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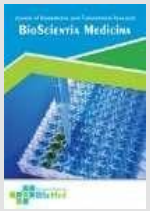

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Unmasking BRASH Syndrome: A Rare and Reversible Cause of Cardiovascular Collapse in the Elderly

Milhan El-Yamani Karim[1*], Tawang Handayani[1], Hardianti Hardmi Putri[2], Setiawan Widodo[3]

[1]Emergency Department, Dewi Sri Hospital, Karawang, Indonesia

[2]Outpatient Department, Gempol Primary Clinic, Karawang, Indonesia

[3]Department of Cardiology and Vascular Medicine, Dewi Sri Hospital, Karawang, Indonesia

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***Corresponding author:**
Milhan El-Yamani Karim

E-mail address:
milhanelyamani@gmail.com

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A B S T R A C T

Background: BRASH syndrome (Bradycardia, Renal failure, AV nodal blockade, Shock, and Hyperkalemia) is an increasingly recognized but still underdiagnosed condition, particularly in elderly patients with multiple comorbidities and those taking AV nodal blocking agents. It represents a synergistic interplay between these factors, leading to a potentially life-threatening state of cardiovascular collapse. This case report aims to highlight the clinical presentation, diagnostic challenges, and successful management of BRASH syndrome in an elderly female patient. **Case presentation:** A 65-year-old female with a history of stage 4 chronic kidney disease and congestive heart failure (ejection fraction of 65%) presented to the emergency department with worsening vomiting over the past week, generalized weakness, dizziness, and palpitations. Her medication list included amlodipine, bisoprolol, candesartan, nitrokaf, furosemide, and aminoral. On examination, she was hypotensive with a blood pressure of 90/60 mmHg and bradycardic with a heart rate of 40 beats per minute. An electrocardiogram (ECG) revealed a junctional escape rhythm with a heart rate of 38 beats per minute and a left bundle branch block. Laboratory investigations showed severe hyperkalemia (potassium 8.1 mmol/L), hyponatremia (sodium 113 mmol/L), elevated creatinine (4.06 mg/dL), and urea (112.3 mg/dL). **Conclusion:** This case underscores the importance of recognizing BRASH syndrome as a distinct clinical entity, especially in elderly patients with pre-existing cardiac and renal conditions who are on AV nodal blocking medications. Prompt diagnosis and management, focusing on correcting hyperkalemia, discontinuing offending medications, and providing supportive care, can lead to favorable outcomes and prevent potentially fatal complications. Increased awareness and further research are crucial for establishing standardized guidelines for the diagnosis and management of this underrecognized syndrome.

1. Introduction

BRASH syndrome is a clinical entity of growing recognition, yet it remains a diagnostic challenge, particularly in complex patients. The acronym encapsulates a constellation of critical clinical findings: Bradycardia, Renal failure, AV nodal blockade, Shock, and Hyperkalemia. This syndrome represents a dangerous convergence of commonly encountered medical conditions and the widespread use of specific pharmacological agents, creating a potentially life-threatening scenario of cardiovascular compromise. The syndrome's pathophysiology is characterized by a deleterious cycle. Atrioventricular (AV) nodal blocking agents, frequently employed in the management of prevalent cardiovascular conditions such as hypertension and heart failure, can precipitate or exacerbate hyperkalemia. Hyperkalemia, in turn, has profound effects on cardiac electrophysiology, contributing to the development or worsening of bradycardia. The resultant bradycardia can compromise renal perfusion, leading to or worsening renal dysfunction. This decline in renal function

further impairs potassium excretion, thus fueling the hyperkalemia and perpetuating the cycle.[1-3]

The true prevalence of BRASH syndrome in the general population is difficult to ascertain. This is attributable, in part, to its relatively recent delineation as a distinct clinical entity. Furthermore, the clinical manifestations of BRASH syndrome can be easily misconstrued as isolated hyperkalemia or attributed to other common conditions, especially in the geriatric population, which often presents with a multitude of comorbidities. However, given the global aging demographic trends and the ubiquitous use of AV nodal blocking medications, it is reasonable to hypothesize that the incidence of BRASH syndrome is likely underrecognized and underestimated in current clinical practice. The failure to promptly recognize and institute appropriate management for BRASH syndrome carries the potential for significant morbidity and mortality. This underscores the critical importance of enhancing awareness of this syndrome among healthcare providers across various medical specialties.[4-6]

Elderly patients represent a particularly vulnerable population for the development of BRASH syndrome. This heightened susceptibility is multifactorial. Older adults frequently have a higher burden of comorbid conditions, including chronic kidney disease and heart failure. These underlying conditions inherently predispose individuals to the development of hyperkalemia and increase the risk of hemodynamic instability. Furthermore, the management of cardiovascular conditions in the elderly often necessitates the prescription of AV nodal blocking agents, such as beta-adrenergic receptor blockers and calcium channel blockers, further increasing the risk of BRASH syndrome. Dehydration and hypovolemia are also commonly encountered in the elderly population. These conditions can further compromise renal function, contributing to the development or exacerbation of hyperkalemia and potentiating the effects of AV nodal blocking medications. The interplay of these factors creates a precarious scenario in which the elderly are particularly susceptible to the deleterious effects of BRASH syndrome.[7-10] This case report aims to contribute to the existing body of knowledge by detailing the clinical presentation, diagnostic process, and subsequent management of an elderly female patient who developed BRASH syndrome.

