ORTHOSTATIC HYPERTENSION DUE TO COEXISTENCE OF RENAL FIBROMUSCULAR DYSPLASIA AND NEPHROPTOSIS

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A 42-year-old woman presented with orthostatic hypertension. Increased plasma renin activity was noted and blood pressure rose gradually with standing. Selective renal arteriography indicated narrowing of the distal portion of the right renal artery and poststenotic dilatation and signs of arterial stenosis due to fibromuscular dysplasia. Greater arterial narrowing resulted from tortion due to nephroptosis brought about by excessive renin secretion. Thus, both renal arterial stenosis and nephroptosis were considered responsible for the present orthostatic hypertension. Percutaneous transluminal renal angioplasty was found very effective for normalizing standing blood pressure and renal blood flow.

NEPHROPTOSIS, abnormal mobility of the kidney, is considered a benign disorder by most clinicians. However, it sometimes leads to other disorders that must be treated. It remains uncertain whether severe nephroptosis causes orthostatic hypertension.¹ The failure of adequate reflex adaptation due to diseases and drugs is known to cause orthostatic hypotension, but hypertension on standing is a term far less familiar to many clinicians.

Orthostatic hypertension was first described in 1922.² Recently, Streeten, et al³ investigated 1,800 hypertensive patients and found 181 to have recumbent and standing diastolic pressures below and above 90 mmHg, respectively. They suggested that excess sympathetic nerve stimulation induced by abnormal peripheral blood pooling on standing may be responsible for the increased standing blood pressure. Abnormal renal vasculature accompanied by abnormal renal

mobility may also cause hypertension on standing.⁴ The present study describes a patient who showed orthostatic hypertension resulting from enhanced renal vascular narrowing, the cause possibly being nephroptosis. Percutaneous transluminal renal angioplasty (PTRA) was found to be a very effective treatment.

CASE REPORT

A 42-year-old female was first found to have hypertension (systolic blood pressure = 150 mmHg) without related symptoms during a routine check-up in April 1985. Six months later, her blood pressure rose to 200/100 mmHg and she began to feel occasional frontal headaches and to become easily fatigued. There was also numbness of the right thigh. Since medication at a local clinic was not effective in reducing the high blood pressure, she was referred to the Kitasato University Hospital for evaluation. She had previously received in 1980 drug therapy for cholelithiasis and her mother is presently taking antihypertensive drugs.

At the outpatient clinic, her blood pressure

Key words:

Orthostatic hypertension
Nephroptosis
Renal fibromuscular dysplasia
Percutaneous transluminal renal angioplasty

(Received November 20, 1987; accepted July 23, 1988)

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Fig.1. Changes in blood pressure and plasma levels of renin, angiotensin and aldosterone during hospitalization.

Abbreviations: PRA = plasma renin activity; AI = plasma angiotensin I; AII = plasma angiotensin II; Aldo. = plasma aldosterone level; Ps = systolic pressure; and Pd = diastolic pressure.

was 160/100 mmHg in the supine position and there was no abrupt change on standing. A physical examination revealed no abdominal bruit or hypertensive vascular change in the optic fundi. The laboratory examination indicated high plasma renin activity (PRA; 13.6 ng/ml/hr), high plasma angiotensin II (87 pg/ml) and high plasma aldosterone (38 ng/dl) after 15 min of bed-rest. Renal arterial stenosis was thus considered responsible for the high blood pressure and she was admitted to the hospital for further evaluation.

At admission, the laboratory examination revealed no abnormality in peripheral blood analysis and normal urinalysis except for mild pyuria (WBC: 5–8/HPF). Arterial blood gas analysis showed a mild metabolic alkalosis (pH 7.42, $p\text{CO}_2$ 43 mmHg, $p\text{O}_2$ 93 mmHg, HCO_3^- 29 mEq/l). Serum electrolytes were: Na^+ (139 mEq/l), K^+ (3.5 mEq/l), Cl^- (112 mEq/l), Ca^{2+} (9.1 mg/dl), PO_4^{3-} (2.9 mg/dl), Mg^{2+} (2.8 mg/dl). Serum creatinine and blood urea nitrogen levels were 0.8 and 19 mg/dl, respectively. Creatinine clearance was slightly decreased to 76.5 ml/min

and renal plasma flow (para-aminohippurate clearance) was 423 ml/min. X-ray films of the chest and abdomen, an electrocardiogram and an ultrasonic cardiogram showed no abnormalities.

