

[CASE REPORT]

A Unique Case of Renovascular Hypertension due to Fibromuscular Dysplasia in an Extra-renal Artery

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Abstract:

A 33-year-old man was admitted to our hospital to undergo an evaluation to determine the cause of secondary hypertension. Computerized tomography angiography (CTA) showed bilateral multiple renal arteries with significant stenosis of the right extra-renal artery due to fibromuscular dysplasia and segmental impairment of renal perfusion. Although the plasma aldosterone concentration and plasma renin activity were within the normal ranges, percutaneous balloon dilatation of the stenotic lesion resolved his hypertension, leading to a diagnosis of renovascular hypertension caused by segmental renal ischemia due to extra-renal artery stenosis. CTA should be considered during the examination of patients with early-age hypertension, even if the plasma renin activity is not sufficiently elevated.

Key words: renovascular hypertension, extra-renal artery

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Introduction

Ten percent of renovascular hypertension (RVH) cases are due to fibromuscular dysplasia (FMD), which is a potentially treatable cause of secondary hypertension (1, 2). Renal artery variation is common. The frequency of extra-renal arteries is reported to be 24-25% (3, 4). However, there are few reports of RVH due to FMD in an extra-renal artery, and the condition has not been sufficiently explored. We describe a unique case of RVH resulting from FMD in an extra-renal artery that was successfully treated with percutaneous transluminal angioplasty (PTA).

Case Report

A 33-year-old man with headache was referred to a nearby clinic. An initial examination revealed a blood pressure of 180/100 mmHg. The administration of amlodipine and olmesartan did not control his hypertension sufficiently. He was referred to our department to undergo further evaluation to determine the cause of secondary hypertension. He

had a family history of hypertension (father and uncle) and was not a smoker. His blood pressure was 144/82 mmHg. Twenty-four-hour ambulatory blood pressure monitoring showed a riser pattern (Table 1). He demonstrated unremarkable changes on cardiovascular, respiratory, and central nervous system examinations. There was no abdominal bruit. General laboratory tests showed a mild decrease in the patient's creatinine clearance (73 mL/min). Ophthalmoscopy revealed Scheie H1S1 changes and abdominal ultrasonography revealed asymmetric kidneys: the right kidney was 87×42 mm in length; the left was 106×45 mm. Computerized tomography angiography (CTA) revealed bilateral multiple renal arteries (Fig. 1A). Two renal arteries supplied the right kidney (anterior and posterior) and left kidney (anterior and posterior), respectively. A string of beads appearance was observed in the middle portion of the right and left anterior renal arteries, suggesting FMD (Fig. 1B and D). The right posterior renal artery showed significant stenosis in comparison to the left. In addition, computed tomography showed that perfusion was reduced in the right posterior renal area, particularly around the lower pole (Fig. 1C). A quantitative analysis of the lower pole cross-section revealed that the ar-

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Table 1. Results of 24 Hours Ambulatory Blood-pressure Monitoring on Admission and after PTA.

	On admission	After PTA
24 hours-SBP (mmHg)	138	128
24 hours-DBP (mmHg)	89	77
24 hours-PR (bpm)	64	68
awake-SBP (mmHg)	136	132
awake-DBP (mmHg)	88	79
awake-PR (bpm)	64	70
sleep-SBP (mmHg)	142	110
sleep-DBP (mmHg)	93	66
sleep-PR (bpm)	61	58
pattern	riser	dipper

SBP: systolic blood pressure, DBP: diastolic blood pressure, PR: pulse rate, PTA: percutaneous transluminal angioplasty

areas of decreased and preserved perfusion were 4.6 cm² (in blue) and 10.8 cm² (in red), respectively (Fig. 1E and F). Selective renal angiography and CTA also revealed significant stenosis of the right posterior renal artery (Fig. 2A). The significant stenosis of the right posterior artery was located on the peripheral side of the upper pole branch bifurcation, which was consistent with the decreased perfusion of the right posterior renal area, particularly around the lower pole.

