Received: 20 April 2022 | Revised: 16 July 2022 | Accepted: 20 July 2022

DOI: 10.1002/emp2.12800

JACEP OPEN
JOURNAL OF THE AMERICAN COLLEGE OF EMERGENCY PHYSICIANS OPEN
A GLOBAL JOURNAL OF EMERGENCY MEDICINE
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CASE REPORT

General Medicine

Brugada phenocopy secondary to hyperkalemia and hyponatremia in primary adrenal insufficiency

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Funding and support: By *JACEP* Open policy, all authors are required to disclose any and all commercial, financial, and other relationships in any way related to the subject of this article as per ICMJE conflict of interest guidelines (see www.icmje.org). The authors have stated that no such relationships exist.

Abstract

Introduction: The Brugada phenocopy represents electrocardiogram (ECG) changes nearly identical to the Brugada syndrome but without the congenital abnormality associated with lethal arrhythmias and normalizes with treatment of the underlying etiology. This case highlights the Brugada phenocopy in the setting of moderate hyperkalemia and severe hyponatremia from adrenal insufficiency that resolves with treatment of the underlying metabolic disturbance.

Case Report: A 26-year-old man with no prior medical history presented to the emergency department with syncope, and his ECG revealed a Brugada-like pattern. The patient was found to have significant metabolic derangements, including severe hyponatremia (94 mEq/L), moderate hyperkalemia (6.1 mEq/L), severe hypochloremia (<60 mEq/L), acute kidney injury, and rhabdomyolysis. The patient was diagnosed with primary adrenal insufficiency, and electrolyte correction led to resolution of the Brugada phenocopy.

Conclusion: The Brugada phenocopy on ECG can occur with severe hyponatremia and moderate hyperkalemia and quickly resolves with electrolyte correction.

KEYWORDS
adrenal insufficiency, Brugada phenocopy, case report, hyperkalemia, hyponatremia

1 | INTRODUCTION

Electrolyte imbalance is a common finding during emergency department (ED) visits and a frequent cause for hospitalizations. Presenting signs and symptoms are generally non-specific. Severe derangements can lead to arrhythmias, conduction abnormalities, shock states with end-organ failure, and neurologic dysfunction. Clinicians must manage these abnormalities while unmasking the root cause of these derangements. Primary adrenal insufficiency can be difficult to detect until a severe metabolic disturbance or adrenal crisis occurs. Certain ECG patterns are associated with electrolyte abnormalities, and the Brugada phenocopy has been described with severe hyperkalemia. This case discusses a 26-year-old man with profound hyponatremia, hypochloremia, and moderate hyperkalemia who presented with syncope and an ECG pattern with Brugada phenocopy.

2 | CASE REPORT

A 26-year-old man with a history of attention deficit hyperactivity disorder taking lisdexamfetamine 30 mg daily presented to the ED with profound weakness, palpitations, and syncope in triage. The patient felt unwell for 2 months before presentation, experiencing anxiety, insomnia, loss of appetite, and weakness initially thought to be stress

Supervising Editors: Nichole Bosson, MD, MPH; Nicholas Johnson, MD.

