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Brash Syndrome: A Rare but Critical Etiology of Bradycardia in the Setting of Acute Kidney Injury

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Abstract

The BRASH syndrome is a rare clinical pentad characterised by bradycardia, renal failure, atrioventricular (AV) blockade, shock and hyperkalaemia. Patients with BRASH syndrome typically present with bradycardia and hypotension due to the synergistic effect of AV node blocker and hyperkalaemia, compounded by underlying renal failure. In this report, we present a young patient with a history of chronic kidney disease and hypertension, who was taking regular beta-blockers and calcium channel blockers, and presented with persistent dizziness, headache and lethargy, which progressed into bradycardia and shock. These symptoms were refractory to initial resuscitation, requiring inotropic support and urgent haemodialysis. The patient was discharged in good condition after initiating regular dialysis. A high index of suspicion and early recognition are key to managing BRASH syndrome. Standard advanced cardiac life support algorithms without calcium are generally impractical for BRASH syndrome. The prognosis for BRASH syndrome is excellent with timely recognition and management.

Keywords: Bradycardia, Renal Failure, Hyperkalaemia

Introduction

The BRASH syndrome is a rare clinical pentad characterised by bradycardia, renal failure, atrioventricular (AV) blockade, shock and hyperkalaemia (1). This clinical condition was introduced by Farkas et al. in 2016 (2). Patients with BRASH syndrome typically present with bradycardia and shock caused by the synergistic effect of AV node blocker and hyperkalaemia, compounded by underlying renal failure (2). Bradycardia and shock eventually result in renal hypoperfusion and acute kidney injury, leading to worsening hyperkalaemia. This vicious pathophysiological cycle is life-threatening if not recognised and treated early. Additionally, precipitating events such as hypovolaemia and sepsis can further worsen the condition (1).

Case presentation

A 31-year-old woman with stage 5 chronic kidney disease and hypertension was on Amlodipine 10 mg once daily and Metoprolol 500 mg twice daily. She presented with persistent dizziness, headache and lethargy. She was hypotensive with a blood pressure of 51/34 mmHg and had marked bradycardia with a heart rate of 40 beats per minute. Her cardiac rhythm was regular, and no cardiac murmur was detected. The rest of the examination was unremarkable. Her first electrocardiogram (ECG) showed sinus bradycardia without ischaemia (Figure 1). Her serum potassium level was 5.4 mmol/L. Arterial blood gas analysis revealed metabolic acidosis (pH = 7.4, bicarbonate = 16.2 mmol/L) with appropriate respiratory compensation. Her serum urea and creatinine were elevated to 65.7 mmol/L and 1,366 mmol/L, respectively. The thyroid function test was normal. Chest radiography showed cardiomegaly with normal lung field. A bedside echocardiogram demonstrated left ventricular thickening and an ejection fraction of 30-40%, with no evidence of regional wall motion abnormality or right heart strain.

A guarded fluid bolus of 4 ml per kg normal saline and two doses of intravenous (IV) atropine 0.5 mg were administered. However, the blood pressure and heart rate did not improve after the initial treatment. Consequently, an IV infusion of epinephrine was started. The BRASH syndrome was suspected to correlate with bradycardia, renal failure, refractory hyperkalaemia, hypotension and acidosis. An IV administration of 10 ml of 10% calcium gluconate, 10 units of Actrapid and 50 ml of 50% dextrose

