

[CASE REPORT]

Treatment of Refractory Hypertension with Timely Angioplasty in Total Renal Artery Occlusion with Atrophic Kidney

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Abstract:

Angioplasty for cases of chronic total occlusion of renal artery with/without atrophic kidney is generally not recommended. We herein report a 57-year-old man who presented with renin-mediated refractory hypertension caused by occlusion of a unilateral renal artery leading to kidney atrophy (length: 69 mm). Angioplasty favorably achieved blood pressure control with normalized renin secretion and enlargement of the atrophic kidney to 85 mm. Timely angioplasty can be beneficial in select patients, even with an atrophic kidney and total occlusion, especially in cases with deterioration of hypertension within six months and the presence of collateral perfusion to the affected kidney.

Key words: renal artery stenosis, renovascular hypertension, renin-angiotensin system inhibitors, atherosclerotic renovascular disease, diffusion-weighted MRI

(Intern Med 60: 287-292, 2021)

(DOI: 10.2169/internalmedicine.5290-20)

Introduction

Atherosclerotic renovascular disease (ARVD) is the most common form of renal artery disease and is associated with severe comorbidities, such as renovascular hypertension with refractory hypertension and ischemic nephropathy with a progressive decline in the renal function (1). Percutaneous transluminal renal angioplasty (PTRA) with stenting is considered an effective modality for the correction of occlusive lesions and the subsequent normalization of the reduced renal blood flow. Nonetheless, randomized controlled trials evaluating angioplasty for ARVD have not found any advantages of angioplasty over medical therapy alone in terms of renal protection (2, 3). Based on these negative studies,

guidelines no longer support routine angioplasty for ARVD patients in general (4-6). However, observational evidence indicating the benefits of PTRA in specific high-risk patients has been increasing (7-10). Thus, the correction of occlusive lesions through angioplasty has a beneficial effect in carefully selected patients who will potentially respond well to angioplasty.

Considering the indication for angioplasty, the current expert consensus statement recommends angioplasty as a therapeutic option for patients with developing ischemic nephropathy or high-risk manifestations of renovascular hypertension (11). However, cases with advanced atrophic kidney (pole-to-pole length <7 cm) and kidney with total occlusion of the renal artery have rarely been considered appropriate due to the limited benefits of angioplasty (11, 12).

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Received: May 11, 2020; Accepted: July 6, 2020; Advance Publication by J-STAGE: August 22, 2020

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We herein report a case of ARVD presenting with a sudden deterioration of refractory hypertension and atrophic kidney (length <7 cm) caused by total unilateral renal artery occlusion. In this case, timely revascularization of the occlusion by PTRA favorably achieved blood pressure control and enlargement of the atrophic kidney.

Case Report

A 57-year-old man had hypertension that had been diag-

Table. Laboratory Results of the Patient before PTRA.

White blood count	(/μL)	8,300
Hemoglobin	(g/dL)	12.6
Platelet count	(/μL)	26.2×10 ⁴
Blood urea nitrogen	(mg/dL)	16
Creatinine	(mg/dL)	1.1
eGFR	(mL/min/1.73 m ²)	56
Sodium	(mmol/L)	139
Potassium	(mmol/L)	2.8
Chloride	(mmol/L)	98
Total protein	(g/dL)	6.2
Albumin	(g/dL)	3.7
Total cholesterol	(mg/dL)	200
HbA1c	(%)	5.6
Active renin concentration	(pg/mL)	166
Plasma aldosterone	(pg/mL)	267
Brain natriuretic peptide	(pg/mL)	82
Urine blood	(-)	
Urine protein	(g/g creatinine)	4.6

