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## Case Report

# New onset hypertension-rare intimal variant fibromuscular dysplasia

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### KEYWORDS

Intimal variant  
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**Summary** Fibromuscular dysplasia (FMD) involving the renal arteries commonly presents as hypertension secondary to renal artery stenosis. Atypical patterns involving intima are rare and contribute to less than 10% cases of FMD. We present a relatively uncommon case of new onset hypertension in a 30-year-old woman resulting from intimal variant FMD involving the left renal artery. Renal duplex ultrasonography and angiography showed stenosis of the left renal artery consistent with intimal variant FMD. Percutaneous transluminal angioplasty of the stenotic lesion was successfully performed. Following angioplasty, her blood pressure was normalized. Renovascular hypertension secondary to FMD involving intimal layer is rare and requires a high index of clinical suspicion. Renal duplex ultrasonography is the recommended initial test of screening for renal artery stenosis in appropriate patients. The standard selective renal angiography, intravascular ultrasound, along with or without hemodynamic assessment should be utilized when renovascular intervention is contemplated. Percutaneous transluminal angioplasty is the mainstay of treatment for those who meet the criteria of intervention.

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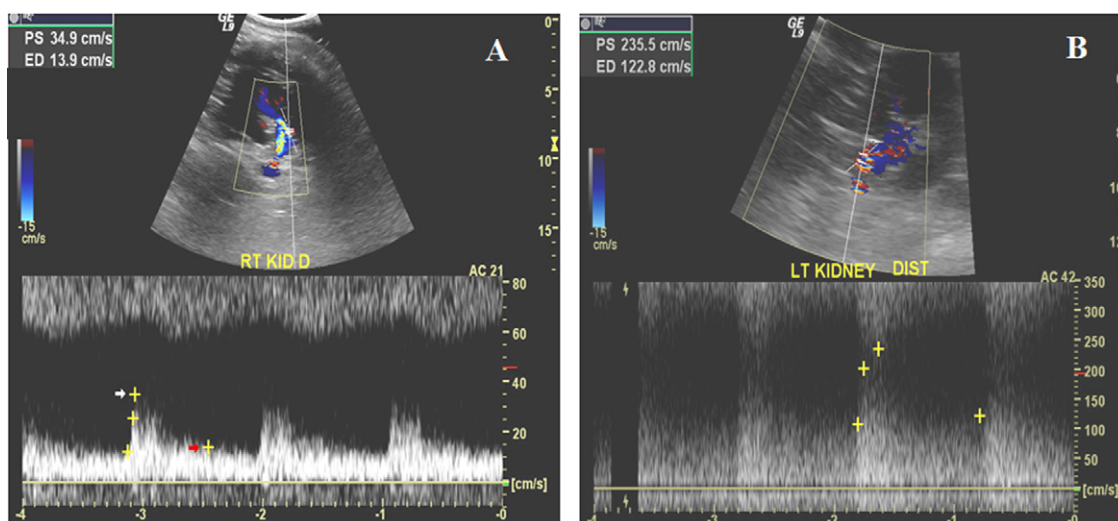
## Introduction

First described by Leadbetter and Burklan in 1938, fibromuscular dysplasia (FMD) is now defined as a multi-

focal, nonatherosclerotic, noninflammatory arterial disease involving the medium- to large-sized arteries. The etiology of FMD is still unclear. While it mostly affects the renal and cephalic arteries, it has been noted in almost every vascular bed [1]. Depending on the arterial segment involvement, the degree of stenosis and the type of FMD, the clinical presentation can range from asymptomatic to multisystem disease. Almost 90% of FMD involves the medial layer of the artery and less than 10% involves the intimal layer. In this report, we present a rare type of FMD involving the intimal layer of the renal artery. We have shown the angiographic

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**Figure 1** Showing color Doppler ultrasound and spectral wave forms of the distal portions of the right renal artery (A) and the left renal artery (B). Peak systolic velocity in distal segments of the right renal artery is 34.9 cm/s and in the left renal artery is 235.5 cm/s suggesting stenosis in the left renal artery.

appearance of this rare type of FMD (intimal variant) and its successful management with percutaneous transluminal angioplasty (PTA).