In the hospital, her blood pressure fluctuated markedly, being often as low as 120/70 mmHg with only dietary salt restriction (NaCl: 5 g/day), as shown in Fig. 1. Recumbent PRA decreased from 7.3 on the second morning to 1.2 ng/ml/hr on the 5th morning after admission and plasma aldosterone decreased from 22 to 10 ng/dl. Recumbent blood pressure followed this reduced renin secretion, decreasing from 162/100 mmHg on the 2nd morning to 140/90 mmHg on the 5th morning. Despite the marked reduction in renin secretion, the plasma catecholamine level showed no change during this period (2nd morning; adrenaline 10 pg/ml, noradrenaline 104 pg/ml, 5th morning; adrenaline 17 pg/ml, noradrenaline 158 pg/ml). An intravenous pyelogram showed mild enlargement of the bilateral pelvis while standing, and upon standing up both kidneys dropped by a length of 2 vertebral bodies (Fig. 2). Four hours of standing induced a

Fig.2. Intravenous pyelography. Left: 10-minute film of supine position showing mild enlargement of left renal pelvis without abnormality in right kidney. Right: Both kidneys have dropped by 2 vertebral bodies during standing. Right renal pelvis slightly enlarged owing to mild urinary stasis. There was no difference in appearance time between the two kidneys in two-minute film of the supine position.

Fig.3. Changes in blood pressure, PRA and plasma aldosterone levels during 4 hours' standing following 10 hours' bed-rest.

gradual increase in blood pressure, PRA and plasma aldosterone, as evident from Fig. 3. The effect of plasma catecholamine on blood pressure with posture change was also examined. Plasma adrenaline was increased to 200 pg/ml from 88 pg/ml by 15 min of standing without a significant change in blood pressure. It was thus considered

that the hypertension in this case was caused by a high angiotensin II level due to hyper renin secretion.

An ^{131}I -hippuran renal scintigram showed delayed perfusion in the right kidney and normal function of the left kidney when in the supine position. Perfusion was delayed and peak activity was much less when sitting than when supine (Fig. 4), indicating an exaggerated impaired right renal blood flow while sitting. The arteriogram (Fig. 5) revealed an appearance typical of fibromuscular dysplasia, involving the distal portion of the renal artery and causing characteristic irregularity and mild poststenotic dilatation when supine. At a 70° head-up tilt, the renal artery was twisted and stenosis became more apparent. From these findings, the patient was considered to have right renal arterial stenosis caused by fibromuscular dysplasia (FMD), which was made more severe on standing by nephroptosis. This would explain the patient's hypertension while standing and reduced blood pressure while in the recumbent position.

Percutaneous transluminal renal angiography (PTRA) was carried out as treatment for this renal arterial stenosis. Fig. 6 shows the im-

Fig.4. ¹³¹I-hippuran renogram. A. supine position, B. sitting position. The perfusion rate was markedly delayed in the right kidney in both positions. Maximum count for the right kidney was 70%, while supine, and 48%, while sitting, of the counts obtained for the left kidney. Abbreviations: R = right kidney; L = left kidney; B = bladder.

Fig.5. Selective renal arteriography before treatment. Left: Right renal artery in supine position has narrowed and shows poststenotic dilatation, both typical features in fibromuscular dysplasia. Right: renal artery has stretched and stenotic lesion is more prominent in the 70° head-up tilt position.

provement in the stenosis under conditions of a 70° head-up tilt after PTR. No significant increase was noted in blood pressure, PRA or plasma aldosterone during 4 hours of standing. Creatinine clearance, renal plasma flow (para-aminohippurate clearance) and fractional ex-

cretion of Na⁺ (Table I) markedly improved. Since discharge from the hospital, the patient's blood pressure has remained stable with no rise in PRA for 1 year, with a daily dose of 300 mg of ticlopidine hydrochloride to prevent recurrence of the occlusion.

Fig. 6. Selective renal arteriography following PTR treatment. Left: In the supine position, Right: 70° head-up tilt.