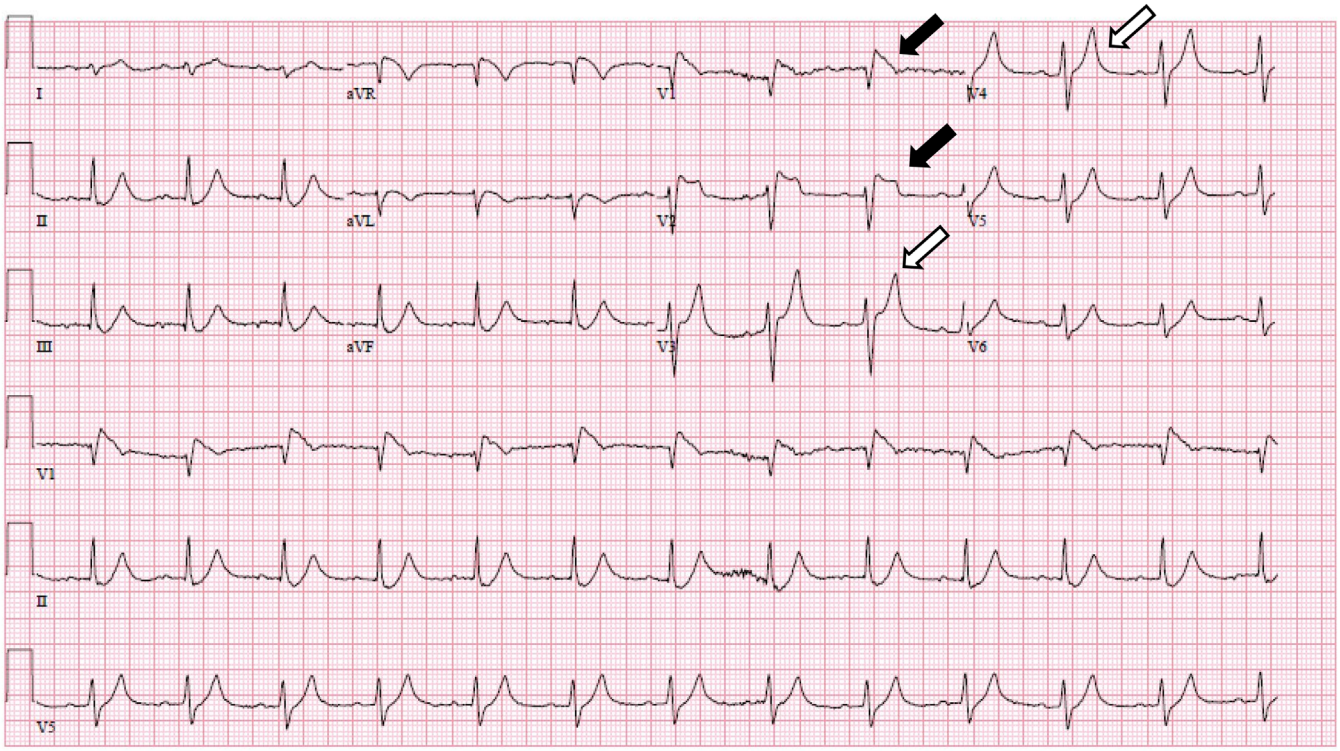

FIGURE 1 Initial electrocardiogram (ECG) with a Brugada type 1 pattern in V1 and a Brugada type 2 pattern in V2 (black arrows) with peaked T-waves in V3 and V4 (white arrows)

related. He was a runner and a triathlon athlete but stopped exercising as a result of fatigue and myalgias. He was prescribed clonazepam 1 mg as needed and started cannabidiol oil drops without relief of his insomnia and anxiety. In addition, he developed nausea, weight loss, and 2 weeks of intermittent non-bloody emesis and diarrhea. The night before ED presentation, he had 1 episode of syncope as well. He denied smoking, vaping, illicit drug use, alcohol use, travel, or sick contacts. Family medical history was significant for his mother having Grave's disease. Physical examination revealed dry mucous membranes with cool dusky extremities and poor skin turgor, but no focal neurologic deficits or murmurs. Initial vital signs were a blood pressure of 120/60 mmHg, heart rate 77 beats per minute, oxygen saturation (SpO_2) 100% on room air, respiratory rate of 24 breaths per minute, and a temperature of 97.4°F. An ECG (Figure 1) performed shortly after arrival demonstrated down-sloping ST elevation in V1 concerning for a Brugada type 1 pattern, and V2 had a saddleback ST segment resembling a Brugada type 2 pattern. In addition, V3 and V4 demonstrated peaked T-waves, and leads II, III, and augmented vector foot had ST segment depression. Relevant laboratory findings include sodium 94 mEq/L, potassium 6.1 mEq/L, chloride <60 mEq/L, creatinine 2.5 mg/dL, serum osmolarity 215 mOsm/kg, lactic acid 3.7 mmol/L, creatine kinase (CK) 20,000 U/L, and a negative urine drug screen. The patient had a normal echocardiogram 4 days before ED presentation.

Shortly after presentation to the ED, 1 L of 0.9 normal saline bolus was initiated with 1 g intravenous calcium gluconate, 25 g intravenous dextrose, and 5 U intravenous regular insulin for hyperkalemia. Hypertonic saline was initiated, and a repeat sodium was 103 mEq/L. Repeat ECG demonstrated resolution of the Brugada phenocopy and improvement of peaked T-waves (Figure 2). In the ICU, serum creatinine returned to normal, CK improved, and a random cortisol level resulted at 7.8 mcg/dL. Baseline cortisol level was 8.1 mcg/dL (reference range, 6–18.4 mcg/dL). Adrenocorticotropic hormone (ACTH) stimulation test using 250 mcg of intravenous cosyntropin demonstrated a 30- and 60-minute cortisol of 8.4 and 8.7 mcg/dL, respectively suggesting a lack of response and a positive test.[1] The ACTH level was 1142 pg/mL (reference range, 7.2–63.3 pg/mL), aldosterone was <4 ng/dL (reference range, <21 ng/dL), paraneoplastic antibodies were negative, and 21-hydroxylase antibodies were positive. These laboratory abnormalities are consistent with autoimmune primary adrenal insufficiency (Addison's disease).[1] Sodium slowly corrected during the course of 5 days with intermittent 3% saline infusion, 2 g salt tablets, and corticosteroid replacement. The patient was discharged on hospital day 5 with a diagnosis of primary adrenal insufficiency resulting in severe electrolyte abnormality causing Brugada phenocopy on ECG.

