Case Report

A Case of Hyperreninemic Hypertension with Bilateral Positive Captopril Renography but without Renovascular Stenosis

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A 34-year-old woman was admitted to our hospital because of hypertension with hypokalemia. Her past medical history revealed that at age 24 she had been diagnosed with left renal lithiasis and had undergone extracorporeal shock-wave lithotripsy (ESWL). Physical examination showed that her peripheral pulses were intact and no peripheral edema or audible bruits were detected. Her serum potassium concentration was 2.7 mEq/mL, her plasma aldosterone concentration (PAC) was 96.7 ng/dL, and her plasma renin activity (PRA) was 28.1 ng/mL/h. Intrarenal lobar artery flow pattern assessed by Doppler ultrasound showed no abnormality. A renogram demonstrated a normal symmetrical tracing pattern. However, administration of 50 mg captopril induced delayed transit of tracer in both kidneys. Selective angiographic studies showed no stenotic lesions in the proximal to distal renal arteries. Blood sampling from each renal vein showed no laterality of PRA. While the possibility of the Page kidney phenomenon resulting from ESWL could not be excluded completely, the patient was diagnosed as a very rare case of hyperreninemic essential hypertension with positive captopril renography in both kidneys. (*Hypertens Res* 2008; 31: 383–386)

Key Words: hyperreninemia, renovascular stenosis, captopril renography

Introduction

The common cause of renovascular hypertension (RVH) in elderly subjects is renal stenosis caused by atherosclerosis and that in young women is medial fibromuscular dysplasia (1). Captopril renography is a very useful technique for diagnosing RVH, since it has a sensitivity and specificity of approximately 90%, for each (2, 3). Captopril renography has been shown to detect bilateral abnormalities in the presence of renal failure (4, 5) and also in a case of atherosclerotic lesions involving both renal arteries (6). We report a rare case of hyperreninemic hypertension with abnormal bilateral captopril renography in the absence of renal artery stenosis and renal failure.

Case Report

A 34-year-old woman was admitted to our hospital because of hypertension with hypokalemia. On admission, her blood pressure was 176/110 mmHg despite the fact that she was taking antihypertensive medication (amlodipine 5 mg, which was discontinued after the admission). Her past medical history showed that at age 24 she had been diagnosed with left renal lithiasis and had undergone extracorporeal shock-wave lithotripsy (ESWL). At 3 months before administration of ESWL, she had a checkup for a headache in a local doctor's office. She was diagnosed with hypertension with hypokalemia for the first time and treated with amlodipine. No other medication including diuretics was taken until the admission. Physical examination did not reveal signs of the excessive

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Fig. 1. A basic renogram of a normal symmetrical tracing pattern (A). Administration of 50 mg of captopril induced delayed transit of tracer in both kidneys (B).

adrenocortical steroid levels seen in Cushing's syndrome. Her height was 150 cm and body weight was 44 kg. All peripheral pulses were intact and no peripheral edema or audible bruits were detected. Urine examination showed no hematuria or cast, although the 24-h excretion of protein was 3.7 g. The urinary excretions of potassium and chloride were 35.2 mEq/day and 81.4 mEq/day, respectively. Serological evaluation for immunoglobulins, complement, anti-nuclear antibodies, antineutrophilic cytoplasmic antibody and hepatitis B and C virus were all negative. Biochemical assays showed a serum potassium concentration of 2.7 mEq/mL, serum creatinine concentration of 0.5 mg/dL, plasma aldosterone concentration (PAC) of 96.7 ng/dL and plasma renin activity (PRA) of 28.1 ng/mL/h. Administration of 50 mg captopril caused a marked decrease in blood pressure to pre-shock levels (98/64 mmHg) at 1 h after administration, associated with a further elevation in PRA (44.7 to 64.1 ng/mL/h) and a reduction in PAC (53.5 to 36.2 ng/dL). Ultrasonography revealed normal symmetrical kidneys, with the length of the right measuring 94 mm and that of the left 95 mm. A Doppler ultrasound of the intrarenal lobar arteries showed that the pulsatility index ($[\text{max pulse wave velocity} - \text{minimum pulse wave velocity}] / \text{mean pulse wave velocity}$; PI) and resistive index ($[\text{max pulse wave velocity} - \text{minimum pulse wave velocity}] / \text{max pulse wave velocity}$; RI) were both within the normal range. A renogram using Tc-99m mercaptoacetyl triglycine (MAG3)

demonstrated a normal symmetrical tracing pattern (Fig. 1A). However, administration of 50 mg captopril induced delayed transit of tracer in both kidneys (Fig. 1B). These captopril administration tests suggested that the patient's high blood pressure level was due to bilateral RVH.