eGFR: estimated glomerular filtration rate

nosed 2 years earlier and was presently being administered amlodipine 5 mg per day with good blood pressure control. He smoked cigarettes (20 per day for 37 years) and did not have diabetes mellitus, hyperlipidemia, or obesity (body mass index: 22 kg/m²). He presented with relatively sudden deterioration of blood pressure (195/115 mmHg) with massive proteinuria (4.6 g/g creatinine) and polyuria. When an angiotensin II receptor blocker (ARB; olmesartan 20 mg per day) was added to control his blood pressure, his serum creatinine level increased from 1.1 to 2.2 mg/dL. After olmesartan was discontinued, the serum creatinine returned to 1.1 mg/dL. A laboratory examination showed hypokalemia and excessive elevation of the active renin and aldosterone concentrations (Table). Doppler ultrasound did not detect flow signals in the right renal artery, and enhanced computed tomography (CT) revealed total occlusion of the right renal artery with atrophy of the right kidney (Fig. 1A, B). The pole-to-pole length of the right kidney had decreased to 69 mm, while that of the left kidney was 111 mm (Fig. 1C). Technetium-99m-labelled diethylenetriamine-pentaacetic acid (^{99m}Tc-DTPA) renography revealed no peak curve of the right kidney, suggesting no residual function in the affected kidney. On magnetic resonance imaging (MRI), diffusion-weighted images demonstrated a high signal intensity with reduced apparent diffusion coefficients in the right kidney parenchyma (Fig. 1D, E), indicating restricted water diffusion due to severe ischemic changes (13-15). He presented with a regular pulse rate of 104 beats per minute and no evidence of thrombophilic disorders, aortic lesion, carotid artery stenosis, or ischemic heart disease. Based on these findings, we diagnosed him with renovascular hypertension

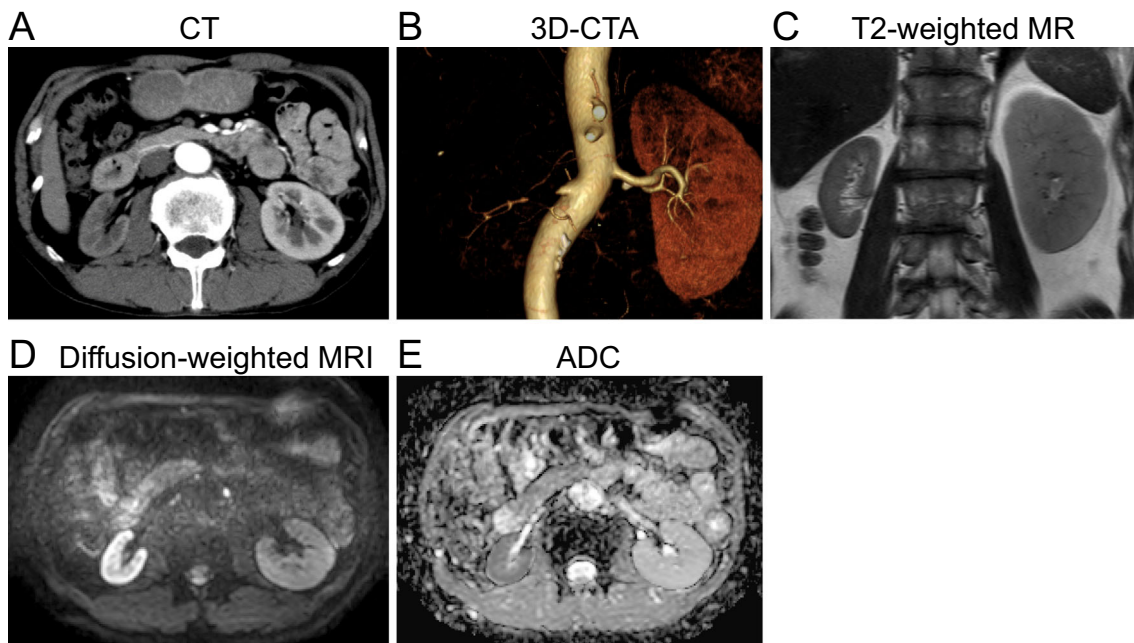


Figure 1. Total occlusion of the right renal artery, leading to renal atrophy. A: Enhanced computed tomography (CT) image. B: Three-dimensional CT angiography image. C: T2-weighted magnetic resonance imaging (MRI) scan. D: Diffusion-weighted MRI scan. E: Apparent diffusion coefficient (ADC) in diffusion-weighted MRI scan.



