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Defying The Vicious Cycle: An Intriguing Case of BRASH Syndrome

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Defying The Vicious Cycle: An Intriguing Case of BRASH Syndrome

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Abstract

BRASH Syndrome is a rare and life-threatening condition marked by the combination of bradycardia, renal failure, atrioventricular (AV) nodal blockade, shock, and hyperkalemia. This case report presents a 79-year-old female with acute kidney injury, hyperkalemia, and severe bradycardia without typical EKG changes associated with hyperkalemia. The aim of this article is to provide a comprehensive overview of BRASH syndrome, including its clinical manifestations, underlying pathophysiology, diagnostic approaches, and management strategies. The patient's presentation, laboratory findings, and response to treatment support the diagnosis of BRASH syndrome. The syndrome's pathogenesis involves a vicious cycle of bradycardia, renal failure, AV nodal blockade, and hyperkalemia, necessitating early recognition and prompt management to prevent life-threatening complications. Increased awareness and understanding among healthcare providers are crucial for improved patient outcomes in BRASH syndrome cases.

Keywords

BRASH, hypertension, hyperkalemia, beta blockers, bradycardia, renal failure, AV nodal blockade, shock

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Conflict of Interest Statement

The authors declare that there is no conflict of interest regarding the publication of this case report. They have no financial, personal, or professional relationships that could influence the the information presented. The manuscript represents an unbiased and objective contribution to the scientific community.

Cover Page Footnote

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CASE REPORT

Defying the Vicious Cycle: An Intriguing Case of BRASH Syndrome

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Abstract

BRASH Syndrome is a rare and life-threatening condition marked by the combination of bradycardia, renal failure, atrioventricular (AV) nodal blockade, shock, and hyperkalemia. This case report presents a 79-year-old female with acute kidney injury, hyperkalemia, and severe bradycardia without typical EKG changes associated with hyperkalemia. The aim of this article is to provide a comprehensive overview of BRASH syndrome, including its clinical manifestations, underlying pathophysiology, diagnostic approaches, and management strategies. The patient's presentation, laboratory findings, and response to treatment support the diagnosis of BRASH syndrome. The syndrome's pathogenesis involves a vicious cycle of bradycardia, renal failure, AV nodal blockade, and hyperkalemia, necessitating early recognition and prompt management to prevent life-threatening complications. Increased awareness and understanding among healthcare providers are crucial for improved patient outcomes in BRASH syndrome cases.

Keywords: BRASH, Hypertension, Hyperkalemia, Beta blockers, Bradycardia, Renal failure, AV nodal blockade, Shock

1. Introduction

The emergence of BRASH Syndrome as a distinct disease process in 2016 has brought attention to a unique clinical entity with potentially serious implications. BRASH, an acronym for Bradycardia, Renal failure, AV-nodal blockade, Shock, and Hyperkalemia, involves a complex interplay of factors that lead to a cycle of hypoperfusion and bradycardia. This syndrome primarily affects patients who are on AV-nodal blocking agents, such as beta-blockers or calcium-channel blockers, and subsequently develop acute renal injury. As renal function deteriorates, hyperkalemia ensues, further exacerbating the AV-nodal blockade. Consequently, the synergistic effects of hyperkalemia and AV-nodal blockade result in bradycardia and hypotension, leading to compromised end-organ perfusion and perpetuating the vicious cycle of BRASH Syndrome. In this case report, we present a detailed analysis of a 79-year-old patient diagnosed with BRASH Syndrome,

shedding light on its pathophysiological mechanisms, clinical implications, and management.

