Successful treatment of focal renal artery fibromuscular dysplasia by balloon dilatation demonstrated via fractional flow reserve

Authors: Xuhe Gong,[A] Jixuan Liu,[B] Daokuo Yao[C] and Rongchong Huang[C]

ABSTRACT

We present a rare case of fibromuscular dysplasia (FMD) manifesting in the mid segment of right renal artery, which led to the development of refractory hypertension. The patient received balloon angioplasty to a severe lesion on the middle of right renal artery and subsequently had normalisation of blood pressures. Fractional flow reserve (FFR) detection of the renal artery before and after balloon dilatation was 0.71 and 0.98, respectively. The patient showed renal artery stenosis (RAS) with distal tumour-like dilatation, and multiple tortuosity and stenosis in carotid artery and coronary artery. At follow-up 2 months later, her blood pressures had normalised.

KEYWORDS: fibromuscular dysplasia, renal artery stenosis, FFR-guided renal artery balloon dilatation

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Introduction

Fibromuscular dysplasia (FMD) is a rare vascular disorder that can have significant clinical significance. Its aetiology remains unclear.[1] The clinical manifestations of FMD depend on the affected arterial vessels, which can cause vascular stenosis, aneurysm, dissection, occlusion or arterial tortuosity.[2] Multiple arterial vessel involvement is one of the characteristics of FMD, and the renal arteries are most commonly affected.[3] FMD has been found to present as stubborn hypertension or even renal artery infarction. We present a case of stubborn hypertension resulting from FMD that ultimately improved through FFR guided renal artery balloon dilation.

Case presentation

A 36-year-old woman was hospitalised in July 2023 for hypertension. She had no history of chronic kidney disease or autoimmune disease. The patient had begun to experience hypertension in late pregnancy 4 years previously, with a maximum blood pressure of 180/120 mmhg. It was accompanied by symptoms of dizziness, headache and palpitations. She took various antihypertensive drugs include beta-receptor blockers, calcium channel blockers and angiotensin converting enzyme inhibitors (ACEI); however, her blood pressure remained difficult to control.

Renal artery ultrasound showed severe stenosis in the middle segment of the right renal artery, with a peak systolic velocity (PSV) of 255 cm/s, while the PSV of the left renal artery was only 63 cm/s. Further renal artery enhancement CT angiogram (CTA) (Fig 1) confirmed severe stenosis in the middle segment of the right renal artery with local cystic dilatation at the distal end of the stenosis. The narrow segment was about 6 mm in length, with the narrowest part of the lumen almost occluded, and the cystic dilated part was the widest by 0.8 cm. Racers (^{99m}Tc-DTPA 8 mCi) were used for renal blood flow imaging, and the results showed that the concentration of the tracer in the renal parenchyma reached its peak within 2 minutes, with the peak value in the right kidney being lower than that in the left kidney, indicating slightly poor blood flow perfusion in the right kidney.

We conducted imaging examinations on the coronary artery, upper and lower limb arteries, subclavian artery and head and neck arteries simultaneously. CTA of the head/neck indicated uneven thickness in the starting segment of the left internal carotid artery (Fig 2). Coronary angiography showed tortuous diffuse lesion in multiple coronary arteries (Fig 3). There were no abnormal structural features in the subclavian artery and upper/lower limb arteries.

