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Pathophysiology of Hyperkalemia Presenting as Brugada Pattern on Electrocardiogram (ECG)

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Study Design A
Data Collection B
Statistical Analysis C
Data Interpretation D
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Patient: Male, 26-year-old
Final Diagnosis: Acute encephalopathy • Brugada pattern • hyperkalemia
Symptoms: Brugada pattern
Medication: —
Clinical Procedure: —
Specialty: Toxicology

Objective: Unknown ethiology

Background: Brugada phenocopies (BrP) are clinical and electrocardiographic (ECG) entities elicited by reversible medical conditions speculated to have pathogenesis rooted in ion current imbalances or conduction delays within the myocardial wall. During an inciting pathologic condition, it produces ECG patterns identical to those of congenitally-acquired Brugada syndrome and subsequently returns to normal ECG patterns upon resolution of the medical condition. This case report describes a 26-year-old man presenting to the Emergency Department (ED) for suspected heroin overdose with a rare ECG consistent with BrP secondary to acute hyperkalemia.

Case Report: A 26-year-old man with a history of substance abuse and a seizure disorder presented to the ED for acute encephalopathy secondary to a heroin overdose complicated by severe rhabdomyolysis and acute renal failure. Laboratory investigations showed acute hyperkalemia (potassium of 7.2 mmol/L) in addition to an elevated creatine kinase, severe transaminitis, and elevated creatinine. His ECG on admission revealed Brugada-like changes in leads V1-V2, with subsequent resolution upon bicarbonate administration and normalization of potassium. After initial stabilization, the patient was admitted to the Intensive Care Unit (ICU). His rhabdomyolysis and acute kidney injury improved after copious rehydration. He was found to have community-acquired pneumonia, with a negative infectious disease workup, that improved with antibiotics. Upon resolution of his hypoxemic respiratory failure and improvement in mentation, he was discharged from the hospital.

Conclusions: Our case report adds to the growing literature on BrP and highlights the importance of recognizing its characteristic ECG pattern as a unique presentation of a common electrolyte derangement.

MeSH Keywords: Brugada Syndrome • Drug Overdose • Hyperkalemia

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Background

Interest in understanding the ionic channel dysfunction, arrhythmogenic potential, diagnosis, and treatment of Brugada phenocopies has grown markedly since the characterization of the condition in 2012 [1]. Identical to congenital Brugada syndrome, the ECG patterns characterizing BrP can be classified into 2 patterns: the typical type 1 "coved" and the type 2 "saddleback" [2,3]. Over 100 cases have been reported in the medical literature, with causative medical conditions falling into 6 general categories: (1) metabolic abnormalities, (2) mechanical compression, (3) ischemia and pulmonary embolism, (4) myocardial and pericardial disease, (5) ECG modulation, and (6) miscellaneous (electrical injury, Ebstein's anomaly). Of these causes, metabolic derangements are the most common. One specific electrolyte disturbance, hyperkalemia, causes a multitude of ECG changes ranging from peaked T waves to sine waves. However, knowledge of its association with the Brugada pattern continues to grow. Here, we supplement the mounting number of cases detailing hyperkalemia as the driver of the reversible electrocardiographic phenomenon known as BrP.

Case Report

A 26-year-old man with a history of cocaine and heroin abuse, as well as a seizure disorder, was brought to the ED by Emergency Medical Services (EMS) after being found lying down and unresponsive for approximately 10 hours due to an apparent overdose. EMS stated that the patient was found hypoxic, with an oxygen saturation of 68%, which improved to 95% on Venturi-mask. Both intranasal and IV Narcan were given, without success. On arrival to the ED, pertinent subjective information, including a personal history of syncope or family history of sudden cardiac death, was unable to be obtained because the patient was obtunded. Arousing on occasion and responding to noxious stimuli, there was a possibility of previous seizure activity and being post-ictal. A bolus of Levetiracetam was given and a head CT was done, revealing no acute changes. Vitals showed a temperature of 99.1°F (37.2°C), heart rate of 106 beats per minute, blood pressure 116/78 mmHg, respiratory rate of 19 breaths per minute, and an oxygen saturation of 95% on Venturi-mask. ECG showed a type 1 Brugada pattern in leads aVR, V1, and V2, which normalized after administering sodium bicarbonate (Figure 1).

