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Syncope caused by hyperkalemia during use of a combined therapy with the angiotensin-converting enzyme inhibitor and spironolactone

Omdlenie spowodowane hiperkaliemią podczas stosowania terapii skojarzonej inhibitorem konwertazy angiotensyny i spironolaktonem

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Abstract

A 76 year-old woman with a history of coronary artery bypass grafting and prior myocardial infarction was transferred to the emergency room with loss of consciousness due to marked bradycardia caused by hyperkalemia. The concentration of serum potassium was high, and normal sinus rhythm was restored after correction of the serum potassium level. The cause of hyperkalemia was considered to be several doses of spiranolactone, an aldosterone antagonist, in addition to the long-term intake of ramipril, an ACE inhibitor. This case is a good example of electrolyte imbalance causing acute life-threatening cardiac events. Clinicians should be alert to the possibility of hyperkalemia, especially in elderly patients using ACE/ARB in combination with potassium sparing agents and who have mild renal disturbance.

Key words: angiotensin-converting enzyme inhibitors, hyperkalemia, aldosterone, antagonist, syncope

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INTRODUCTION

Evidence has grown to support the combination therapy of angiotensin converting enzyme inhibitor (ACEI) with spironolactone as the standard regimen for the treatment of patients with heart failure along with essential hypertension [1]. Combination therapy has resulted in rare adverse events. However, there have been several reports that simultaneous administration of ACEI and spironolactone may cause a higher risk of developing hyperkalemia [2]. Severe hyperkalemia is responsible for conduction disturbances, dangerous arrhythmias, cardiogenic syncope and sudden cardiac death [3]. To our knowledge, however, syncope due to severe bradycardia caused by a combination of spironolactone and ACEI has not been reported before. We report here the case of a patient who had presented with syncope and electrocardiographic (ECG) evidence of marked bradycardia caused by hyperkalemia in association with a combination therapy of ACEI and spironolactone in mildly decreased renal function background.

CASE REPORT

A 76 year-old woman was transferred to the hospital emergency room with loss of consciousness. On the day of presentation, she developed abdominal pain, diarrhoea, nausea and vomiting. These symptoms were followed by dizziness and an episode of syncope. On admission to the hospital, she had heart rate of 28 bpm, respiratory rate of 18 breaths/min, blood pressure of 120/59 mm Hg and oxygen saturation of 99% on 4 L/min of oxygen administration through nasal canula. The patient's medical history revealed a coronary artery bypass grafting operation in

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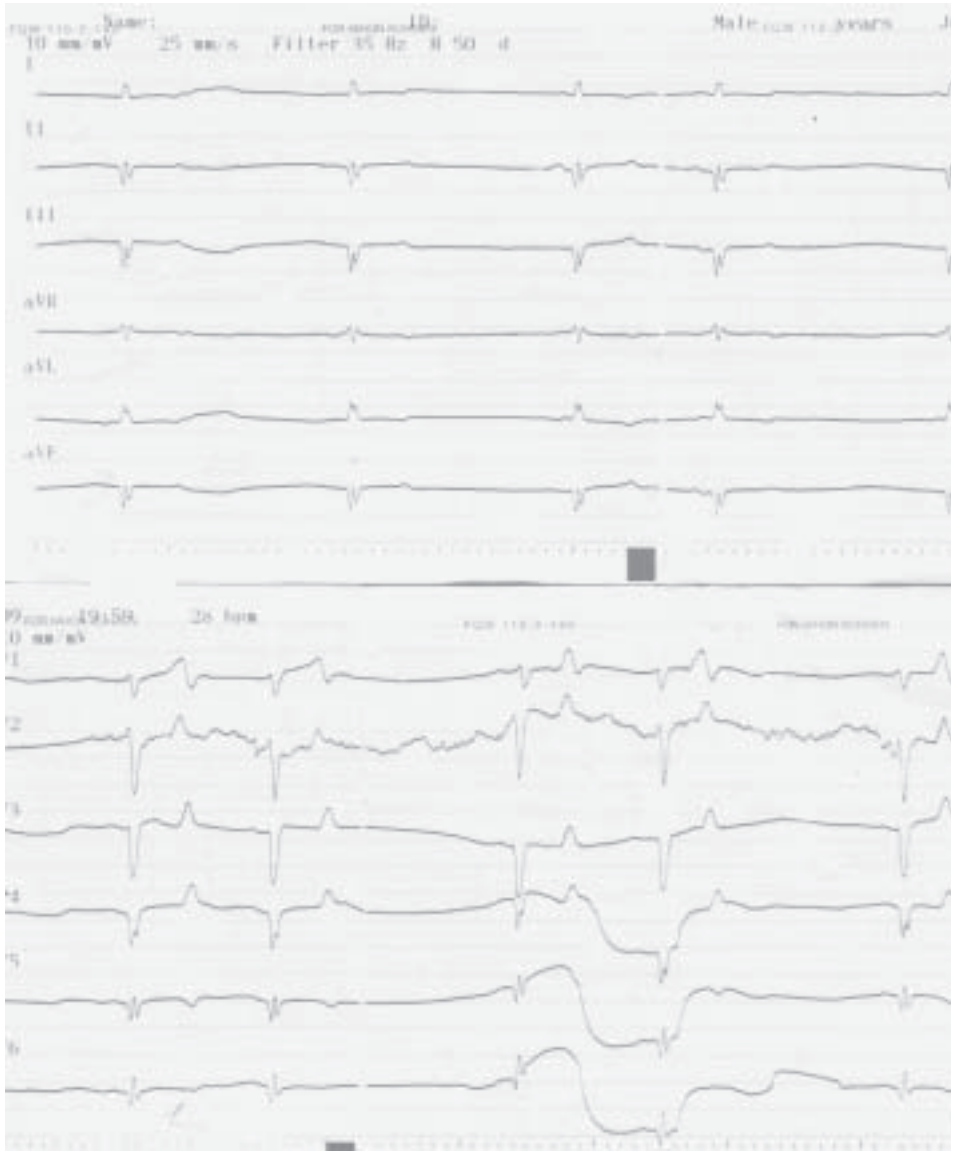