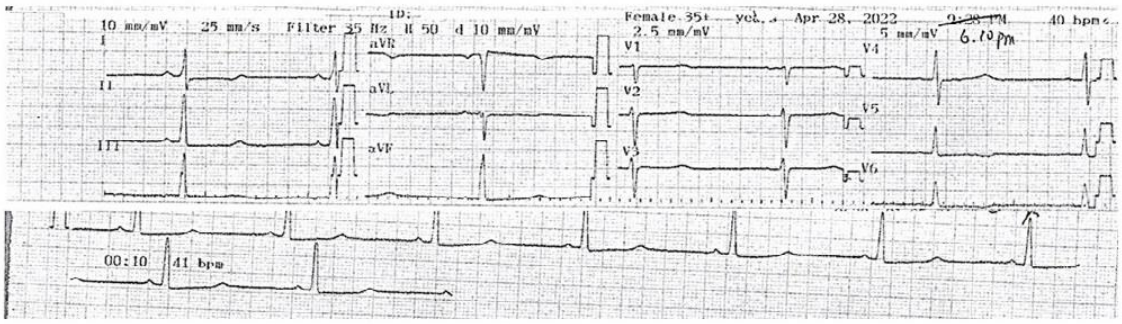

Figure 1: The patient's ECG upon arrival, showing sinus bradycardia.

was given for hyperkalaemia. The post-lytic cocktail ECG is shown in Figure 2. The patient's amlodipine and beta-blocker were withheld due to hypotension and bradycardia. Unfortunately, her heart rate and blood pressure remained persistently low, requiring inotropic support. Several haemodialysis sessions were performed in the ward to facilitate potassium excretion. Her heart rate returned to normal as her uraemic acidosis and refractory hyperkalaemia were managed, as shown in Table 1. The ECG post-haemodialysis is shown in Figure 3. The patient's inotropic support was successfully weaned off as her heart rate returned to normal on day 4 of admission. She was discharged in good condition and has required regular dialysis since then.

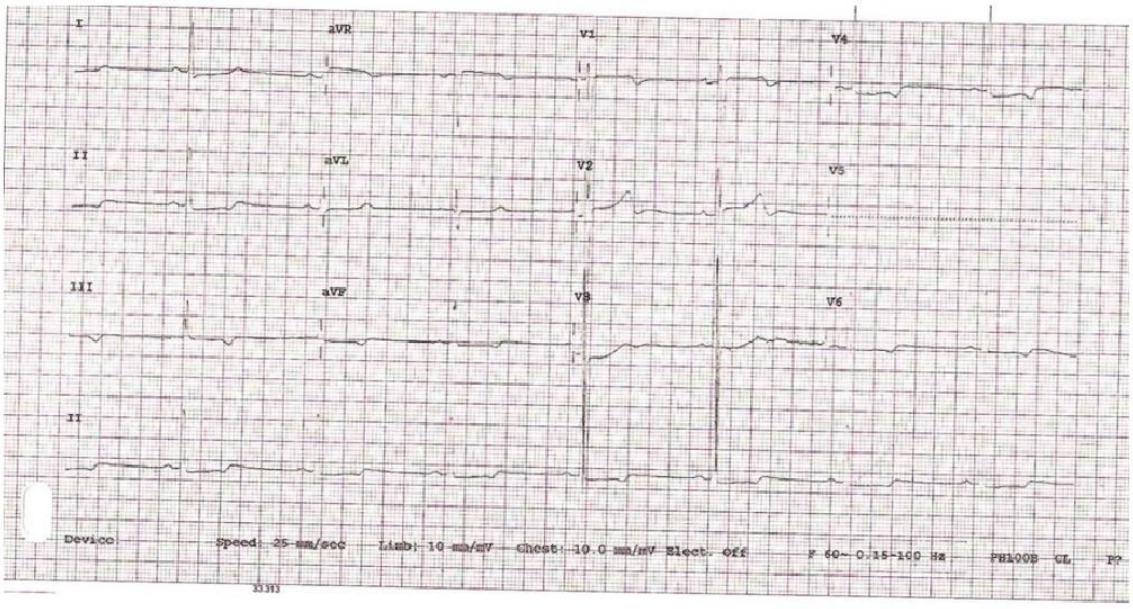

Figure 2: The patient's ECG post-lytic cocktail, showing no improvement in heart rate.