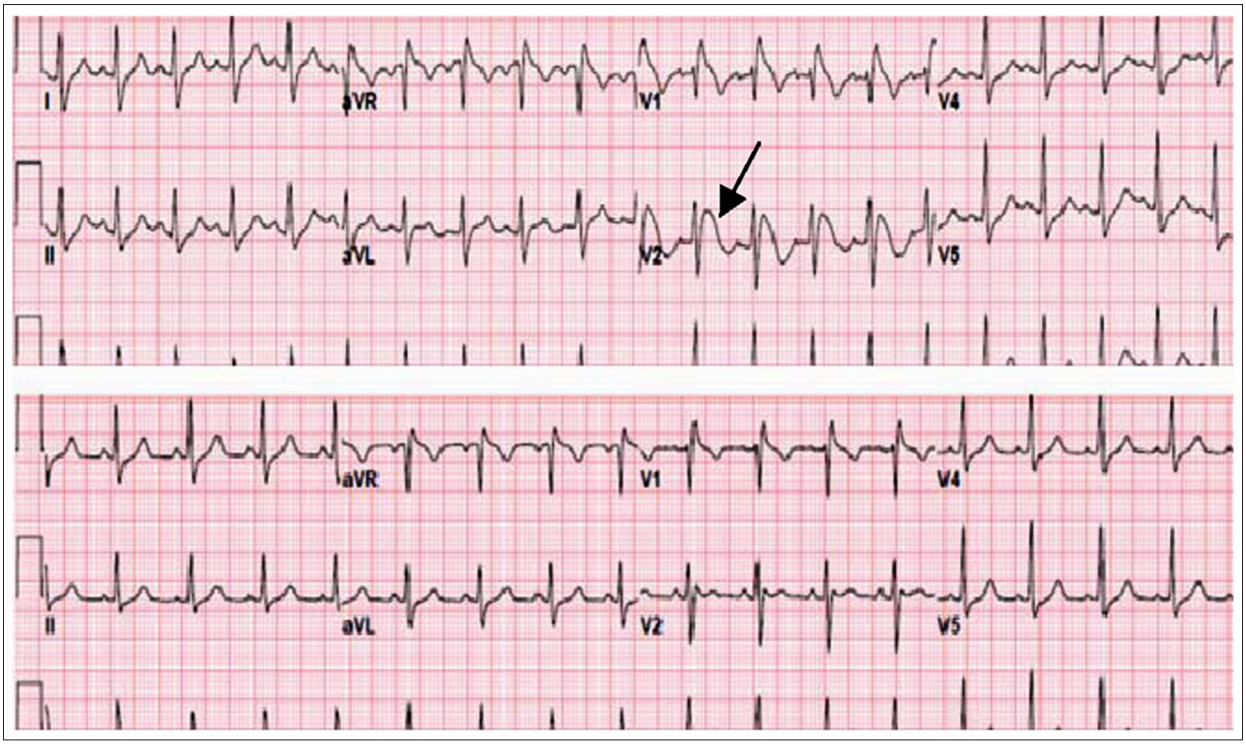

Figure 1. Electrocardiogram (ECG) tracing in a 26-year-old male presenting with acute encephalopathy, acute hypoxic respiratory failure, and acute hyperkalemia, resulting in Brugada-like ECG changes. Top ECG tracing obtained while serum potassium measured 7.2 mmol/L, demonstrating the type 1 "coved" Brugada pattern with concave, ST-segment elevation most prominent in leads V1 and V2 (arrow). Bottom ECG tracing demonstrating resolution of ST-segment changes after correction of serum potassium to 4.4 mmol/L.

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Laboratory studies revealed a myriad of derangements, including: acute hyperkalemia (potassium of 7.2 mmol/L) and elevated creatine kinase (29,270 units/L on admit with maximum of 74,750 units/L) thought to be secondary to drug overdose-related crush myopathy, and transaminase elevation (AST 4,052 units/L ALT 5,960 units/L) thought to be secondary to shock liver *vs.* rhabdomyolysis itself. Repeat potassium was 4.4 mmol/L after administration of calcium gluconate, insulin, glucose, and sodium bicarbonate. Additionally, lactate levels were elevated at 3.5 mmol/L, venous blood gas was 7.33/35 mmHg/61 mmHg/18 mmol/L consistent with anion gap acidosis, and creatinine above 3 mg/dL suggesting acute kidney injury, which improved following fluid supplementation. Urine drug screening performed in the ED was positive for Levetiracetam, Fentanyl, and Norfentanyl.

