

THE INTERPLAY OF DIGOXIN AND RENAL IMPAIRMENT IN BRASH SYNDROME: A CASE REPORT ON MANAGEMENT STRATEGIES

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ABSTRACT

BRASH syndrome (Bradycardia, Renal failure, AV-nodal blockade, Shock, and Hyperkalemia), a frequently underdiagnosed condition, arises from a synergistic, self-perpetuating interaction between atrioventricular-nodal blockers and renal impairment, often initiated by hypovolemia. Management requires a high index of suspicion, focusing on rapid correction of hyperkalemia, fluid resuscitation, and inotropic support. Early recognition is essential; timely, targeted intervention interrupts this vicious cycle and optimizes the clinical prognosis.

KEYWORDS

Bradycardia, digoxin, hyperkalemia, hypovolemia, renal insufficiency, shock

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INTRODUCTION

BRASH (bradycardia, renal failure, atrioventricular node blockade, shock, and hyperkalemia) syndrome – acronym for bradycardia, renal failure, atrioventricular nodal blockade, shock, and hyperkalemia – is a frequently underrated condition. The clinical presentation, typically profound bradycardia, is out of proportion to the hyperkalemia or use of an atrioventricular nodal blocker. A growing body of clinical research suggests that these two factors may act synergistically to cause severe bradycardia. This creates a vicious cycle: bradycardia may induce or exacerbates renal dysfunction, which further intensifies hyperkalemia, and thereby compounding the bradycardia.¹ If the condition remains unrecognized, it inevitably progresses to multi-system organ failure.²

In this article, we report a case of BRASH syndrome occurring in the setting of digoxin therapy for the rate control of atrial fibrillation.

CASE REPORT

We present the case of a 68-year-old male who presented with altered sensorium for three hours prior to arrival at the Emergency Department. He had a one-day history of decreased urine volume with passage of dark-colored urine compared to baseline. There was no history suggestive of fluid loss, including diarrhea, vomiting, excessive sweating or recent blood loss. He denied fever, headache, neck stiffness, focal weakness, or seizures. He did not have history of burning micturition, urgency, or flank pain. Palpitations, chest pain, or syncope were not reported.

On further inquiry, he reported decreased oral

intake (<1 Liter/day). He had been on torsemide (20 mg/day) and digoxin (0.25 mg/day) since discharge one week prior following a diagnosis of heart failure with reduced ejection fraction precipitated by atrial fibrillation. There was no history suggestive of digoxin toxicity, with the patient denying anorexia, nausea, vomiting, or visual disturbances. There were no recent changes on medication doses or addition of interacting drugs, and his baseline renal function was normal. As per the spouse, he was compliant to his medications. His other medications included inhaled bronchodilators for chronic obstructive pulmonary disease (COPD), amlodipine for hypertension, rivaroxaban, and combination of metformin and glimepiride for diabetes mellitus.

Our patient was obtunded, lethargic and dehydrated. His pulse was irregularly irregular,