3 | DISCUSSION

Brugada syndrome is attributed to a sodium channelopathy with a characteristic ECG pattern caused by a genetic defect predisposing an individual to ventricular dysrhythmias and sudden cardiac death in the

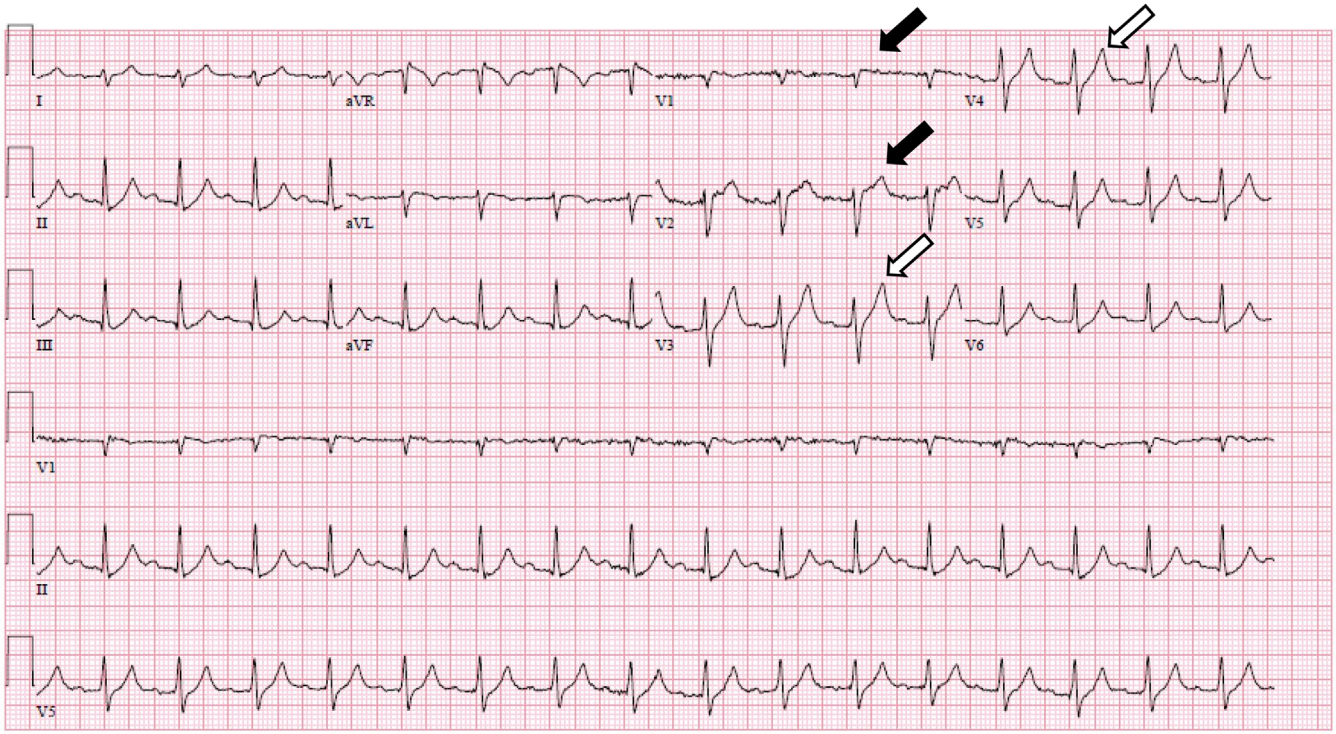

FIGURE 2 Subsequent electrocardiogram (ECG) with resolution of the Brugada phenocopy pattern (black arrows) and improvement of peaked T-waves (white arrows)

