Reversible Renin-dependent Renovascular Hypertension Successfully Treated With Percutaneous Transluminal Renal Angioplasty and Stenting

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SUMMARY

A 37-year old woman was suspected of having renovascular hypertension because of recent onset severe hypertension (blood pressure 220/135 mmHg; compared to 132/65 mmHg two years earlier) and an abdominal bruit. A captopril renal scan indicated the presence of right renal artery stenosis. Additionally, a captopril plasma renin activity (PRA) provocation test showed a positive result for renovascular hypertension (baseline PRA = 291 μU/mL; 1 hour post-captopril PRA = 1444 μU/mL). Selective renal angiography demonstrated a severe critical stenotic lesion at the distal portion of the right renal artery. Blood pressure (BP) decreased to 136/80 mmHg one day after successful percutaneous transluminal renal angioplasty and stenting. Repeat renal angiography six months after the procedure revealed no evidence of in-stent restenosis. Blood pressure (BP = 137/76 mmHg) and plasma renin profile (baseline PRA = 23.8 μU/mL; 1 hour post-captopril PRA=22.3 μU/mL) also were normal six months following initial revascularization. Moreover, blood pressure (137/84 mmHg) and renin profile remained normal 2.5 years after the procedure (baseline PRA = 24.3 μU/mL; 1 hour post-captopril = 25.6 μU/mL). The results of this study have thus demonstrated a case of renin-dependent renovascular hypertension in which both the blood pressure and plasma renin activity profile normalized following successful percutaneous transluminal angioplasty and stenting. (Int Heart J 2005; 46: 339-345)

Key words: Renovascular hypertension, Fibromuscular dysplasia, Angioplasty, Stenting, Plasma renin activity

RENOVASCULAR hypertension is the most common form of potentially curable secondary hypertension and accounts for up to 3% of the hypertensive population.1) In 1934 Goldblatt2) demonstrated that partial occlusion of one renal artery resulted in significantly increased blood pressure. The importance of the renin-angiotensin system in initiating this state has subsequently been demonstrated.3,4) This study describes a case of reversible renin-dependent renovascular
hypertension. Blood pressure and renin profile normalized following successful percutaneous transluminal renal angioplasty and stenting.

**CASE REPORT**

A 37-year-old woman visited our emergency department due to episodic severe headache, nausea, and vomiting that had persisted for 2 days. The woman denied any previous history of hypertension. Blood pressure was 132/65 mmHg two years earlier, as recorded in her chart. The woman had experienced episodic headache during the past month, but had not visited a doctor. On admission, her blood pressure was 220/135 mmHg, temperature 36.5°C, pulse 84 beats per minute, and respiratory rate 18 breaths per minute. Laboratory examinations showed her hemoglobin was 15.2 gm% and white blood cell count $7.11 \times 10^3/\text{mm}^3$. Additionally, biochemistry examination revealed blood urea nitrogen of 14 mg%, creatinine 0.9 mg%, cholesterol 195 mg%, triglycerides 38 mg%, and potassium 3.87 meq/L. Physical examination was unremarkable except for the presence of an abdominal bruit. The woman was suspected to have renovascular hypertension because of recent onset severe hypertension and an abdominal bruit. A captopril renal scan was arranged and indicated right renal ischemia. A captopril plasma renin activity provocation test (CRT) revealed a positive result for renal artery stenosis (baseline PRA = 291 $\mu$U/mL; normal: 7-76 $\mu$U/mL, one hour post-captopril 50 mg = 1444 $\mu$U/mL). Renal angiography subsequently was performed and revealed a critical stenotic lesion at the distal portion of the right renal artery (Figure 1 upper panel), while the left renal artery was patent. The woman underwent percutaneous transluminal renal angioplasty using a Viva balloon catheter (2.5 × 20 mm), but the result was suboptimal. Subsequently, an AVE GFX stent (3.5 × 12 mm) was deployed successfully (Figure 1 middle panel). Blood pressure decreased to 136/80 mmHg one day after interventional revascularization without any antihypertensive medication (Figure 2). Repeat renal angiography six months after initial revascularization revealed no evidence of in-stent restenosis (Figure 1, lower panel). Blood pressure was 137/76 mmHg without any antihypertensive medication 6 months after initial revascularization (Figure 2). Repeat CRT was negative for renal vascular hypertension (baseline PRA = 23.8 $\mu$U/mL; one hour post-captopril = 22.3 $\mu$U/mL) (Figure 3). Two and a half years after initial revascularization, her blood pressure (137/84 mmHg) (Figure 2) remained normal and CRT was still negative (basal PRA = 24.3 $\mu$U/mL; one hour post-captopril = 25.6 $\mu$U/mL) (Figure 3).
Figure 1. Angiograms of right renal artery. 
**Upper**: a discrete critical stenotic lesion at the distal right renal artery. **Middle**: after successful percutaneous transluminal renal angioplasty and stenting. **Lower**: repeat renal angiography six months following initial percutaneous transluminal stent placement revealing no evidence of in-stent restenosis.
DISCUSSION

