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Two Years Efficacy of Paclitaxel-Coated Balloon Dilation for In-Stent Renal Artery Restenosis Due to Takayasu Arteritis

Authors' Contribution:
Study Design A
Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
Literature Search F
Funds Collection G

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Conflict of interest: None declared

Patient: Female, 19
Final Diagnosis: Renovascular hypertension
Symptoms: Hypertension
Medication: Anti-hypertensive agents
Clinical Procedure: Percutaneous transluminal renal angioplasty
Specialty: Cardiology

Objective: Unusual or unexpected effect of treatment

Background: Endovascular procedures for renal artery stenosis induced by Takayasu arteritis include renal angioplasty (RA); sometimes renal artery bypass surgery may be required. Recently, there have been several reports about the use of drug-coated balloon (DCB) for renal artery stenosis in patients with Takayasu arteritis.

Case Report: A 19-year-old female was diagnosed with ulcerative colitis in 2012 and was on oral therapy. In 2015, she developed type V Takayasu arteritis, with 90% stenosis of the bilateral common carotid arteries, 90% stenosis of the right renal artery, and 75% stenosis of the infrarenal abdominal aorta. Her abdominal aortic stenosis reduced blood flow to the lower extremities and revascularization was required, so balloon dilatation of the abdominal aorta and renal angioplasty for right renal artery were performed at another hospital in March 2016. However, in-stent restenosis occurred 2 times, we performed renal angioplasty again with DCB. The patient has subsequently shown a stable course without recurrence of hypertension. At 2 years after renal angioplasty with the DCB, her serum renin and aldosterone levels were normal, there was no change of the right renal artery blood flow rate, and the blood pressure was normal.

Conclusions: This case suggests that dilation of in-stent restenosis with a DCB is an effective strategy for renal artery stenosis in patients with Takayasu arteritis. It seems desirable to consider expanding the indications for use of DCB to include renal artery stenosis.

MeSH Keywords: Hypertension, Renovascular • Renal Artery • Takayasu Arteritis

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Background

Takayasu arteritis is a large vasculitis that causes stenosis and obstruction in the aorta and its branches and causes clinical symptoms. Vasculitis causes fibrosis and sclerosis in all layers (intima, media and adventitia) of the artery featured by inflammatory cell infiltration, fibrous thickening of adventitia, smooth muscle cell loss of media, and elastic fiber destruction, intimal thickening. The cause of Takayasu arteritis is assumed to be involved in some form of autoimmune disease, but it has not been clarified yet, and its association with histocompatibility antigens (human leukocyte antigen-B52 and B67) has been clarified [1,2].

In patients with Takayasu arteritis, endovascular therapy is increasingly being selected as a treatment strategy for renal dysfunction or blood pressure abnormalities caused by renal artery stenosis. However, the outcomes of treating renal artery stenosis in this disease are poor, and the restenosis rate after renal angioplasty (RA) is reported to be a very high 78% [3].

Recently, there have been several reports about use of drug-coated balloon (DCB) for renal artery stenosis in patients with Takayasu arteritis [4,5]. However, to the best of our knowledge, use of a DCB for in-stent restenosis of the renal artery in a patient with Takayasu arteritis has not been reported before. We employed this strategy in the patient reported here and achieved good secondary patency for 2 years.

