Brugada Phenocopy: A Case of Incessant Ventricular Tachycardia in a Patient with Tricyclic Antidepressant Overdose

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ABSTRACT: Brugada electrocardiographic pattern, or Brugada phenocopy (BrP), can be found in conditions other than Brugada syndrome. We present the case of a 34-year-old woman who was found convulsing at home followed by ventricular tachycardia (VT) cardiac arrest upon arrival to the emergency department. Electrical direct cardioversion led to a return of spontaneous circulation, and she was started on intravenous amiodarone. The patient had four additional episodes of pulseless VT that returned to sinus rhythm with electrical cardioversion. A subsequent electrocardiogram taken in sinus rhythm revealed a right bundle branch block pattern with a coved ST segment elevation and inverted T waves in leads V1 and V2, suggestive of BrP type 1. Further inquiry revealed that an empty bottle of nortriptyline was found at her home. Nortriptyline intoxication was subsequently confirmed by a serum level of 1581 ng/mL. Treatments with intravenous sodium bicarbonate resolved the BrP, and she fully recovered with supportive care.

Intoxication with drugs that inhibit cardiac sodium channels, such as nortriptyline, can trigger a BrP in otherwise normal individuals. Nortriptyline and other tricyclic antidepressants (TCAs) are used to treat chronic pain, depression, and other conditions but have dose-related side effects and can lead to fatal overdose. Intoxication by these TCAs should be on the differential when a BrP is observed.

INTRODUCTION

Brugada phenocopy (BrP) is a clinical entity similar in presentation to a true congenital Brugada syndrome (BrS) yet etiologically distinct. It is defined by electrocardiographic (ECG) patterns identical to BrS (both type 1 and 2) but provoked by various clinical circumstances, usually myocardial ischemia or metabolic derangement. ECG changes in BrP resolve after the underlying cause is treated. Compared with patients with BrS, those with BrP have an acquired sodium channel dysfunction, evidenced by a negative sodium channel blocker challenge test once the insult is resolved.[1]

According to the international database of BrP, there are more than 130 cases of BrP recognized in medical literature.[2] Among others, tricyclic antidepressant (TCA) poisoning is recognized as a rare cause of BrP secondary to severe sodium channel blockade presenting as BrP type 1.[3] We report a case of incessant ventricular tachycardia in a patient with TCA overdose and Brugada-like ECG manifestations.

CASE PRESENTATION

A 34-year-old female with a history of hypertension and bipolar disorder was found convulsing at home. Upon arrival to the emergency department (ED), the patient had a tonic-clonic seizure and was intubated for airway protection. She was febrile (38.8°C), tachycardic (heart rate of 140 bpm), tachypneic (respiratory rate of 25 rpm), and mildly hypertensive (blood pressure of 139/77 mm Hg). Blood work done before intubation revealed metabolic and respiratory acidosis (pH of 6.94, pCO_2 of 74 mm Hg, pO_2 of 33 mm Hg, bicarbonate of 16 mmol/L in venous blood gases) with a lactate level > 15 mmol/L. The patient initially was treated with 50 mEq of sodium bicarbonate and normal saline. However, 15 minutes after the intubation, she had a pulseless polymorphic ventricular tachycardia (VT) that required cardiopulmonary resuscitation and electrical cardioversion with 200 J (Figure 1).[4] Although her pulse recovered, she went on to have four additional episodes of pulseless VT, each lasting around 5 minutes. She was managed according to the advanced cardiac life support protocol and was started on intravenous amiodarone infusion. A subsequent ECG in sinus rhythm revealed a right bundle branch block pattern with a coved ST-segment elevation and inverted T waves in leads V1 and V2, suggestive of BrP type 1 (Figure 2).[4] Repeated venous blood gases showed correction of acidemia (pH of 7.35; pCO_2 of 50 mm Hg, pO_2 of 46 mm Hg, bicarbonate of 28 mmol/L) and lactate of 6.5 mmol/L.