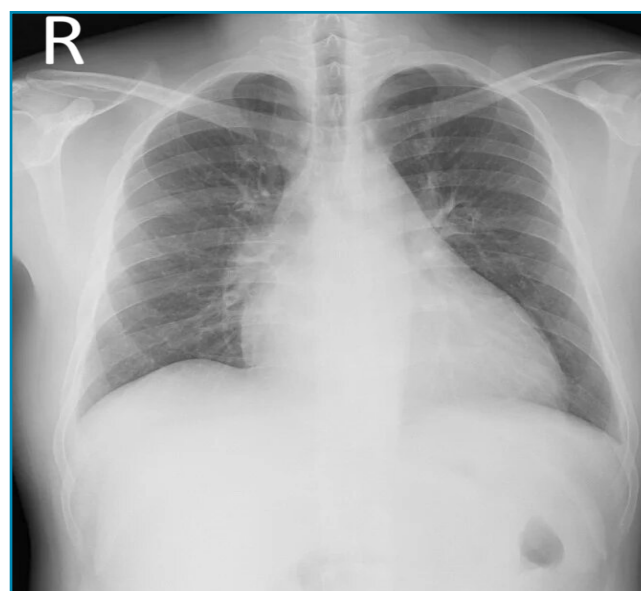


Fig. 2: Chest X-ray shows cardiomegaly without pulmonary edema

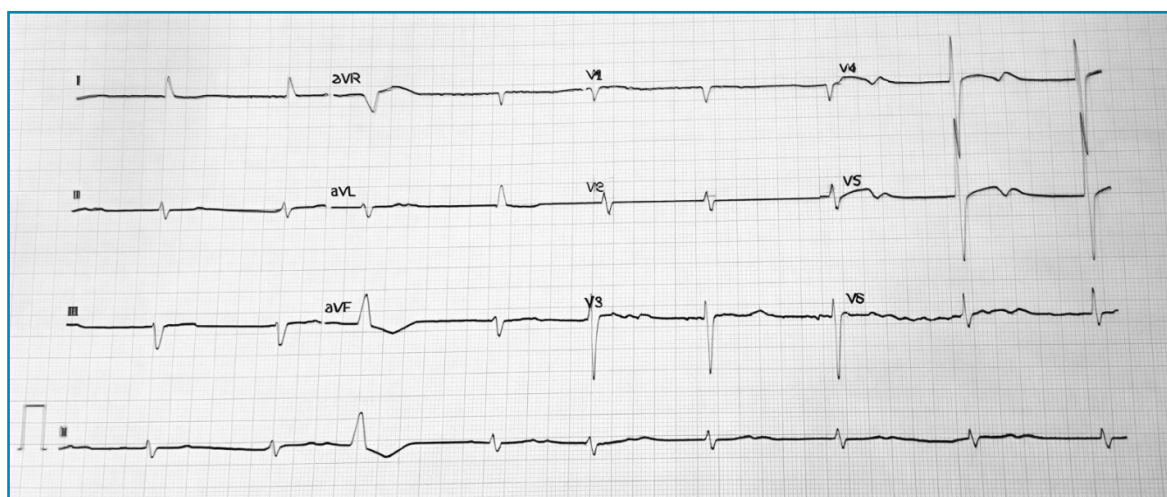


Fig. 1: ECG shows atrial fibrillation with high-grade AV block and junctional escape