2. Case Presentation

The patient, a 65-year-old female, presented to the emergency department exhibiting a constellation of symptoms that ultimately led to the diagnosis of BRASH syndrome. Her presentation was notable for a primary complaint of worsening vomiting, a symptom that had been progressively increasing in severity over the preceding week. This primary symptom was accompanied by a cluster of associated symptoms, including generalized weakness, dizziness, and palpitations. These symptoms, taken in conjunction with the patient's medical history and the findings of the physical examination and laboratory investigations, formed a clinical picture consistent with the complexities of BRASH syndrome. The patient's medical history was significant for several chronic conditions. She had a documented history of stage 4 chronic kidney disease, a condition that inherently predisposes individuals to electrolyte imbalances and cardiovascular complications. In addition to her chronic kidney disease, the patient also had a history of congestive heart failure. The patient's ejection fraction, a key indicator of the heart's pumping efficiency, was reported to be 65%. While an ejection fraction of 65% is generally considered to be within the normal range, it is important to note that the patient had a history of congestive heart failure, a condition that can fluctuate in severity and may be associated with other structural or functional cardiac abnormalities. Importantly, the patient's medical history did not include any reported history of diabetes mellitus or other significant medical conditions. This absence of diabetes is noteworthy, as diabetes is a common comorbidity in elderly patients and can contribute to both renal and cardiovascular complications. The patient's medication regimen was

complex, reflecting the management of her chronic medical conditions. She was taking several regular medications, including amlodipine 5 mg once daily, bisoprolol 5 mg once daily, candesartan 8 mg once daily, Nitrokaf (isosorbide dinitrate) 5 mg three times daily, furosemide 40 mg once daily, and Aminoral (a combination of amino acids) one tablet three times daily. Amlodipine is a calcium channel blocker commonly used in the management of hypertension and angina. Bisoprolol is a beta-blocker, another class of medication frequently used for hypertension, heart failure, and other cardiovascular conditions. Candesartan is an angiotensin II receptor blocker (ARB) used for hypertension and heart failure. Nitrokaf, containing isosorbide dinitrate, is a nitrate medication used for the management of angina. Furosemide is a loop diuretic, commonly used to manage fluid overload associated with heart failure and other conditions. Aminoral, a combination of amino acids, is often used as a nutritional supplement, particularly in patients with chronic kidney disease. Notably, there were no recent changes to the patient's medication regimen reported, suggesting that the current presentation was not attributable to an alteration in her prescribed medications. However, the presence of bisoprolol, an AV nodal blocking agent, is a critical factor in the context of BRASH syndrome. The physical examination revealed several important findings. The patient's general appearance was described as frail and mildly dehydrated. Frailty is a common condition in elderly individuals and is characterized by decreased physiological reserve and increased vulnerability to stressors. Mild dehydration is also a frequent finding in the elderly and can contribute to a variety of medical complications, including renal dysfunction and electrolyte imbalances. In terms of vital signs, the patient was hypotensive, with a blood pressure reading of 90/60 mmHg. Hypotension, or low blood pressure, can be a sign of inadequate tissue perfusion and can be associated with a variety of underlying medical conditions. The patient was also bradycardic, with a heart rate of 40 beats per minute. Bradycardia, or a slow heart rate, can be a manifestation of underlying cardiac conditions, medication effects, or electrolyte imbalances. The patient's respiratory rate was 20 breaths per minute, which is within the normal range. Her oxygen saturation was 98% on room air, indicating adequate oxygenation. The cardiovascular examination revealed no jugular venous distension or peripheral edema. The absence of jugular venous distension suggests that there was no significant elevation in central venous pressure, which can be seen in conditions such as heart failure. The absence of peripheral edema suggests that there was no significant fluid retention in the extremities. The patient's cardiac rhythm was described as regular but bradycardic. There were no murmurs or gallops auscultated, suggesting that there were no significant valvular abnormalities or other abnormal heart sounds. The respiratory examination revealed that the lungs were clear to auscultation bilaterally, with no crackles or wheezes. This suggests that there was no evidence of significant pulmonary congestion or other respiratory abnormalities. The abdominal examination revealed that the abdomen was soft and non-tender, suggesting that there was no acute abdominal pathology. The neurological examination was reported to be unremarkable, indicating that there were no obvious neurological deficits. An electrocardiogram (ECG) was performed, revealing a junctional escape rhythm with a ventricular rate of 38 beats per minute. A junctional escape rhythm is a type of bradyarrhythmia that originates from the AV junction, rather than the sinoatrial (SA) node, which is the normal pacemaker of the heart. The ventricular rate of 38 beats per minute is significantly below the normal range, indicating significant bradycardia. The ECG also revealed a left bundle branch block, a conduction abnormality that affects the left ventricle. There were no acute ischemic changes noted on the ECG, suggesting that there was no evidence of acute myocardial ischemia or infarction. Laboratory investigations revealed several significant abnormalities. The serum potassium level was 8.1 mmol/L, indicating severe hyperkalemia. The

