

Case Report

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Two Cases of BRASH Syndrome

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ABSTRACT

BRASH syndrome is a rare entity that is often underdiagnosed. Recently known in 2016, it falls within the scope of drug toxicity. BRASH syndrome consists of bradycardia, renal failure, shock, and hyperkalemia, secondary to atrioventricular node blocking drugs. We report two cases of BRASH syndrome in order to encourage the physician to think about it in front of bradycardia associated with hyperkalemia in chronic renal patients and to intensify the monitoring of renal insufficiency under atrio-ventricular node blocker.

The first case was a 59-year-old man, hypertensive-diabetic, suffering from a stage IV chronic renal disease not dialyzed, having taken as antihypertensive drugs: Carvedilol 12.5 mg and Amlodipine 10 mg, presenting a picture of BRASH syndrome triggered by the intake of diuretic.

The second case was a 64-year-old hypertensive-diabetic man, presenting a mixed vascular and diabetic nephropathy stage V not dialyzed, under Carvedilol 12.5 mg and Amlodipine 10 mg making a picture of shock and severe bradycardia with aggravation of a hyperkalemia labeled as BRASH syndrome on bacterial pneumonia.

In both cases we initiated medical treatment of hyperkalemia with emergency administration of atropine and use of the positive inotropic substance Dobutamine. Atrioventricular node blocking drugs were discontinued. Haemodialysis was indicated but was not available for the first case for financial reasons. The evolution was fatal for the first case on a picture of refractory cardiogenic shock. On the other hand, it was favourable for the second case with normalization of heart rate and hemodynamic status of the patient and biologically a normalization of the kalemia.

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Introduction

BRASH syndrome is a rare condition that is often underdiagnosed [1]. It was recently described in 2016 by Josh Farskas in Pulmicrit [2]. It is a syndromic association of bradycardia, renal failure, at least one atrioventricular node blocker, shock and hyperkalemia. It is part of a drug toxicity that increases the effect of hyperkalemia on cardiac conduction. We report two cases of BRASH syndrome in order to encourage the physician to think about it when faced with bradycardia associated with hyperkalemia in chronic renal patients and to intensify the monitoring of renal insufficiency patients under atrio-ventricular node blockers.

Observation

First Case

The patient was a 59-year-old man, a smoker, admitted for anemia, with a history of grade III hypertension treated with Carvedilol 12.5 mg/d and Amlodipine 10 mg/d, insulin-requiring type II diabetes, and stage IV chronic renal failure due to diabetic and vascular nephropathy that was not dialyzed. He had presented a spontaneous epistaxis for two weeks. On admission, the patient was afebrile at 37°C and presented a poorly tolerated anemic syndrome with tachycardia at 110 beats per minute, asthenia and

mucocutaneous pallor. A blood pressure (BP) of 130/80 mmHg, a respiratory rate of 17 cycles per minute with SpO₂ of 96% were observed. In addition, he had a syndrome of hydric overload with discrete crepitating rales of the two pulmonary bases and edemas of the lower limbs. Paraclinical investigations showed an increase in creatinine level to 840 µmol/L with a baseline creatinine level of 303 µmol/L, hyperazotemia to 40 mmol/L, hyperkalemia to 6.8 mmol/L and normochromic normocytic anemia to 6.2 g/dL. The hemostasis and hepatic workup was normal. We initiated the hyperkalemia protocol with administration of intravenous Calcium 1g, Kayexalate 15 g three times a day, rapid insulin 10 IU in 500 of GHS 10% and Salbutamol 5 mg aerosol. Blood cell transfusion and intravenous Furosemide 300 mg/24h were done.

On the second day of hospitalization, we noticed a melting of the edemas and the lungs were free. However, he had presented with non-syncopal sinus bradycardia at 35 beats per minute (Figure 1). In addition, he was profoundly asthenic with arterial hypotension at 60/40 mmHg and coldness of the extremities. At the biological control, a worsening of hyperkalemia to 7.6 mmol/L was objectified. Emergency hemodialysis was indicated but not performed for financial reasons. Antihypertensive drugs were

stopped. Intravenous Atropine 0.5 mg was administered as an emergency measure. Positive inotropic substances such as Dobutamine were started at a dose ranging from 5 to 20 gamma/kg/h. We continued the medical treatment of hyperkalemia. The evolution was marked by the persistence of the bradycardia and the state of shock that had taken the patient.

