



Clinical Communications: OB/GYN

EPINEPHRINE ADMINISTERED FOR ANAPHYLAXIS UNMASKING A TYPE 1 BRUGADA PATTERN ON ELECTROCARDIOGRAM

Peter V. Bui, MD, Nathan L. Haas, MD, Nicholas W. C. Herrman, MD, Matthew Macias, MD, Victoria Hoch, MD, William Schaeffer, DO, and Christopher Wallace, MD

Department of Emergency Medicine, University of Michigan, Ann Arbor, Michigan

Reprint Address: Nathan L. Haas, MD, University of Michigan, Taubman Center B1354, 1500 E Medical Center Drive, SPC 5303, Ann Arbor, MI 48109-5305

Abstract—Background: Brugada pattern on electrocardiography (ECG) can manifest as type 1 (coved pattern) and type 2 (saddleback pattern). Brugada syndrome represents an ECG with Brugada pattern in a patient with symptoms or clinical factors, including syncope, cardiac arrest, ventricular dysrhythmias, and family history. Brugada syndrome is caused by a genetic channelopathy, but the Brugada pattern may be drug-induced. Epinephrine-induced Brugada pattern has not been reported previously. **Case Report:** A 63-year-old man developed anaphylaxis secondary to a bee sting, had a transient loss of consciousness, and self-administered intramuscular epinephrine. He subsequently presented to the emergency department and was found to have a type 1 Brugada pattern on ECG that resolved during observation. A historic ECG was reviewed that demonstrated a baseline type 2 Brugada pattern. His anaphylaxis was managed with steroids and antihistamines. He was observed without subsequent dysrhythmic events on telemetry or any further symptoms. **Why Should an Emergency Physician Be Aware of This?:** The differential diagnosis for syncope includes dysrhythmia, such as Brugada syndrome. Among other possible drugs, epinephrine may induce a type 1 Brugada pattern. Patients with Brugada pattern on ECG should be referred immediately to electrophysiology for consideration of implantation of a cardioverter-defibrillator device, given the association of Brugada pattern with sudden cardiac arrest and ventricular dysrhythmias. © 2018 Elsevier Inc. All rights reserved.

Keywords—Brugada syndrome; Brugada pattern; electrocardiography; syncope; anaphylaxis

INTRODUCTION

In 1992, Brugada et al. described a pattern on electrocardiography (ECG) associated with sudden cardiac death (1). Three Brugada patterns were initially described, but were later modified to type 1 (coved pattern) and type 2 (saddleback pattern), although the medical literature may still refer to all three types (2,3). Diagnostic criteria for Brugada syndrome were established in 2002 (2). The most recent diagnostic criteria for Brugada pattern require ST-segment elevation with type 1 morphology ≥ 2 mm in leads V1 or V2 positioned in the second, third, or fourth intercostal space, occurring either spontaneously or after provocative drug test with i.v. administration of class I antidysrhythmic drugs (typically sodium channel blockers) (4,5).

A clinical distinction may be made between the Brugada pattern, an ECG with Brugada morphology in a patient without symptoms or clinical factors, and the Brugada syndrome, an ECG with Brugada morphology in a patient with symptoms or clinical factors (2,3,6). Clinical factors include but are not limited to syncope, cardiac arrest, ventricular dysrhythmias, and family history. Brugada syndrome is a result of a cardiac channelopathy involving sodium, calcium, and potassium channels, with an autosomal dominant inheritance pattern (7). In a study of patients with implantable cardioverter-defibrillators (ICDs) for

primary and secondary prevention in Brugada syndrome, approximately 20% experienced appropriate shocks for ventricular dysrhythmias during the roughly 2-decade study period (8).

The Brugada pattern may be drug-induced, and as the underlying pathology relates to a channelopathy, pharmaceutical agents, and antidysrhythmic medications in particular, can induce and thereby diagnose Brugada syndrome (9). Prior to Brugada syndrome being described, the Cardiac Arrhythmia Suppression trial performed in 1991 showed flecainide and encainide (sodium channel blockers) increased antidysrhythmic deaths in patients who had suffered myocardial infarctions, which may have been due to unmasking of Brugada syndrome (10,11).

