

Challenges in diagnosing and treating a patient with renal artery fibromuscular dysplasia: case report

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Background

We present a patient with history of sinus venous thrombosis and hypertension during the last year. Her blood pressure was not controlled despite drugs, diet, and exercise. She denied symptoms. She does not smoke nor drink alcohol. Her body mass index was 20 kg/m², NYHA Class I/IV.

Case summary

A 40-year-old Latin-American female patient, concerned because despite taking verapamil 160 mg/day, losartan 100 mg/day, and hydrochlorothiazide 25 mg/day her diastolic blood pressure was over 100 mmHg. Routine serum and urine lab tests and a transthoracic echocardiogram were done and were normal. The treatment was increased over the next consultations but without control of her blood pressure. She developed resistant hypertension, and she was taking four antihypertensive drugs and two diuretics. A first renal artery Doppler was normal. Because of a high clinical suspicion a renal angio-CT was performed showing bilateral fibromuscular dysplasia. The patient underwent a renal artery angioplasty with balloon with excellent results and better control of her blood pressure after the procedure. Over the next month, her doctors were able to decrease her treatment to two drugs at intermediate doses. Currently, she is doing well and asymptomatic.

Discussion

Renal artery fibromuscular dysplasia (FMD) could be a challenging disease to be diagnosed. Patients with this condition may suffer from symptomatic and resistant hypertension. Many patients do not have abnormalities on their physical exam or in the routine lab tests. Treatment includes renal artery angioplasty if patient is symptomatic and blood pressure is resistant.

Keywords

Hypertension • Renal fibromuscular dysplasia • Renal artery stenosis • Renal artery angioplasty • Case report

Learning points

- Renal fibromuscular dysplasia (FMD) is an uncommon disease. High clinical suspicion is necessary for making this diagnosis.
- Secondary hypertension and kidney failure due to renal FMD are potentially curable diseases when treated opportunistically. Those patients who are not cured through initial treatment may benefit from invasive treatment to improve blood pressure control and renal function.
- The most common and initial imaging method for diagnosing renal FMD is duplex ultrasound (US). Duplex US can show a false negative depending on the operator's experience, patient's obesity, or gas interposition. If duplex US is negative and clinical suspicion is still high, then an angio-CT or angio-MR should be done.
- Invasive treatment for symptomatic renal FMD includes renal angioplasty or surgical revascularization.

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Introduction

Fibromuscular dysplasia (FMD) is an idiopathic, non-atheromatous, non-inflammatory disease affecting the muscular layer of arteries. FMD produces stenosis in small and medium-sized vessels.¹ Women are more commonly affected than men, especially those between 30 and 50 years of age.²

The prevalence of symptomatic renal FMD is 0.4%. Arterial hypertension is the most frequent presentation of FMD with many cases being classified as resistant.²

Fibromuscular dysplasia results in distortion of arteries. Affected arteries look like rosary beads with segmented stenosis. Up to 60% of renal FMD may be bilateral.³

Image aids for diagnosing renal FMD are: duplex ultrasound, angio-CT, angio-RM, and arteriography.

Invasive options for treating symptomatic renal FMD includes balloon angioplasty, stenting, or surgical bypass.

Timeline

regular and rhythmic, and her point of maximal impulse (PMI) was non-displaced. No murmurs nor bruits were found on her anterior abdomen or on her lumbar regions. Her body mass index was measured at 20 kg/m².

Her prior treatment plan included verapamil 160 mg po qd, losartan 100 mg po qd, hydrochlorothiazide 25 mg po qd, aspirin 100 mg po qd, and clopidogrel 75 mg po qd. Despite treatment, the patient was found with diastolic blood pressures >100 mmHg. In that visit, verapamil was increased to 240 mg po qd.

Her laboratory results included: creatinine 0.55 mg/dL (NV 0.4–1.1 mg/dL), BUN 11.4 mg/dL (NV 3–20 mg/dL), K 4.27 mEq/L (NV 3.5–5.1 mEq/L), glucose 86 mg/dL (NV 70–99 mg/dL), total cholesterol 191 mg/dL (NV < 200 mg/dL), HDL 65 mg/dL (NV 50–60 mg/dL), triglycerides 72 mg/dL (NV < 100 mg/dL), and uric acid 2 mg/dL (NV 1.9–7.5 mg/dL). She had a normal electrocardiogram and thoracic echocardiogram.