reference range for serum potassium is typically 3.5-5.0 mmol/L, so this value is significantly elevated. Hyperkalemia, or elevated serum potassium, can have profound effects on cardiac electrophysiology and can lead to bradycardia and other arrhythmias. The serum sodium level was 113 mmol/L, indicating hyponatremia. The reference range for serum sodium is typically 135-145 mmol/L, so this value is significantly decreased. Hyponatremia, or low serum sodium, can be associated with a variety of medical conditions and can cause neurological symptoms. The serum creatinine level was 4.06 mg/dL, which was elevated. The patient's baseline creatinine was approximately 3.5 mg/dL, indicating a worsening of renal function. Elevated serum creatinine is a marker of renal dysfunction. The blood urea nitrogen (BUN) level was 112.3 mg/dL, which was also elevated. The reference range for BUN is typically 7-20 mg/dL, so this value is significantly increased. Elevated BUN is another marker of renal dysfunction. The hemoglobin level was 11.5 g/dL, which is within the normal range. The white blood cell count was 7.2 x 10^3/L, which is also within the normal range. The platelet count was 210 x 10^3/L, which is within the normal range as well. Based on the totality of the clinical presentation, including the patient's history, physical examination findings, ECG results, and laboratory investigations, the clinical diagnosis of BRASH syndrome was established. The presence of bradycardia, renal failure, AV nodal blockade (as evidenced by the junctional escape rhythm and the use of bisoprolol), shock (as evidenced by hypotension), and hyperkalemia, all in the context of an elderly patient with chronic kidney disease and heart failure, supported this diagnosis. The patient's medication regimen, which included bisoprolol, an AV nodal blocking agent, was a key contributing factor to the development of BRASH syndrome. The episode of worsening vomiting likely led to dehydration and a prerenal acute kidney injury, which exacerbated the hyperkalemia and further contributed to the syndrome. The interplay of these factors resulted in a life-threatening condition that required prompt recognition and aggressive management (Table 1).

The management of the 65-year-old female patient diagnosed with BRASH syndrome involved a comprehensive and multifaceted approach, initiated with the patient's immediate transfer to the intensive care unit (ICU). This decision underscored the severity of her condition and the necessity for close monitoring and intensive management of her complex physiological derangements. The transfer to the ICU facilitated continuous observation of her vital signs, laboratory parameters, and overall clinical status, allowing for timely interventions and adjustments in her treatment plan. The cornerstone of the patient's management focused on addressing the life-threatening hyperkalemia that characterized her presentation. Hyperkalemia, defined as an elevated serum potassium level, poses a significant risk of cardiac arrhythmias and other adverse cardiac events. In this patient, the serum potassium was markedly elevated at 8.1 mmol/L, necessitating immediate and aggressive treatment. The initial intervention to mitigate the cardiac effects of hyperkalemia involved the intravenous administration of calcium gluconate. Calcium gluconate acts by stabilizing the cardiac cell membranes, thereby reducing the risk of arrhythmias induced by hyperkalemia. It does not lower the serum potassium level itself but rather antagonizes its deleterious effects on the heart. A dose of 1 gram of intravenous calcium gluconate was administered as a standard initial dose in the management of severe hyperkalemia. Following the administration of calcium gluconate, further measures were implemented to reduce the serum potassium concentration. Intravenous boluses of 10 units of regular insulin in conjunction with 50 mL of 40% dextrose (D40) were given for two cycles. This therapeutic strategy aims to shift potassium intracellularly, effectively lowering the serum potassium level. Insulin stimulates the sodium-potassium ATPase pump, which promotes the movement of potassium from the extracellular to the intracellular space. The administration of dextrose is crucial to prevent hypoglycemia, a potential complication of insulin therapy. The protocol of