Angiography revealed severe stenosis, focal middle segment vessel disease with greater than 95% stenosis, and dilatation at the distal end of the stenosis in right renal artery, highly suggestive of FMD (Fig 4a). The middle segment lesion was treated with balloon angioplasty (Fig 4b, c). The intervention had good angiographic results, with $<30\%$ residual stenosis and no complications. We adopted an intervention therapy strategy guided by FFR during the surgery, gradually increasing the diameter of the dilated balloon, with a maximum balloon diameter of 4.0 $\times$ 9 mm selected. The FFR of renal artery before and after balloon dilatation was 0.71 and 0.98, respectively. The preoperative resting pressure gradient was 35 mmhg, while

Authors: [A]deputy chief physician, Beijing Friendship Hospital, Capital Medical University, Beijing, China; [B]attending physician, Beijing Friendship Hospital, Capital Medical University, Beijing, China; [C]medical professor, Beijing Friendship Hospital, Capital Medical University, Beijing, China

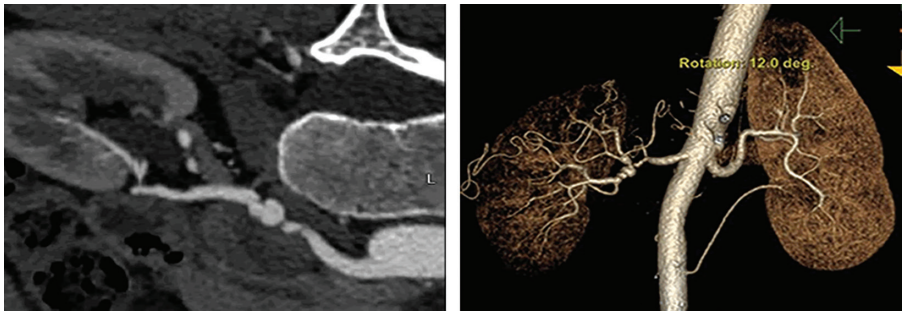

Fig 1. Images of renal artery CT angiogram. Severe stenosis in the middle segment of the right renal artery with local cystic dilatation at the distal end of the stenosis.

the postoperative pressure gradient was only 3mmhg. Balloon dilation significantly reduced the pressure gradient (Fig 5).

The patient was discharged 4 days after surgery and stopped taking all antihypertensive drugs. At follow-up 2 months later, her blood pressure remained at a normal level.

Management

This report describes a young female patient with RAS caused by FMD. FMD is an idiopathic, segmental, non-atherosclerotic and non-inflammatory disease of the musculature of arterial walls, leading to stenosis of small and medium-sized arteries. FMD can occur in any artery in the human body, such as the renal, extracranial carotid or vertebral arteries.[4] Renal artery involvement is the most common and can cause hypertension; the next most common is involvement of the carotid artery, which can lead to symptoms like dizziness, transient ischemic attack or stroke. Coronary artery involvement may cause acute coronary syndrome and myocardial ischemia. Multiple vascular involvement is one of the characteristics of FMD, this case presented with renal artery, internal carotid artery, and coronary artery involvement. However, the patient did not experience symptoms related to heart and cerebrovascular diseases.

Fig 2. CT angiogram of the head/neck. Arrows indicate uneven thickness in the starting segment of the left internal carotid artery.

It is estimated to affect approximately 3–4% of the population, with a higher prevalence among women than men, with a ratio of 9:1.[1] The aetiology of FMD is unknown, although various hormonal and mechanical factors have been suggested, including endogenous/exogenous oestrogen exposure (oral contraceptives or hormonal replacement therapy) and smoking, as well as an underlying genetic predisposition.[5] Currently, many studies are focusing on the relationship between genes and the pathogenesis of FMD. Unfortunately, genetic screening studies targeting these genes (mainly FBN1, ACTA2, SMAD3, TGFBR1/2 and COL3A1) have only identified mutations of uncertain significance in few FMD patients.[6] In terms of signal pathways, elevated plasma levels of TGF-β1 and TGF-β2 were detected in a cohort of 47 (43 women) FMD patients, suggesting that the pathophysiology may also be associated with abnormal regulation of TGF-beta signaling.[7] However, a recent study found no enrichment for mutations in genes in the TGF-β pathway in FMD patients.[8] Overall, the genetic research on FMD is still unclear.