The patient was diagnosed with right posterior ischemic nephropathy due to FMD of the right posterior renal artery. To determine whether the right posterior renal artery stenosis was associated with hypertension, an endocrinological examination was performed after the discontinuation of olmesartan. The plasma aldosterone concentration was 147 pg/mL (normal range 30-159 pg/mL). The plasma renin activity (PRA) was 1.5 ng/mL/h (normal range 0.2-2.7 ng/mL/

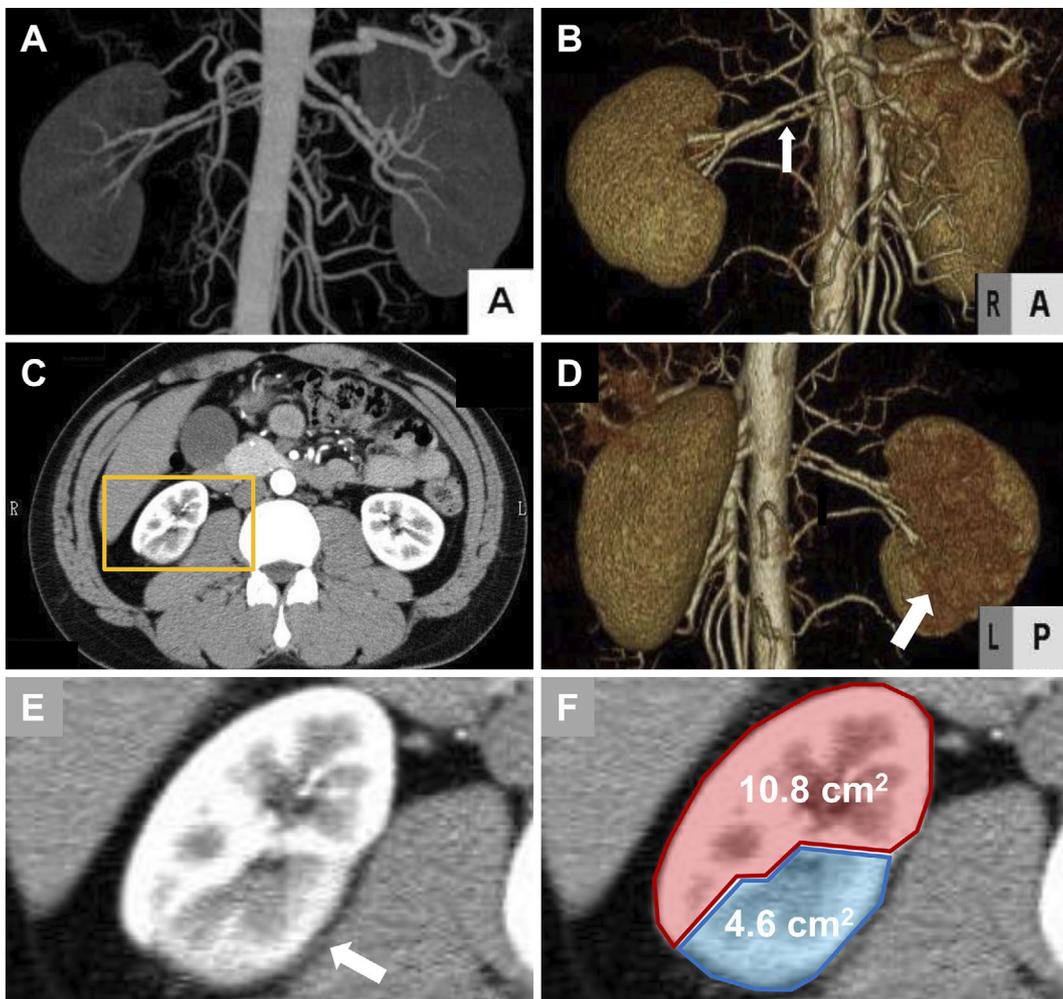


Figure 1. Computed tomography (CT) and computed tomography angiography (CTA) images on admission. (A) CTA and 3D maximum intensity projection indicated bilateral multiple renal arteries. (B) Anterior views of CTA and 3D multiplanar reconstruction indicated significant stenosis of the posterior right renal artery (arrow). (C) (D) CT and posterior views of CTA and 3D multiplanar reconstruction indicated decreased perfusion of the posterior right renal area (arrow). (E) (F) A magnified view of the right kidney revealed decreased perfusion of the right posterior renal area (arrow). The areas of decreased and preserved perfusion were 4.6 cm² (in blue) and 10.8 cm² (in red), respectively.

