


Electrolyte Imbalance–Induced Brugada Phenocopy: A Complex Intersection of Hyperkalemia, Hyponatremia, and Acidosis – Case Report

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ABSTRACT

Introduction: Brugada phenocopies (BrP), which are different from real congenital Brugada syndrome (BrS), are clinical entities with different etiology. BrP can manifest in a range of conditions, such as metabolic disturbances like hypokalemia, hyperkalemia, hypophosphatemia, hyponatremia, and acute toxicity. **Case:** Brugada phenocopy was observed in the ECG of a 68-year-old male, resolved following the correction of hyperkalemia, hyponatremia, and acidosis. The patient presented with septic shock and multiorgan dysfunction, which contributed to severe electrolyte imbalance and metabolic derangements. Despite initial stabilization and improvement in ECG findings after targeted correction, the patient ultimately developed progressive clinical deterioration. **Discussion:** Recognizing BrP helps identify reversible causes of the ECG changes, allowing for proper treatment and prevention of complications. This case highlights the importance of evaluating underlying metabolic and systemic conditions when encountering Brugada-like ECG patterns. **Conclusion:** Brugada phenocopy can occur in hyperkalemia and hyponatremia in an acidosis state. Clinicians should consider comprehensive clinical assessment, laboratory evaluation, and ECG monitoring to distinguish BrP from congenital BrS, especially in critically ill patients.

Keywords: Brugada phenocopy, Brugada syndrome, case report, electrolyte imbalance.

ABSTRAK

Pendahuluan: Fenokopi Brugada (BrP), berbeda dari sindrom Brugada kongenital (BrS), adalah entitas klinis dengan etiologi berbeda. BrP dapat muncul pada berbagai kondisi, seperti gangguan metabolik, termasuk hipokalemia, hiperkalemia, hipofosfatemia, hiponatremia, dan toksisitas akut. **Kasus:** Fenokopi Brugada ditemukan pada elektrokardiogram (EKG) seorang pria berusia 68 tahun dan kembali normal setelah koreksi hiperkalemia, hiponatremia, dan asidosis. Pasien mengalami syok septik dan disfungsi multiorgan, yang menyebabkan ketidakseimbangan elektrolit yang parah dan gangguan metabolik. Meskipun terjadi stabilisasi awal dan perbaikan pada temuan EKG setelah koreksi yang ditargetkan, pasien akhirnya mengalami perburukan klinis yang progresif. **Diskusi:** Mengenali BrP membantu mengidentifikasi penyebab reversibel dari perubahan EKG, memungkinkan penanganan yang tepat dan pencegahan komplikasi. Kasus ini menyoroti pentingnya mengevaluasi kondisi metabolik dan sistemik yang mendasari saat menemui pola EKG serupa Brugada. **Simpulan:** Fenokopi Brugada dapat terjadi pada hiperkalemia dan hiponatremia dalam keadaan asidosis. Tenaga medis perlu mempertimbangkan penilaian klinis komprehensif, evaluasi laboratorium, dan pemantauan EKG untuk membedakan BrP dari sindrom Brugada kongenital, terutama pada pasien kritis. **Yuddy Imowanto, Taufiq Abdullah, Sri Wahyuni. Ketidakseimbangan Elektrolit-yang Menyebabkan Fenokopi Brugada: Interaksi Kompleks Hiperkalemia, Hiponatremia, dan Asidosis – Laporan Kasus.**

Kata Kunci: Fenokopi Brugada, sindrom Brugada, laporan kasus, ketidakseimbangan elektrolit.