2. Case presentation

A 79-year-old female patient with a history of stage IV chronic kidney disease (CKD) characterized by a baseline creatinine level ranging from (1.8–2.3 mg/dL), essential hypertension, and well-controlled diabetes mellitus was referred to the emergency department (ED) by her primary care provider. The patient presented with a slow heart rate of 34 beats per minute, along with complaints of dizziness. Upon examination in the ED, laboratory tests revealed hyperkalemia with a level of (6.1 mmol/L), acute kidney injury (AKI), and a blood glucose level of 72 mg/dL, which occurred in the context of her pre-existing CKD condition. Importantly, she had been non-compliant with sodium zirconate (Lokelma) therapy and admitted to not following a strict low-potassium diet. The patient denied experiencing diarrhea, nausea, vomiting, or

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recent changes in medication. Upon evaluation in the ED, her heart rate was recorded at 36 beats per minute, and her blood pressure measured 157/101 mmHg, otherwise had vitals within normal range.

The patient was on an AV nodal blocker, metoprolol succinate 50 mg daily, for hypertension. Other home medications included hydralazine, amlodipine, dulaglutide, insulin, sodium zirconium cyclosilicate, and torsemide. Laboratory tests revealed severe hyperkalemia (potassium level of 6.1 mmol/L), AKI on CKD (creatinine level of 3.2 mg/dL), and normal anion gap metabolic acidosis with a venous pH of 7.29. The electrocardiogram revealed sinus bradycardia, as shown in Fig. 1. Notably, other features of hyperkalemia were absent in the ECG.

The patient received temporizing treatment for hyperkalemia with calcium gluconate, insulin, and dextrose. Additionally, she received patiromer, fludrocortisone, isotonic bicarbonate, and intravenous furosemide. These interventions successfully lowered her potassium to (5.4 mmol/L), however despite that she remained bradycardic with heart rate of 39. It is important to note that metoprolol succinate was not restarted. Upon further lowering the potassium to 4.6 mmol/L her bradycardia, acute kidney injury (AKI), and acidosis gradually resolved. The repeat ECG is shown in Fig. 2. A diagnosis of BRASH syndrome was made based on

the patient's presentation of severe bradycardia with hyperkalemia in the setting of AV nodal blocker use and the absence of any hyperkalemia-related EKG changes.

3. Discussion

BRASH is a clinical syndrome, represented by an acronym that encompasses a vicious cycle of Bradycardia, Renal failure, AV nodal blockade, Shock, and Hyperkalemia.¹ BRASH is becoming more prevalent due to the aging population and the use of pharmaceuticals targeting cardiac output.² The patient in this case report presented with BRASH syndrome, which can be attributed to several likely precipitating factors. Firstly, the patient's use of beta-blocking agents might have played a role in the syndrome's development. Secondly, the condition was further complicated by hyperkalemia, which arose due to non-compliance with Lokelma treatment and dietary indiscretion. Additionally, it is important to note that all these factors occurred in the context of the patient's stage IV chronic kidney disease (CKD). Additionally, commonly encountered triggers for BRASH syndrome encompass volume depletion and the escalation of AV nodal-blocking drugs or medications that provoke hyperkalemia, such as renin-angiotensin-aldosterone system inhibitors and mineralocorticoid antagonists.