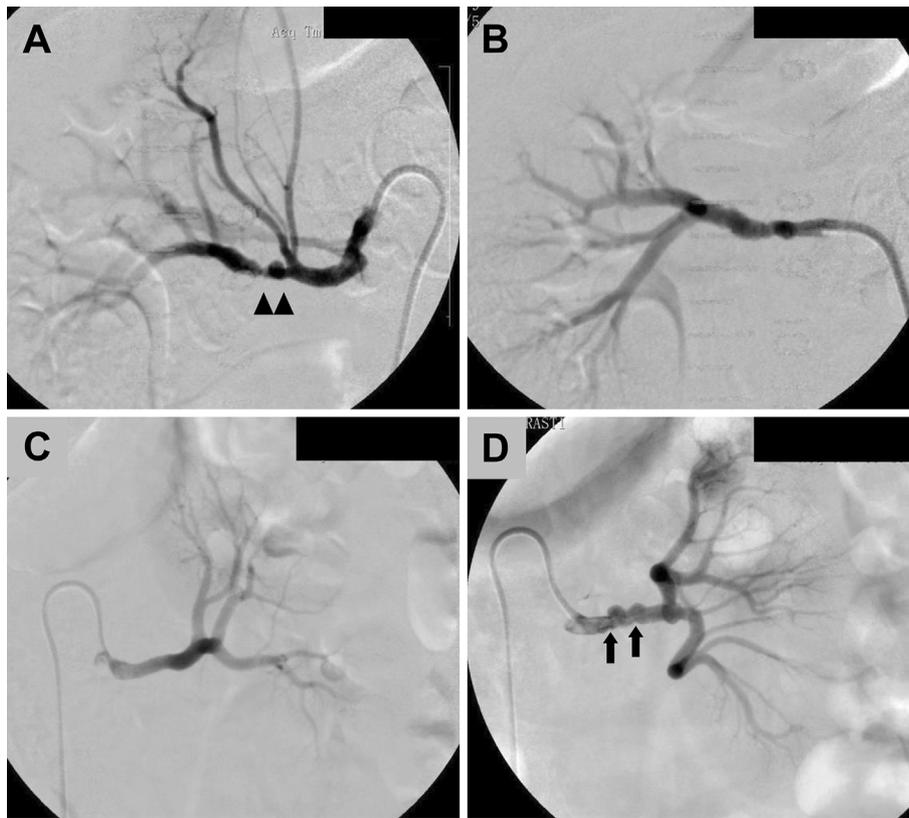


Figure 2. Selective renal angiography. (A) The right posterior renal artery showed a string-like appearance with significant stenosis (arrowhead). (B) Right anterior artery. (C) Left posterior artery. (D) The left anterior artery showed a string-like appearance without significant stenosis (arrow).

Table 2. Results of Captopril 50 mg Renin Provocation Test on Admission and after PTA.

	On admission		After PTA	
	Pre	60 min	Pre	60 min
PRA (ng/mL/h)	1.5	11.9	1.1	2.5
PAC (pg/mL)	119	150	97	70

PTA: percutaneous transluminal angioplasty, PRA: plasma renin activity, PAC: plasma aldosterone concentration

Table 3. Selective Renal Venous Sampling.

Right renal vein PRA (ng/mL/h)	1.9
Left renal vein PRA (ng/mL/h)	1.5
Ratio (Right:Left)	1.3:1
IVC PRA (ng/mL/h)	1.8

PRA: plasma renin activity, IVC: inferior vena cava

h). A renin provocation test using captopril (50 mg) showed an excessive response, as a more than 4-fold increase of the peak PRA from a baseline PRA of <3 ng/mL/h is indicative of RVH (5) (Table 2). The removal of the suppressive effect of high angiotensin II levels on renin secretion caused the exaggerated secretion of renin from the right posterior ischemic renal area, which was possibly linked to the increase in the plasma aldosterone concentration.

Next, renal venous sampling was performed. The renin ratio was calculated by dividing the renin value on the significantly stenotic side (right) by that on the contralateral side (left). The renin ratio of this patient was 1.3 (Table 3). Notably, a cut-off value of 1.5 has been proposed for this ratio (6). Renography using ^{99m}Tc -MAG3 also showed non-specific changes. These results indicated that the correlation between the right posterior renal artery stenosis and hypertension was obscure.

