The vicious cycle of BRASH syndrome: A case report and a brief review of literature

CHARIF H., PATRICK M., NJIE M., JAMA D., B.E Ovaga,HABOUB M. AROUS S., BENNOUNA E.M. , DRIGHIL A. , AZOUZI L., HABBAL R.

Department of Cardiology, Ibn Rochd University Hospital, Casablanca, Morocco.

Faculty of Medicine and Pharmacy, Hassan II University of Casablanca, Casablanca, Morocco.

ABSTRACT

BRASH syndrome is a medical condition characterized by the combination of bradycardia and shock in individuals with renal failure, the use of atrioventricular (AV) nodal blocking agents, and hyperkalemia. This syndrome typically occurs in elderly individuals who have compromised kidney function and a history of taking AV nodal blocking medications regularly(1). Major risk factors for BRASH syndrome include hypovolemia and worsening kidney function. It's important to recognize that these manifestations should be viewed as part of a syndrome rather than isolated findings because they are interconnected and have synergistic effects on each other. These underlying physiological processes create a harmful cycle of bradycardia and reduced cardiac output, leading to organ dysfunction, including renal failure with hyperkalemia, which in turn exacerbates the bradycardia. BRASH syndrome is associated with significant morbidity and mortality(2). Typically, the treatment approach for BRASH syndrome involves increasing renal blood flow by enhancing cardiac output through the administration of catecholamines. In rare cases, interventions like intralipid emulsion and continuous renal replacement therapy (CRRT) may be necessary, depending on the specific circumstances. Early recognition of BRASH syndrome is crucial as it can help prevent diagnostic delays and reduce mortality rates. In the case presented here, the patient's medical history provided important clues that led to the early identification and aggressive treatment of BRASH syndrome. This timely intervention prevented the onset of shock, reduced morbidity, and improved overall outcomes.

Keywords: atrioventricular node blocker; bradycardia; BRASH; hyperkalemia; renal failure; shock

INTRODUCTION

The term "BRASH syndrome," which stands for Bradycardia, Renal failure, Atrioventricular (AV) nodal blocking agent, Shock, and Hyperkalemia, was first introduced in 2016 by Dr. Josh Farkas. Dr. Farkas proposed a pathophysiologic cycle of events that results in a vicious cycle initiated by renal failure, leading to hyperkalemia and the accumulation of AV nodal blocking agents such as beta-blockers (BB) or calcium channel blockers (CCB)(3). Both hyperkalemia and AV nodal blockers contribute to bradycardia and reduced perfusion, which further worsen

renal failure. Many cases of BRASH syndrome are often misdiagnosed and managed as isolated electrolyte abnormalities, such as hyperkalemia, which can have catastrophic consequences if left untreated. Recognizing the interconnected nature of these clinical features is crucial for accurate diagnosis and timely intervention.

CASE PRESENTATION

In this report, we present a 66-years-old male, who presented with generalized fatigue, vomiting and many episodes of syncope. The patient was a known case of coronary artery disease, heart failure with low ejection fraction (25%), stage 3 chronic kidney disease, type-2 diabetes mellitus, and hypertension. He was compliant with his medications, including bisoprolol 2.5 mg once daily (OD), sacubitril/valsartan 25 mg twice daily, Furosemide 40 mg OD, and spironolactone 12.5 mg OD. On first medical contact, the patient was mildly drowsy but oriented to time, place, and person. His Glasgow Coma Scale upon presentation was 15/15. He was dehydrated. His blood pressure was 76/55 and his heart rate was 25 beats per minute. The rest of his physical examination was unremarkable. He had an electrocardiogram (ECG) which was remarkable for bradycardia with a junctional rhythm (Figure1).The results of his routine biochemistry blood tests revealed severe hyperkaliemia 6 mEq/L, Metabolic acidosis, acute on chronic kidney failure (creatinine at 35 g/L , GFR of 17mls/min which had deteriorated from a baseline of 40 mls/min) .The rest of his biochemistry blood tests were within the normal range.

Fluid resuscitation was initiated with vasopressor agents. Urgent treatment of his hyperkaliemia with calcium gluconate, regular insulin with dextrose, salbutamol inhalation was undertaken. In evolution, his heart rate, and blood pressure improved, urgent dialysis was arranged due to his refractory hyperkaliemia (5.4 mmol/L), and a temporary transvenous pacemaker was inserted for ~~his~~ initial stabilization due to the persistence of bradycardia.