Figure 2. Angioplasty for total occlusion in the renal artery. **A:** First percutaneous transluminal renal angioplasty (PTRA) procedure for the right renal artery. Angiography obtained by cannulating the adrenal artery providing collateral flow to the right kidney before PTRA and renal artery angiography after PTRA. **B:** Computed tomography one month after the first PTRA procedure showing thrombotic in-stent re-occlusion (arrows) **C:** Second PTRA procedure for the right renal artery.

secondary to atherosclerotic renal artery occlusion, leading to kidney atrophy.

Despite treatment with multiple antihypertensive medications (nifedipine 80 mg, doxazosin 8 mg, and clonidine 150 µg per day), the blood pressure remained uncontrollable at 160-200/100-130 mmHg. Thus, we decided to perform PTRA. At four months after the onset of deterioration of blood pressure, renal angiography showed occlusion of the right renal artery with collateral flow to the kidney from the adrenal artery (Fig. 2A). Balloon dilation and placement of 2 stents in the lesion revascularized the right kidney, although a systolic pressure gradient of 20 mmHg remained across the treated lesion. He was started on aspirin 100 mg the following day. After the procedure, his blood pressure and the plasma renin level decreased; however, they increased again one month after the treatment. CT showed thrombotic in-stent re-occlusion of the right renal artery (Fig. 2B). Thus, we performed endovascular balloon dilatation for the lesion again, and revascularization was achieved (Fig. 2C). After the second treatment, the plasma renin concentration dramatically decreased to 11 pg/mL, and the blood pressure was controlled at 130/85 mmHg with antihypertensive medication, including the ARB azilsartan (20 mg) without a rapid decline in the renal function (Fig. 3). The urinary protein also decreased to 0.5 g/g creatinine.

One month after the procedure, Doppler ultrasonography demonstrated a normalized intrarenal blood flow pattern and enlargement of the atrophic right kidney (length: 85 mm), and ^{99m}Tc -DTPA scintigraphy showed partial recovery of the right kidney function (Fig. 4). After 6 months, the patient

presented with favorable control of blood pressure (120/70 mmHg) and a stable renal function (serum creatinine: 1.2 mg/dL), and no features of re-stenosis have been observed on follow-up evaluations by Doppler ultrasonography.

Discussion

In the present case, the timely resolution of the total occlusion of the renal artery by PTRA favorably achieved blood pressure control and functional and size recovery of the affected atrophic kidney in a patient with refractory hypertension. This suggests that PTRA can have a beneficial effect in select ARVD patients, even with an atrophic kidney and total occlusion of the renal artery, when the procedure is performed at an appropriate time. Thus, clinicians cannot exclude PTRA as a potential treatment for such patients and should carefully evaluate each individual case to decide whether or not performing PTRA promptly would provide any beneficial effect and thereby avoid missing the appropriate timing of PTRA.

Although the current expert consensus states that PTRA for ARVD with advanced atrophic kidney and/or chronic total occlusion is rarely appropriate (11), several case studies have reported a positive outcome in such patients (16-20). In the present case, the occlusive lesion appeared to progress during the time when hypertension had suddenly worsened. Angioplasty was performed four months after the onset of the deterioration of hypertension. In previous case reports as well, angioplasty achieved favorable blood pressure control in patients with advanced atrophic kidney who presented