administering insulin and dextrose was repeated to ensure a sustained reduction in serum potassium. In addition to addressing the hyperkalemia, the patient's hyponatremia was also carefully corrected. Hyponatremia, a state of low serum sodium, can lead to serious complications, including cerebral edema and seizures. The patient's serum sodium was 113 mmol/L, significantly below the normal range of 135-145 mmol/L. The correction of hyponatremia requires a careful and gradual approach to avoid the risk of osmotic demyelination syndrome, a potentially devastating neurological complication that can occur with rapid correction. The patient's hyponatremia was corrected with a slow infusion of intravenous isotonic saline, with close monitoring of serum sodium levels to ensure a safe rate of correction. Given the patient's hypotension and bradycardia, hemodynamic support was deemed necessary. An intravenous infusion of dopamine was initiated to provide hemodynamic support and potentially increase heart rate. Dopamine is a catecholamine that acts on various receptors, including beta-1 adrenergic receptors in the heart, leading to increased heart rate and contractility, and dopaminergic receptors, leading to renal vasodilation. The infusion rate of dopamine was carefully titrated based on the patient's blood pressure and heart rate response. To further promote potassium excretion, furosemide, a loop diuretic, was continued at a dose of 40 mg three times daily. Furosemide acts on the loop of Henle in the kidneys to increase the excretion of sodium and potassium in the urine. This helps to lower the serum potassium level and also aids in managing fluid overload. Additional potassium-lowering measures were implemented to augment the effects of insulin, dextrose, and furosemide. Salbutamol, a beta-2 adrenergic agonist, was administered at a dose of 8 mg twice daily via nebulizer. Beta-2 agonists also promote the intracellular shift of potassium, contributing to a further reduction in serum potassium. Intravenous sodium bicarbonate was administered three times daily. Sodium bicarbonate can enhance potassium elimination and also help to correct any underlying metabolic acidosis. These additional measures were taken to ensure a comprehensive approach to managing the patient's severe hyperkalemia. A critical aspect of the patient's management involved the discontinuation of offending medications. Bisoprolol and Nitrokaf, both of which can contribute to bradycardia and hypotension, were immediately discontinued. Bisoprolol, a beta-blocker, is an AV nodal blocking agent that can exacerbate bradycardia. Nitrokaf, containing isosorbide dinitrate, can cause hypotension. Discontinuing these medications was crucial to breaking the cycle of BRASH syndrome and preventing further deterioration of the patient's condition. Other medications were also temporarily held and later re-evaluated. Amlodipine and candesartan were held temporarily. Amlodipine, a calcium channel blocker, can contribute to hypotension. Candesartan, an ARB, can potentially affect renal function and potassium levels. These medications were held as a precautionary measure and their resumption was considered based on the patient's clinical course. Aminoral was continued as per her chronic medication regimen. Aminoral, a combination of amino acids, was continued as it was part of her routine management for chronic kidney disease. Throughout the patient's hospital stay, serial laboratory monitoring was conducted to assess her response to treatment and to guide further management decisions. Serial monitoring revealed a gradual decrease in serum potassium levels, indicating the effectiveness of the potassium-lowering therapies. After the initial interventions, the potassium level decreased to 6.9 mmol/L, and the patient's clinical condition showed improvement. This improvement in potassium levels correlated with an improvement in the patient's overall clinical status. There was also a notable improvement in the patient's heart rate and blood pressure. Her heart rate increased to approximately 70 beats per minute, and her blood pressure improved, allowing for a gradual weaning of the dopamine infusion. The increase in heart rate reflected the improvement in bradycardia, and the improvement in blood pressure indicated

better hemodynamic stability. The gradual weaning of dopamine demonstrated the patient's improving ability to maintain adequate blood pressure without pharmacological support. A repeat 12-lead ECG demonstrated a change in rhythm to sinus rhythm with a heart rate of 70 beats per minute. This was a significant improvement from the initial junctional escape rhythm with a heart rate of 38 beats per minute. The return to sinus rhythm indicated improved cardiac function and resolution of the bradyarrhythmia. The left bundle branch block persisted. While the rhythm improved, the left bundle branch block remained, suggesting that the underlying conduction abnormality was still present. The patient's renal function remained impaired, but she did not require acute dialysis during this episode. While the patient had chronic kidney disease, the acute episode did not necessitate renal replacement therapy, indicating that the interventions were effective in stabilizing her renal function. The patient's renal function was closely monitored throughout her hospital stay. The correction of hyponatremia was conducted gradually, and her overall clinical status improved significantly over the next few days. The gradual correction of hyponatremia was essential to prevent complications. The patient's overall improvement was evident in her improving vital signs, laboratory parameters, and general condition. She was able to tolerate oral intake and was transitioned to oral medications. As her condition stabilized, the patient was able to resume oral intake, and her medications were transitioned from intravenous to oral formulations. This transition reflected her improving clinical status and readiness for discharge. Prior to discharge, her medications were reviewed. A thorough medication review is a crucial step in the management of complex patients with multiple comorbidities. Decisions were made to continue furosemide, salbutamol, aminoral, and sodium bicarbonate. These medications were deemed necessary for the continued management of her underlying conditions. The bisoprolol was not restarted, and alternative management for her hypertension was considered for outpatient follow-up. Given its role in the development of BRASH syndrome, bisoprolol, the beta-blocker, was not restarted. Alternative strategies for managing her hypertension were planned for outpatient follow-up to ensure adequate blood pressure control without the risk of recurrent BRASH syndrome. The patient was discharged home in stable condition. The patient's condition at discharge was stable, indicating that the treatment interventions were successful in resolving the acute episode of BRASH syndrome. The patient was discharged with instructions for close follow-up with her cardiologist and nephrologist. Close follow-up with her cardiologist and nephrologist was crucial for the ongoing management of her chronic heart condition and kidney disease, as well as for the management of her hypertension. At her one-month follow-up appointment, she reported feeling well. The patient's subjective report indicated a positive recovery and a return to her baseline functional status. Her laboratory parameters showed stable renal function and normokalemia. The laboratory parameters at the one-month follow-up demonstrated stable renal function and normal potassium levels, indicating the sustained effectiveness of the treatment interventions and the absence of recurrence of hyperkalemia. This positive follow-up confirmed the successful management of BRASH syndrome and the patient's recovery (Table 2).