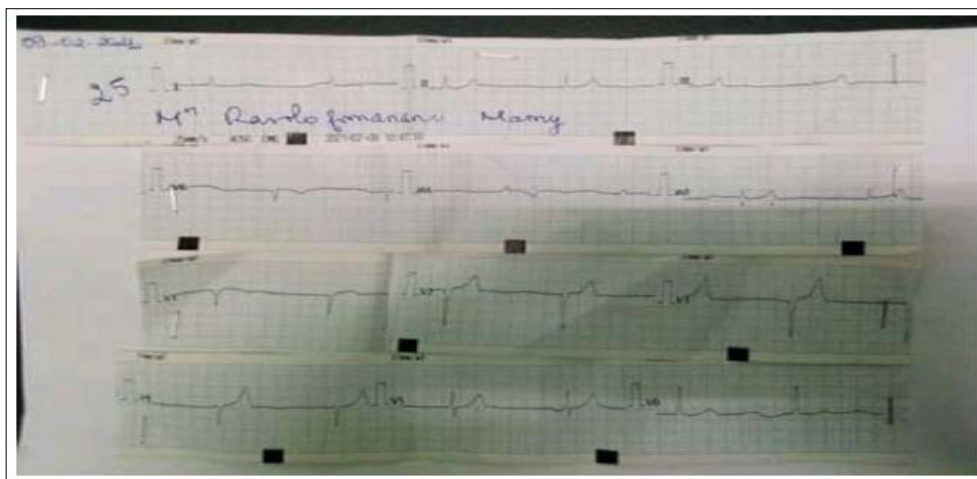


Figure 1: ECG of 1e case: sinus bradycardia

Second Case

This was a 64-year-old man admitted to our department for a febrile chest cough that had been evolving for four days in a patient with non-dialysis CKD-G5 with hypertensive nephropathy and diabetes. He was on Carvedilol 6.25 mg/d, Amlodipine 10 mg/d, Methyldopa 750 mg/d long term and insulin therapy on a basal bolus schedule. Clinical examination on admission showed a fever of 39°C, hypotension of 80/40 mmHg with bradycardia of 40 beats/minute (Figure 2) accompanied by profuse sweating and coldness of the extremities. Respiratorily, he had a left basal pulmonary condensation syndrome. There were no signs of fluid overload. Diuresis was estimated at 800 ml/24H. Biological examination revealed hyperkalemia at 6.31 mmol/l, an inflammatory syndrome with a C-reactive protein (CRP) of 45 mg/l, a predominantly neutrophilic hyperleukocytosis at 11.7 G/l and a moderate normochromic anemia at 9.8 g/dl. Creatinine was elevated to 643 µmol/L with a previous value of 482 µmol/L. Blood urea was 38 mmol/L. The chest X-ray showed an alveolar syndrome in the left lower lobe. In view of this picture, the diagnosis of BRASH syndrome triggered by a bacterial pneumonia was retained. We stopped the antihypertensive drugs. The protocol of medical treatment of hyperkalemia was instituted with urgent extra-renal purification. The pneumonia was treated with Amoxicillin clavulanate. The evolution was favorable with an increase of the heart rate to 65 beats per minute and a blood pressure of 100/60 mm Hg.

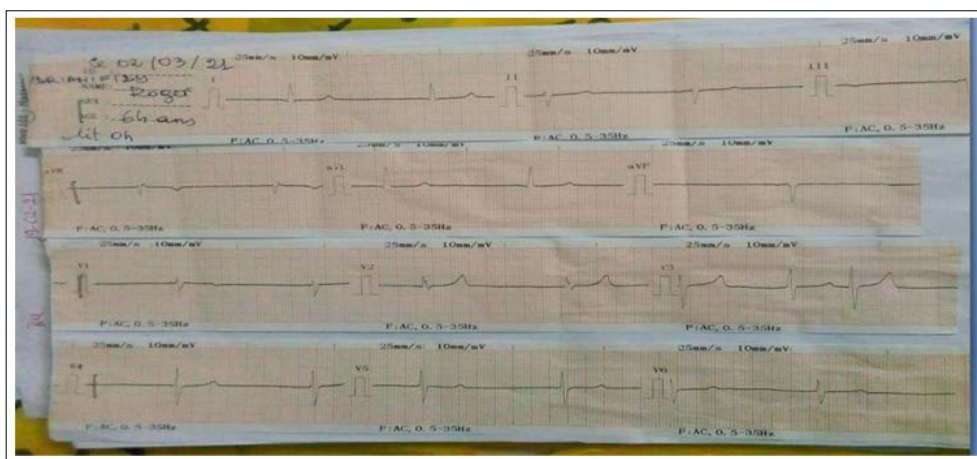


Figure 2: ECG of the 2e case: sinus bradycardia

Discussion

The BRASH syndrome results from a synergistic effect between hyperkalemia and the atrioventricular node blocker leading to bradycardia. It constitutes a vicious circle that starts with an aggravation of renal insufficiency leading to hyperkalemia which is, with the atrio-ventricular node blocker, responsible for a bradycardia causing hypoperfusion which aggravates renal failure and maintains hyperkalemia [1].