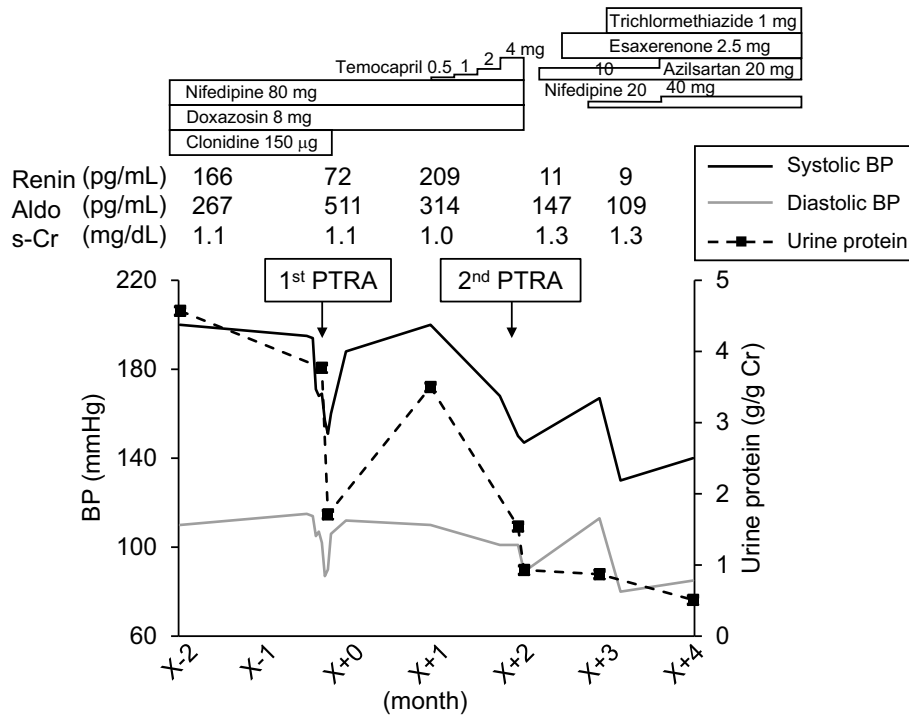


Figure 3. Clinical course. BP: blood pressure, PTRA: percutaneous transluminal renal angioplasty, Renin: active renin concentration, Aldo: aldosterone, s-Cr: serum creatinine

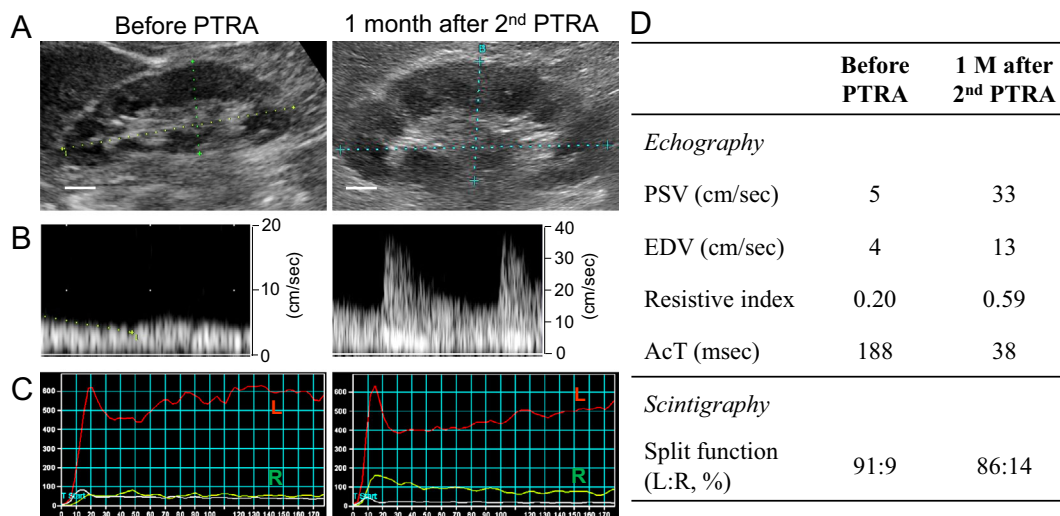


Figure 4. Kidney enlargement and improved intrarenal hemodynamics after the second PTRA procedure. A: The right kidney image on ultrasonography. Scale, 1 cm. B: The intrarenal flow velocity pattern in the interlobar region in the right kidney. C: ^{99m}Tc-DTPA scintigraphy during the vascular phase. L: left kidney, R: right kidney. D: Parameters on ultrasonography and scintigraphy before and after PTRA. Pressure systolic velocity (PSV), endo diastolic velocity (EDV), resistive index, and acceleration time (AcT) were measured in the interlobar region in the right kidney.