3. Discussion

The patient's initial presentation to the emergency department was characterized by a cluster of symptoms, with worsening vomiting taking precedence. While vomiting, in isolation, is a relatively common symptom with a broad differential diagnosis, its progressive nature and association with generalized weakness, dizziness, and palpitations suggest a more complex underlying process. The symptom of vomiting itself can lead to a cascade of physiological disturbances, including fluid and electrolyte imbalances, which can significantly contribute to the development or exacerbation of conditions like BRASH syndrome.

Table 1. Summary of patient's clinical findings.

Category	Finding	Details
Patient demographics	Age	65 years old
	Gender	Female
Chief complaint	Primary Symptom	Worsening vomiting
	Associated Symptoms	Generalized weakness, dizziness, palpitations
Past medical history	Chronic Conditions	Stage 4 chronic kidney disease
		Congestive heart failure (ejection fraction of 65%)
		No history of diabetes mellitus or other significant medical conditions reported
Medications	Regular Medications	Amlodipine 5 mg once daily
		Bisoprolol 5 mg once daily
		Candesartan 8 mg once daily
		Nitrokaf (isosorbide dinitrate) 5 mg three times daily
		Furosemide 40 mg once daily
		Aminoral (combination of amino acids) one tablet three times daily
	Recent Changes	No recent changes to the medication regimen reported
Physical examination	General Appearance	Frail and mildly dehydrated
	Vital Signs	Blood pressure: 90/60 mmHg (hypotensive)
		Heart rate: 40 beats per minute (bradycardic)
		Respiratory rate: 20 breaths per minute
		Oxygen saturation: 98% on room air
	Cardiovascular	No jugular venous distension or peripheral edema
		Regular but bradycardic rhythm, no murmurs or gallops on auscultation
	Respiratory	Lungs clear to auscultation bilaterally, no crackles or wheezes
	Abdomen	Soft and non-tender
	Neurological	Unremarkable
Electrocardiogram (ECG)	Rhythm	Junctional escape rhythm with a ventricular rate of 38 beats per minute (Figure 1)
	Other Findings	Left bundle branch block
		No acute ischemic changes
Laboratory investigations	Serum Potassium	8.1 mmol/L (severe hyperkalemia) (Reference range: 3.5-5.0 mmol/L)
	Serum Sodium	113 mmol/L (hyponatremia) (Reference range: 135-145 mmol/L)
	Serum Creatinine	4.06 mg/dL (elevated, baseline approximately 3.5 mg/dL)
	Blood Urea Nitrogen (BUN)	112.3 mg/dL (elevated) (Reference range: 7-20 mg/dL)
	Hemoglobin	11.5 g/dL
	White Blood Cell Count	7.2 x 10^3/L
	Platelet Count	210 x 10^3/L
Clinical diagnosis		BRASH Syndrome

Table 2. Treatment and follow-up.