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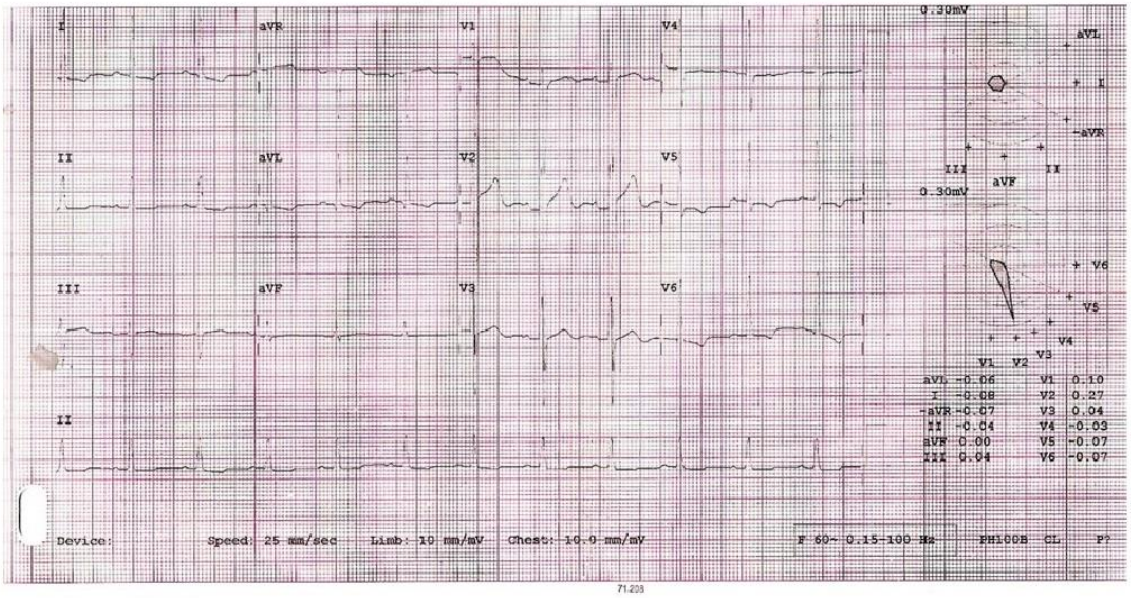

Figure 3: The patient's ECG post-haemodialysis. Her heart rate normalised after haemodialysis, corresponding to decreasing urea and creatinine levels.

Table 1: Summary of patient progress. Heart rate normalised after Continuous Veno-venous Hemofiltration (CVVH) was initiated, corresponding to decreasing urea and creatinine levels.

Date	Urea (mmol/L)	Creatinine (µmmol/L)	Potassium Level (mmol/L)	Heart Rate (HR) (bpm)	Blood Pressure (BP) (mmHg)	Remark
Baseline		701.0		N/A	N/A	N/A
On arrival	65.7	1366.0	5.4	40	51/34	Initial treatment as mentioned.
Day 1	62.1	1423.5	5.1	39	112/70	Started on IVI epinephrine, completed Hemodialysis.
Day 2	44.8	1127.9	4.7	41	140/73	BP was unsupported, but the patient remained bradycardic.
Day 3	45.4	1134.8	4.7	53	102/70	Transferred into intensive care unit (ICU) and started on CVVH
Day 4	33.8	685.3	3.6	82	114/69	CVVH day 2.
Day 5	16.6	366.9	3.8	101	148/79	CVVH ended.
Day 6	15.7	330.9	3.8	99	140/79	Beta-blocker was restarted.
Day 7	21.7	424.4	4.1	87	160/95	Optimizing antihypertensive medications.
Day 8	25.7	473.3	3.5	87	133/86	On regular hemodialysis.

N/A: Not available
CVVH: Continuous Veno-venous Hemofiltration

Discussion

The BRASH syndrome is a rare phenomenon that is often under-recognised. The name BRASH syndrome was derived from the symptoms it presents with, namely bradycardia, renal failure, AV node blockade, shock and hyperkalaemia (1).