After initial stabilization, the patient was admitted to the ICU still requiring Venturi-mask secondary to his mental status and acute hypoxic respiratory failure. Collateral history was obtained from the patient's family and was significant for chest discomfort, diaphoresis, and a dry scratchy throat for 1 week prior to presentation. Hyperkalemia protocols were initiated and normalized the potassium level to 3.9 mmol/L. His rhabdomyolysis and acute kidney injury resolved with vigorous hydration that restored his kidney function to baseline. He was noted to have community-acquired pneumonia with a negative infectious workup (negative blood cultures, negative urinary Streptococcus pneumoniae and Legionella antigens, and negative respiratory viral panel) for which he finished a course of Azithromycin and Ceftriaxone, resulting in resolution of hypoxia. The patient's mentation improved, and he was discharged from the hospital.

Discussion

Hyperkalemia causes ECG alterations, including tall, peaked, and tented T waves, widened and flattened P waves, widening of the QRS complex, AV blocks, sine wave rhythms, and asystole. However, presentation with coved ST-segment elevation representing a Brugada pattern is uncommon. In our case, the etiology of hyperkalemia causing Brugada-like changes was likely multifactorial, indicating a combination of rhabdomyolysis, acidosis, and acute renal failure, resulting in increased potassium release from muscle breakdown, transcellular shifts, and impaired excretion. Rapid treatment with calcium gluconate, insulin, and sodium bicarbonate resulted in ECG normalization, likely reflecting an improvement in both hyperkalemia and acidemia. Levetiracetam, which inhibits N-type calcium channels and delayed rectifier potassium currents, was administered, but this took place after the initial ECG showing Brugada-like changes, and thus was probably not an important contributing factor. The transient nature of the ECG alteration is a hallmark in differentiating Brugada syndrome from Brugada phenocopy [4].

The congenitally-acquired channelopathy known as Brugada syndrome (BrS) and the reversible conditions leading to Brugada phenocopy differ in many clinically relevant ways. BrS is an autosomal dominant disorder that predisposes patients to lethal arrhythmias and sudden cardiac death without identifiable structural abnormalities. The most common cause is inheriting one of the approximately 290 pathogenic variants that have been identified in the *SCN5A* gene, which encodes for a specific cardiac sodium channel. Nevertheless, many other genes can cause the disorder, including genes coding for subunits of sodium channels or other ionic channels [5]. This locus and allelic heterogeneity account for the variable penetrance associated with BrS. Two-thirds of patients are asymptomatic at diagnosis, while one-third are identified after non-specific symptomatology (e.g., syncope and aborted sudden cardiac death). Once a patient is identified and risk-stratified according to risk of sudden cardiac death, a complex management begins. However, the only proven effective therapy is implantation of an implantable cardioverter device (ICD) to terminate lethal arrhythmias. Recently, ablation of the arrhythmic electrophysiological substrate (AES), purported to be in the epicardium of the right ventricular anterior wall and outflow tract, has been suggested as a possible therapeutic option resulting in correction of ECG abnormalities [5,6].

The causes and management strategies mentioned above for BrS differ significantly from those for BrP. The proposed pathogenesis of these reversible Brugada-like patterns is largely described by two theories. The repolarization theory describes ion current imbalances during phase 1 of the myocyte action potential in which partial repolarization occurs as the precluding abnormality. Specifically, an increased transient outward potassium current (I_{to}) or decreased inward currents, either through L-type calcium currents or peak sodium currents, create focal ionic imbalances that give rise to reentry arrhythmias [7–10]. Alternatively, the depolarization theory describes a focus in the right ventricular outflow tract that undergoes delayed depolarization and establishes an electrical gradient for the rest of the right ventricular circuitry, creating a dysrhythmia [7–10]. More recent studies using simulations of the anterior ventricular wall showed that potassium concentration, fibrosis, and I_{to} are all involved the development of the Brugada pattern and act synergistically to shape the characteristic pattern [11]. As presented in our case, high levels of extracellular potassium lead to an increase in the normal resting membrane potential and subsequent inactivation of the sodium channels and delayed conduction. The subsequent creation of ionic imbalances lends support to repolarization as the driver of ECG changes in our case. Nevertheless, much of the current speculation is based on studies from BrS due to the relative rarity of BrP

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and lack of animal models. Furthering the distinction between BrS and BrP, there are no data showing an increase in the risk of SCD in those with BrP; therefore, treatment should focus on amelioration of the underlying condition rather than cardioverter-defibrillator implantation.

Conclusions

The differences between Brugada syndrome and Brugada phenocopy shed light on both the challenge and importance of an accurate diagnosis of BrP in providing appropriately tailored therapy. It has been well documented that the hyperkalemic-induced Brugada pattern carries a grim prognosis [12]. Thus, we hope that our case report increases awareness and recognition of a rare presentation of a common electrolyte disorder.

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