Case Report

A 19-year-old female was diagnosed with ulcerative colitis in 2012 and was on oral therapy. In 2015, she developed type V Takayasu arteritis, with 90% stenosis of the bilateral common carotid arteries, 90% stenosis of the right renal artery, and 75% stenosis of the infrarenal abdominal aorta. Drug treatment was started with prednisolone 30 mg per day for aortitis syndrome. The patient's medical condition was stable by continuing to gradually decrease prednisolone from 30 mg per day and continuing at a minimum of 2.5 mg per day. Her abdominal aortic stenosis reduced blood flow to the lower extremities and revascularization was required, so balloon dilatation of the abdominal aorta was performed at another hospital in March 2016. Although, the renogram showed normal pattern for both kidneys and there was no abnormality of blood pressure, or elevation of serum renin and aldosterone levels, right renal angioplasty by bare metal stent (Express Vascular 5.0/19 mm, Boston Scientific) was also performed because mild right renal artery blood flow decreased in renogram (Figure 1). The post operational course was favorable, with improvement of lower extremity blood flow. In July 2016, she developed elevation of blood pressure (144/76 mmHg) and serum renin and aldosterone levels, while renal artery ultrasound revealed an increase of the right renal artery blood flow rate (359 cm/s), leading to a diagnosis of renovascular hypertension. As renal arteriography demonstrated in-stent restenosis of the right renal artery, cutting balloon angioplasty (CBA) was performed with a cutting balloon (Flextome Cutting Balloon 3.0/15 mm, Boston Scientific, Starling 5.0/20 mm, Boston Scientific) (Figure 2). Postoperatively, there was transient improvement of the blood pressure, the serum renin and aldosterone levels, and the right renal artery blood flow rate (221 cm/s). However, her blood pressure increased again (156/88 mmHg) in October 2016, along with elevation of the serum renin and aldosterone levels and an increase of the renal artery blood flow rate (359 cm/s) on renal artery ultrasound. Repeat renal arteriography showed in-stent re-restenosis of the right renal artery. Because recurrence was noted only 3 months after RA, it seemed that repeating RA with a normal balloon would not be effective. Therefore, we decided to perform RA with a DCB. After predilatation with non-slip element (NSE) percutaneous transluminal angioplasty (PTA) balloon catheter 5.0/20 mm (Nipro), RA was done with 60 seconds inflation of the SeQuent Please

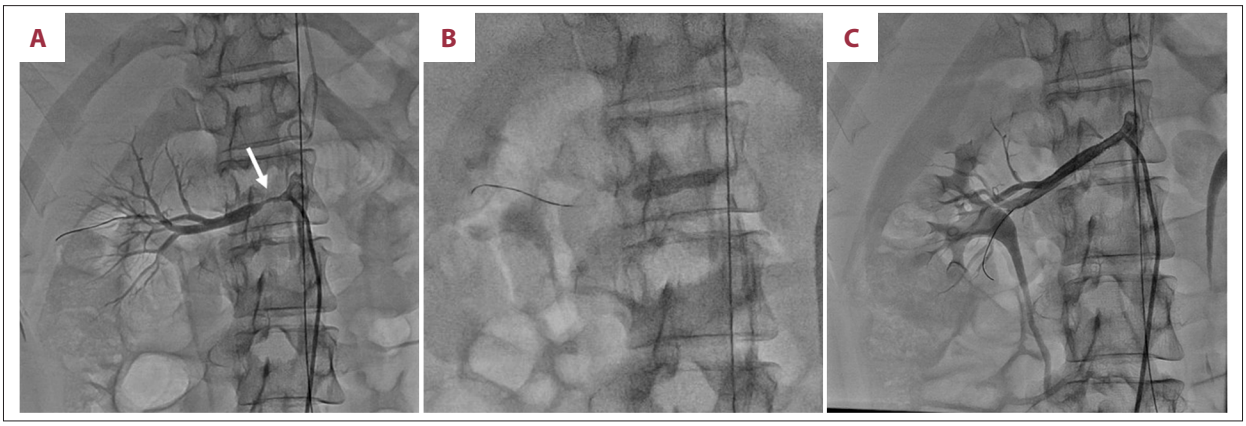

Figure 1. Renal angioplasty (RA) performed at another hospital. (**A**) Pretreatment right RA performed at another hospital. (**B**) Implantation of a bare metal stent in the right renal artery. (**C**) Right RA after stenting. → – stenosis.