To improve the ischemic nephropathy of the right posterior renal area, percutaneous balloon dilatation of the stenotic lesion (middle portion of the right posterior renal artery) was performed using a 3-mm balloon catheter (Fig. 3). Balloon inflation at pressures of up to 5 atm for 30 seconds, twice succeeded in dilating the lesion without any significant residual stenosis. Restenosis is reported to generally occur within 1 year in 10-30% of patients undergoing PTA for atherosclerotic renal artery stenosis (1). In particular, smaller arteries have a risk for restenosis after PTA, which is caused by atherosclerosis. In contrast, over a 10-year period, restenosis occurred in <10% of patients with renal artery stenosis due to FMD (1). In the present case, following angioplasty, the patient's blood pressure was normalized over a period of several years without antihypertensive medication. To evaluate the effects of PTA on ischemic nephropathy and hypertension, we performed CTA, a renin provocation test, and 24-h ambulatory blood pressure monitoring at 1 year after PTA. CTA revealed no evidence of recurrent renal artery

stenosis and showed the improvement of the ischemic nephropathy of the right posterior renal area (Fig. 4). A renin provocation test using captopril (50 mg) showed a normal response (Table 2). Captopril inhibited the synthesis of angiotensin II, leading to a reduction in the plasma aldosterone concentration. In contrast, PRA was increased by the removal of negative feedback. Twenty-four-hour ambulatory blood pressure monitoring showed a dipper pattern; however, the patient's body weight, alcohol consumption, and sleeping hours remained unchanged (Table 1). Based on these clinical findings, the patient was diagnosed with RVH due to FMD in the right extra-renal artery.



Figure 3. Selective renal angiography of the right posterior renal artery showed improvement of the stenotic lesion after percutaneous balloon dilatation (arrowhead).

Discussion

We described a unique case of RVH due to FMD in an extra-renal artery. The mere presence of renal artery stenosis and hypertension does not establish a diagnosis of RVH. A three-step approach to the diagnosis of RVH has been suggested (2, 7). The first step is the appropriate selection of patients who are more likely to have RVH. RVH is to be considered when hypertension develops at an early age, is of new onset or worsens in the elderly. RVH should also be considered in patients with accelerated hypertension, where there is a sudden and persistent worsening of previously controlled blood pressure, with resistant hypertension, where the condition cannot be controlled with three antihypertensive agents including one diuretic, or with malignant hypertension, where there is hypertension with acute end organ damage (8). Second, the patient's renal arteries should be imaged to confirm the presence of renal artery stenosis. Resolution or improvement in blood pressure control should occur with reversion of the stenosis. The present case fulfilled these criteria. Segmental renal ischemia due to extra-renal artery stenosis was found to be the cause of the patient's RVH.

In our case, the 24-h ambulatory blood pressure monitoring showed a riser pattern and a dipper pattern before and after PTA, respectively. Before PTA, the morning administration of amlodipine and olmesartan might not have sufficiently suppressed the nocturnal blood pressure in comparison to the awake blood pressure. In general, a higher morn-