Postema et al. compiled a list of drugs that may be pro-dysrhythmic in patients with Brugada syndrome (12). While these drugs fall into several disparate categories, the mechanism is postulated to be the effect of the drug or its metabolites on ion channels (13). β -blockers, tricyclic antidepressants, neuroleptics, propafenone, and lithium have been linked with unmasking Brugada syndrome previously. In addition to pharmaceutical agents, non-medication etiologies of unmasking Brugada syndrome have been reported, including fever, hypokalemia, hyperkalemia, hypercalcemia, alcohol, and cocaine (6,9,14–17). In a study of 18 patients with unexplained cardiac arrest, infusion of epinephrine was not associated with a Brugada pattern (18). In our review of the medical literature, we were unable to find a case of epinephrine-induced Brugada pattern.

We describe a case of a male patient with baseline type 2 Brugada pattern who was found to have a transient type 1 Brugada pattern following intramuscular epinephrine administration for anaphylaxis.

CASE REPORT

A 63-year-old man with a history of ankylosing spondylitis, allergy to bees, and no other medical problems presented to the emergency department (ED) with anaphylaxis and syncope. He was stung by a bee in the left foot and shortly thereafter developed a sensation of throat scratching, swelling inside his mouth, nausea, and lightheadedness. After administering 0.3 mg of intramuscular epinephrine, his symptoms resolved. He subsequently called emergency medical services. He reported that he experienced three consecutive transient episodes of loss of consciousness after administering the epinephrine. He had no prior episodes of syncope and did not have a family history of early or unexplained cardiac death. He did not experience chest pain, shortness of breath, or any other symptoms prior to presentation to the ED.

On arrival to the ED, vital signs were temperature 36.7°C, blood pressure 164/93 mm Hg, heart rate was 75 beats/min, respiratory rate was 18 breaths/min, and oxygen saturation 99% on room air. On physical examination, he appeared well, had no mucosal edema, stridor, or wheezing, and had a normal cardiopulmonary examination without murmurs. His anaphylaxis resolved following further management with corticosteroids and antihistamines. An ECG demonstrated a type 1 Brugada pattern (Figure 1). A subsequent ECG several hours later demonstrated resolution of the type 1 Brugada pattern (Figure 2). An ECG from 7 years earlier was consistent with a baseline type 2 Brugada pattern (Figure 3). He was admitted for observation and telemetry and did not have additional dysrhythmias. He was evaluated by electrophysiology the following morning.

Electrophysiology ultimately attributed his unresponsiveness to anaphylaxis and not to dysrhythmic syncope, and it was recommended that placement of an ICD was not indicated. He was subsequently discharged with planned outpatient electrophysiology follow-up and was advised to have his first-degree relatives screened with ECGs for Brugada pattern.

DISCUSSION

We present the first reported case of an epinephrine-induced type 1 Brugada pattern in a patient with a baseline type 2 Brugada pattern in the setting of anaphylaxis to a bee sting.

The mechanism for epinephrine-induced Brugada pattern is unclear, but may be related to the adrenergic and sympathomimetic effects, based on previously

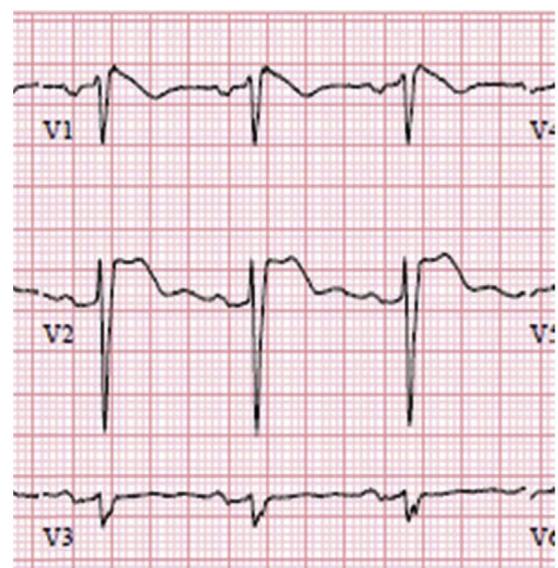


Figure 1. Electrocardiogram on arrival to the emergency department demonstrating a type 1 Brugada pattern.