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INTRODUCTION

Brugada syndrome (BrS) is an inherited arrhythmia disorder characterized by type 1 and type 2 electrocardiogram (ECG) patterns in leads V1–V3, which predisposes individuals to life-threatening ventricular arrhythmias and sudden cardiac death.[1,2] In contrast to true congenital Brugada syndrome, Brugada phenocopies (BrP) are clinical conditions with a different underlying etiology.[1,2]

BrS is a relatively rare condition, with a

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global prevalence estimated at 0.05%, while the Brugada phenocopy is found in approximately 0.4% of the population. In Asia, the prevalence of asymptomatic BrS is estimated to range from 0.00% to 1.77%, whereas Brugada phenocopy is reported in 0.014% to 15.96% of the cases.[3]

BrPs are classified based on ECG morphology in leads V1 and V2.[4] Type 1 BrP is characterized by J-point elevation of at least 2 mm, followed by a coved ST segment and a negative T wave. In contrast, type 2 BrP features a J-point elevation of 2 mm or more, with a saddleback-shaped ST segment. Both BrP and BrS exhibit similar ECG patterns, making it challenging to distinguish between the two.[4,5]

The six etiological categories of Brugada phenocopy are metabolic disturbances, myocardial ischemia, peri-myocardial diseases, mechanical disorders such as tumors, poor ECG filters, and other causes.[4] Metabolic conditions account for nearly half of the BrP cases (63 out of 135) included in the international registry. The mean age of affected individuals is 48 ± 18 years, with a male predominance (47 males, 14 females, and 2 cases with unknown gender).[6] The most common metabolic conditions are electrolyte disturbances, including hypo-hyperkalemia, hyponatremia, and hypophosphatemia.[4] It is important to differentiate Brugada phenocopy from Brugada syndrome because misdiagnosis can lead to unnecessary treatments like implanting a defibrillator, which is needed for BrS but not for BrP.[7]

CASE

A 68-year-old male with a history of allergic dermatitis, who has been taking dexamethasone 5 mg three times daily for four months, presented to the emergency department with loss of consciousness, dyspnoea, and lesions on the skin of the leg and scrotum. A scratch mark on the left waist spreads to the left thigh and scrotum, accompanied by pain for a week. Initially, the wound was small, resembling small bumps filled with fluid, then it spread and became itchy. For the past week, the patient has stopped taking dexamethasone because he has been bedridden. The day before presenting to the emergency department, his family reported that the patient tended to be sleepy and difficult to communicate with. He also experienced a fluctuating fever for a week. A history of diabetes mellitus and hypertension was denied. He had no family history of arrhythmias or sudden cardiac death.

Upon admission, the patient's Glasgow coma scale (GCS) was 7, and his vital signs revealed unmeasurable blood pressure, a pulse rate of 140 bpm, oxygen saturation (SpO_2) of 97% on a non-rebreathing mask delivering 15 L/minute of oxygen, a respiratory rate of 43 bpm, and a temperature of 36.8°C. Physical examination revealed cold and wet extremities, poor skin turgor, and erythematous maculae in the abdominal and femoral regions. Necrotic tissues were found in the bilateral scrotal region. A 12-lead ECG performed upon admission revealed a J-point elevation of ≥ 2 mm with downsloping ST elevation in leads V1 and V2, consistent with the Brugada type 1 pattern **(Figure 1).** Laboratory tests indicated mild hyperkalemia (5.5 mmol/L), severe hyponatremia (115 mmol/L), and random blood sugar was low (below 10 mg/dL). Blood gas analysis demonstrated metabolic acidosis with a pH of 7.28 and a base excess of -14.9.

The patient was treated with a 1 L bolus of 0.9% normal saline along with 100 mL of 40% intravenous dextrose. After fluid administration, blood pressure was 96/40 mmHg with a heart rate of 134 bpm. Intravenous drip of norepinephrine 0.1 mcg/kg/minute was initiated, then the blood pressure rose to 105/57 mmHg with a heart rate of 138 beats per minute. Due to the routine use of dexamethasone and hypoglycemia, hyponatremia and hyperkalemia, adrenal insufficiency was suspected; therefore intravenous hydrocortisone 100 mg was given. The patient was diagnosed with septic shock due to scrotal Fournier gangrene, electrolyte imbalance, and suspected adrenal insufficiency.