The optimal imaging strategy for diagnosis of FMD lesions has still to be defined. Due to the low diagnostic spatial resolution of non-invasive imaging modes (CTA or MRA), it is difficult to detect slight changes in blood vessels, some FMD cases are overlooked, catheter-based angiography remains the gold standard for diagnosis. The diagnosis of renal artery FMD is now based mostly on angiographic appearance, and the binary angiography classification of renal artery FMD lesions as multifocal or focal is increasingly recognised.[9] Multifocal FMD was characterised by the classical 'string of beads' appearance, yet this case is a focal lesion. In a cohort of mostly young Chinese patients, renovascular hypertension associated with FMD was frequently as focal type, with a lower hypertension cure rate.[10]

In general, it is not difficult to differentiate FMD from atherosclerosis. Atherosclerotic RAS is more common at the age of ≥55 years, and is associated with multiple cardiovascular risk factors. RAS is more common at the proximal end, which

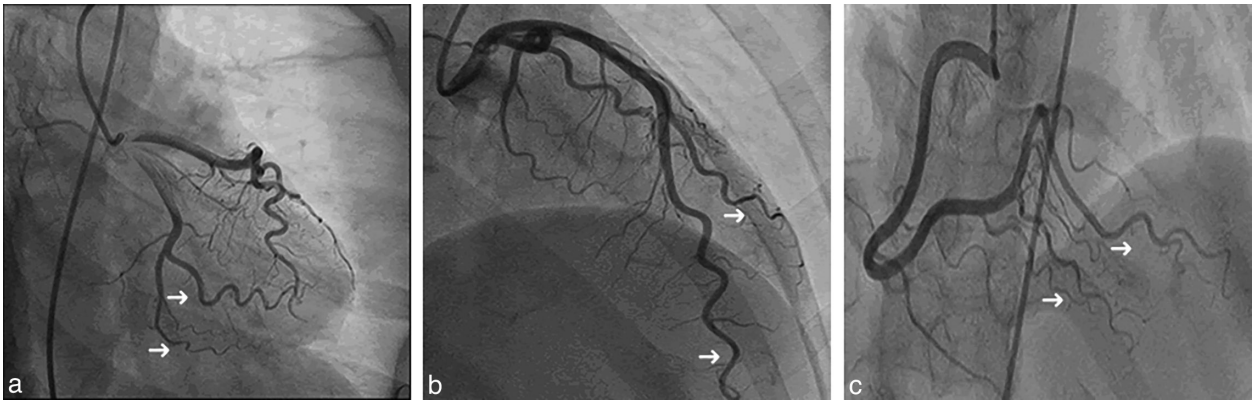

Fig 3. Coronary artery catheterisation findings. (a) Arrows indicate tortuous diffuse lesion in the left circumflex artery. (b)The image shows tortuous diffuse lesion in distal LAD and diagonal branch. (c) Arrows indicate tortuous diffuse lesion in posterior descending branch and left ventricular posterior branch of RCA.

can be combined with atherosclerotic changes in other parts. In some cases, it may be difficult to distinguish between FMD and arteritis. Unless an acute infarction occurs in FMD, it is generally not accompanied by anaemia, thrombocytopenia or elevated inflammatory factors in the acute phase. However, arteritis is an autoimmune inflammatory disease with elevated inflammatory factors. Generally, arteritis involving the renal artery is more common in young women (under 40 years old) with fewer cardiovascular risk factors, and RAS is more common in the opening.

The aetiology of renal artery FMD (RA–FMD) is unknown, so targeted treatment is not possible, whether active intervention is needed for asymptomatic RA–FMD remains uncertain. Several management options for FMD include medical therapy solely, revascularisation and surgery. To date, there have been no randomised trials comparing revascularisation with medical therapy alone in FMD patients. Clinical decision making is nowadays largely guided by the evidence available in atherosclerotic disease. Usually, as recommended by the European consensus,[5] revascularisation of FMD-related lesions is considered only in cases of symptomatic FMD (eg hypertension for RA–FMD, signs of organ ischemia).