with a sudden deterioration of blood pressure control, and PTRA was performed within six months after the onset of the episode (18, 19). When the sudden onset of hypertension or deterioration of blood pressure control leads to the diagnosis of ARVD, the involvement of a stenotic/occlusive lesion is very likely the cause of the blood pressure elevation. Thus, in patients with such features, angioplasty is theorized to improve hypertension. In addition, long-standing ischemia

in the kidney would decrease the reversibility of renal parenchymal damage and reduce the beneficial effect of PTRA. Nevertheless, the role of these episodes in predicting the responsiveness of patients to angioplasty has not been evaluated in previous studies. The present case suggests that the timely resolution of the occlusive lesion by PTRA would exert a beneficial effect in patients who have had recent deterioration of blood pressure control (i.e. within the past six

months), including those with atrophic kidneys.

Chronic total occlusion is defined as complete stenosis for more than three months (21). For the treatment of chronic total occlusion of the renal artery, angioplasty may functionally salvage the kidney with a preserved sub-segmental flow from the collateral arteries (22). Even without a blood supply from the main renal artery, the presence of collateral circulation can prevent renal infarction in the affected kidney, although the insufficient perfusion would cause renal ischemia and inappropriate renin secretion, leading to refractory hypertension. In such situations, revascularization can allow recovery of the function of the “hibernating” kidney and normalize the hyper-renin secretion because the kidney is not yet “dead” (16, 23). Indeed, although the present case showed almost no residual function in the affected kidney before PTR, the function partially recovered, suggesting reversibility of the ischemic kidney that was only barely perfused by collateral supply. Previous reports showed that the recanalization of total renal artery occlusion in kidneys with collateral flow was feasible in the group of patients with refractory hypertension and high plasma rennin activity (22). Thus, when considering revascularization of the kidney with total renal artery occlusion, it is important to check for evidence of collateral flow to the kidney. To evaluate hibernating kidney, kidney function imaging has been performed (24). The present case indicates the beneficial use of diffusion-weighted MRI to detect kidney ischemia associated with renovascular disease, as we previously reported (13). However, further studies are warranted to more definitively elucidate the efficacy of diffusion-weighted MRI for evaluating the reversible hibernating kidney.

The present case showed in-stent re-occlusion after the first PTR procedure. The residual stenosis indicated by the translesional pressure gradient may have contributed to the thrombus formation, although aspirin was prescribed to prevent re-occlusion after the treatment. In addition, a previous study on coronary artery disease showed that angioplasty for chronic total occlusion carries a higher risk of in-stent restenosis after treatment than that for non-occlusive stenosis (25).

The patient showed a slight increase in the serum creatinine concentration after PTR, although it improved renal perfusion in the affected kidney. Regarding the pathophysiology of unilateral renal artery stenosis, while the post-stenotic kidney has reduced perfusion, the contralateral kidney undergoes hyperperfusion and glomerular hyperfiltration associated with renin-angiotensin activation (1). The persistence of hyperperfusion results in parenchymal injury in the contralateral kidney. PTR improves the renal reduced blood flow in the affected kidney and simultaneously normalizes compensatory hyperfiltration in the contralateral kidney (26). In addition, we administered a renin-angiotensin inhibitor in the present study, which also normalized the glomerular hyperfiltration (27). Thus, the increased creatinine concentration after the combination of PTR and medication with renin-angiotensin inhibitors was attributed

to the normalization of hyperfiltration in the contralateral kidney. Nevertheless, reducing the glomerular filtration via normalization of the activated renin-angiotensin system is thought to be beneficial for long-term renal protection (27).

In conclusion, PTR is an effective option for treating ARVD patients who have refractory hypertension, even with an atrophic kidney and chronic total renal artery occlusion, especially in cases that meet specific criteria, such as recent blood pressure deterioration and the presence of collateral perfusion to the affected kidney. Clinicians should carefully evaluate patients by combining information from the clinical data, imaging modalities, and their timeline before deciding whether or not revascularization would be of any benefit.

The patient provided his informed consent.

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

Yuri Sasaki and Eikan Mishima contributed equally to this work.

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