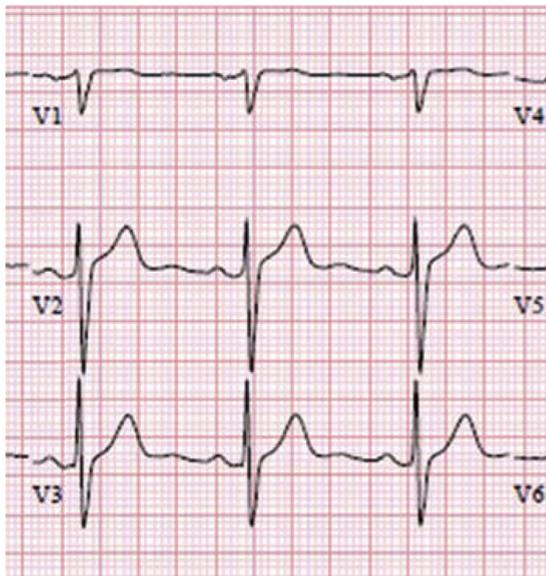


Figure 2. Electrocardiogram several hours later demonstrating resolution of the type 1 Brugada pattern.

published case reports of drugs with similar mechanisms. Leiria et al. previously proposed that the sudden increase in vagal tone once the adrenergic effects of brompheniramine and phenylephrine had worn off may have caused a drug-induced Brugada pattern (19). In a case report of cocaine-induced Brugada morphology, Alraies et al. suggested that the mechanism may be related to sodium channel blocking effects, sympathomimetic effects leading to increased ventricular irritability and decreased fibrillation threshold, decreased vagal activity promoting sympathomimetic effects, and afterdepolarization and triggered ventricular dysrhythmias caused by increased intracel-

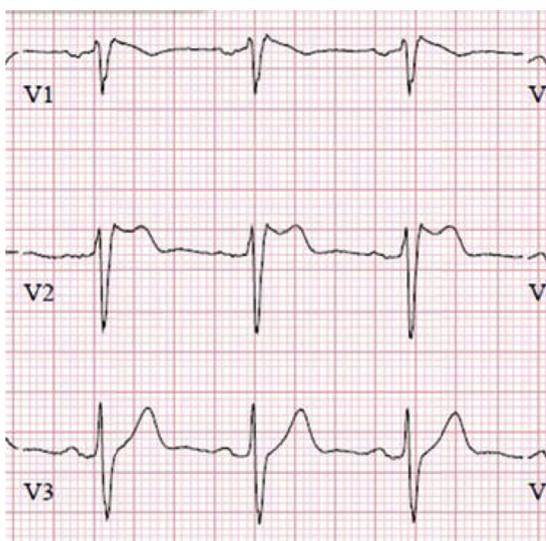


Figure 3. Historic electrocardiogram from 7 years prior demonstrating baseline type 2 Brugada pattern.

lular calcium (20). Similarly, Littman et al. described a case of cocaine-induced Brugada pattern (21).

Given the limited available data, we hypothesize that the adrenergic effects of epinephrine or its metabolites, or the subsequent sudden increase in vagal tone as they were degraded, may have led to the type 1 Brugada pattern on ECG through an ion channel-related mechanism.

WHY SHOULD AN EMERGENCY PHYSICIAN BE AWARE OF THIS?

An ECG with Brugada pattern is a relevant finding in the setting of syncope because of the possible short-term and long-term management and mortality implications. Channelopathies, including Brugada syndrome, are an important contributor to patients presenting with sudden cardiac arrest. We describe the first case of epinephrine inducing a transient type 1 Brugada pattern. Patients with Brugada pattern on ECG should be referred immediately to electrophysiology for consideration of implantation of an ICD, given the association of Brugada pattern with sudden cardiac arrest and ventricular dysrhythmias.

