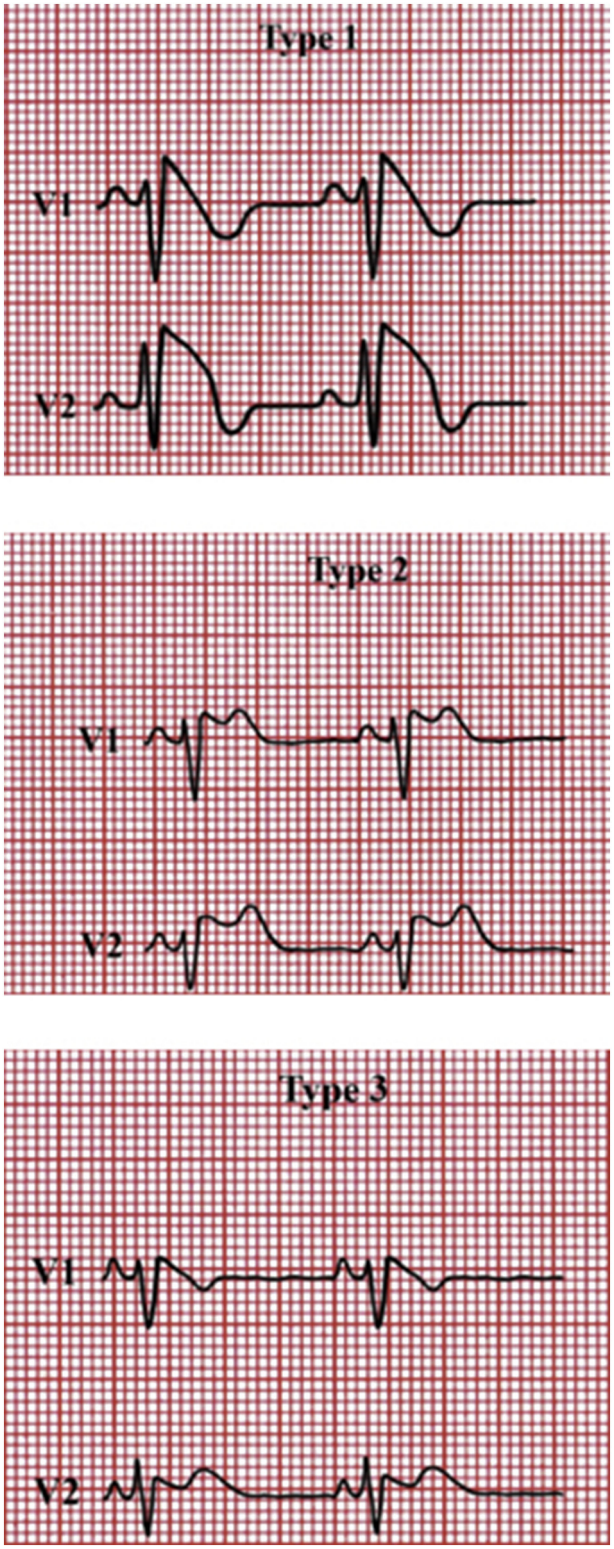


**Fig. 2.** Examples of Brugada type patterns I-III. Top: Type I – "Coved" ST elevations in right precordial leads (V1–3) >2 mm followed by an abrupt T-wave inversion. Middle: Type II – "Saddleback" ST elevation as above the first part of the T wave has an abrupt elevation >2 mm above baseline. Bottom: Type III – "Mixed Pattern" these may be either saddleback or cove but the elevation is no >1 mm above baseline. Used with permission by Jason Ausman, MD.

followed by oral quinidine therapy for VF or VT storm in Brugada patients, these studies all show positive results in either termination of arrhythmia or decreasing the frequency of arrhythmia in Brugada syndrome patients [30]. Additionally, the use of quinidine alone or in combination with isoproterenol is well described in the electrophysiology (EP) literature as a method to control electrical storm in Brugada syndrome [29]. Although the use of an oral medication in an emergent condition such as Brugada associated electrical storm may seem suboptimal, the literature seems to suggest that Brugada induced electrical storm may recur rapidly after cessation of the isoproterenol infusion and that addition of quinidine decreases the recurrence of electrical storm once the infusion is stopped. Given this information and the available evidence, those with suspected Brugada syndrome in refractory ventricular tachycardia, especially those who are refractory to or worsened by standard ACLS medications, a reasonable alternative treatment would be IV isoproterenol coupled with oral quinidine if available [18]. The complexity of this treatment decision, however, necessitates expert consultation should it be available.

## 4. Conclusion

For the emergency physician, this case illustrates the critical importance of Brugada ECG phenotype recognition. Additionally, the emergency physician should consider the possibility of covert Brugada syndrome when there is clinical deterioration, especially in a younger patient with ventricular tachycardia, that does not follow a predicted course after use of anti-arrhythmic medications. Lastly, in cases refractory to or elicited by standard ACLS medications or those refractory to electrical cardioversion, evidence suggests that IV isoproterenol coupled with oral quinidine is a reasonable alternative treatment for the EM physician.

## Conflicts of interest

None.

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