Figure 1. ECG on arrival showing marked bradycardia and tented T waves

1999, and history of acute anterior myocardial infarction at the age of 65. Her ejection fraction decreased moderately (EF: 40%). She also had hypertension and hypercholesterolaemia. Her daily medication regimen consisted of ramipril + hydrochlorothiazide 5/12.5 mg, carvedilol 12.5 mg, atorvastatin 20 mg, and acetyl salicylic acid 100 mg. Her family physician started spironolactone 25 mg for her worsening oedema control two weeks ago. The 12-lead ECG at admission showed absence of sinus P-waves, a persistent slow regular idioventricular-like rhythm at a rate of 28 bpm and upright and symmetrical peaked T-waves in right precordial leads (QTc, 0.42 s) (Fig. 1). Temporary percutaneous pacing was begun immediately, resulting in an immediate stabilisation of the haemodynamic status. A laboratory examination of peripheral venous blood revealed no elevation of serum cardiac muscle enzymes, but there was hyperkalemia (9.2 mEq/L). Creatinine level was 1.3 mg/dL. The glomerular filtration rate and the creatinine clearance estimated by predictive equations were 42 mL/min per 1.73 m^2 (MDRD 2 — Modification of Diet in Renal Disease study equation) showing a mild loss in renal function [4]. A rapid arterial blood gas analysis showed plasma pH 7.38, pCO_2 34.7 mm Hg, pO_2 95.0 mm Hg, and bicarbonate 22.0 mEq/L, with an anion gap of 7 mEq/L. Her blood potassium level decreased from 9.2 mEq/L to 5.2 mEq/L after six hours of glucose-insulin-bicarbonate infusion. Control ECG showed restored sinus rhythm at a rate of 70 bpm with the signs of an old myocardial infarction.

DISCUSSION

The classical sequence of ECG changes in hyperkalemia includes the appearance of tall and peaked T waves followed by PQ- and QRS-interval prolongation. Eventually, P waves may disappear, and progressive QRS lengthening may result in a sinusoidal pattern. Hyperkalemia also may manifest as a conduction block at different levels, including bundle branch block or atrioventricular (AV) block. Generally, the ventricular myocardium and Purkinje fibers are believed to be more sensitive than the AV node to the effects of hyperkalemia, but several cases of hyperkalemia-induced complete AV block with narrow QRS complex have been reported in the literature [5, 6]. However, there has been no case report in which hyperkalemia may manifest as a conduction defect at sinoatrial (SA) node. The disappearance of the P wave was probably due to SA block and/or sinoventricular conduction; that is, transmission of the sinus impulse from the SA node to the AV node without activation of the surrounding atrial myocardium.

Hyperkalemia is a known complication of the use of ACEI. The incidence of hyperkalemia appears to be relatively low (0–6%) in patients with normal renal function, but becomes increasingly common (5–50%) in those with renal insufficiency. Development of life-threatening hyperkalemia during the use of ACEI, although relatively rare, has been reported. Additional factors reported to increase the risk of hyperkalemia during the use of ACEI have included advanced age, congestive heart failure, the use of potassium-sparing diuretic agents, potassium supplements, and NSAIDs [7]. On the other hand, thiazide and loop diuretics are associated with a reduced risk of hyperkalemia. Indeed, hyperkalemia has not recurred in our patient since she was prescribed ramipril and a hydrochlorothiazide.

Though the risk of hyperkalemia remains a serious concern, this concern was not evident in the RALES trial, which reported an incidence of serious hyperkalemia of only 2% in the spironolactone treatment group, close to the 1% incidence observed in the placebo group. However, it's a fact that the publication of RALES was associated with abrupt increases in the rate of prescriptions for spironolactone and in the rate of hyperkalemia-associated morbidity and mortality [8]. In addition, this concern has been verified by a study of 25 patients with serious hyperkalemia caused by a combination of spironolactone and ACEI [2]. The defined serious hyperkalemia was a potassium concentration of > 6.0 mEq/L. The mean daily dose of spironolactone was 57 mg and the mean serum creatinine concentration was 3.8 mg/dL. Two patients died, and two others were resuscitated and survived. Haemodialysis was necessary in 17 patients and 12 patients were admitted to the intensive care unit. Our patient presented a similar clinical course as the most serious cases in that report.

As a consequence, clinicians who want to avoid acute life-threatening cardiac events should monitor especially elderly patients who have risk factors for hyperkalemia and are at high risk for this electrolyte imbalance.

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