Although stenting has been widely used in the treatment of atherosclerotic RAS, it is not recommended for RA–FMD patients

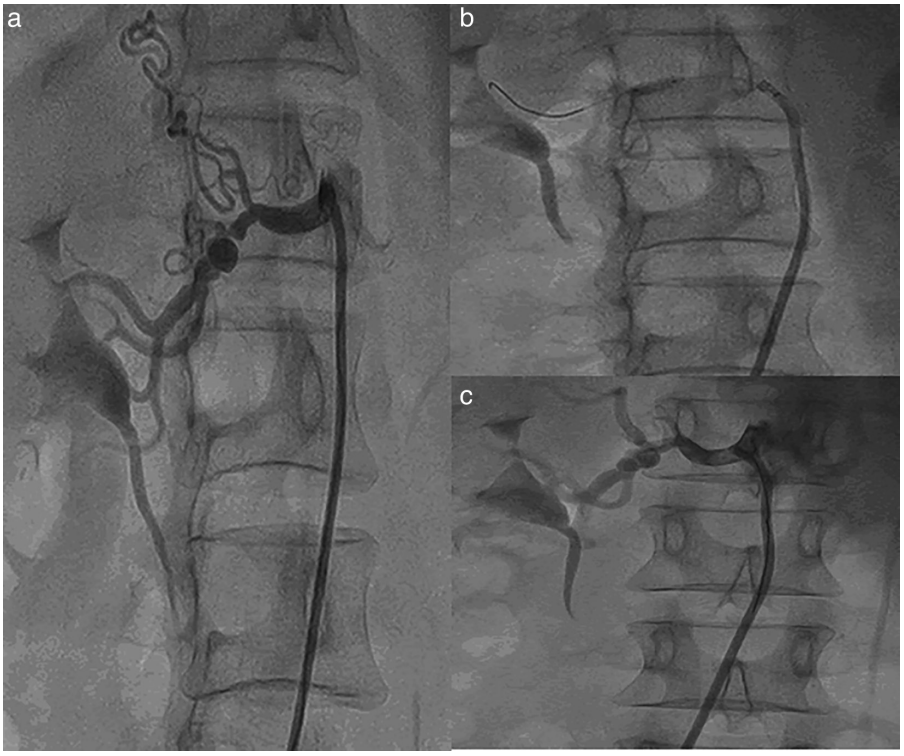

Fig 4. Interventional treatment of renal artery stenosis. (a) Fibromuscular dysplasia lesion with a classic focal appearance shows areas of severe stenosis and post-stenotic dilations in the middle segment of right renal artery. (b) Balloon is dilated over an area of stenosis in the right renal artery. (c) Post-dilation image shows excellent angiographic results.