We next performed computed tomographic renal angiography and selective renal angiography (Fig. 2). These angiographic studies showed no stenotic lesions in the proximal to distal renal arteries. Selective blood sampling from each renal vein showed no laterality of renin secretion. On the basis of these clinical findings, the patient was diagnosed with hyperreninemic essential hypertension. During hospitalization, her blood pressure remained high and the hypokalemia continued, so she was treated with 25 mg spironolactone and 5 mg bisoprolol. After 2 weeks of this treatment, her blood pressure decreased to 122/80 mmHg, her proteinuria fell to 0.4 g/day and her serum potassium level was normalized, without an elevation in creatinine.

Discussion

In this paper we report the case of a hypertensive patient with hypokalemia due to hyperreninemia and hyperaldosteronism without renal artery stenosis. Secondary hyperaldosteronism and a hyperreninemic state are usually observed in patients with RVH. Angiographically, we did not detect stenosis in the

Fig. 2. Selective renal angiography showed no stenotic lesions in the proximal to distal renal arteries in both kidneys.

proximal to distal renal arteries in either kidney. Reviewing the patient's medical history, we noted she had undergone ESWL 10 years previously. ESWL has been reported to initiate the development of hypertension with hyperreninemia (7, 8), with histological studies in experimental animals showing ESWL may injure all the tissues within the focal region of the shock wave, especially veins and small arteries (9). These histological changes may induce a Page (cellophane-wrapped) kidney effect, leading to elevation of PRA (8, 9). The Page kidney was established in these earlier experiments of induced hypertension by wrapping canine kidneys with cellophane. There are now numerous clinical reports of Page kidney occurring in association with secondary hypertension, or acute or chronic unilateral subcapsular or perinephric hematomas (8). Any significant external compression of the kidney causes renal hypoperfusion and water retention, ultimately leading to hypertension. The most common cause of Page kidney is bleeding secondary to trauma resulting from contact sports or motor vehicle accidents. Subcapsular bleeding is also a complication of renal biopsies and ESWL and may indicate a Page kidney phenomenon. Sasaguri *et al.* reported a case of hyperreninemic hypertension after ESWL (7). In this patient, renography showed reduced rates of renal excretion and uptake of the tracer in the left kidney that had been treated by ESWL, but a normal right kidney. The ratio of PRA in the left vein to that in the right renal vein was 1.7. In this earlier case of ESWL-induced hypertension, the kidney injured by ESWL secreted more renin than the lateral kidney. However, in our case, selective blood sampling from each renal vein showed no laterality of renin secretion. Janetschek *et al.* reported that patients with new onset hypertension following ESWL had an elevation in the intrarenal resistive index (10). Both intrarenal PI and RI were within the normal range in our case and showed no laterality. However, despite these findings we could not exclude the possibility of ESWL-induced hyperreninemic hypertension in our patient.

Captopril induced a reduction in the uptake and a slowing

of excretion of Tc-99m MAG3 in both kidneys in our patient. Bilateral abnormalities in captopril renography are seen in glomerular diseases, especially those with a vasculitis etiology, and also in sodium depletion associated with activation of the renin-angiotensin aldosterone axis and bilateral renal artery stenosis (11, 12). None of these conditions were observed in our patient.

In addition to RVH and Page kidney, reninomas have been reported to cause hyperreninemic hypertension, with renin secreting juxtaglomerular cell tumors elevating renin-angiotensin activity, thereby leading to hypertension. In such cases, angiotensin converting enzyme inhibitors and angiotensin II receptor antagonists produce marked decreases in blood pressure, despite plasma renin levels remaining high (13). In our case, although the PRA level was extremely high at admission, the reduction in blood pressure was associated with a decrease in PRA, which after 3 months of treatment had fallen to 4.86 ng/mL/h. Yung *et al.* also reported that captopril did not influence the patterns of renograms in renin secreting tumors or Page kidneys and concluded that captopril renography was therefore not useful for diagnosing these two conditions (14).

We are not able to exclude the possibility that long term exposure to very high blood pressure levels by conditions such as unilateral Page kidney or reninomas may cause hypertensive renal damage. Advanced hypertensive nephrosclerosis may enhance renin secretion and reduce uptake and excretion of Tc-99m MAG3 in both kidneys during captopril renography. Another possible diagnosis in our patient was an extrarenal reninoma. In order to exclude such a possibility, we performed whole body computer tomography and positron emission tomography and found that no extrarenal tumor was present. However, we are also not able to rule out the extrarenal reninoma completely.

On the basis of these clinical and laboratory findings, we conclude that our patient was a very rare case of hyperreninemic hypertension with positive captopril renography in both

kidneys. However, in order to establish the cause of this hyperreninemic hypertension, we need more experience in the treatment of patients with physiological changes similar to those seen in our patient.

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