REFERENCES

1. Brugada P, Brugada J. Right bundle branch block, persistent ST segment elevation and sudden cardiac death: a distinct clinical and electrocardiographic syndrome. A multicenter report. *J Am Coll Cardiol* 1992;20:1391–6.
2. Wilde AA, Antzelevitch C, Borggrefe M, et al. Proposed diagnostic criteria for the Brugada syndrome: consensus report. *Circulation* 2002;106:2514–9.
3. Bayés de Luna A, Brugada J, Baranchuk A, et al. Current electrocardiographic criteria for diagnosis of Brugada pattern: a consensus report. *J Electrocardiol* 2012;45:433–42.
4. Priori SG, Wilde AA, Horie M, et al. HRS/EHRA/APHRS expert consensus statement on the diagnosis and management of patients with inherited primary arrhythmia syndromes: document endorsed by HRS, EHRA, and APHRS in May 2013 and by ACCF, AHA, PACES, and AEPIC in June 2013. *Heart Rhythm* 2013;10:1932–63.
5. Priori SG, Blomström-Lundqvist C, Mazzanti A, et al., ESC Scientific Document Group. 2015 ESC guidelines for the management of patients with ventricular arrhythmias and the prevention of sudden cardiac death: the task force for the management of patients with ventricular arrhythmias and the prevention of sudden cardiac death of the European Society of Cardiology (ESC). Endorsed by: Association for European Paediatric and Congenital Cardiology (AEPIC). *Eur Heart J* 2015;36:2793–867.
6. Antzelevitch C, Brugada P, Borggrefe M, et al. Brugada syndrome: report of the second consensus conference: endorsed by the Heart Rhythm Society and the European Heart Rhythm Association. *Circulation* 2005;111:659–70.
7. Sarquella-Brugada G, Campuzano O, Arbelo E, Brugada J, Brugada R. Brugada syndrome: clinical and genetic findings. *Genet Med* 2016;18:3–12.
8. Hernandez-Ojeda J, Arbelo E, Borrás R, et al. Patients with Brugada syndrome and implanted cardioverter-defibrillators: long-term follow-up. *J Am Coll Cardiol* 2017;70:1991–2002.
9. Minoura Y, Kobayashi Y, Antzelevitch C. Drug-induced Brugada syndrome. *J Arrhythm* 2013;29:88–95.
10. Echt DS, Liebson PR, Mitchell LB, et al. CAST Investigators. Mortality and morbidity in patients receiving encainide, flecainide, or

- placebo. The Cardiac Arrhythmia Suppression Trial. *N Engl J Med* 1991;324:781–8.
11. Konigstein M, Rosso R, Topaz G, et al. Drug-induced Brugada syndrome: clinical characteristics and risk factors. *Heart Rhythm* 2016; 13:1083–7.
 12. Postema PG, Wolpert C, Amin AS, et al. Drugs and Brugada syndrome patients: review of the literature, recommendations, and an up-to-date website (www.brugadadrugs.org). *Heart Rhythm* 2009; 6:1335–41.
 13. Yap YG, Behr ER, Camm AJ. Drug-induced Brugada syndrome. *Europace* 2009;11:989–94.
 14. Piroette MJ, Mueller JG, Poprawski T. A case report of Brugada-type electrocardiographic changes in a patient taking lithium. *Am J Emerg Med* 2008;26:113.e1–3.
 15. Aksay E, Okan T, Yanturali S. Brugada syndrome, manifested by propafenone induced ST segment elevation. *Emerg Med J* 2005; 22:748–50.
 16. Unlu M, Bengi F, Amasyali B, Kose S. Brugada-like electrocardiographic changes induced by fever. *Emerg Med J* 2007;24(1):e4.
 17. Berbata VS, Summers S. Brugada electrocardiographic pattern induced by cocaine toxicity. *Ann Emerg Med* 2007;49:827–9.
 18. Krahn AD, Gollob M, Yee R, et al. Diagnosis of unexplained cardiac arrest: role of adrenaline and procainamide infusion. *Circulation* 2005;112:2228–34.
 19. Leiria TL, Mantovani A, de March Ronsoni R, Martins Pires L, Lapa Kruse M, Glotz de Lima G. Brugada syndrome after using cold medicine: is there any relation? *Rev Port Cardiol* 2013;32: 415–7.
 20. Alraies MC, Chamsi-Pasha MA, Baibars M, Alraiyes AH, Shaheen K. Brugada pattern electrocardiogram unmasked with cocaine ingestion. *Case Rep Cardiol* 2013;2013:704859.
 21. Littmann L, Monroe MH, Svenson RH. Brugada-type electrocardiographic pattern induced by cocaine. *Mayo Clin Proc* 2000;75: 845–9.