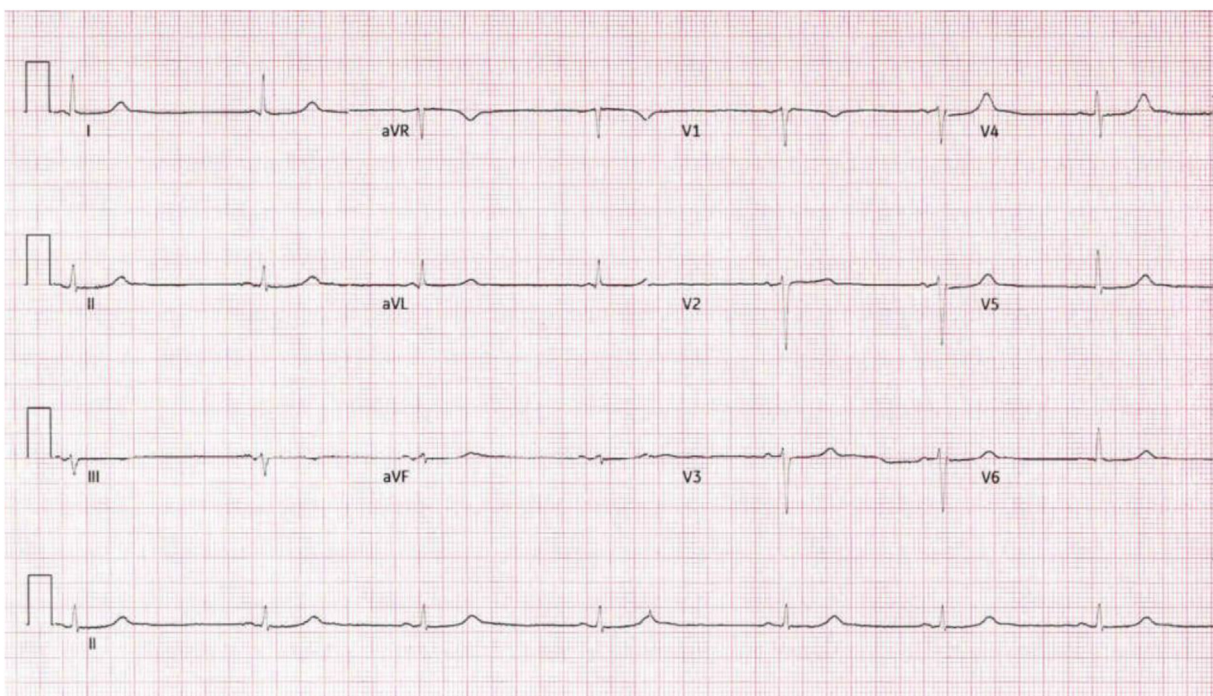


Fig. 1. ECG at presentation showing sinus bradycardia without other features of hyperkalemia.

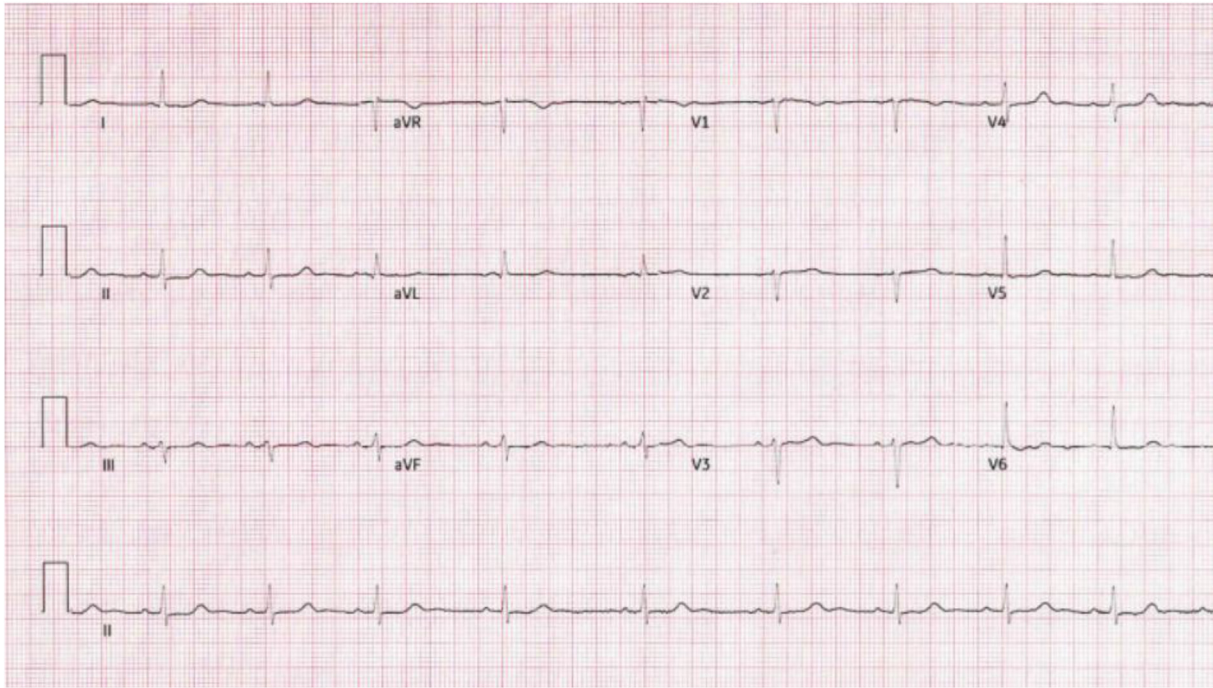


Fig. 2. Normalization of EKG upon correction of hyperkalemia.