After 2 days in the intensive care unit (ICU) and correction of the presence of hyponatremia with NaCl 3% 12 mEq/24 hours, a repeat electrolyte examination showed a normal result with a sodium level of 143 mmol/L and a potassium level of 4.87 mmol/L. Blood gas analysis revealed metabolic acidosis with a pH of 7.31 and a base excess of -7.3. A repeat ECG demonstrated resolution of the Brugada ECG pattern **(Figure 2).** The patient was treated in the ICU for 9 days and was declared deceased due to septic shock after cardiopulmonary resuscitation.

DISCUSSION

Clinical conditions referred to as BrP are characterized by ECG patterns similar to

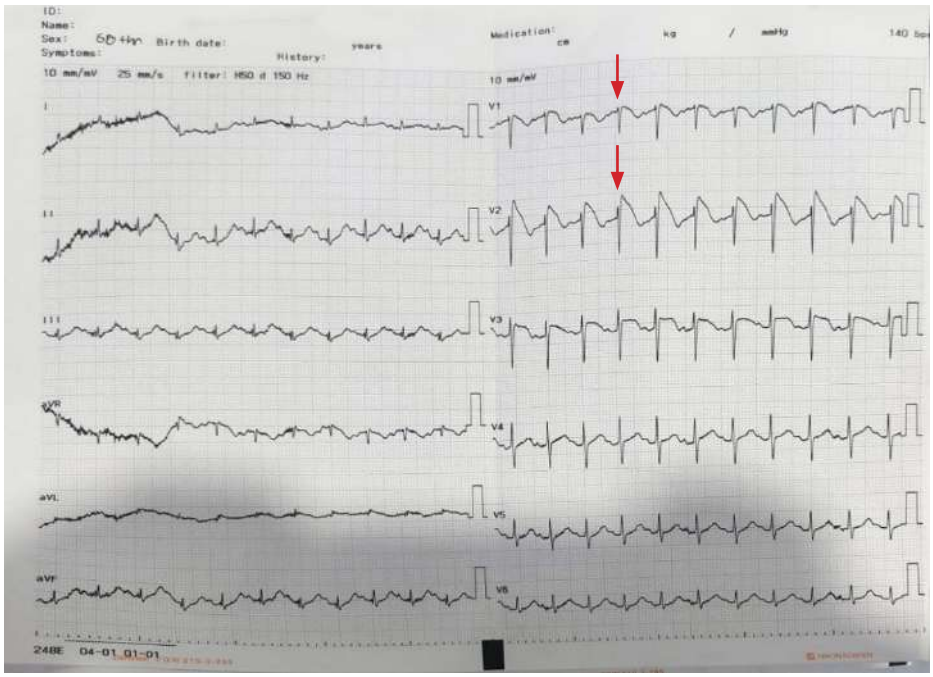

Figure 1. ECG at admission (red arrow).

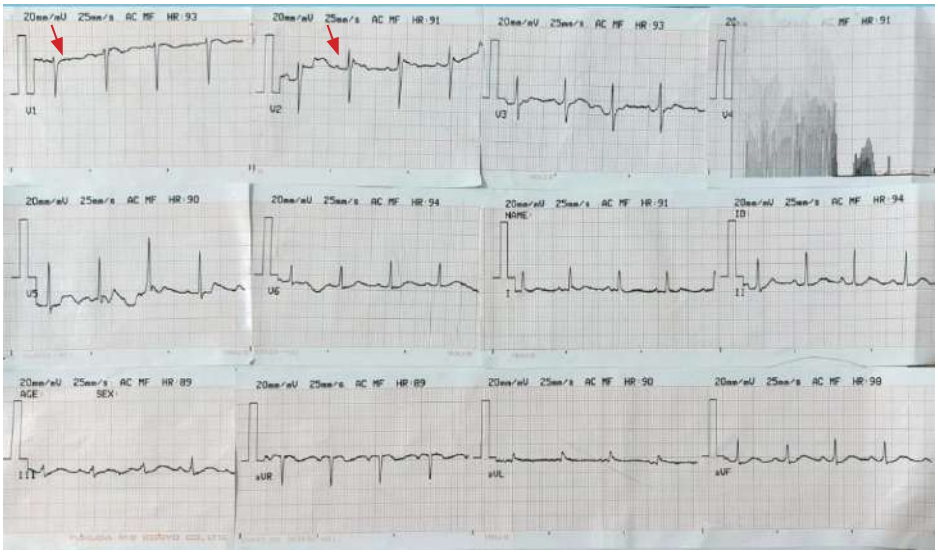

Figure 2. ECG post electrolyte correction (red arrow).

