Case Report

Dilation of Renal Artery Stenosis after Administration of Losartan

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Transluminal angioplasty with a balloon catheter is effective to dilate renal artery stenosis (RAS) caused by fibromuscular dysplasia (FMD), but lesions resistant to the angioplasty exist. In this report, we describe the case of a young woman with RAS of FMD that was difficult to dilate even by cutting-balloon angioplasty. To facilitate the formation of a smooth intimal covering at the site of angioplasty, we administered losartan, an angiotensin receptor blocker, for 4 months after the angioplasty. Although re-stenosis was detected at 5 months after the angioplasty, the normotensive state continued without antihypertensives and the re-stenosis gradually dilated afterwards. The present case suggests the possibility of remodeling the renal artery during the normotensive state by administering losartan after the angioplasty. (*Hypertens Res* 2007; 30: 999–1002)

Key Words: renal artery stenosis, fibromuscular dysplasia, hypertension, angiotensin, angioplasty

Introduction

Fibromuscular dysplasia (FMD) often disturbs renal perfusion by its stenotic lesions and causes renovascular hypertension (RVH) (1). Re-canalization of renal artery stenosis (RAS) by percutaneous transluminal angioplasty with a conventional balloon catheter is the primary mode of treatment (2). However, some lesions are resistant to this treatment. Stainless-steel endoprosthesis (stenting) and cutting-balloon angioplasty are often performed in these resistant lesions and improve the rate of re-canalization, but they can cause adverse effects (3, 4). Stenting may cause in-stent re-stenosis, which is difficult to re-canalize (5). Cutting-balloon angioplasty may cause intimal dissection and arterial perforation at the site of angioplasty (6). Therefore, several of the reported cases of resistant RAS have necessitated surgical reconstruction (7), which not only costs more but also has a higher rate of complications than transluminal angioplasty (1).

We report a case of RVH caused by FMD, in which the

RAS was resistant to transluminal angioplasty. The resistant RAS, however, showed dilation during the normotensive state that was achieved by administration of losartan after the angioplasty.

Case Report

A 22-year-old woman with hypertension (160/90 mmHg) was referred to our hospital for suspicion of RVH. Renal arteriography revealed characteristic images of FMD: stenotic lesions on the distal portion of the right upper trunk and on the left primary branches, and an aneurysmal deformity on the right upper trunk (Fig. 1A). The calculated minimal diameters of the stenotic lesions were 0.5 mm, 1.9 mm, and 1.7 mm in the right upper trunk, the left upper branch, and the left lower branch, respectively. Because these lesions had a mean pressure gradient (PG) >40 mmHg, we performed transluminal angioplasty. Although the angioplasty with a conventional balloon catheter reduced the mean PG to <15 mmHg in all these lesions, residual stenosis remained on the left branches

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(minimal diameters: 2.8 and 2.5 mm in the upper and lower branches, respectively). The plasma renin activity in the right and left renal vein before the angioplasty was 1.1 and 0.9 ng/mL/h, respectively; this indicated that her hypertension had already been volume-dependent before the angioplasty. The angioplasty reduced the arterial blood pressure (BP) to 135/85 mmHg, but administration of atenolol (25 mg/day) and losartan (25 mg/day) was needed to reduce it to <130/85 mmHg.

At 6 months after the angioplasty, only losartan (25 mg/day) maintained the normotensive state, but repeated arteriography revealed re-stenosis (Fig. 1B). Therefore, we performed a second angioplasty. The re-stenosis in the right upper trunk could be dilated by a conventional balloon catheter (Fig. 1C, left), and the PG at the stenosis disappeared (mean: from 77 to 0 mmHg). However, the re-stenosis in the left branches could not be dilated even by a cutting-balloon (Boston Scientific, Natick, USA), and residual stenosis remained (minimal diameters: 2.5 and 2.0 mm in the upper and lower branches, respectively) (Fig. 1C, right). Consequently, the PG in the left branches was reduced but did not disappear (mean: from 41 to 6 mmHg in the upper branch and from 56 to 14 mmHg in the lower branch).

The arterial BP was further reduced (115/75 mmHg) after the second angioplasty, but we continued administration of losartan (25 mg/day) for an additional 4 months. Although cessation of losartan did not increase the arterial BP, a computed tomographic angiography (CTA) detected re-stenosis in the left branches at 5 months after the second angioplasty (Fig. 2A). We did not perform further angioplasty, because the normotensive state continued without antihypertensives. During the normotensive state, CTA detected gradual dilation of re-stenosis at 16 and 40 months after the second angioplasty (Fig. 2B, C). The calculated minimal diameters of the lesions are summarized in Table 1.