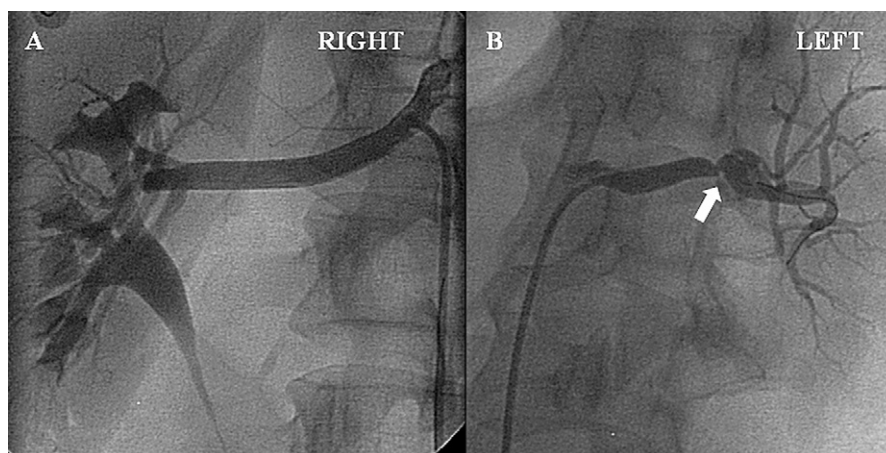
## Case report

We present a 30-year-old Caucasian woman without any significant past medical history who has had multiple admissions to an outlying facility for uncontrollable hypertension. On a routine physical examination during her initial admission, she was found to have a very high blood pressure of 240/144 mmHg. At that time she had an elevated aldosterone level with low potassium and normal renin levels. She was treated with labetalol and eventually transitioned to an angiotensin-converting enzyme inhibitor (ACEI) and a diuretic. She was discharged home on these medications. After four months she was readmitted with chest pain, dizziness, and a blood pressure of 248/148 mmHg. Physical examination, electrocardiogram, and laboratory values were normal. Electrocardiogram and echocardiogram revealed left ventricular hypertrophy. She was discharged home with a blood pressure of 120/60 mmHg on three anti-hypertensive medications, including a beta-blocker (metoprolol), a diuretic (aldactone), and an ACEI (lisinopril). Following the discharge on medical therapy, she began having recurrent episodes of upper abdominal discomfort. A computed tomography (CT) scan of the abdomen showed hypoperfusion of the lateral half of the left kidney, suggestive of renal infarction or ischemia. Given the history and CT scan findings, embolic phenomenon was suspected. In light of the patient's age and sex, FMD was considered as one of the possibilities for her resistant hypertension. Renal duplex ultrasonography (RDU) was abnormal, revealing elevated velocity (236 cm/s) in the distal segment of the left renal artery (Fig. 1) along with post stenotic turbulence, renal/aortic ratio (RAR – calculated by dividing the highest peak systolic velocity in the renal artery by the normal aortic velocity) of 2.4 and resistive index (RI

– ratio of peak systolic and end diastolic velocity derived from the Doppler spectrum) of 0.56. There was 1.8 cm discrimination in the size of right and left kidney. Angiographic evaluation was planned. Left femoral artery access was obtained using a modified Seldinger technique. A 7F sheath was placed in the common femoral artery. A pig tail catheter was advanced to the level of L1 and abdominal angiogram was performed. Angiogram revealed a possible stenosis of the left distal renal artery. Following this a 7F guiding catheter was placed in the left renal artery ostium. Selective angiography revealed a 6 mm renal artery with the presence of greater than 70% stenosis of the left distal renal artery. The angiographic appearance of the lesion suggested intimal variant FMD as described by Slovut and Olin [1] (Fig. 2). There was also a moderate stenosis (40–50%) in a sub-branch of the left renal artery. A SpartaCore (0.014") wire was advanced across the stenosis into the distal bed. A 5 mm diameter balloon was advanced to the lesion and two inflations at 8 atm pressure for 60 s each were performed. The balloon was removed and angiography showed an excellent angiographic result with less than 10% residual stenosis (Fig. 3). Within 24 h after the angioplasty, her blood pressure was normalized in response to the intervention and her medications were titrated off. On further follow-up of two years, her blood pressure remained well-controlled on reduced doses of only one antihypertensive medication.