Further evaluation revealed a history of empty bottles of alprazolam and nortriptyline found by her side at home. She had no suicide attempts before this episode, and her family members

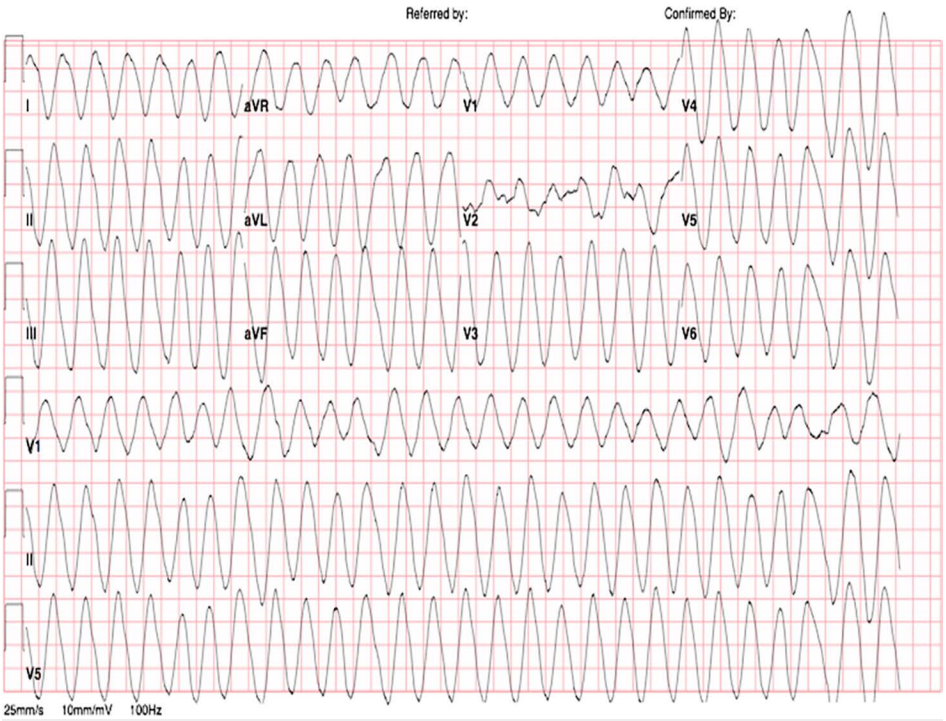

Figure 1.
Electrocardiogram showing polymorphic ventricular tachycardia.[4] Reprinted with permission from Elsevier.