Category	Intervention/Monitoring	Details
Initial management	Transfer to ICU	Patient was immediately transferred to the intensive care unit for close monitoring and management.
	Management of Hyperkalemia	
		Intravenous calcium gluconate (1 gram) was administered to antagonize the cardiac effects of hyperkalemia.
		Intravenous bolus of 10 units of regular insulin along with 50 mL of 40% dextrose (D40) was given for two cycles to shift potassium intracellularly.
	Correction of Hyponatremia	Hyponatremia was carefully corrected with a slow infusion of 3% hypertonic saline to avoid osmotic demyelination syndrome.
	Hemodynamic Support	Intravenous infusion of dopamine was initiated to provide hemodynamic support and potentially increase heart rate.
	Promotion of Kaliuresis	Furosemide (20 mg three times daily) was continued to promote potassium excretion.
	Additional Potassium Lowering Measures	Salbutamol (8 mg twice daily via nebulizer) and intravenous sodium bicarbonate (three times daily) were also administered to further assist in potassium lowering.
	Discontinuation of Offending Medications	Bisoprolol and nitrokaf, both of which can contribute to bradycardia and hypotension, were immediately discontinued.
	Temporary Holding of Other Medications	Amlodipine and candesartan were held temporarily and later re-evaluated.
	Continuation of Aminoral	Aminoral was continued as per her chronic medication regimen.
Monitoring and subsequent course	Serial Laboratory Monitoring	Serial laboratory monitoring revealed a gradual decrease in serum potassium levels.
	Improvement in Potassium Levels	After the initial interventions, the potassium level decreased to 6.9 mmol/L, and the patient's clinical condition showed improvement.
	Improvement in Heart Rate and Blood Pressure	Her heart rate increased to approximately 70 beats per minute, and her blood pressure improved, allowing for a gradual weaning of the dopamine infusion.
	Repeat ECG	A repeat 12-lead ECG demonstrated a change in rhythm to sinus rhythm with a heart rate of 70 beats per minute (Figure 2).
		The left bundle branch block persisted.
	Renal Function	The patient's renal function remained impaired, but she did not require acute dialysis during this episode.
	Correction of Hyponatremia and Overall Improvement	Her hyponatremia was corrected gradually, and her overall clinical status improved significantly over the next few days.
	Tolerance of Oral Intake	She was able to tolerate oral intake and was transitioned to oral medications.
Pre-discharge management	Medication Review	Prior to discharge, her medications were reviewed.
	Medications Continued	A decision was made to continue furosemide, salbutamol, aminoral, and sodium bicarbonate.
	Bisoprolol Management	The bisoprolol was not restarted, and alternative management for her hypertension was considered for outpatient follow-up.
	Discharge Condition	The patient was discharged home in stable condition.
	Discharge Instructions	The patient was discharged with instructions for close follow-up with her cardiologist and nephrologist.
Follow-up	One-Month Follow-Up	At her one-month follow-up appointment, she reported feeling well.
		Her laboratory parameters showed stable renal function and normokalemia.

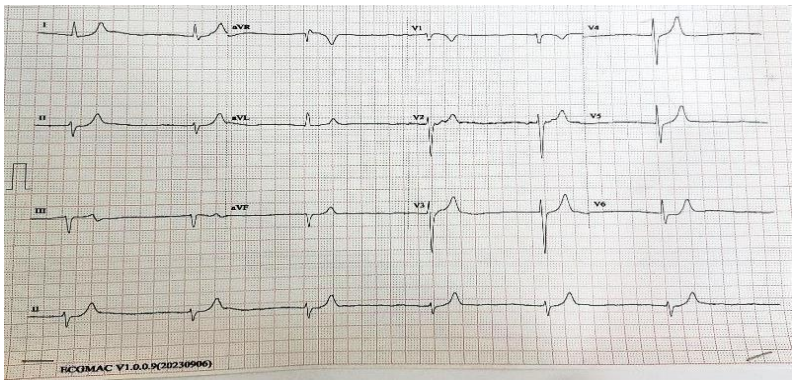

Figure 1. Initial ECG revealed a junctional escape rhythm, characterized by a heart rate of 38 beats per minute.

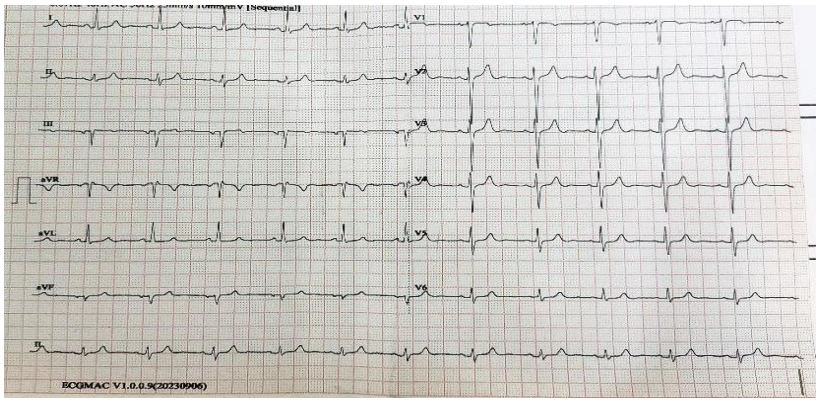

Figure 2. ECG post-therapy revealed a sinus rhythm, with a heart rate of 70 beats per minute.