## Discussion

FMD can involve almost every arterial bed but most often affects the renal and internal carotid arteries. This case of new-onset hypertension in an apparently healthy young woman illustrates an unusual and atypical variant of FMD involving the intimal layer. FMD tends to affect the population between 15 and 50 years of age [1]. The actual incidence of FMD is unknown as significant numbers of patients are asymptomatic. Renal FMD



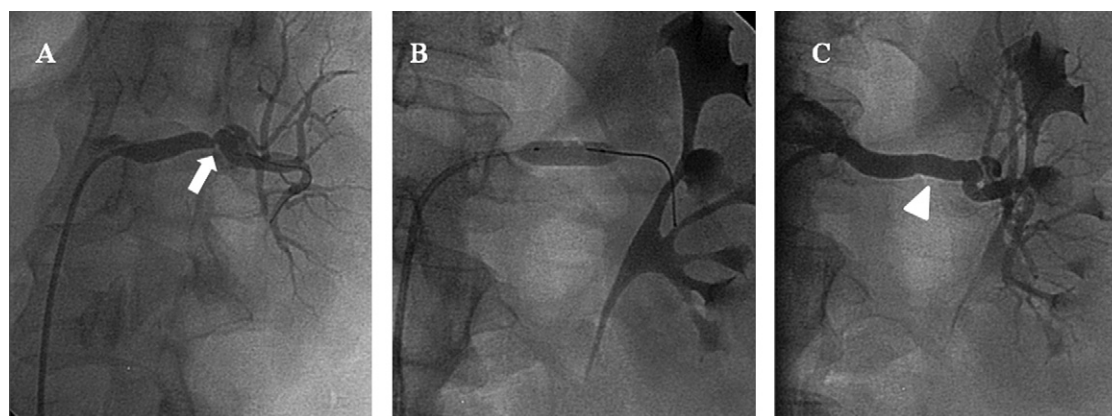
**Figure 2** Renal angiography: (A) the right renal artery and (B) the left renal artery with tight distal stenosis (white arrow).

tends to affect women with 3:1 or 4:1 predominance over men. Renovascular hypertension is defined as hypertension caused by renal artery stenosis and accounts for less than 5% of all cases of hypertension in the general population.

The two main etiologies of renal artery stenosis are atherosclerosis and FMD. Renal artery aneurysms, dissection, thromboemboli, Takayasu's arteritis are few other rare causes of renal artery stenosis [2]. Atherosclerosis accounts for 70–90% of cases of renal artery stenosis, especially in older patients with cardiovascular risk factors, and involves the proximal portion of the main renal artery [3]. FMD involving renal arteries commonly presents as hypertension which contributes to less than 10% of renovascular hypertension. In contrast, FMD occurs in middle or distal arterial segments in younger patients with few or no cardiovascular risk factors. FMD may involve any layer of the visceral artery. It is histologically classified as intimal, medial, or adventitial variant. It is most common in the medial layer (~90%), rare in intimal layer (<10%), and very rare in adventitial layer (<1%) [4]. Angiographic classification of FMD includes: (a) multiple stenoses and 'string-of-beads' appearance which is classic for medial fibroplasias and (b) the focal stenosis, which is more suggestive of intimal fibroplasias.

Intimal fibroplasia on angiography can appear as focal stenosis due to circumferential or eccentric deposition of collagen in the intima with no lipid or inflammatory component, or as a long smooth narrowing similar to that seen in large artery vasculitides such as giant cell arteritis or Takayasu arteritis. The very rare adventitial hyperplasia (<1% of FMD), with limited angiographic information, has been observed as sharply located tubular areas of stenosis. A high index of suspicion and careful, complete angiographic visualization of the renal vasculature is critical to identify the type of FMD.

Renal angiography remains the most accurate method for the diagnosis of renal artery stenosis. However, noninvasive diagnostic techniques such as RDU, magnetic resonance angiography (MRA), and computed tomographic angiography (CTA) have been proved to be accurate in the assessment of renal artery stenosis and provide valuable alternatives to diagnostic angiography [5–7]. RDU is the recommended initial screening modality to establish the diagnosis of renal artery stenosis [2,8]. It provides both the anatomical and the functional assessment of the renal arteries. It can accurately detect the elevated blood flow velocities based on the site of stenosis especially proximal- and mid-vessel stenosis. It has a sensitivity of 84–98% and a specificity of 62–99%



**Figure 3** Percutaneous transluminal angioplasty: (A) the angiography of the left renal artery revealed a tight distal stenosis (white arrow). (B) The balloon dilatation of the left renal artery. (C) The post-stenotic dilatation (white arrow head).

for detecting renal artery stenosis [9–13]. In the literature for significant renal artery stenosis that is >60% stenosis was considered when peak systolic velocity >180–200 cm/s, RAR >3.5, acceleration time >0.07s, acceleration index <300 cm/s, and difference in renal or segmental RI >0.15. Peak systolic velocity is the best non-invasive RDU parameter. A meta-analysis of 88 studies showed that peak systolic velocity was more accurate than renal-aortic ratio and acceleration index with a sensitivity of 85% and specificity of 92% [14]. In another study, peak systolic velocity was better correlated with translesional pressure gradient for hemodynamically significant renal artery stenosis compared to RAR and percent diameter stenosis [15]. Utilization of captopril, color coding can increase the reliability of the RDU [16,17].