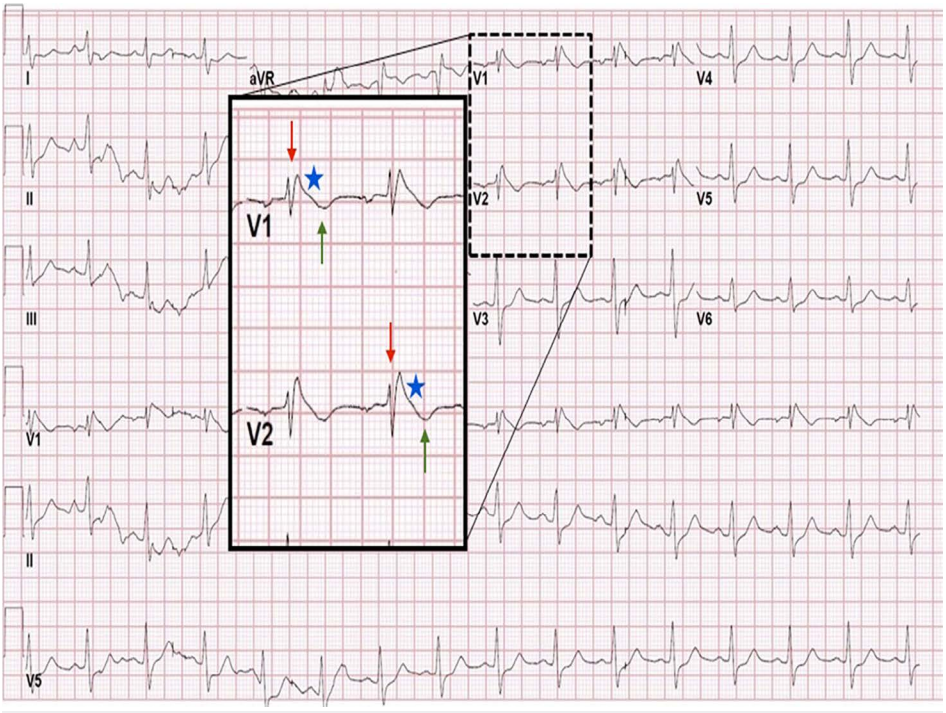

Figure 2.
Electrocardiogram showing sinus rhythm with right bundle branch pattern (red arrow), coved ST segment elevation (blue star), and inverted T waves (green arrow).[4] Reprinted with permission from Elsevier.

did not know how many pills she had ingested. The patient had no personal or family history of BrS or sudden cardiac death. She was transferred to the intensive care unit, where treatment was continued with sodium bicarbonate infusion (15-20 mEq/h) to maintain a blood pH of 7.5 to 7.55 due to suspicion of TCA overdose. Her blood level of nortriptyline was high at 1,581 ng/mL (normal is 50-150). Her urine toxicology was negative, and blood levels of salicylate, alcohol, acetaminophen, and alprazolam were undetectable. She had a normal blood count and coagulation profile and normal levels of potassium, magnesium, calcium, and TSH. In addition, her chest x-ray, brain magnetic resonance imaging, and echocardiography were also normal. She fully recovered with supportive care and was successfully extubated. Treatments with intravenous sodium bicarbonate led to resolution of the BrP. When an ECG showed improved QRS to < 120 ms and QTc < 500 ms, her bicarbonate drip was discontinued (Figure 3).[4] The patient's mental status improved to baseline and she was discharged from the hospital on day 6.

DISCUSSION

Brugada syndrome was described by the Brugada brothers in 1992 as a clinical and electrocardiographic syndrome.[5] It is an autosomal dominant heart disease caused by dysfunctional ion channel with a classical ECG pattern and a predisposition to malignant ventricular arrhythmias and sudden cardiac death. It is usually recognized by three types of ECG patterns and confirmed by provocative challenge test with sodium channel blockers. Nevertheless, the ECG pattern may not always be present and easy to identify and may be only unmasked by metabolic or different derangements.[6]

The term "BrP pattern" was first proposed by Riera and later described by Baranchuk et al.[6] BrP manifests when an