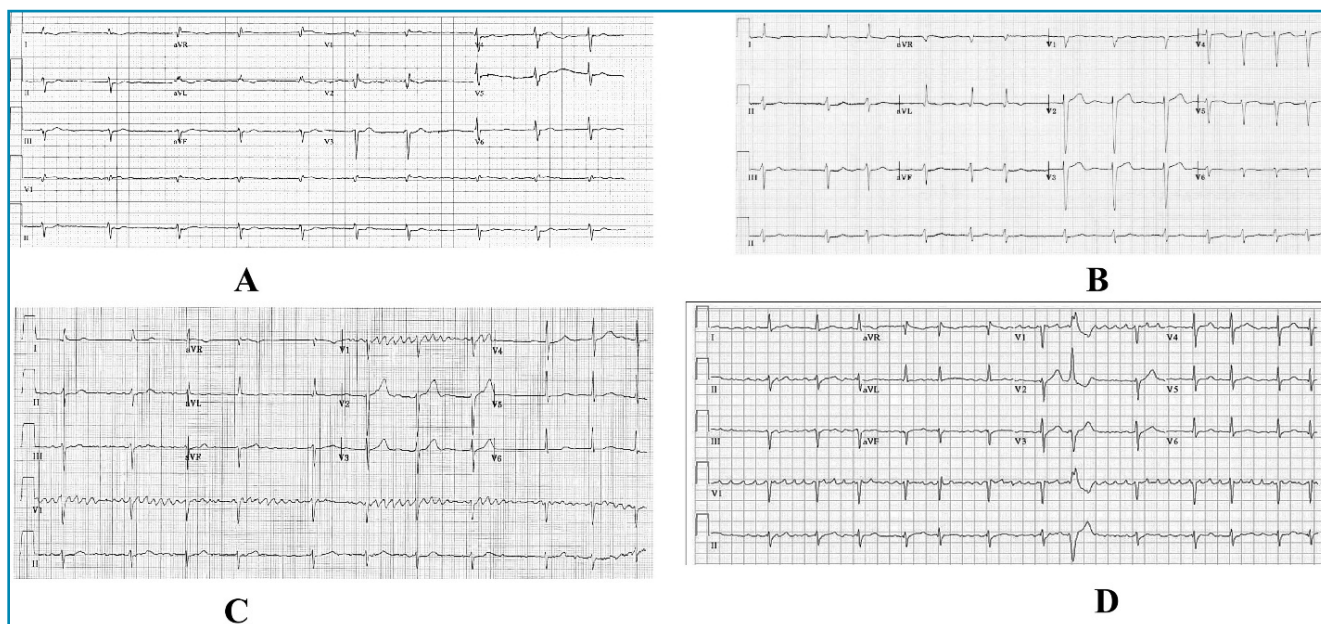


Fig. 3: A – A 12-hour follow-up ECG demonstrates atrial flutter with high-grade, variable AV block and characteristic digitalis-induced ST-segment scooping. B – Day 3 ECG shows atrial fibrillation with an improving ventricular rate, representing the initial resolution of high-grade AV blockade. C – Day 7 ECG shows a return to baseline atrial fibrillation with normalized AV conduction and narrow QRS complexes, signifying the resolution of the high-grade blockade. D – Day 14 ECG demonstrates sustained baseline atrial fibrillation with a normal ventricular rate and an isolated ventricular premature complex (VPC).

Table 1: Trends in clinical and laboratory parameters

Parameters (Unit)	Reference range	Day 1	Day 2	Day 4	Day 7
Vital signs					
Heart rate (bpm)	60-100	36-50	40-60	60-80	60-80
Blood pressure (mmHg)	–	80/54	92/60	128/74	130/88
Fluid balance					
Urine output (ml/kg/hour)	>0.5	<0.1	0.3	0.8	>1
Laboratory results					
Hemoglobin (g/dL)	12-18	18	14	13	13
Packed cell volume (%)	34-48	53.6	41.8	40	40
WBC count (/cumm)	4000-11000	8500	8400	9000	8800
Urea (mg/dL)	15-45	92	76	59	41
Creatinine (mg/dL)	0.5-1.2	2.6	2.3	1.5	1.1
Sodium (mEq/L)	135-145	128	132	136	135
Potassium (mEq/L)	3.5-5.0	6.2	5.4	4.6	4.0

with a rate of 36-50 beats/minute and variable volume. Respiratory rate, blood pressure, temperature, and SpO₂ were 22 breaths/minute, 80/54 mmHg, 98.6°F, and 96%, respectively. Bilateral basal crepitations were present, with otherwise normal heart sounds. GCS was 12/15 (E3 V4 M5), and remainder of the examination was unremarkable. Electrocardiogram (ECG) showed a fluctuating ventricular rate with junctional escape and no discernible P-waves (Fig. 1). Chest X-ray revealed cardiomegaly

without pulmonary edema (Fig. 2). Fluid resuscitation was initiated, intravenous calcium gluconate was administered for hyperkalemia (6.2 mEq/L), and digoxin was discontinued. The patient was transferred to the intensive care unit (ICU).

In the ICU, fluid therapy was guided by urine output, passive leg raise testing, and inferior vena cava diameter and collapsibility. Anti-hyperkalemic measures included insulin

with dextrose and nebulized salbutamol. As hypotension persisted despite fluid resuscitation, an epinephrine infusion was initiated for hemodynamic support. Serum digoxin levels were not obtained due to limited availability and delayed turnaround time in the acute setting, limiting their utility in immediate clinical decision-making.

With improvement in blood pressure and heart rate, cognition, renal function, and urine output gradually recovered over the following days. He was transferred to the medical ward on Day 4 where he remained stable and continued to improve. Laboratory parameters are summarized in Table 1. His ECGs slowly returned to his baseline rhythm (Fig. 3). After resolution of his acute illness and improvement in renal function on Day 7, he was discharged with close cardiology follow-up and advised to continue home medications except digoxin. At 2-week follow-up, he was clinically stable, and initiation of low-dose β -blocker therapy for rate control was being considered in view of atrial fibrillation with heart failure and supporting evidence.