TABLE I CLINICAL DATA BEFORE AND AFTER PTR

	Before PTR			After PTR		
	Before	1 hr	4 hrs	Before	1 hr	4 hrs
<i>A. Effects of standing</i>						
PRA (ng/ml/hr)	0.2	1.0	2.2	0.8	1.6	1.0
Aldosterone (ng/dl)	5	11	21	9	9	10
BP (mmHg)	120/70	146/80	180/100	126/70	120/76	134/84
<i>B. Renal function (supine)</i>						
C _{cr} (ml/min)		76.5			131	
RPF (ml/min)		423			591	
F.F.		0.18			0.22	
FENa (%)		2.7			0.8	

*RPF (renal plasma flow) was measured by paraamino-hippurate clearance. F.F. stands for filtration fraction and FENa, the fractional excretion of Na.

DISCUSSION

The present case of orthostatic hypertension was caused by FMD of the right renal artery, complicated by nephroptosis. Stenosis was enhanced by torsion of the artery on standing. Even though the stenosis was considerable, the patient showed normal blood pressure with normal levels of PRA, angiotensins I and II and

plasma aldosterone when in the supine position. The stenosis was sufficiently severe to stimulate renin secretion when standing, as evident in Fig. 5. Thus, no immediate change in blood pressure was noted with change in posture. Plasma catecholamine levels at the time of admission were within normal limits, instead of a high blood pressure. The noradrenaline level increased to 200 pg/ml during 15 min of standing,

but blood pressure showed no significant increase.

The present arterial stenosis exhibited characteristics of FMD, including distal renal arterial stenosis and irregularity of the arterial wall. Both nephroptosis and F.M.D. are generally observed only in females. De Zeeuw, et al found abnormal renal mobility in 12 of 14 female patients with F.M.D., with mean mobilities of the right (8.6 cm) and left kidneys (6.8 cm) which significantly exceeded ($p < 0.001$) those in women with hypertension due to other causes (6.3 cm and 4.0 cm, respectively), and also those of healthy women (3.4 cm and 3.5 cm, respectively).¹ They considered excessive torsion of the renal artery due to abnormal renal mobility to possibly be one cause of FMD. A report has also appeared on coincidental renal arterial stenosis complication due to aortitis syndrome and nephroptosis.⁴ Though a significant correlation has been found between orthostatic hypertension and nephroptosis in female patients, orthostatic hypertension apparently does not depend on renal mobility in male patients.⁵ No satisfactory explanation for this sex difference can be given at the present but the much higher incidence of nephroptosis in women is surely a major participating factor.

Whether severe nephroptosis should be treated has long been a controversial issue. In 1940, McCann and Romansky observed marked decreases in renal blood flow in nephroptotic hypertensive females.⁶ Recently, de Zeeuw, et al presented data in support of this, from measurements of effective renal blood flow.⁷ Bianchi, et al also found marked reduction in GFR as measured by ¹³¹I-hypaque clearance.⁸ Some reports indicate possibly higher incidences of nephrolithiasis and recurrent pyelonephritis in female nephroptotic patients than in other females.^{9,10} Careful examination is required to detect disturbances to renal blood flow and renal functions resulting from severe nephroptosis.

In our case, PTRa was used to treat renal arterial stenosis. It was found highly effective for treating renovascular hypertension and safer than surgical revascularization.^{11,12} The long-term follow-up was also satisfactory and normotension has been maintained for about 37 months following termination of PTRa. Blood pressure during standing was successfully reduced and renal function improved. There is no satisfactory explanation for observed increases in fractional excretion of sodium before PTRa. Some micropuncture studies have suggested that

the proportion of filtered fluid and sodium reabsorbed by the proximal tubules falls when the glomerular filtration rate is reduced by renal ablation, glomerulonephritis or experimental pyelonephritis.¹³ Since in this study PTRa normalized creatinine clearance and fractional excretion of sodium without any delay, tubular function before PTRa might have been impaired without any organic damage. Thus in this case PTRa treatment virtually abrogated the orthostatic hypertension. Without organic narrowing of the renal artery, it would not have been possible for torsion of the renal artery alone to raise the blood pressure and PRA levels, since the degree of ptosis was not very severe.

In summary, the present case was found to be one of orthostatic hypertension caused by excessive renal arterial narrowing arising from abnormal renal mobility. Renovascular stenosis was improved by PTRa and the outcome of this therapy was found quite satisfactory.

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