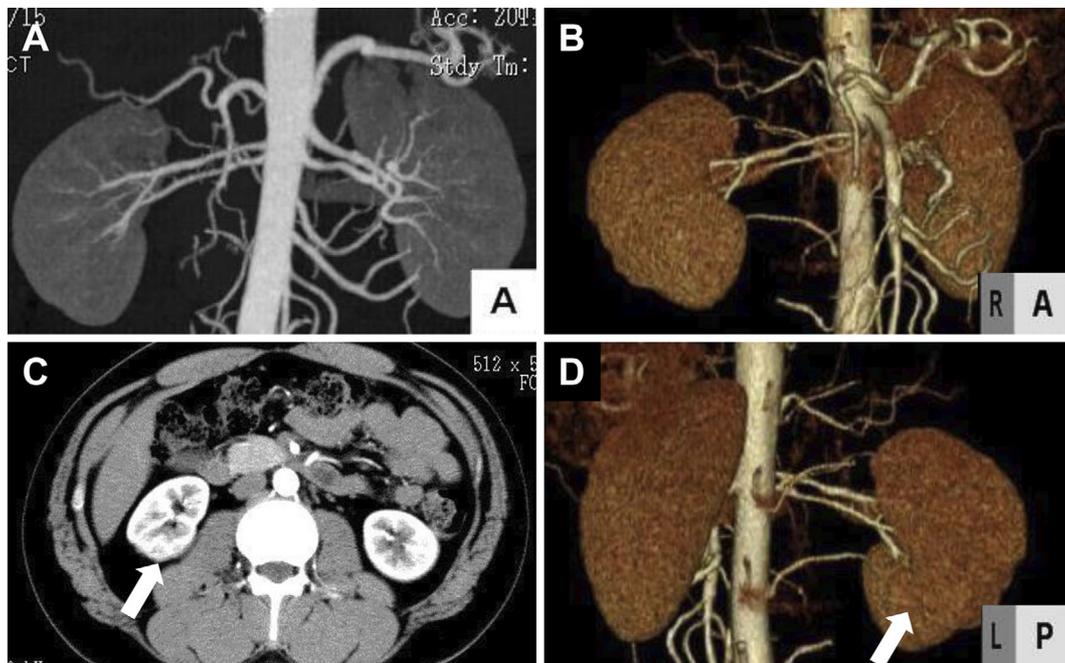


Figure 4. Computed tomography (CT) and computed tomography angiography (CTA) images at 1 year after percutaneous transluminal angioplasty (PTA). (A) (B) Anterior views of 3D maximum intensity projection and 3D multiplanar reconstruction indicated no evidence of recurrent renal artery stenosis. (C) (D) CT and posterior views of CTA and 3D multiplanar reconstruction indicated the improvement of the posterior right renal perfusion (arrow).

ing home blood pressure relative to office blood pressure occurs because of a non-dipper pattern or a riser pattern of nocturnal blood pressure (9). A recent study reported that PTA significantly decreased both office and home morning and evening blood pressures and morning home systolic blood pressure variability (10). Our findings and previous data suggest that PTA may have beneficial effects on the actual blood pressures values and on the circadian rhythm.

In general, the frequency of extra-renal arteries is 24-25% (3, 4), while bilateral multiple renal arteries are present in 5-7.7% of people. Extra-renal arteries are divided into 2 groups: hilar and polar arteries. Hilar arteries enter the kidneys from the hilus with the main renal artery, whereas polar arteries enter the kidneys directly from the capsule outside the hilus (3). In the present case, bilateral multiple renal arteries were defined as bilateral double hilar arteries.

In general, reduced renal perfusion with preserved oxygenation can activate renin secretion, leading to RVH (11). The renal artery divides into the anterior and posterior division, both of these divisions further divide into segmental arteries, which represent the end artery and form independent renal segments (12). Based on these findings, segmental perfusion impairment due to stenosis of the extra-renal artery can cause RVH. Segmental perfusion impairment was found to cause RVH (13-15). CTA is known to detect renal FMD in either the main renal or extra-renal arteries with high sensitivity (16). It was noted that RVH was not directly linked to extra-renal arteries; however, the presence of extra-renal artery stenosis should be considered a potential risk factor for hypertension (17).

It was also reported that cure rates using current definitions for hypertension (blood pressure <140/90 mmHg) were only 36% after angioplasty in patients with renal artery stenosis caused by FMD (18). Based on these findings, it is important to evaluate the correlation between extra-renal artery stenosis and hypertension using functional tests, such as the baseline PRA, captopril renin provocation test, renography, and renal venous sampling for the confirmation of angioplasty.

In the present case, these functional tests did not entirely indicate RVH. Thus, the correlation between the patient's stenosis and hypertension remained obscure until PTA was performed. A conventional cut-off value in functional tests may not be suitable for evaluating segmental renal ischemia due to the existence of extra-renal artery stenosis; thus, while the frequency of extra-renal arteries is 24-25%, RVH due to extra-renal artery stenosis is rarely diagnosed. A more specific evaluation of dysfunction in the unilateral local renal area might be needed. Some previous reports have described RVH due to FMD in extra-renal arteries (13, 19, 20), and the evaluation of dysfunction in the unilateral local renal area was attempted. Ergün et al. reported that drawing more than one region of interest over the kidneys by dividing each kidney into zones makes it possible to evaluate the parenchyma separately on a renogram (13). It was also noted that the accuracy of selec-

tive renal sampling could be enhanced by the prior administration of an ACE-inhibitor, which would increase renin secretion on the affected side (14). However, a cut-off value in the functional test for RVH due to extra-renal artery stenosis has not been established. The accumulation of patients and further examinations is required.

Conclusion

We described a unique case of RVH due to FMD in an extra-renal artery that was cured using PTA. Segmental renal ischemia due to extra-renal artery stenosis was identified as the cause of RVH. CTA should be considered during the examination of patients with early-age hypertension, even if the PRA is not sufficiently elevated.

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

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