Successful Treatment with an Antihypertensive Drug Regimen Including Eplerenone in a Patient with Malignant Phase Hypertension with Renal Failure

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Abstract

A 28-year-old man was referred to our hospital for the treatment of congestive heart failure and severe hypertension. The patient was diagnosed with malignant phase hypertension based on the presence of marked hypertension with left ventricular hypertrophy, exudate retinopathy, and renal failure. Intensive therapy for hypertension and heart failure with a combination of antihypertensive drugs including nitroglycerin, nifedipine, eplerenone and candesartan successfully lowered his blood pressure and further improved the renal function. Eplerenone could be one of the choices of antihypertensive drugs in combination therapy in patients with malignant phase hypertension with progressive heart and renal failure.

Key words: hypertensive emergency, renin-angiotensin-aldosterone system, eplerenone

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Introduction

Malignant phase hypertension, which is characterized by marked hypertension and acute end-organ damage, is relatively uncommon, occurring in 1% of the hypertensive population (1). Although the prognosis of malignant phase hypertension has improved with multiple antihypertensive medications, renal involvement is associated with higher morbidity and mortality (1, 2). Renin-angiotensin system (RAS) blockers such as angiotensin-converting enzyme inhibitors (ACE-Is) or angiotensin receptor blockers (ARBs) are recommended for the treatment of malignant phase hypertension (2). However the efficacy of mineralocorticoid receptor (MR) antagonists has not yet been studied. We herein report the case of a 28-year-old man with malignant phase hypertension complicated by heart and renal failure that was successfully treated with an antihypertensive drug regimen including eplerenone, an MR antagonist.

Case Report

A 28-year-old man was referred to our hospital to undergo treatment of congestive heart failure and severe hypertension in mid-December of 2011. He had not undergone a medical checkups for 10 years. He had been well until 1 month earlier, when he experienced cough and dyspnea. Seven days earlier, he had visited a general practitioner and had received medication for asthma. His blood pressure was not checked at that time. On admission, the patient’s blood pressure was 236/138 mmHg (without left-right difference), and the pulse rate was 90/min and regular. He was obese, with a weight of 97 kg, height of 167 cm, and body mass index of 34.8 kg/m2. Grade 2/6 systolic ejection murmurs and coarse crackles were heard on auscultation of the chest. There was moderate pitting edema of the legs. No bruit was audible in the abdomen. Fundoscopic findings revealed exudate retinopathy with papilledema, suggestive of malignant phase hypertension.

The urine was measured at 2+ for protein. Renal dysfunction was noted, with blood urea nitrogen levels of 75 mg/dL.
Discussion

Malignant phase hypertension is a hypertensive emergency characterized by a severe elevation of blood pressure and acute target organ damage, including progressive renal failure and heart failure (1, 3). The present patient showed a typical clinical presentation of malignant phase hypertension, such as marked hypertension with left ventricular hypertrophy, exudate retinopathy, and progressive renal failure. Although essential hypertension is the most common cause, any secondary form of hypertension could develop into malignant phase hypertension (1). Although renovascular hypertension should be considered at the outset of juvenile malignant phase hypertension, the present patient’s physical findings did not suggest renovascular hypertension and the renal arteriogram assessed by magnetic resonance angiography was normal. Endocrine hypertension, such as Cushing’s syndrome, pheochromocytoma, and primary aldosteronism, was not suggested by endocrinological studies and by the findings of CT. Renal parenchymal hypertension, however, was not ruled out because a renal biopsy was not performed.
in this patient. In any case, obesity might have been associated with the development of hypertension in this patient (4).

The activation of the renin-angiotensin-aldosterone (RAA) system plays an important role in the pathogenesis of malignant phase hypertension (1, 5, 6). Hyperreninemia due to diffuse intrarenal ischemia and secondary aldosteronism are frequently present, and elevated renin and aldosterone levels most likely exacerbate the hypertensive process in patients with malignant phase hypertension (5, 6). Among the vicious cycle of the RAA system, blood pressure, and renal injury, Naruse et al. has emphasized the role of aldosterone and the vascular RAS in the development of malignant phase hypertension (6). Aldosterone has been reported to be involved in renal injuries, including renal inflammation, oxidative stress, fibrosis, mesangial cell proliferation, and podocyte injury in various animal models (7, 8).

In the present patient, high PRA levels suggested the activation of RAS. In addition, hypokalemia suggested the effect of aldosterone, although the PAC was within the normal range. It is possible that decreasing levels of potassium, resulting from the activation of the RAA system, further inhibited aldosterone secretion despite increasing PRA in this patient (5). RAS blockers such as ACE-Is or ARBs are recommended for the treatment of malignant phase hypertension (2). However, the response to RAS blockers is variable and unpredictable and depends on the patient’s plasma volume and PRA. Moreover, RAS blockers are contraindicated when the patient has bilateral renal artery stenosis, which is difficult to assess immediately (9).

Eplerenone is a selective MR antagonist that has been shown to be effective as an antihypertensive agent (10), in preventing cardiovascularr and renal end-organ damage in patients with essential hypertension (11), and in reducing morbidity and mortality in short- and long-term in patients with heart failure and left ventricular systolic dysfunction after myocardial infarction (12). However, the efficacy and safety of eplerenone for patients with malignant phase hypertension has not yet been documented. Regarding non-selective MR antagonists, Oka et al. reported the use of multiple antihypertensive drugs including spironolactone for a patient with malignant hypertension caused by primary aldosteronism (13). In patients with resistant arterial hypertension including chronic kidney disease (CKD), Vaclavik et al. reported that the addition of spironolactone to their antihypertensive medications significantly lowered the systolic blood pressure (14). In the present patient, the independent efficacy of eplerenone could not be evaluated. However, the addition of eplerenone to the antihypertensive treatment for malignant phase hypertension normalized the patient’s hypokalemia and did not worsen the renal function.

Several clinical studies have confirmed the antialdosteronemic effects of MR antagonists given in addition to ACE-Is or ARBs in patients with diabetes or CKD (15, 16). In the present patient, the urinary albumin level decreased during the clinical course. However, it is not clear whether this was due to the effect of the antagonizing MR or the decrease in blood pressure. Hyperkalemia is considered one of the most serious adverse effects of MR antagonist therapy in patients with an impaired renal function. In a recent review, however, Shavit et al. demonstrated that the increased risk of hyperkalemia in MR antagonist-treated patients has been exaggerated and the risk of developing hyperkalemia in both CKD and end-stage renal disease patients is significantly lower than considered previously (8). In the present patient, combination treatment with eplerenone and ARBs did not induce hyperkalemia throughout the clinical course.

In summary, we herein reported a case of malignant phase hypertension that was successfully treated with multiple antihypertensive drugs including eplerenone. Eplerenone could be one of the choices for antihypertensive drugs in combination therapy in patients with malignant phase hypertension with the activation of the RAA system. Both the renal functions and the serum potassium level should be monitored carefully if eplerenone is prescribed for a patient with malignant phase hypertension.

The authors state that they have no Conflict of Interest (COI).

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