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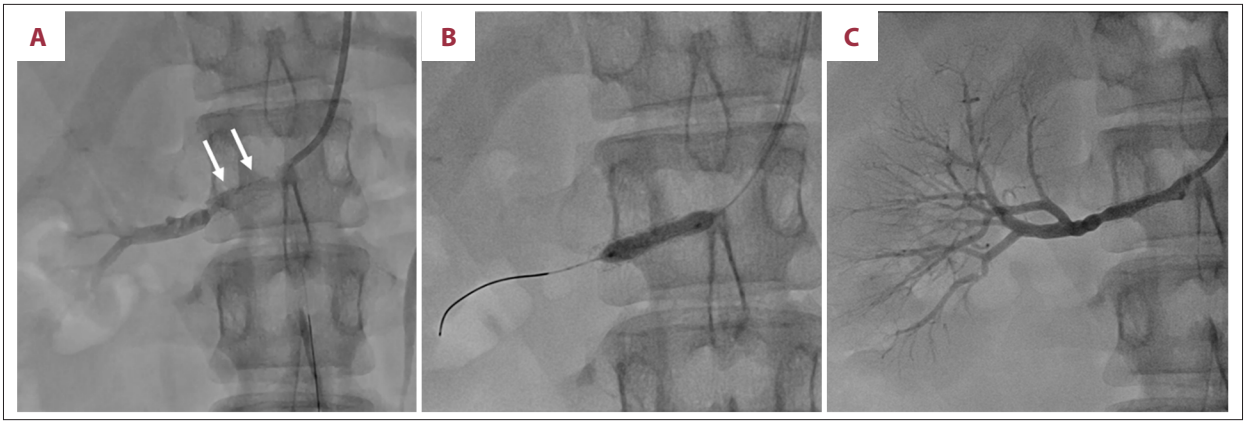

Figure 2. Renal angioplasty for first in-stent restenosis. (**A**) In-stent restenosis of the right renal artery at 4 months after stent implantation. (**B**) Cutting balloon angioplasty. (**C**) Arteriography after balloon dilatation of the right renal artery. → – stenosis.

