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Case Report

BRASH Syndrome as a Cause of Severe Bradycardia

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Abstract

BRASH Syndrome is a newly defined cause of severe bradycardia that can manifest in a number of ways. This syndrome can easily arise in the setting of polypharmacy and does so in the context of some of the most frequently prescribed medications in current practice. This case demonstrates how this syndrome can occur with medication initiation and lead to a critical status.

Keywords: *BRASH Syndrome; SGLT-2 inhibitor; Bradycardia; Hyperkalemia; Acute kidney Injury*

Abbreviations:

AV: Atrioventricular
AKI: Acute Kidney Injury
ACEi: Angiotensin Converting Enzyme Inhibitor
ARB: Angiotensin II Receptor Blocker
BRASH: Bradycardia, Renal failure, Atrioventricular nodal blockade, Shock and Hyperkalemia
SGLT2 inhibitor: Sodium-Glucose Cotransporter-2 inhibitor

Introduction

BRASH Syndrome describes the cumulative effect of AV-nodal blocking agents, kidney injury, hypotension, and hyperkalemia. After an initial insult, these factors can evoke a spiraling feedback loop causing shock and multiorgan failure. Identification and reversal of the original injury is critical in the effective management of the overall syndrome. This clinical syndrome can progress rapidly and is often refractory to typical vasopressor support alone. We present a case of BRASH Syndrome in the setting of the recent initiation of a SGLT2 inhibitor.

Case

A 77-year-old female with a past medical history of hypertension, type 2 diabetes mellitus, non- obstructive coronary artery disease, and group II pulmonary hypertension initially presented to the emergency department with dizziness for the past 36 hours. She was found to be bradycardic to 36 beats per minute [FIGURE 1] and developed junctional rhythm [FIGURE 2]. On physical examination she had dry mucous membranes. Her initial laboratory results were notable for a creatinine elevation to 2.9 mg/dL from a baseline of 0.9 mg/dL, potassium of 5.8 mEq/L. The high-sensitivity troponin trended from 38 to 35 ng/dL. Atropine and glucagon were administered without significant response.

She was then started on fluid resuscitation and a dopamine drip. Despite this, the patient became progressively more hypotensive and bradycardic, requiring 4 more liters of fluid boluses and an aggressive increase in her dopamine drip. As the patient's kidney function returned to baseline and she became euvolemic, her bradycardia improved and dopamine was successfully titrated off.

Of note, the patient was started on dapagliflozin 3 days prior to admission and was on atenolol for years. Once she recovered, she stated that she was experiencing polyuria prior to presentation with the recent dapagliflozin initiation.

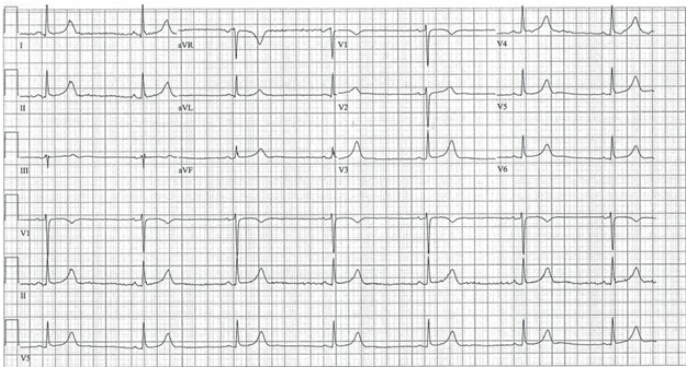

Figure 1: Patient's initial electrocardiogram with significant bradycardia (40 beats per minute present)