Discussion

In the present case, the images of the renal artery showed dilation of re-stenosis after angioplasty. Because the dilation of re-stenosis followed achievement of the normotensive state, continuation of the normotensive state is thought to have induced the dilation. The angiographic appearance of the RAS in the present case indicated that the RAS was intimal fibroplasia type (8). In this type, intimal hyperplasia is thought to occur during the process of re-stenosis (9), and the blood flow on the intima is known to affect the hyperplasia; ruffled flow facilitates and unruffled flow prevents the hyperplasia (8, 10). Because reduction of the arterial BP would reduce the turbulence of flow at the stenotic lesions, it would facilitate dilation of the lesions by preventing intimal hyperplasia. Supporting this notion, in a previously reported case of FMD, dilation of RAS without angioplasty was recognized after the continuous normotensive state that was achieved by antihypertensives (11).

Antihypertensives capable of suppressing the renin-angio-

Fig. 1. Renal arteriography. *A:* Initial arteriography detected a lesion with 90% stenosis, a 6 mm-diameter aneurysm in the right upper trunk, and lesions with 70% stenosis in the primary branches of the left renal artery. The stenotic lesions were dilated by transluminal angioplasty. *B:* A second arteriography detected re-stenosis (70% of each). *C:* Repeated arteriography after the second angioplasty confirmed successful dilation in the right upper trunk, but there was residual stenosis in the left branches.

tensin cascade, a potential enhancer of intimal hyperplasia (12), were used in the reported case of RAS-dilation after the continuous normotensive state (11). The authors suggested the possibility that inhibition of the cascade might have facilitated the dilation, although antihypertensives with the potential to activate the renin-angiotensin cascade were also used in the case. Administration of losartan, an angiotensin II receptor blocker (ARB), during the period of intimal healing might also have facilitated the dilation of re-stenosis in the present case (10, 13). Losartan would have facilitated the smooth covering of the luminal surface at the site of angioplasty, and the smooth covering would have reduced the turbulence of blood flow, which could have induced the dilation. Considering the effectiveness of calcium channel blockers to reduce the arterial BP, the combination of a calcium channel blocker and an ARB might be a preferable way to maintain a normo-

Fig. 2. CTA maximum intensity projection images of the left renal artery. A: At 5 months after the second angioplasty (1 month after cessation of losartan), re-stenosis was detected in the primary branches. B: At 16 months after the second angioplasty, the lesions with re-stenosis were enlarged. C: At 40 months after the second angioplasty, the lesions were further enlarged.

Table 1. Minimal Diameter of Stenosis in Left Renal Arterial Branch

Size (mm)	Pre-angioplasty 1	Pre-angioplasty 2	Post-angioplasty 2		
			5 months	16 months	40 months
Upper	1.9	1.8	1.4	2.4	2.7
Lower	1.7	1.4	1.5	1.9	2.2

tensive state (14).

Brief blockage of the renin-angiotensin cascade has also been reported to contribute to achieve a continuous reduction of the total peripheral vascular resistance in young hypertensive animals (15, 16). Reduction in the media/lumen ratios of the resistance vessels was noted in these animals, indicating that a brief blockade of the cascade induced remodeling of the resistance vessels. The present case is thought to have demonstrated that even in young adult human a short-term blockage of the cascade could induce vascular remodeling of the renal artery at least during the process of intimal healing after angioplasty and contribute to long-term reduction of the arterial BP. The participation of the renin-angiotensin cascade in the architecture of the arterial wall has also been revealed in the aorta and heart (17–19). The inhibition of the renin-angiotensin cascade could prevent the progression of the aortic aneurysm and cardiovascular structural changes.

Converting angiotensin I to angiotensin II, the angiotensin-converting enzyme (ACE) is a key enzyme in the renin-angiotensin cascade, and two different types of ACE are known to exist: the tissue ACE and the serum ACE. The ACE inhibitors are agents that can block both types, but the dose of the ACE inhibitors normally used for antihypertensive treatment cannot block the tissue ACE (20). In contrast to the ACE inhibitors, ARBs can block the effect of angiotensin II produced by either type of ACE (21). Because the degree of intimal hyper-

plasia is known to correlate with the tissue ACE rather than the serum ACE (12), we used an ARB during the period of intimal covering at the site of angioplasty (9). Because losartan has the added effect of suppressing platelet-aggregation, we selected losartan from the ARBs (13).

In conclusion, administration of losartan could be used to prevent re-stenosis after angioplasty of RAS caused by FMD, although further studies are needed to establish its efficacy. The administration would facilitate smooth covering of the damaged luminal surface at the site of angioplasty. Reduced turbulence of the blood flow on the smoothly covered luminal surface would prevent intimal hyperplasia and re-stenosis.

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