In this context, the reported worsening of vomiting over the preceding week likely played a crucial role in precipitating the patient's acute presentation. The patient's past medical history revealed two significant chronic conditions: stage 4 chronic kidney disease and congestive heart failure with a reported ejection fraction of 65%. Stage 4 chronic kidney disease represents a substantial decline in renal function. This decline has profound implications for the body's ability to maintain electrolyte homeostasis, particularly concerning potassium regulation. The kidneys play a central role in potassium excretion, and their impaired function in chronic kidney disease predisposes individuals to hyperkalemia. Furthermore, chronic kidney disease is frequently associated with cardiovascular complications, including hypertension and heart failure, creating a complex interplay of factors that can increase the risk of conditions like BRASH syndrome. Congestive heart failure, even with a preserved ejection fraction of 65%, indicates underlying cardiac dysfunction. Heart failure can be associated with structural or functional abnormalities of the heart, as well as neurohormonal dysregulation, which can impact cardiovascular stability and increase susceptibility to arrhythmias. The fact that the patient had both stage 4 chronic kidney disease and congestive heart failure highlights the complexity of her medical history and the potential for interactions between these conditions to contribute to acute presentations. The patient's medication regimen was notable for including several drugs with cardiovascular effects. Amlodipine, a calcium channel blocker, is commonly used for hypertension and angina. Bisoprolol, a beta-blocker, is another mainstay in the treatment of hypertension, heart failure, and other cardiac conditions. Candesartan, an angiotensin II receptor blocker (ARB), is used for hypertension and heart failure management. Nitrokaf,

containing isosorbide dinitrate, is an organic nitrate used for angina. Furosemide, a loop diuretic, is frequently used to manage fluid overload in heart failure and other edematous states. Aminoral, a combination of amino acids, is often used as a nutritional supplement, particularly in patients with chronic kidney disease. Among these medications, bisoprolol, a beta-blocker, is of particular significance in the context of BRASH syndrome. Beta-blockers are AV nodal blocking agents, and their use can contribute to bradycardia and hypotension, especially in the presence of hyperkalemia and renal dysfunction. The patient's chronic use of bisoprolol likely played a key role in the development of BRASH syndrome in this case. The physical examination revealed critical findings. The patient's frail and mildly dehydrated appearance is a common presentation in elderly patients and can contribute to a variety of complications, including electrolyte imbalances and renal dysfunction. The vital signs demonstrated hypotension and bradycardia. Hypotension, with a blood pressure of 90/60 mmHg, suggests inadequate tissue perfusion and may be indicative of shock. Bradycardia, with a heart rate of 40 beats per minute, is a significant finding that can result from a variety of causes, including medication effects, electrolyte disturbances, or underlying cardiac conditions. The cardiovascular examination was notable for a regular but bradycardic rhythm, while the respiratory and abdominal examinations were largely unremarkable. The neurological examination was also unremarkable, suggesting that there were no acute gross neurological deficits at the time of initial presentation. The electrocardiogram (ECG) is a fundamental tool in the evaluation of patients with suspected cardiac involvement. In this case, the ECG revealed a junctional escape rhythm with a slow ventricular rate of 38 beats per minute, along with a left bundle branch block. A junctional escape rhythm is a bradyarrhythmia that originates from the AV junction, rather than the sinoatrial (SA) node, and indicates a failure of the normal pacemaker of the heart. This finding, in the context of beta-blocker use and hyperkalemia, is highly suggestive of AV nodal dysfunction. The left bundle branch block indicates a conduction abnormality within the heart's electrical system. Laboratory investigations provided further critical diagnostic information. Severe hyperkalemia, with a serum potassium level of 8.1 mmol/L, was a prominent finding. Hyperkalemia has significant implications for cardiac electrophysiology and can lead to life-threatening arrhythmias. Hyponatremia, with a serum sodium level of 113 mmol/L, was also present. Hyponatremia can be associated with various conditions and can contribute to neurological dysfunction. Elevated serum creatinine and blood urea nitrogen (BUN) levels confirmed the presence of renal dysfunction. The constellation of clinical findings, including the patient's history of chronic kidney disease, heart failure, and beta-blocker use, combined with the physical examination findings of hypotension and bradycardia, the ECG evidence of a junctional escape rhythm, and the laboratory confirmation of severe hyperkalemia and renal dysfunction, collectively pointed towards a diagnosis of BRASH syndrome. The diagnostic process in BRASH syndrome necessitates a careful and systematic approach. It requires the integration of clinical information, including the patient's medical history, medication history, physical examination findings, ECG results, and laboratory data. The varied and sometimes subtle presentation of BRASH syndrome can pose a significant diagnostic challenge. As seen in this case, the initial symptoms, such as vomiting, can be non-specific and may overlap with other common conditions. This underscores the importance of considering a broad differential diagnosis and maintaining a high index of suspicion, particularly in vulnerable populations such as the elderly.[11-15]