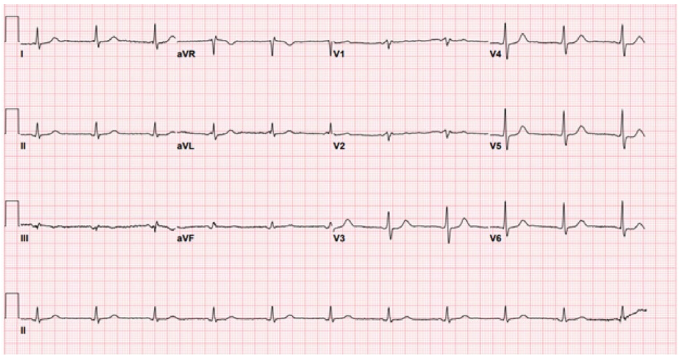

Figure 2: Patient in junctional rhythm

Discussion

BRASH Syndrome is a vicious feedback loop that can be precipitated by medications frequently prescribed in the healthcare field. ACEi and ARB therapies are widely prescribed for highly prevalent conditions such as hypertension, diabetes, or coronary artery disease. It is well understood that ACEi/ARB medications can lower the threshold for AKI due to their reduction in renal perfusion pressure and glomerular filtration rate [1]. With the onset of AKI, concurrent use of AV-nodal blocker agents is problematic due to decreased renal excretion of the medications and an exacerbation of their effects [2]. It is theorized that hyperkalemia from AKI and decreased clearance of AV-nodal blocker agents creates a synergistic effect that presents as BRASH Syndrome [2]. In a review of reported cases of BRASH Syndrome, around 37% of patients were taking either ACEi or ARB therapies in combination with an AV-nodal blocking agent [2]. However, the use of SGLT2 inhibitors as an offending agent leading to BRASH Syndrome is less reported. Current evidence of an association between SGLT2 inhibitors and BRASH Syndrome is limited to Wright et al.'s recent case report [3]. Our case is significant in that our patient experienced concomitant profound hypotension unresponsive to vasopressors. SGLT2 inhibitors were first approved by the Food and Drug Association in 2013, and have been increasingly prescribed for type II diabetes and heart failure. SGLT2 inhibitors are also known to cause AKI due to osmotic diuresis leading to intravascular volume contraction [4]. The most common initial insult for BRASH Syndrome is AKI. This kidney injury is often prerenal in nature, precipitated by etiologies such as limited oral intake or relative hypovolemia.

Initially patients with BRASH syndrome may be minimally symptomatic before spiraling into a critical status. Other initial presentations may be severe symptomatic bradycardia or multiorgan failure. Treatment is targeted towards the initial insult, and usually involves improving renal perfusion status. While presentations may vary, this patient's BRASH Syndrome was characterized by preexisting AKI caused by SGLT2 inhibitor initiation and hyperkalemia causing hypotension and bradycardia, resulting in decreased end organ perfusion leading to further kidney injury [5]. This patient's initial presentation with dizziness in the setting of known coronary artery disease, type 2 diabetes, hypertension, and pulmonary hypertension could lead her to easily be considered suffering from an acute coronary injury or ischemic event. Implantation of a permanent pacemaker can be avoided with proper recognition of this syndrome. In cases of extreme bradycardia, a temporary pacemaker can be considered. Thankfully, cardiac pacing could be avoided in this patient with successful stabilization of her cardiac status and reversal of the renal injury. History gathering is particularly valuable in this syndrome to determine the initial insult and guide towards symptomatic management rather than permanent pacemaker implantation. We highlight here a rare case of BRASH Syndrome that was precipitated by SGLT-2 inhibitor initiation, a medication with growing use in the heart failure, diabetic, and chronic kidney disease patient population.

Conclusion

BRASH Syndrome has only recently been identified as a clinical entity, and patients may present with a variety of symptoms and may suffer from multiorgan failure. It is essential that we maintain a high index of suspicion as BRASH has an in-hospital mortality of 5.7% [2]. If this diagnosis is overlooked, it can result in patients requiring renal replacement therapy or invasive therapies such as cardiac pacing in a setting where such therapy can be avoided.

Consent obtained from patient 09/25/2023

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