The pathophysiologic characteristic of BRASH syndrome involves a vicious cycle of specific medication use, hyperkalaemia and renal failure, as shown in Figure 4. The proposed mechanism is that renal failure may trigger hyperkalaemia, leading to the accumulation of AV node blockers. AV node blockers may increase plasma potassium levels by inhibiting aldosterone release, resulting in reduced potassium uptake by cells. The synergic effects of AV node blockers and hyperkalaemia can lead to bradycardia and hypoperfusion, further worsening renal function. This phenomenon is often unnoticed but may contribute to rapid clinical deterioration (3). This case report highlights the importance of recognising BRASH syndrome and initiating appropriate treatment.

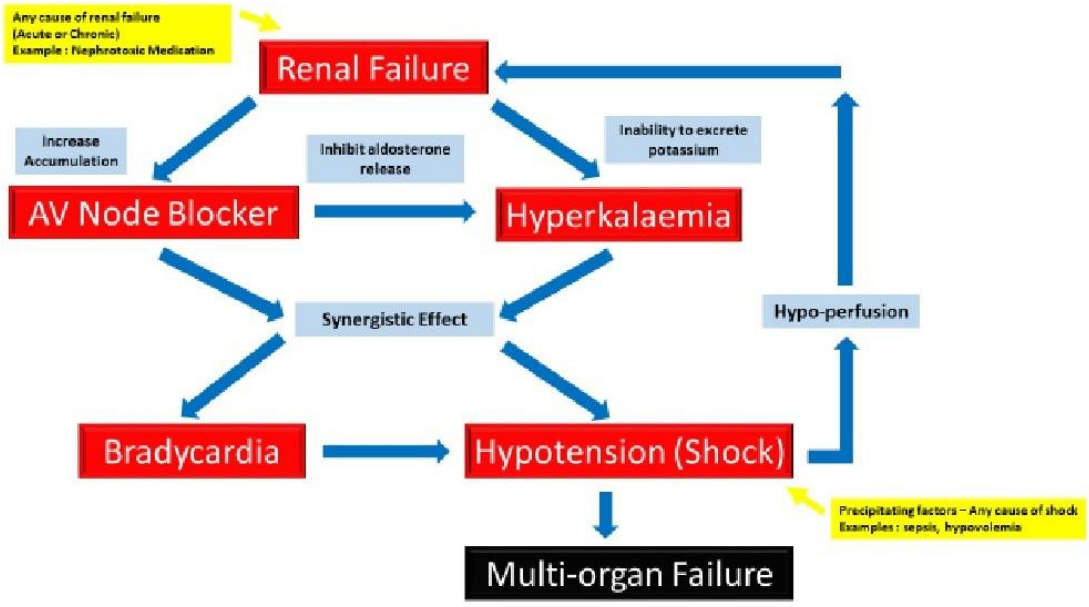

Figure 4: Vicious cycle of BRASH syndrome.

AV Node Blocker: Atrioventricular Node Blocker.
References: J. D. Farkas et al. (1) and RECAPEM (10)

One of the most common triggering factors of BRASH syndrome is hypovolaemia. It often causes hypoperfusion to the kidneys and results in acute kidney injury. Patients with reduced kidney function are at risk of developing BRASH syndrome (4). The elderly have a higher prevalence of BRASH syndrome due to their cardiac and renal comorbidities, and AV node blockers are frequently prescribed in this age group (1). In previous literature, the age group reported with BRASH syndrome ranged from 43 to 89 years (5). However, in this case, the patient was a 31-year-old woman, suggesting that younger patients with similar comorbidities may also be at risk of developing BRASH syndrome. Any event that promotes renal failure or hyperkalaemia can potentially trigger BRASH syndrome. However, BRASH syndrome is typically characterised by its clinical presentation rather than the precipitating factors (2).

BRASH syndrome diagnoses are based on history taking, ECG findings and laboratory investigations. The presentation is often non-specific, with patients potentially presenting with asymptomatic bradycardia, ranging from mild symptoms to cardiopulmonary arrest (1, 2, 4).