Table I: Comparative Table of Our Cases with Some Cases Reported in Literature

Authors	land	Medicines	Triggering factor	Brady- cardie	Hyperk alemia	Treatment	Evolution
1 st case	Man 59 years old HTA Diabetes	Carvedilol 12.5 mg Amlodipine 10 mg	Diuretic	42 bpm	7.6 mmol/L	(GCa) GHS10% + Insulin Atropine	Unfavorable
2 nd case	Male 64 years old HTA Diabetes	Carvedilol 6.25 mg Amlopress 10 mg	Infection	37 bpm	6,3 mmol/L	GCa GHS+ (GHS +) Insulin EER	favorable
Arif et al[2]	Woman 55 years old HTA Diabetes	Diltiazem	Diuretic	30-40 bpm	5.4 mmol/l	Atropine Dopamine EER	favorable
Sattar et al[3]	Female 66 years old HTA Diabetes Coronary artery disease Dyslipidemia	Carvedilol 25mg	Infection	35bpm	6.2mmol/l	GCa GHS+ (GHS +) insulin	favorable
Wong and Jaffar [4]	Woman 62 years old HTA Diabetes	Atenolol 50mg Diltiazem 60 mg	diuretic	40 bpm	6.3mmol/l	Atropine	favorable

HTA: Hypertension, GCa : Calcium Gluconate, bpm : beat per minute, EER : Extra-Renal Purification, IBS : Isotonic Bicarbonate Serum, HGS : Hypertonic Glucose Serum

Table II: Comparative Table of Our Cases with Some Cases Reported in Literature

Authors	land	Medicines	Triggering factor	Brady- cardie	Hyperk alemia	Treatment	Evolution
1 st case	Male 59 years old HTA Diabetes	Carvedilol 12.5 mg Amlodipine 10 mg	Diuretic	42 bpm	7.6 mmol/L	GCa SGH10% + Insulin Atropine	Unfavorable
2 nd case	Male 64 years old HTA Diabetes MRC-G5 ND	Carvedilol 6.25 mg Amlopress 10 mg	Pneumo pathy	37 bpm	6,3 mmol/L	GCa GHS+ (GHS +) Insulin EER	favorable
Grigorov et al[5]	Woman 43 years old HTA Diabetes Heart disease	Metoprolol 50mg Diltiazem 180mg	infection	35bpm	7.6 mmol/l	GCa GHS+ (GHS +) Insulin Noradrenaline	favorable
Zaidi et al[6]	Woman 88 years old HTA Diabetes Insufficiency	Ranolazine	Dehydration on vomiting and diarrhea	32bpm	6.8 mmol/l	Noradrenaline Atropine GCa SGH+ (GHS) Insulin	favorable
"Diribe and the [7]"	"Man 51 years old HTA Diabetes Cancer Hypothyroidism"	"Trimethopri me /Sulfam ethoxazole"	Otitis media	20bpm	8.6 mmo /l	"GCa GHS+ (GHS +) Insulin Hydrocortisone EER	favorable
"Simmons and Blazar [8]"	"Male 24 years old HTA Trans-renal planted"	Metoprolol	"Aggravation of renal failure"	40 bpm	7.4 mmol/l	"Atropine GCa SBI"	favorable
"Prabhu et al[9]"	"Female Elderly HTA"	"Carvedilol verapamil"	Covid infection	Covid infection	6.5 mmol/l	"Atropine GCa SGH+ (GHS) Insulin SBI Dopamine"	Favorable

HTA: Hypertension, GCa: Calcium Gluconate, bpm: beat per minute, EER: Extra-Renal Purification, IBS: Isotonic Bicarbonate Serum, HGS: Hypertonic Glucose Serum

In the literature, this pathology mainly affects elderly polytheistic subjects but a few cases in young adults have been reported [5,8].

The main drugs frequently encountered are beta-blockers and calcium channel blockers taken on a long-term basis [1,10]. However, authors have reported the responsibility of other drugs in the genesis of BRASH syndrome [6,7]. The severity of bradycardia varies from patient to patient. The diagnosis of BRASH syndrome requires a systematic search for triggering factors, i.e. all factors that aggravate pre-existing renal insufficiency, which could be hypovolemia, diabetic imbalance, an excess of diuretic drugs as in our first case, or an infection in the second case [1,5,6,9].

It is a diagnostic and therapeutic emergency, and the discontinuation of the atrioventricular neural blocking drug is imperative. In the acute phase, management is based on the treatment of hyperkalemia. The use of emergency EER and positive inotropic substances are often necessary [11, 12].

The evolution is generally favorable after correction of hyperkalemia, but can be severe if not properly managed. In the long term, regular clinical and biological monitoring, focused on prevention and search for aggravating factors of renal failure in patients undergoing atrioventricular node blockers, is the main preventive treatment for BRASH syndrome.

Conclusion

BRASH syndrome is a diagnostic and therapeutic emergency. The diagnosis is based on the syndromic association of bradycardia, renal failure, atrio-ventricular node blocking drugs, shock and hyperkalemia. Few data are available in the African literature on this subject, nevertheless this article constitutes an overview in the management of BRASH syndrome and encourages physicians to think about it before any bradycardia and to intensify the monitoring of renal failure patients on atrio-ventricular node blockers.

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