The renin-angiotensin system has been demonstrated to play an important role in the initiation of hypertension in renal artery stenosis. Renal hypoperfusion results in reduced preglomerular pressure and flow that increase renin secretion with the production of angiotensin II. Angiotensin II is not only a potent vasoconstrictor but also stimulates the secretion of aldosterone that causes sodium retention and volume expansion. Although peripheral renin activity is
usually elevated in patients with renovascular hypertension, approximately 20% of patients with renovascular hypertension have normal plasma renin activity, while up to 16% of patients with essential hypertension may have elevated plasma renin activity.\(^5,6\) Therefore, the measurement of peripheral renin activity has been shown to be inadequate for the diagnosis of renovascular hypertension. Case and Laragh\(^7\) were the first to show that the reactive rise in renin following administration of captopril is greater in patients with renovascular hypertension than in those with essential hypertension. Later, Muller, \textit{et al}\(^8\) proposed the captopril renin test (CRT) for distinguishing renovascular hypertension and essential hypertension. The original captopril renin test criteria were as follows: (1) post-captopril renin exceeding 12 ng/mL/hour, (2) an absolute increase of 10 ng/mL/hour or more, and (3) a percentage increase of 150% or more or a 400% increase if the basal renin is below 3 ng/mL/hour. They found that CRT had a sensitivity of 100% and a specificity of 95%. Subsequent studies have confirmed the value of the CRT,\(^9,10\) but never obtained such a high sensitivity and specificity. The reported overall sensitivity is around 61% while the specificity is 86%.\(^11\) In the present case, the basal plasma renin activity was markedly elevated (291/76 = 3.8 fold above the upper normal level) and the PRA increased 496% (1444/291) after stimulation with captopril, so the result was strongly positive for renovascular hypertension when using the original Muller criteria. Six months and 2.5 years following initial successful revascularization the basal PRA was normal and CRT was negative. In the present case, the blood pressure was quite high at baseline (220/135 mmHg); however, blood pressure declined to normal (136/80 mmHg) 1 day after successful revascularization and the BP remained normal (137/84 mmHg) 2.5 years after initial revascularization (without any antihypertensive medication). Correlating the BP and renin profile data before and after successful revascularization revealed that our case was a typical case of reversible renin-dependent renovascular hypertension. There are two major causes of renovascular hypertension.\(^12,13\) Atherosclerotic renovascular hypertension accounts for 90% of cases and tends to affect older populations (usually over 50 years old) and usually involves the proximal third of the renal artery. Fibromuscular dysplasia accounts for less than 10% of cases and tends to affect young populations, particularly female populations and usually involves the middle and distal third of the renal artery. The present patient is a young female with recent onset severe resistant hypertension, and thus fibromuscular dysplasia is the likely cause of her renal artery stenosis. The available literature indicates that the blood pressure control achievable in patients with fibromuscular dysplasia renal artery stenosis is consistently greater than in patients with atherosclerotic renal artery stenosis. In the review by Ramsey \textit{et al},\(^14\) the cured, improved, and unchanged rates of hypertension in patients with fibromuscular dysplasia by percutaneous translum-
nal renal angioplasty were 50%, 42%, and 8%, respectively, whereas in patients with atherosclerotic renal artery stenosis the respective figures were 19%, 51%, and 30%. In another study of percutaneous transluminal renal angioplasty for treating renovascular hypertension by Morganti, et al.\textsuperscript{15} the results of blood pressure control in both types of renal artery stenosis are similar to that reported by Ramsey, et al.\textsuperscript{14} Only 3% of 66 patients with atherosclerotic renovascular hypertension were cured, 38% were improved, and 59% were unchanged; in contrast, 45% of 47 patients with fibromuscular dysplasia were cured, 23% achieved improvement, and 32% remained unaffected. Why is the blood pressure response after successful revascularization quite different between these two types of renal artery stenosis? This study postulates that the fibromuscular dysplasia form of renovascular hypertension is initially renin-dependent; however, if it is not diagnosed and treated early, long-term hypertension may cause nephrosclerosis that may further contribute to the exacerbation of hypertension. This phenomenon may explain why not all patients with the fibromuscular dysplasia form of renovascular hypertension are cured following successful revascularization. Additionally, theoretically the likelihood of a cure of hypertension following successful revascularization should increase with the promptness of the diagnosis and treatment. The hypertension may be of mixed origin in the atherosclerotic form of renovascular stenosis. A renovascular component may exist solely, or more frequently may be superimposed on essential hypertension. These mechanisms may explain why the cure rate of hypertension following successful revascularization is less successful for atherosclerotic than for fibromuscular disease. No parameter is yet available for predicting what subgroup of patients with renovascular hypertension can benefit most from blood pressure control by revascularization. From the observations of the present case, we would like to propose conducting a prospective large-scale study that would determine renin profiles (including basal PRA and CRT) before and after revascularization. The renin profiles could then be compared in three groups of patients in regard to the blood pressure response to revascularization (cured, improved, and unchanged groups). These analyses may enable us to determine whether the renin profile can serve as a parameter for predicting the blood pressure response by revascularization.

REFERENCES