Based on the results of the October 2015 visit, the treatment plan was changed to: verapamil/trandolapril 240/4 mg po qd, hydrochlorothiazide 25 mg po qd, and spironolactone 25 mg po qd. In addition, ambulatory blood pressure monitoring (ABPM) was ordered as a precautionary measure (Figure 1).

The patient was followed up between October 2015 and June 2017.

2015 August	First contact with a cardiovascular group. History of hypertension and a previous episode of sinus venous thrombosis. Treatment with verapamil, losartan, hydrochlorothiazide, aspirin, and clopidogrel.
2015 October	Uncontrolled blood pressure. Change of antihypertensive treatment to: verapamil + trandolapril, hydrochlorothiazide, and spironolactone. Order of 24 h ambulatory blood pressure monitoring (ABPM).
2015 December	Good control of blood pressure. Spironolactone suspended due to patient intolerance.
2016 March	Normal Doppler of renal arteries.
2016 July	Episodes of moderate to severe headache that was resolved with common analgesics. Non-controlled blood pressure. Start of prazosin and eplerenone in addition to the previous treatment.
2016 September	Non-controlled blood pressure despite anti-hypertensive treatment and non-pharmacological strategies (diet, physical activity).
2017 May	Angio-CT of renal arteries shows bilateral fibromuscular dysplasia of renal arteries.
2017 June	Abnormal Doppler of renal arteries. Stenosis of 60% in right renal artery. Prolonged acceleration times. Intra-renal blood flow with spectrum 'tardus et parvus'. Left renal artery checked without abnormalities.
2017 June	Patient underwent bilateral renal arteriography and balloon angioplasty. Procedure was successful.
2017 June	After discharge, patient displayed better blood pressure control. Patient had regular follow-up with Cardiology and treatment was diminished to losartan + amlodipine. Other anti-hypertensive drugs were suspended.

Case report

In October 2015, a 40-year-old female patient with a history of sinus venous thrombosis and hypertension sought medical consultation. Her blood pressure was resistant despite treatment. She had a good NYHA Class I/IV and exercised frequently. She was adherent to dietary approach to stop hypertension (DASH) and regularly attended medical visits.

A review of systems was negative. She did not have toxic habits. On her physical exam she had normal respiratory sounds, her cardiac exam was normal without murmurs or rubs, the heart sounds were

She was seen again in December of 2015; the ABPM showed good blood pressure control, but the patient complained of intolerance to spironolactone, which was subsequently stopped (Figure 1).

A renal artery Doppler was completed in March of 2016 with all results being normal.

In July 2016, the patient complained of frontal headaches that were resolved with conventional analgesics. Her systolic blood pressure was 170 mmHg, so her treatment plan was supplemented with prazosin 3 mg po qd and eplerenone 25 mg po qd.

Despite the pharmacological changes, her blood pressure remained greater than 160/100 mmHg.

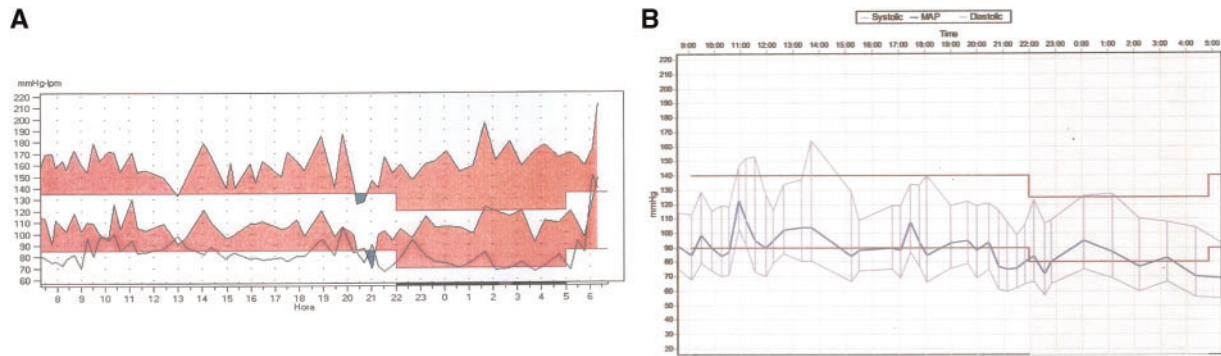


Figure 1 Ambulatory monitoring of blood pressure (AMBP). Before (A) and after (B) balloon angioplasty of renal arteries affected by fibromuscular dysplasia.