true congenital Brugada syndrome (BrS) but triggered by various clinical conditions, including electrolyte imbalances, ischemia, pulmonary embolism, and metabolic disorders.[6] ECG alone cannot differentiate between the two conditions.[7] It is crucial to make a clear differentiation between BrP and BrS. The difficulty lies in the fact that BrS may arise unexpectedly, without a clear personal or familial background of the condition, and without recognized genetic defects.[4]

Based on the International Registry of Brugada Phenocopies **(Table)**, BrP is diagnosed based on the presence of an ECG showing a Brugada ECG pattern, with resolution after addressing the underlying causes; an anamnesis not suggestive of BrS, negative provocative tests using sodium channel blockers, and negative genetic testing. Several medications for provocative tests include ajmaline, flecainide, procainamide, and pilsicainide.[2,4]

Based on the diagnostic criteria, Brugada phenocopy cases can be categorized into three classes: A, B, and C. Class A, is assigned when a case meets all mandatory diagnostic criteria, including a negative provocative challenge. Class B, is assigned when a case shows high suspicion of BrP, but not all mandatory diagnostic criteria are fulfilled. This is due to the inability to perform the provocative challenge test, such as in fatal cases, lost to follow-up, or refusal of further examination. Class C, in cases with high suspicion of BrP, where provocative testing is not required, such as in instances involving recent surgical manipulation of the right ventricular outflow tract or changes to the ECG filter.[4,8]

Table. Diagnostic criteria of Brugada phenocopy.[1]

1.	Brugada ECG pattern (type 1 or type 2)
2.	There is an underlying condition consistent with the six categories of etiology.
3.	The Brugada ECG pattern resolves once the underlying causes are treated.
4.	Considering the anamnesis, medical history, and family history, the likelihood of the patient having Brugada syndrome is low.
5.	Provocative tests with sodium channel blockers (ajmaline, flecainide, or procainamide) yielded negative results.
6.	Provocative testing is not required if surgical RVOT manipulation happened within the past 96 hours.
7.	Genetic testing results are negative (low sensitivity, not mandatory).

Abbreviations: ECG: Electrocardiogram; RVOT: Right ventricular outflow tract
Adapted from Anselm, *et al.*

According to the Brugada phenocopy diagnostic criteria, the ECG pattern in this case presents a type 1 Brugada morphology with an identifiable underlying condition (mild hyperkalemia, severe hyponatremia, and acidosis), which resolved after the resolution of the electrolyte imbalance. The likelihood of Brugada syndrome is low, as indicated by the absence of symptoms, medical history, and family history. Provocative testing with sodium channel blockers and genetic testing could not be performed due to the patient's condition and the unavailability of genetic testing at our hospital.

The literature has repeatedly connected a Brugada ECG pattern to metabolic disorders and electrolyte imbalances, and new cases are still being reported each month.[6,7] A transient channel malfunction brought on by an electrolyte imbalance could produce the distinctive ECG pattern.[6]

Hyperkalemia is believed to induce a Brugada ECG pattern by inactivating cardiac sodium channels, leading to an imbalance in sodium ion currents. This causes a reduction in the resting membrane potential. Sodium channel inactivation is more pronounced in the anteroseptal region compared to other areas, resulting in the Brugada ECG pattern observed in V1–V2. The outward shift in ion currents, particularly in the right ventricle, is caused by an increase in transient outward potassium current (Ito). It primarily occurs in the epicardium of the right ventricle compared to the endocardium and M cells, leading to the loss of the AP dome, which can result in a type-1 Brugada ECG pattern.[6,9]

Although Baranchuk, *et al*., suggest that acidosis may amplify the gradient imbalance between different myocardial layers, its exact role remains unclear.[6] The Brugada ECG pattern hasn't always completely resolved once acidosis has been corrected, which is an interesting observation. This implies that modulating the ionic channel may require more than just acidosis "per se".[6] In this case, the patient presented with metabolic acidosis with a pH of 7.28 and a base excess of -14.9. After resuscitation and 2 days of ICU treatment, the patient remained acidotic but improved with a pH of 7.31 and a base excess of -7.3, and the ECG continued to show


resolution of the Brugada ECG pattern despite the patient still being in a state of acidosis.