BRASH syndrome is not simply an additive effect of its individual components; rather, it's characterized by a detrimental synergy between AV nodal blocking medications, hyperkalemia, and often, underlying renal dysfunction. This interplay creates a vicious cycle that, if left unaddressed, can rapidly lead to

severe cardiovascular compromise. At the core of BRASH syndrome lies the complex interaction between hyperkalemia and AV nodal blockade. Hyperkalemia, an electrolyte disturbance marked by an elevated serum potassium concentration, exerts profound effects on cardiac electrophysiology. The resting membrane potential of cardiac myocytes, crucial for the generation and propagation of action potentials, is highly sensitive to changes in extracellular potassium concentration. Elevated potassium levels decrease the resting membrane potential, bringing it closer to the threshold for activation. This seemingly paradoxical effect leads to a reduction in membrane excitability. The most critical impact of hyperkalemia on cardiac function involves its disruption of repolarization. Repolarization, the process by which cardiac myocytes return to their resting state after depolarization, is essential for proper cardiac rhythm and contractility. Potassium ions play a vital role in this phase. Hyperkalemia interferes with the normal flow of potassium ions across the cell membrane during repolarization, prolonging the action potential duration. This prolongation can manifest on the electrocardiogram (ECG) as changes in the T wave and QRS complex. The consequences of hyperkalemia on cardiac conduction are significant. The slowing of conduction can lead to bradycardia, as seen in BRASH syndrome. In more severe cases, hyperkalemia can precipitate life-threatening arrhythmias, such as ventricular fibrillation or asystole. The severity of hyperkalemia's effects on the heart is influenced by both the absolute level of potassium and the rapidity with which the hyperkalemia develops. AV nodal blocking medications, such as beta-blockers (like bisoprolol in this case), constitute another key component of BRASH syndrome's pathophysiology. These medications exert their effects primarily by targeting the AV node, a critical structure in the heart's electrical conduction system responsible for regulating the transmission of electrical impulses from the atria to the ventricles. Beta-blockers, specifically, act by antagonizing beta-1 adrenergic receptors located in the AV node. This antagonism reduces the influence of the sympathetic nervous system on heart rate and AV nodal conduction. By slowing AV nodal conduction, beta-blockers can effectively control heart rate in various clinical scenarios. However, this effect becomes problematic in the setting of hyperkalemia. The combined effect of hyperkalemia-induced slowing of cardiac conduction and beta-blocker-induced AV nodal blockade results in a synergistic depression of cardiac electrical activity. This synergy is a hallmark of BRASH syndrome, often leading to profound bradycardia that is disproportionate to what would be expected from either hyperkalemia or beta-blocker use alone. Renal dysfunction plays a crucial role in the development and progression of BRASH syndrome. The kidneys are the primary route of potassium excretion from the body. In patients with underlying chronic kidney disease, the kidneys' ability to eliminate potassium is impaired. This impairment predisposes individuals to hyperkalemia, even in the absence of other precipitating factors. When an additional insult, such as dehydration or acute kidney injury, further compromises renal function, the risk of hyperkalemia escalates dramatically. In the context of BRASH syndrome, renal dysfunction not only contributes to the development of hyperkalemia but also exacerbates the effects of hyperkalemia and AV nodal blockers on the heart. The reduced potassium excretion associated with renal dysfunction perpetuates the hyperkalemia, sustaining its negative impact on cardiac electrophysiology. Hypovolemia, a state of decreased blood volume, frequently complicates the pathophysiology of BRASH syndrome, particularly in elderly patients. Reduced fluid intake, diuretic use, or conditions leading to fluid loss (such as vomiting, as in this case) can all contribute to hypovolemia. Hypovolemia compromises renal perfusion, further impairing the kidneys' ability to excrete potassium and contributing to the development or worsening of hyperkalemia. Furthermore, decreased renal blood flow can precipitate or worsen acute kidney injury, creating a feedback loop that further exacerbates the electrolyte

imbalances characteristic of BRASH syndrome. The interplay of these factors—AV nodal blockade, hyperkalemia, renal dysfunction, and hypovolemia—establishes a vicious cycle. Hyperkalemia potentiates the effects of AV nodal blockers, leading to bradycardia. Bradycardia and hypovolemia reduce renal perfusion, worsening renal dysfunction and further impairing potassium excretion. This, in turn, fuels the hyperkalemia, perpetuating the cycle. This cycle can rapidly progress to life-threatening cardiovascular collapse if not promptly recognized and interrupted.[16-20]

4. Conclusion

In conclusion, this case report underscores the critical importance of maintaining a high index of suspicion for BRASH syndrome, particularly in elderly patients presenting with non-specific symptoms such as vomiting, especially in the presence of pre-existing renal dysfunction, heart failure, and the use of AV nodal blocking agents. The diagnosis of BRASH syndrome requires a comprehensive evaluation, integrating clinical findings, ECG interpretation, and laboratory investigations. The case highlights the detrimental synergy between AV nodal blockade, hyperkalemia, and renal dysfunction, which can precipitate a rapid deterioration in cardiovascular function. Prompt recognition and aggressive management, including the correction of hyperkalemia, discontinuation of offending medications, and hemodynamic support, are essential to interrupt the vicious cycle of BRASH syndrome and prevent life-threatening complications. This case also emphasizes the need for careful medication review and consideration of alternative management strategies in the outpatient setting to prevent recurrence in susceptible individuals. Increased awareness among healthcare providers and further research are crucial to improve the timely diagnosis and management of this underrecognized but potentially reversible cause of cardiovascular collapse in the elderly.

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