Patients presenting similarly would often demonstrate refractoriness to antidotes and chronotropic medications. In such situations, transvenous pacing and/or renal replacement therapy are often utilized.^{3,4} A recent systematic review and meta-analysis demonstrated that more than half of all patients who presented with BRASH had a non-severe hyperkalemia (<6.5 mmol/L). Beta blockers accounted for most of the implicated nodal agents, with the average mean arterial pressure of 62 and heart rate of 36 beats per minute. Most patients presented with junctional escape rhythm, and less commonly sinus bradycardia and complete heart block. The big majority of patients did respond to medical management with 20% requiring renal replacement therapy. A third of the patients eventually did require transcutaneous pacing.⁵

Several salient clinical features in our case strongly support the diagnosis of BRASH syndrome. These include the presence of disproportionate bradycardia despite the absence of severe hyperkalemia, the lack of characteristic electrocardiographic changes associated with hyperkalemia, the absence of an overdose history involving AV nodal blockers, and the subsequent resolution of bradycardia following the normalization of potassium levels.

Hyperkalemia can cause bradycardia because of effects on the sinoatrial, atrioventricular and ventricular conduction apparatuses.⁶ However, this

effect is usually seen above potassium level of 7 mmol/L.^{7,8} The presence of bradycardia at modest potassium elevation and remaining bradycardic while potassium dropped to 5.4 further supports that in this case BRASH syndrome might be the result of the potentiation and synergistic effect of concurrent AV nodal blockade.^{5,9}

Kidneys primarily excrete some AV nodal blocking agents and in the presence of AKI; they may accumulate, thereby potentiating the AV nodal effect. These include hydrophilic beta-blockers like atenolol, bisoprolol, nadolol and acebutolol.¹⁰ However, the inciting medications do not need to be renally cleared. Metoprolol, which was used in our case, is largely metabolized by the liver, and the metabolites, which are excreted by kidneys, do not have any beta blocker activity.¹¹ There is also propensity of beta-2 blockade to prevent transcellular transport of potassium causing hyperkalemia.¹²

Modest hyperkalemia and AV nodal blockade mutually potentiate the risk of bradycardia. Bradycardia decreases cardiac output and causes prerenal AKI.¹³ This, in turn, increases the risk of hyperkalemia and leads to further accumulation of renally cleared AV nodal blocking agents. Consequently, this vicious cycle can culminate in circulatory shock and multiorgan dysfunction if not appropriately managed. Treatment modalities encompass the management of hyperkalemia, fluid resuscitation, and circulatory support with pressors. The

administration of membrane stabilizing agents such as calcium gluconate is crucial, even in the absence of severe hyperkalemia or classic electrocardiographic findings associated with hyperkalemia. In the presence of metabolic acidosis, fluid resuscitation with isotonic bicarbonate is preferred. In cases of anuric AKI or lack of improvement, dialysis may be necessary. ACLS protocol for management of bradycardia may be useless in absence of aforementioned measures.^{1,14}

4. Conclusion

BRASH Syndrome is a rare, yet potentially life-threatening condition characterized by a confluence of Bradycardia, Renal failure, AV node block, Shock, and Hyperkalemia. The pathophysiology of this syndrome is intricate and multifactorial, and its diagnosis requires an increased awareness and a thorough assessment of the patient's clinical history, physical examination, and laboratory findings. Early recognition and expeditious management of BRASH syndrome are imperative to avoid potentially life-threatening complications.

Conflict of interest

The authors have no conflicts of interests to report.

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