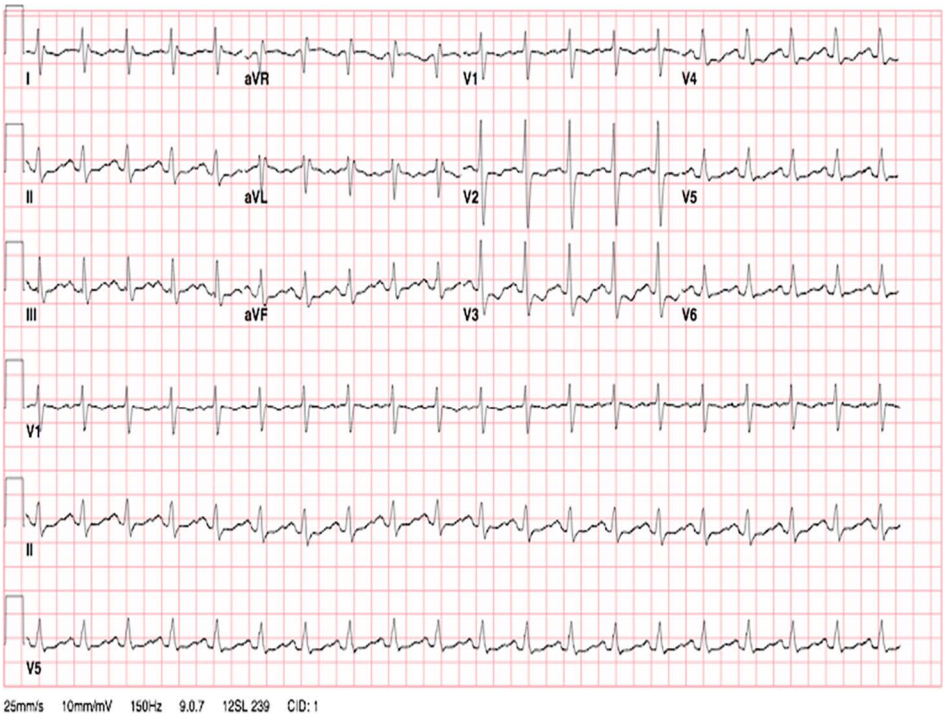

Figure 3.
Electrocardiogram showing resolution of Brugada phenotype after treatment with intravenous sodium bicardonate.[4] Reprinted with permission from Elsevier.

acquired ionic dysfunction and imbalance in potassium, calcium, and sodium currents are present during phase 1 of the action potential, creating a transmural gradient in the epicardium of the right ventricular outflow tract (depolarization model).[6,7] At late phase 1 of the action potential, these shifts cause all-or-none repolarization of some epicardial sites, inducing focal dispersion of repolarization that leads to local re-excitation and phase 2 re-entry arrhythmias.[7] BrP is most often caused by metabolic abnormalities (usually hyper- or hypokalemia), ischemia, or pulmonary embolism,[6] but it has also been attributed to myocardial/pericardial diseases, mechanical compression, non-Hodgkin lymphoma, etc.[6] The International Registry of BrP proposed several criteria to recognize BrP based on determining a typical ECG Brugada pattern with low test probability of BrS, provocative challenge, and genetic testing.[2]

Tricyclic antidepressants (TCA) antagonize fast sodium channels, alpha 1 adrenergic, muscarinic acetylcholine (central and peripheral), histamine 1, and CNS gamma-aminobutyric acid type A receptors, thus causing neurologic, cardiac, and anticholinergic toxicity when poisoning occurs. Usual neurological manifestation of TCA poisoning is sedation, although confusion, delirium, or hallucinations and seizures may occur. Cardiac conduction abnormalities, arrhythmias, and hypotension are also common.[7] By antagonizing cardiac sodium channels, TCAs cause prolongation of QRS (> 100 milliseconds) with abnormal QRS morphology, right bundle branch block, right-axis deviation, low-amplitude P waves, and prolonged PR or QT intervals.[2,8-10] Severe sodium channel blockage may present as a transient BrP type 1 ECG pattern and sustained ventricular tachycardia.[2,8-10]

TCA cardiac toxicity is due mainly to the quinidine-like actions on cardiac tissues. Slowing of the action potential depolarization may slow the conduction through the His-Purkinje system and myocardium; this is responsible for QRS prolongation and atrioventricular block and contributes to ventricular arrhythmias and hypotension. Also, the administration of intravenous sodium bicarbonate to achieve a systemic pH of 7.5 to 7.55 reduces QRS prolongation, reverses hypotension, and improves mental status in patients with moderate to severe TCA poisoning.

The presence of BrP type 1 in the setting of TCA overdose may not always be a reason to perform sodium challenge or genetic testing to diagnose a concealed BrS if high-risk characteristics such as history of recurrent syncope, polymorphic VT, or a family history of BrS were not reported[2,3]; in fact, provocative testing was not performed in our patient during her hospital stay. Nevertheless, while there were no red flags pointing to BrS, we recommended that the patient undergo outpatient challenge testing as well as genetic testing, if possible.

CONCLUSION

Intoxication with drugs that inhibit cardiac sodium channels, such as tricyclic antidepressants, can trigger a BrP in otherwise normal individuals. Tricyclic antidepressants are used for the treatment of chronic pain, depression, and other conditions but have dose-related side effects and can lead to fatal overdose. Intoxication by these drugs should be on the differential when a BrP is observed.

Conflict of Interest Disclosure:
The authors have completed and submitted the *Methodist DeBakey Cardiovascular Journal* Conflict of Interest Statement and none were reported.

Keywords:
Brugada phenocopy, nortriptyline overdose, ventricular tachycardia

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