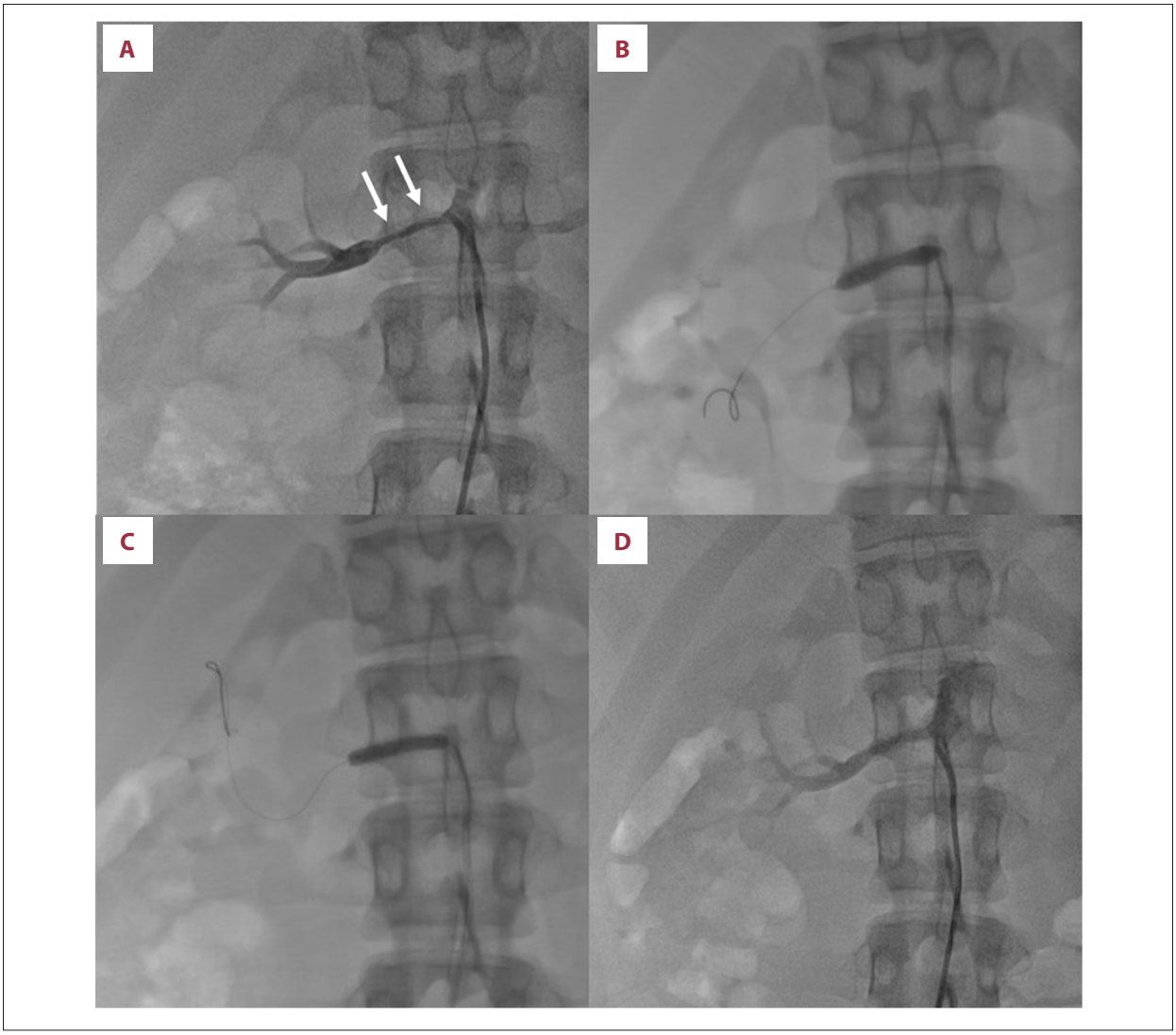

Figure 3. Renal angioplasty (RA) for second in-stent restenosis. (**A**) Right RA at the time of re-restenosis. (**B**) Cutting balloon angioplasty. (**C**) Dilatation with drug-coated balloon (DCB) for 60 seconds. (**D**) Final angiogram after dilatation with the DCB. → – stenosis.

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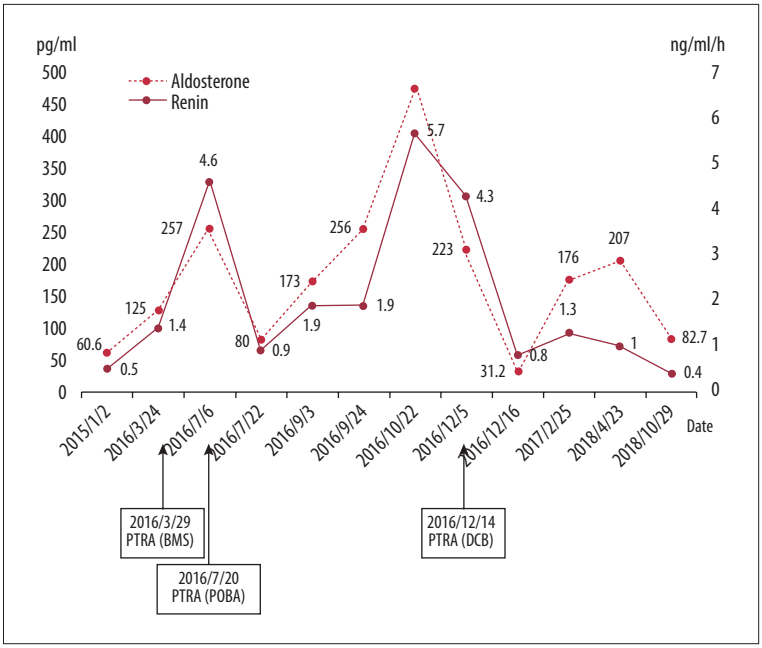

Figure 4. Trends in serum renin and aldosterone. Levels of renin and aldosterone in relation to the endovascular procedures. Renin and aldosterone levels decreased immediately after each endovascular procedure. However, the levels increased again soon after renal angioplasty with a bare metal stent and cutting balloon angioplasty. Following treatment with a drug-coated balloon, renin and aldosterone levels have remained stable for about 2 years.

4.0/20 mm (Nipro) (Figure 3). Immediately after the procedure, there was improvement of the blood pressure (99/53 mmHg), normalization of renin and aldosterone, and improvement of the right renal artery blood flow rate (199 cm/s). The patient has subsequently shown a stable course without recurrence of hypertension. In October 2018, at 2 years after RA with the DCB, her serum renin and aldosterone levels were normal (Figure 4), there was no change of the right renal artery blood flow rate (212 cm/s), and the blood pressure was normal (100/65 mmHg).