absence of structural heart disease.[2] The classic Brugada type 1 ECG pattern has coved-shaped ST-segment elevation of at least 2 mm starting at the J point and sloping downward into the T wave in leads V1 through V3. T-wave inversion in V1 attributed to prolonged depolarization is also a component of the Brugada type 1 pattern and is not clearly present on this patient's ECG (see Figure 1). The Brugada type 2 pattern has >2 mm of ST-segment elevation in a saddleback appearance. The Brugada type 3 pattern has either the coved-shaped ST segments or saddleback ST segments but <2 mm of elevation. Brugada syndrome is diagnosed with the typical ECG pattern and ventricular dysrhythmia, a personal or family history of syncope, or sudden cardiac death.[3] Brugada syndrome is caused by a mutation in the cardiac sodium channel gene *SCN5A*, which encodes for the alpha subunit of the sodium channel, leading to a reduction of the inward sodium current.[4] The Brugada ECG pattern without Brugada syndrome is referred to as Brugada phenocopy and is not associated with genetic mutations or structural heart disease. The Brugada phenocopy may be attributed to electrolyte disturbance, fever, pulmonary embolism, ischemia, myocardial or pericardial diseases, and sodium channel–blocking xenobiotics such as anti-dysrhythmics, cocaine, diphenhydramine, lithium, and tricyclic antidepressants.[3–5]

The Brugada phenocopy has occurred in the setting of severe hyperkalemia typically with a potassium >6.5 mmol/L with an average potassium of 7.45 ± 0.89 mmol/L.[5,6] In cases of hyperkalemia-induced Brugada phenocopy, the high extracellular potassium potentially inactivates cardiac sodium channels by decreasing the resting membrane potential, thus resulting in the outward potassium current dominating.[6] This negative hyperkalemic effect causes delayed depolarization resulting in ST-segment elevation in the anteroseptal region of the ECG with the Brugada type 1 pattern predominantly.[6] This patient's Brugada phenocopy occurred with a potassium of 6.1 mmol/L, less than commonly described, but likely caused by a combination of severe hyponatremia with moderate hyperkalemia. A transmural voltage gradient of reduced inward positively charged ions (sodium) with an accentuated outward current (potassium) resulted in the characteristic ECG pattern.[5] The Brugada phenocopy with severe hyponatremia alone has not been well documented with only a few case reports found.[7]

The profound hyponatremia appeared to be multifactorial and was likely acute on chronic. The patient was hypovolemic on exam with orthostatic symptoms, dry mucous membrane, and poor skin turgor, but urine electrolyte studies resulted in a urine Na^+ of 52 mEq/L and urine osmolarity of 422 mOsm/L with a serum osmolarity of 215 mOsm/kg, suggesting a concurrent euvolemic hyponatremia. The differential diagnosis of euvolemic hyponatremia includes a syndrome of inappropriate antidiuretic hormone secretion, adrenal insufficiency, severe hypothyroidism, medication induced, or iatrogenic etiologies.[8,9] The diagnosis of severe adrenal insufficiency should be considered in moderate to severe hypo-osmolar hyponatremia in the absence of overt volume overload attributed to salt wasting. Because of the non-specific symptoms, a delayed diagnosis is common in adrenal insufficiency, with <50% of patients being diagnosed in the first 6 months of symptom onset and >66% consulting at least 3 physicians.[10] Unfortunately, this delay in diagnosis fre-

quently results in the development of adrenal crisis, with severe hyponatremia being a common electrolyte abnormality at the time of crisis.[11] This patient's ACTH stimulation test and antibody tests are consistent with autoimmune primary adrenal insufficiency (Addison's disease). With correction of hyperkalemia from 6.1 to 4.9 mEq/L and improvement of sodium from 94 to 103 mEq/L, the Brugada phenocopy resolved quickly (Figure 2). With corticosteroid replacement, the patient's hyponatremia improved gradually during the course of 6 days.

This patient presented with syncope in the ED triage area, and the initial ECG can cause a confusing situation leading to potential errors in management as the treatment for Brugada syndrome is an implantable cardioverter-defibrillator. A combination of hyponatremia and hyperkalemia attributed to underlying primary adrenal insufficiency were likely responsible for the Brugada phenocopy on initial ECG at presentation, and syncope was likely an orthostatic or vasovagal event.[6,7] Resolution of dynamic ECG changes with electrolyte correction suggests against the Brugada syndrome and represents the Brugada phenocopy.

4 | CONCLUSION

The Brugada phenocopy on ECG can occur with severe hyponatremia and moderate hyperkalemia and quickly resolves with electrolyte correction. The Brugada phenocopy must be distinguished from Brugada syndrome as the pathophysiology and management are drastically different. Adrenal insufficiency and crisis should be considered in cases of severe metabolic and electrolyte disturbances.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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How to cite this article: Amusina O, Mehta S, Nelson ME. Brugada phenocopy secondary to hyperkalemia and hyponatremia in primary adrenal insufficiency. *JACEP Open*. 2022;3:e12800. https://doi.org/10.1002/emp2.12800