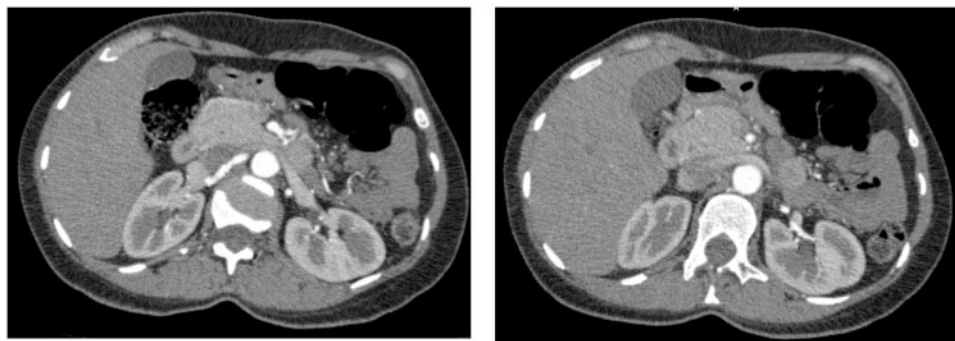


Figure 2 Angio-CT. Fibromuscular dysplasia on both renal main arteries, more evident on the right side.

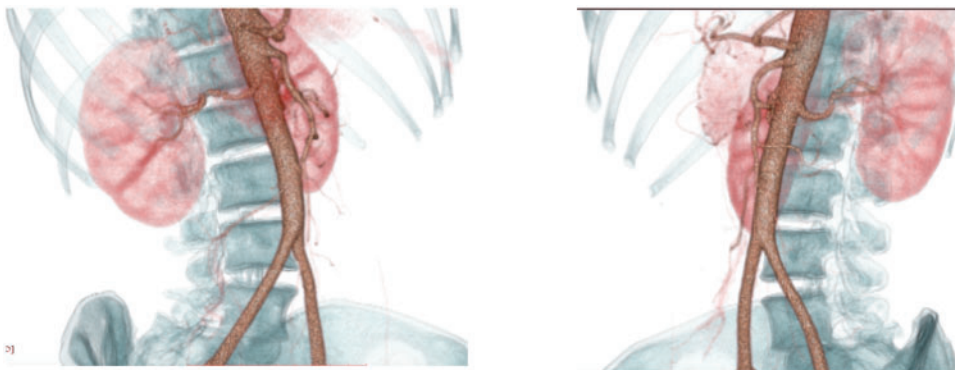


Figure 3 Angio-CT 3D reconstruction. Fibromuscular dysplasia on both renal main arteries.

In May 2017, an angio-CT of the renal arteries was performed (Figures 2 and 3), and it showed bilateral renal fibromuscular dysplasia. The right renal artery was 100% abnormal, and the left renal artery was affected on its distal third.

A subsequent Doppler of renal arteries was completed in June 2017 (Figure 4) and showed abnormal findings. The right renal/aortic index was 3.9; a high suspicion of FMD exists when the renal/aortic index is greater than 3.5. The peak-systolic velocity at the