During the observation period from 2015 to 2018, serum C reactive protein was stable at around 0.5 mg/dL, and erythrocyte sedimentation rate at around 15 mm. The disease activity level seemed to remain low during the year 2015–2018. The patient continued to receive aspirin 100 mg per day. We used modality for stenosis grading was intravascular ultrasound (IVUS) and angiography.

Discussion

We encountered a patient who underwent RA several times for renal artery stenosis caused by Takayasu arteritis, but always rapidly developed restenosis, in whom use of a DCB led to good 2 years secondary patency.

The outcome of RA for vascular stenosis associated with Takayasu arteritis is generally poor, with restenosis rates in the range from 15–20% after 1 to 3 years [6,7]. For renal artery stenosis, a very high restenosis rate of 78% has been reported after RA [1].

Our patient received implantation of a bare metal stent for right renal artery stenosis at another hospital, but she developed restenosis after only 4 months. We performed repeat RA, but re-restenosis occurred within 3 months and the outcome of endovascular therapy was extremely poor. We considered surgical treatment, but the patient was a young woman and she wished to avoid surgery if possible. Thus, we needed to try another endovascular procedure. However, it was easy to predict that restenosis would occur rapidly if we performed RA again with a normal balloon. In principle, endovascular procedures should not be carried out in patients with ongoing inflammation [8], and since implanting a new stent in the renal artery was likely to affect future management, we considered that re-stenting should be avoided.

In Takayasu arteritis, vasculitis affects all layers of the arterial wall (intima, media, and adventitia), starting from the adventitia. Invasion of inflammatory cells into the adventitia is associated with fibrous thickening, loss of smooth muscle cells in the media, destruction of elastic fibers, and intimal thickening/fibrosis, so the pathology is fundamentally different from atherosclerosis [9]. Stent recoil is highly likely to occur in patients with Takayasu arteritis due to inflammation of the media and adventitia plus fibrous thickening. In addition, progressive intimal thickening makes these patients very susceptible to restenosis.

Development of in-stent restenosis is a serious event in patients with coronary artery disease. In recent years, use of DCB for coronary artery in-stent restenosis has been reported to yield favorable outcomes [10], and long-term patency was reportedly achieved with a DCB in renal artery stenosis as

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well [11]. Accordingly, although it was an off-label use, we employed a DCB in the present patient and achieved stable renal artery secondary patency for 2 years. As far as we can determine, there have been no other reports of similar cases in which a DCB was used to treat Takayasu arteritis-induced renal artery stenosis.

There is no report that paclitaxel is effective in renal angioplasty for Takayasu arteritis, and the mechanisms responsible are poorly understood.

In this case report, since IVUS findings showed stent recoil at the initial in-stent restenosis (ISR), adventitial inflammation by Takayasu arteritis might be one of the mechanisms of the ISR. However, in-stent neointimal hyperplasia was also observed by IVUS at the initial ISR and the second ISR. Although the influence of Takayasu arteritis on the neointimal hyperplasia after stent implantation was not well known, Paclitaxel may have affected to reduce the ISR preventing the initial process of neointimal hyperplasia.

NSE PTA balloon is an angioplasty catheter with 3 longitudinal elements attached directly proximal and distal to the balloon, which produce 3 endovascular surgical incisions during balloon dilation. So that using the NSE PTA balloon for predilatation created “cuts” in the intima that subsequently allowed paclitaxel coating the DCB to penetrate the vessel wall.

Therefore, we assume that effectiveness of the DCB in our patient was attributable to suppression of vascular inflammation and cellular proliferation through a mechanism similar to that for paclitaxel-eluting stents [12]. From the aforementioned, it was suggested that DCB used in renal angioplasty had effectiveness for in-stent renal artery restenosis which was due to Takayasu arteritis.

Since systemic anti-inflammatory therapy with steroids or immunosuppressants is effective against inflammatory diseases such as Takayasu arteritis, it seems reasonable to use a DCB for local intravascular anti-inflammatory treatment.

Conclusions

This case suggests that dilation of in-stent restenosis with a DCB is an effective strategy for renal artery stenosis in patients with Takayasu arteritis. It seems desirable to consider expanding the indications for use of DCB to include renal artery stenosis.

Conflict of interest

None.

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