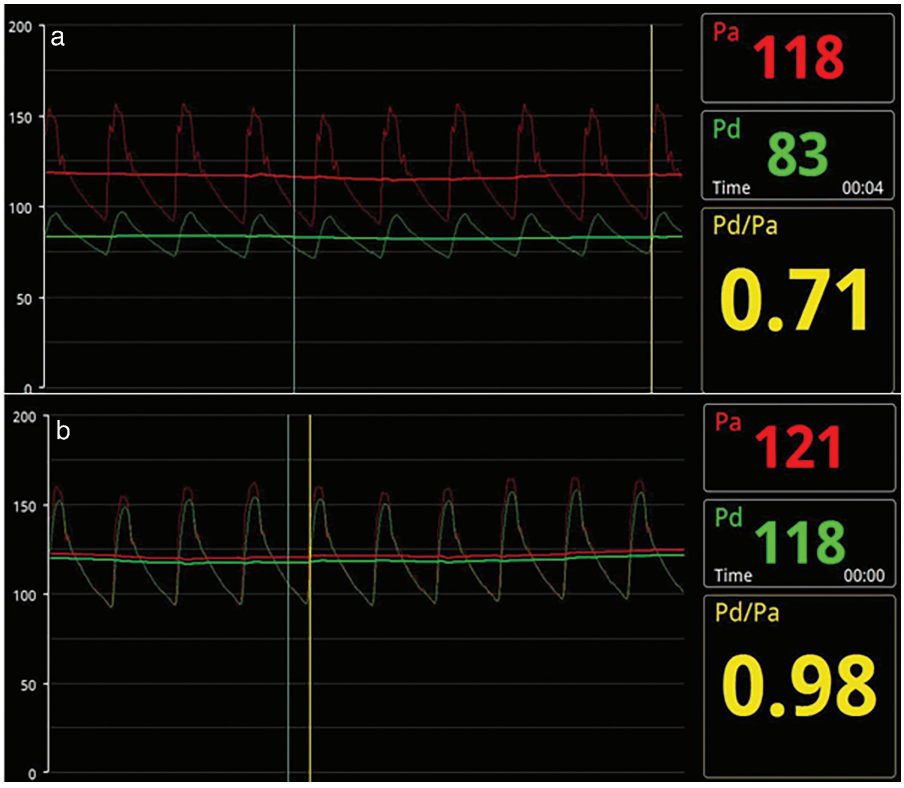

Fig 5. Fractional flow reserve of the renal artery (a) before (b) after balloon dilatation.

at present. For such patients, stent implantation is only used as a remedial measure when balloon dilation is ineffective and renal artery dissection occurs during the operation. The complications of balloon dilation in the treatment of RA–FMD are about 10%, most of which are related to the access vessels, while renal artery perforation, dissection or renal infarction are rare.

Arteriography can only provide imaging evaluation of the degree of stenosis and cannot determine the impact of stenosis on distal blood flow (functional evaluation). FFR is an indicator used to calculate blood flow through pressure measurement. It has become a recognised indicator for functional evaluation of coronary artery stenosis and is gradually being applied to peripheral blood vessels. However, it is currently unclear how to determine the critical value of the lesion. Can a resting pressure gradient greater than 20 mmHg can be used as a basis for judging stenosis? Should systolic blood pressure, mean blood pressure or diastolic blood pressure be used? Should congestion medication be used, and if so what type/dosage of medication should be used? Can resting Pd/Pa (distal pressure/proximal pressure) <0.9 be considered as a critical value? Bernard de Bruyne *et al*[11] published a study in 2006 that included 15 patients with renal artery stenosis exceeding 50%, exploring the relationship between pressure gradient and serum renin concentration. In this study, no congestion drugs were used. The research results show that renal artery stenosis with Pd/Pa >0.9 has no hemodynamic significance, and RAS with Pd/Pa <0.9 should be considered as having significant hemodynamic significance. Therefore, the threshold of 0.9 can be used as a judgment standard for interventional treatment of renal artery stenosis. Of course, this threshold needs to be validated by large sample studies. The FFR of renal artery before balloon dilatation was 0.71 in this case, the postoperative FFR was 0.98, indicating a significant improvement. We believe that FFR guided balloon dilation, after significant improvement in FFR, stops further expansion of larger balloons and greater pressure, and also reduces the possibility of intervention treatment risk. More precise treatment and improved patient prognosis can be achieved through this functional assessment. ■

Summary

RA–FMD often occurs in young women without cardiovascular risk factors, and renal artery angiography is the 'gold standard' for diagnosis. FFR-guided renal artery balloon dilatation provides a good treatment strategy for such patients.

Ethics

The study was approved by the ethics committee of Beijing Friendship Hospital (approval number: 2023-P2-271-01).

Funding

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Address for correspondence: Rongchong Huang, Department of Cardiology, Cardiovascular Center, Beijing Friendship Hospital, Capital Medical University, Beijing 100050, China. Email: rchuang@ccmu.edu.cn