DISCUSSION

The clinical pentad of bradycardia, renal failure, atrioventricular (AV) node blockade, shock, and hyperkalemia – collectively known as BRASH syndrome – frequently remains underestimated, often leading to precipitous clinical decline.³ Older adults with underlying cardiac disease and renal dysfunction along with concurrent use of AV node blocking drugs for management of atrial fibrillation are at the highest risk.^{1,4} Hypovolemia is the most common trigger for BRASH syndrome, though other factors like dehydration, acute kidney injury, and antihypertensives (notably beta blockers, angiotensin-converting enzyme inhibitors, and angiotensin II receptor blockers) often play a role.⁵

AV node blocking drugs reduce cardiac output and renal perfusion, while concomitant hypovolemia – arising from either diminished intake or excessive loss – further precipitates acute kidney injury. As renal function deteriorates, the diminished clearance of potassium and offending agents leads to a pathological synergy. In this setting, hyperkalemia amplifies the effects of the medication, often resulting in critical bradycardia even when potassium levels are only marginally elevated. The consequent drop in cardiac output further compromises renal blood flow, creating a self-reinforcing loop –

the BRASH cycle. If left undiagnosed, this cycle progresses to cardiogenic shock and multi-system organ failure.⁵⁻⁸

The diagnosis of BRASH syndrome in our case required analyzing several overlapping clinical factors. Hypovolemia from diminished fluid intake and diuretics precipitated renal impairment, compromising digoxin clearance and intensifying AV-nodal blockade.⁹ The severe bradycardia and cardiovascular collapse were disproportionate to the degree of hyperkalemia, which usually causes heart block at potassium levels $>7\text{mmol/L}$.¹⁰ The ECG features of hyperkalemia – peaked T waves or sine waves – were absent in our case.¹¹ Although confusion was likely secondary to cerebral hypoperfusion from shock, our patient lacked features of digoxin toxicity – anorexia, nausea, vomiting, abdominal pain, and visual disturbances (blurring, yellow-green vision). Serum levels correlate poorly with clinical status; however, the overall presentation was more consistent with a synergistic BRASH cycle rather than isolated digoxin overdose.¹² Serum digoxin levels were unavailable, but the absence of dose changes, interacting medications, and prior normal renal function made significant toxicity unlikely, though it could not be excluded. In this setting, digoxin likely contributed as an AV nodal blocker within the BRASH cascade rather than representing primary toxicity.

The management of BRASH syndrome includes withdrawal of the offending drug (digoxin in our case), fluid resuscitation, cardiac membrane stabilization, potassium shifting, and improving cardiac output. Intravenous calcium is the first-line treatment, as it stabilizes the myocardium, and improves heart rate and cardiac output. Standard advanced cardiac life support (ACLS) approach to bradyarrhythmias often fails as atropine is ineffective in BRASH physiology and IV calcium is excluded in the algorithm.^{1,3,6} In the setting of refractory bradycardia and shock, epinephrine provides both chronotropic and inotropic support, effectively restoring the hemodynamics and improving renal perfusion. It also shifts potassium into the cells.^{13,14} Other hypokalemic measures are intravenous insulin and nebulized salbutamol.¹⁵ Hypovolemia should be promptly treated with fluid resuscitation, preferably balanced crystalloids, as 0.9% normal saline can cause hyperchloremic acidosis which worsens prognosis.^{1,16} The volume status and fluid responsiveness can be assessed with dynamic indices (e.g., passive leg raise) and noninvasive ultrasound-based methods (e.g. inferior vena cava diameter and collapsibility, cardiac output).¹⁷ Prompt

diagnosis and management usually reverses the condition without the need for advanced measures such as hemodialysis or temporary pacing.^{6,13}

In conclusion, BRASH syndrome poses a unique therapeutic challenge. The typical cohort involves patients on AV nodal blockers who develop bradycardia and shock complicated by

renal insufficiency. A high index of suspicion is essential for prompt recognition as early institution of supportive measures prevent multiorgan failure, thus improving the prognosis.

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