The clinical entity of BRASH syndrome represents an overlap between AV node blocker intoxication and hyperkalaemia (3). To differentiate BRASH syndrome from pure hyperkalaemia, it has been reported that patients with BRASH syndrome often have a mild or moderate level of hyperkalaemia, causing significant bradycardia without other typical hyperkalaemia features appearing on the ECG (1). ECG findings in BRASH syndrome can vary from sinus and junctional bradycardia to third-degree AV block, without other ECG features of hyperkalaemia (4). On the other hand, conduction abnormalities or bradyarrhythmias

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are more common in isolated hyperkalaemia, typically with a potassium level of 7 mmol/L or more (6). Patients with BRASH syndrome may have profound or refractory bradycardia, even with mild hyperkalaemia, due to the synergistic effect of AV node blockers and the vicious cycle of BRASH syndrome (1, 2). A reported patient may remain bradycardic, even after the potassium level normalises, as seen in this case (4).

Distinguishing BRASH syndrome from AV node blocker toxicity can be challenging. Hyperkalaemia may not be present in patients with beta- or calcium-blocker intoxication. In BRASH syndrome, a history of overdose on AV node blocker medication is a key factor to help differentiate the two diagnoses. Patients with BRASH syndrome often have a history of renal insufficiency and regularly take AV node blockers, such as calcium channel blockers or beta blockers, without overdose (2). History of precipitating events such as gastrointestinal losses, recent changes in medication and sepsis is also essential (1). Drug levels should be tested to rule out AV node blocker toxicity if necessary. In this case, the patient was known to have chronic kidney disease and was on two types of AV node blockers. She presented with hypovolaemia, which may predispose her to develop BRASH syndrome.

Urea and creatinine remain elevated in BRASH syndrome. The BRASH syndrome can occur in patients with chronic kidney disease and acute kidney injury. There was a reported case where a patient on an AV node blocker presented acute kidney injury with BRASH syndrome after consuming sulfamethoxazole and trimethoprim (7).

The key to managing BRASH syndrome is early identification and managing the condition as a syndrome rather than treating each abnormality individually. The treatment modality aims to treat hyperkalaemia, bradycardia, hypovolaemia and renal hypoperfusion by fluid resuscitation, IV calcium, triple regimen and withholding the causative agent (8).

In hypovolaemic patients, the recommended choice for fluid replacement is IV isotonic bicarbonate or balanced crystalloid, guided by patient blood gases and volume assessment using bedside ultrasound. Patients with normal anion gap metabolic acidosis may benefit from isotonic bicarbonate infusion (1, 2).

Calcium is a vital myocardium stabiliser, and it helps in improving heart rate and cardiac output (7). It also reduces the need for transvenous pacemaker intervention (2). The recommended dose of calcium gluconate is 10 mL of a 10% solution administered over 5-10 minutes, or calcium chloride 1 gram IV given over 1 to 2 minutes (1). Repeated doses may be given if necessary. Inotropic support, such as epinephrine, and haemodialysis should be considered if initial measures fail (1).

In addition to the usual approach to treating hyperkalaemia by the triple regimen of calcium, dextrose and insulin, the literature suggests that diuretics can help excrete excess potassium through urine (1). However, there is a limitation in patients with hypovolaemia or anuria. A few cases have reported failed inotropic support, necessitating pacing or urgent haemodialysis (5). The standard advanced cardiac life support (ACLS) algorithms without calcium are generally impractical for BRASH syndrome (2). It is also important to note that atropine has no role in the management of BRASH syndrome (9).

Therefore, early haemodialysis should be performed despite hypotension in a patient in shock and suspected BRASH syndrome with concurrent renal failure. The aim is to correct the electrolyte abnormalities and remove the offending agent from the patient's system.

This case demonstrates the importance of early haemodialysis and the limitations of the standard ACLS approach in managing BRASH syndrome. This patient was successfully weaned off inotropic support after a few haemodialysis sessions and was discharged in good condition.

Conclusion

A high index of suspicion and early recognition are key to managing BRASH syndrome, especially in patients with a history of AV node blocker use or chronic kidney diseases. The prognosis of BRASH syndrome is excellent with timely recognition and management.

Informed Consent

Verbal consent for this anonymous case report was obtained from the patient due to logistical constraints.

Competing interest

None declared.

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