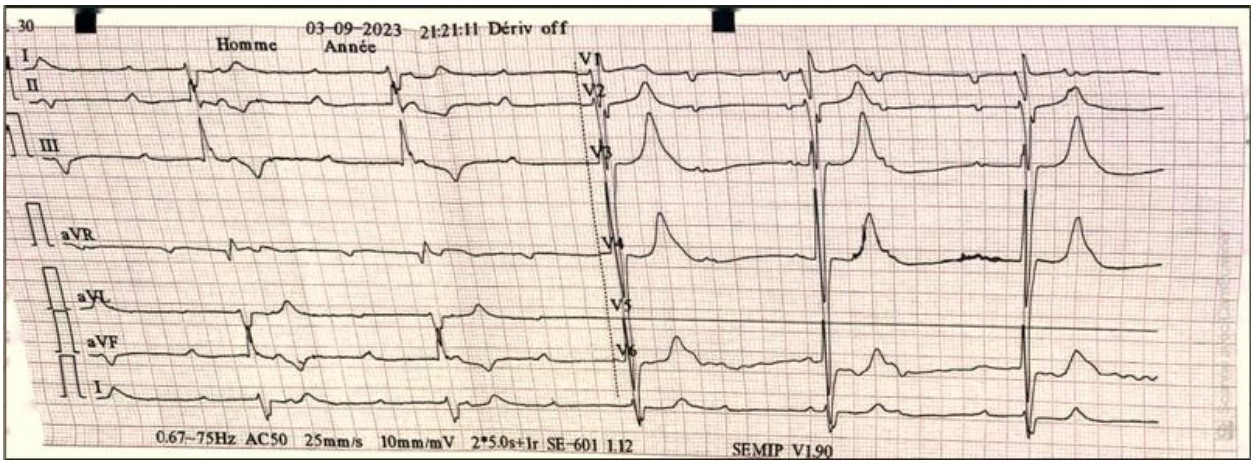

Figure1. ECG bradycardia (25bpm) with a junctional rhythm

Discussion

Hyperkalemia and the use of atrioventricular (AV) nodal blocking agents can lead to bradycardia. However, when bradycardia occurs in the setting of underlying renal dysfunction, it

can exacerbate hyperkalemia, creating a detrimental cycle known as BRASH syndrome (Bradycardia, Renal Failure, AV-nodal blockers, Shock, Hyperkalemia)(4).

The key pathophysiological feature of BRASH syndrome is the synergistic effect of hyperkalemia and AV nodal blockers, resulting in bradycardia. Common causative agents are beta-blockers (BB) or calcium channel blockers (CCB), as seen in the present cases(5). While these medications are generally well-tolerated, they can cause significant AV nodal blockade when patients experience precipitating events such as systemic infections, leading to acute kidney injury and reduced drug clearance, further compromising renal function. Clinicians should exercise caution when prescribing AV nodal blocking agents to patients with a history of chronic kidney disease or those at risk of acute kidney injury, as this can increase the likelihood of developing BRASH syndrome(6).

The diagnosis of BRASH syndrome primarily relies on clinical manifestations, ECG findings, and a complete metabolic panel, after ruling out other potential causes. A high level of suspicion is crucial when encountering patients with refractory bradycardia, elevated serum potassium levels, renal failure, and a history of AV nodal blocking drugs(7).

Early identification of the syndrome is essential for reducing mortality. Initial management focuses on membrane stabilization with calcium gluconate, correction of hyperkalemia through dextrose and insulin infusion, and salbutamol nebulization. Electrolyte correction and fluid replacement are critical even if classic ECG findings of hyperkalemia are absent(8). Additionally, early consideration of hemodialysis can help remove excess potassium from the body. In cases of refractory hemodynamic instability, timely transvenous pacing and judicious use of inotropes can be life-saving(9).

BRASH syndrome poses a diagnostic and therapeutic challenge, underscoring the importance of understanding its pathophysiology and ensuring timely diagnosis for effective management and improved patient outcomes(9).

Conclusion.

BRASH syndrome is a life-threatening yet often underdiagnosed condition. Patients with BRASH syndrome may present with nonspecific symptoms, making diagnosis and treatment challenging. Increased awareness among clinicians is essential, as early diagnosis and addressing precipitating factors can be instrumental in its management. The mainstay of BRASH treatment involves correcting hyperkalemia, improving renal function by addressing underlying causes, and discontinuing AV nodal blocking agents to halt the vicious cycle.

DECLARATIONS

ETHICS APPROVAL AND CONSENT TO PARTICIPATE.