Sepsis or dehydration can cause hypotension and reduced tissue perfusion, which can result in metabolic acidosis.[10] The large intracellular potassium reservoir allows transcellular shifts to exert significant and rapid effects on plasma potassium levels ([K+]). Acute metabolic acidosis promotes the movement of potassium from the intracellular to the extracellular space, a process counteracted by insulin and β-adrenergic signaling.[11] In this case, the patient was diagnosed with septic shock due to Fournier gangrene of the scrotum with mild hyperkalemia and acidosis.

Hyponatremia is thought to reduce the ionic gradient, which decreases the inward sodium current (INa). This allows the transient outward current (Ito) to remain unopposed. The imbalance between sodium and potassium ion currents may lead to the loss of the action potential (AP) dome in the epicardium of the right ventricle. Most patients with hyponatremia-induced BrP also have additional electrolyte abnormalities, such as hyperkalemia, hypokalemia, acidosis, and others. Hyponatremia is thought to play a role in the temporary inactivation of sodium channels.[6] A combination of hypoglycemia, hyperkalemia, and hyponatremia raised suspicion of adrenal insufficiency. Brugada phenocopy was reported by Amusina, *et al*., in a case of electrolyte disturbance due to adrenal insufficiency, which resolved after the underlying metabolic abnormality was treated.[12]

Clinicians must have a strong clinical suspicion of adrenal insufficiency, particularly in cases of nonspecific life-threatening shock. Patients with adrenal insufficiency often present with vague clinical signs and symptoms; hypoglycemia and electrolyte disturbances such as hyponatremia and hyperkalemia can occur. Diagnostic tests include serum cortisol, adrenocorticotropic hormone (ACTH), renin, aldosterone, and a comprehensive chemistry panel. Adrenal insufficiency can be confirmed with a serum cortisol level test, especially when elevated ACTH and plasma renin activity are present.[13] Around half of patients develop adrenal insufficiency either while undergoing oral glucocorticoid therapy or soon after its discontinuation.[14] Despite this, adrenal function testing is performed in less than 1% of patients outside the context of clinical studies. Notably, over 70% of adrenal insufficiency cases are diagnosed during acute hospital admissions.[14]

This case had hypoglycemia, hyperkalemia, and hyponatremia, raising suspicion of adrenal insufficiency due to long-term dexamethasone use without medical advice. A limitation of this case report is the absence of data on cortisol and ACTH levels due to limited of laboratory resources. Sepsis represents a broad clinical spectrum with varying prognoses, with septic shock being the most severe and life-threatening complication.[15] Sepsis can precipitate BrP due to metabolic disturbances, such as electrolyte imbalances.[16–18] The resolution of electrolyte disturbances will be followed by the resolution of Brugada phenocopy.[4,16]

Despite advancements in medical care, septic shock continues to carry a high mortality rate, often exceeding 40%.[15] Severe sepsis remains one of the leading causes of death among hospitalized patients, with outcomes influenced by several factors, including the causative organism, antibiotic resistance, the extent of organ involvement, and patient demographics such as age.[15] Studies indicate that tachypnea and altered mental status serve as strong predictors of poor prognosis.[15] In this case, the patient presented with an altered mental state and tachypnea, accompanied by life-threatening multiple organ dysfunction, resulting in a poor prognosis and death.

CONCLUSION

Brugada phenocopy can occur in hyperkalemia and hyponatremia in an acidosis state. The Brugada ECG pattern alone should not be considered to be Brugada syndrome. Differentiating between Brugada phenocopy and Brugada syndrome is crucial in clinical practice, as it impacts patient management.

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