In addition, Doppler ultrasound is an excellent means by which to assess restenosis after percutaneous or surgical intervention [18,19]. Usually the follow-up is clinical and/or radiological. If the patient develops recurrence of hypertension or unexplained increase in the serum creatinine we can evaluate the renal artery stenosis with reimaging of the renal arteries. RDU has few limitations such as technique-related (e.g. operator and machine dependent), patient-related (e.g. obesity and bowel gas), and anatomy-related (inability to detect distal, branch, and accessory renal arteries stenosis) limitations. In selective cases where RDU is inconclusive we can screen with CTA (normal renal function patients) or MRA to detect renal artery stenosis.

In our patient, left renal artery angiography showed 70% mid-vessel stenosis which was consistent with intimal variant FMD as described by Slovut and Olin [1]. Despite improvements in noninvasive imaging methods, catheter-based angiography remains the most widely used method for diagnosing FMD [1]. Intimal FMD can present as focal webs or long tubular lesions which often make the angiographic assessment of the disease severity difficult. Utilization of RDU, intravascular ultrasound (IVUS) and/or hemodynamic assessment by pressure wire pull-back gradient measurements during and after angioplasty is helpful to assess the clinically significant lesions and has become a standard practice in many centers [15,20,21]. In hemodynamically significant lesions assessment of peak systolic velocity with RDU can be an effective alternative to translesional pressure gradient measurement using 0.014in. pressure wire [15]. Sometimes visual inspection of the treated stenosis is inadequate and requires pressure guide wire assessment (mean gradient of <5 mmHg across the treated segment), IVUS, or post procedure RDU (RAR <3.5) [21,22] to know the effectiveness of the intervention. Assessment of translesional pressure gradient especially hyperemic systolic gradient ( $\geq 21$  mmHg) was proved to be more accurate than IVUS or angiographic assessment in predicting hypertension improvement after stenting of significant RAS [2,23].

Before the advent of PTA, surgical revascularization was the primary therapeutic modality for patients with refractory hypertension [3]. Compared to surgery, PTA is more cost effective, less invasive, can be performed on an outpatient basis, and is associated with lower morbidity. Moreover, if it is unsuccessful, the surgical option is still feasible. PTA with bailout stent placement if necessary has emerged as the mainstay of treatment in patients with FMD who meet the criteria of intervention [2,24,25]. Though there are no

clear-cut guidelines for intervention, the following criteria may be reasonable to perform renal artery revascularization: hemodynamically significant renal artery stenosis and recent onset of hypertension in which the goal is to cure the hypertension, drug-refractory hypertension (three or more drugs), accelerated hypertension, malignant hypertension, hypertension with an unexplained unilateral small kidney, intolerance to antihypertensive medications, progressive renal insufficiency/failure, and, finally, episodes of flash pulmonary edema [2]. Clinical response in patients with renovascular hypertension consists of lowering the blood pressure with a reduction in the number of medications required to control or to decrease serum creatinine level of 30  $\mu$ mol/l after renal artery angioplasty or surgery. Following PTA, the blood pressure in our patient normalized within a couple of hours and is well controlled on a reduced dose of one antihypertensive medication (rather than higher doses of 3 medications required before the procedure). Post-intervention normalization or drop in (>10 mmHg) blood pressure varies in duration. There are no accurate data available in the literature in this regard. In our practice we have noticed drop in blood pressure occurs within a couple of hours to two days post-intervention.

There are no prospective studies on the effect of percutaneous transluminal renal angioplasty (PTRA) on intimal or nonmedial type of FMD. A recent single center retrospective study on non medial, unifocal stenosis showed the restenosis rate of 20% and long-term clinical success rate of 70% which is much less compared to the medial lesions 70–98% [26]. Follow up after PTRA can be done with RDU within 1, 6, and 12 months to detect restenosis. It can be repeated thereafter annually or if there is worsening hypertension [27]. In our case we did not proceed with annual RDU as our patient did extremely well with normal levels of blood pressure and serum creatinine levels.

## Conclusion

Reported cases of renovascular hypertension, secondary to FMD, involving intimal layer are rare and require a high index of clinical suspicion. Multimodality approach with RDU, selective renal angiography, IVUS along with or without hemodynamic assessment should be utilized when renovascular intervention is suspected. PTA is the mainstay of treatment for those who meet the criteria of intervention.

## Disclosures

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