- As per international standard or university standard written ethical approval has been collected and preserved by the author(s)

CONSENT FOR PUBLICATION.

- In accordance with international and academic standards, written consent for publication was obtained from the patient and retained by the authors.

COMPETING INTERESTS

The authors declared no conflicts of interest

AUTHORS' CONTRIBUTIONS

- CHARIF Hana, Patrick M., Njie M., Jama D.: Wrote the article and inserted the references
- M. Haboub, A. Salim, Med G. Benouna, A. Drighil, L. Azzouzi and R. Habbal : corrected the article

This work was carried out in collaboration between all the authors. All authors have read and approved the final manuscript.

- **ACKNOWLEDGEMENTS**
- I thank the whole Department of Cardiology P37, university teaching hospital Ibn Rochd Casablanca for their outstanding collaboration in the support of this work.

- **AUTHORS' INFORMATION**

Department of Cardiology, IBN ROCHD University Hospital, Casablanca, Morocco

REFERENCES

(1)Farkas J. PulmCrit- BRASH syndrome: Bradycardia, Renal failure, Av blocker, Shock. Hyperkalemia 2016 February 15; https://emcrit.org/pulmcrit/brash-syndrome-bradycardia-renal-failure-av-blocker-shock-hyperkalemia/

(2) Calvin J Tan B S. BRASH Syndrome: Profound Bradycardia in the Setting of Mild Hyperkalemia State University of New York – Downstate, College of Medicine; Kings County Hospital Center. https://www.emra.org/siteassets/emra/be-involved/events--activities/casecon/2018-posters/group-2/calvin_tan_final_poster.pdf

(3) Farkas JD, Long B, Koyfman A, Menson K. BRASH Syndrome: Bradycardia, Renal Failure, AV Blockade, Shock, and Hyperkalemia. J Emerg Med. 2020 Aug;59(2):216-223. doi: 10.1016/j.jemermed.2020.05.001. Epub 2020 Jun 18. PMID: 32565167. https://pubmed.ncbi.nlm.nih.gov/32565167/

(4) Sattar Y, Bareeqa SB, Rauf H, Ullah W, Alraies MC. Bradycardia, Renal Failure, Atrioventricular-nodal Blocker, Shock, and Hyperkalemia Syndrome Diagnosis and Literature Review. Cureus. 2020 Feb 13;12(2):e6985. doi: 10.7759/cureus.6985. PMID: 32201662; PMCID: PMC7075507. https://pubmed.ncbi.nlm.nih.gov/32201662/

(5) Srivastava S, Kemnic T, Hildebrandt KR. BRASH syndrome. BMJ Case Rep. 2020 Feb 23;13(2):e233825. doi: 10.1136/bcr-2019-233825. PMID: 32094236; PMCID: PMC7046371. https://pubmed.ncbi.nlm.nih.gov/32094236/

(6) Zhou M and AH Khan, Bradycardia, Renal Failure, AV-Nodal Blockers, Shock, and Hyperkalemia (BRASH) - A New Clinical Syndrome, in American Thoracic Society 2018 International Conference. 2018: San Diego, CA. A3467-A3467. https://pubmed.ncbi.nlm.nih.gov/35475060/

(7) Nathani A, Lingamaneni P, Radigan KA. Brash Syndrome: An Emerging Clinical Entity.A43. CRITICAL CASE REPORTS: TOXICOLOGY AND POISONINGS. American Journal of Respiratory and Critical Care Medicine. 2020; 201A1666 https://www.atsjournals.org/doi/10.1164/ajrccm-conference.2020.201.1_MeetingAbstracts.A1666 [in A43. l.c. p. A1666-A1666]

(8) Saini T, Reny J, Hennawi HA, Cox A, Janga C, DeLiana D, McCaffrey J. The vicious cycle of BRASH syndrome: A case report. Glob Cardiol Sci Pract. 2023 Jan 30;2023(1):e202302. doi: 10.21542/gcsp.2023.2. PMID: 36890842; PMCID: PMC9988297. https://pubmed.ncbi.nlm.nih.gov/36890842/

(9) Shah P, Silangruz K, Lee E, Nishimura Y. Two Cases of BRASH Syndrome: A Diagnostic Challenge. Eur J Case Rep Intern Med. 2022 Apr 8;9(4):003314. doi: 10.12890/2022_003314. PMID: 35520368; PMCID: PMC9067425. https://pubmed.ncbi.nlm.nih.gov/35520368/