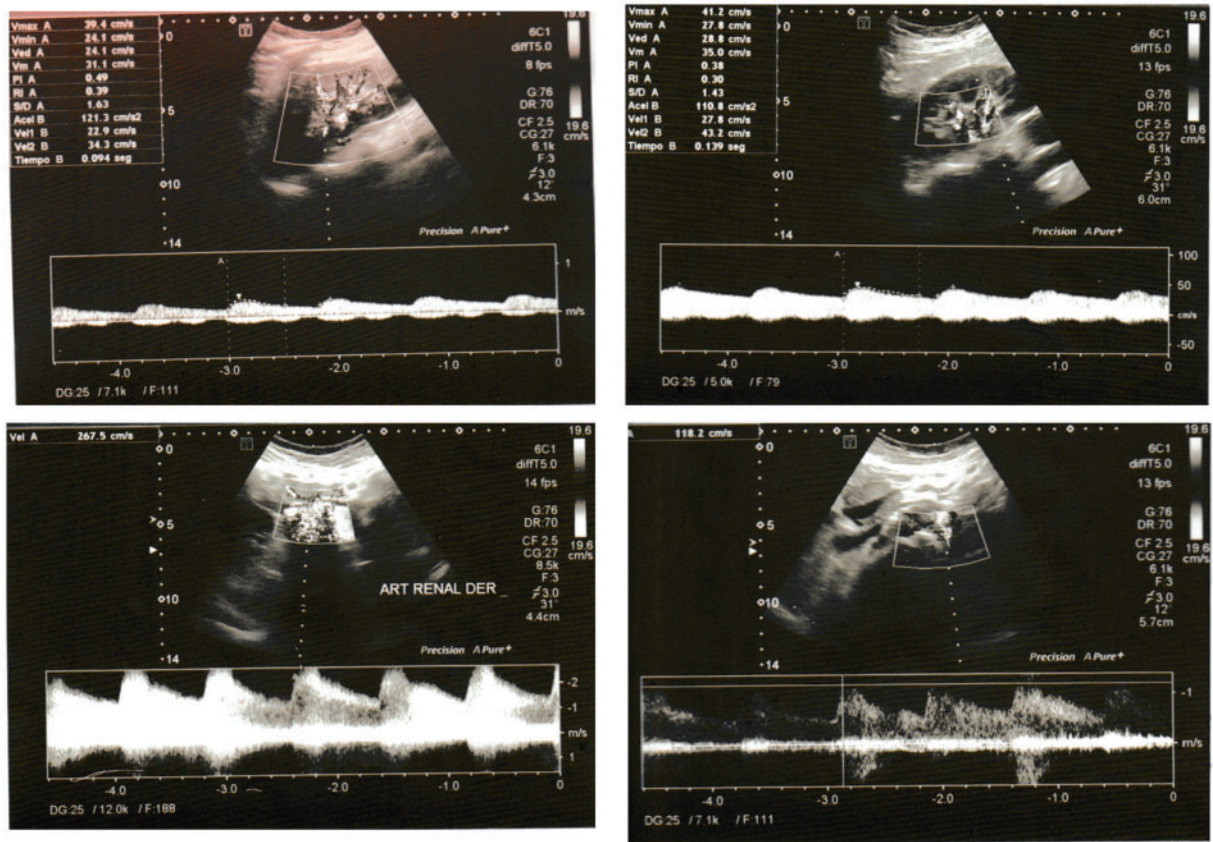


Figure 4 Renal Doppler ultrasound. (A) Right side, lower picture shows peak systolic velocity at right main renal artery of 267.5 cm/s. (B) Left side, lower picture shows peak systolic velocity at left main renal artery of 118.2 cm/s.

right renal artery was measured at 267 cm/s with a stenosis of 60%. The left renal artery was normal; a possible explanation for this normal finding could be the distal FMD at the left renal artery found in the angio-CT. The intra-renal blood flow had a spectrum type tardus et parvus, prolonged acceleration times, and normal resistance indexes.

The patient underwent renal arteriography (Figure 5) and balloon angioplasty in June 2017. The most critical stenosis had a 5 mm diameter on the left side and 6 mm on the right side. 5×40 mm and 6×20 mm balloons were used on the left side, inflated to 8 atmospheres for two and a half minutes. The right side (more severely affected by FMD) was treated with a 6×20 mm balloon starting on the distal part of the vessel, inflated to 8 atmospheres for two and a half minutes. The medium and proximal thirds of the vessel were treated with a 6×20 mm balloon, inflated to 10 atmospheres.

There was a good angiographic result after the procedure, the stenosis improved significantly and there were no spasms or dissections observed. There were no complications. The patient remained in the clinic for a short period to monitor for possible complications and variations in her blood pressure.

After discharge, the patient has displayed good control of blood pressure; she is under treatment with only losartan/amlodipine 50/

2.5 mg po qd. She has been asymptomatic and in good overall clinical condition.

Discussion

Patients with critical renal artery stenosis may have abdominal murmurs/bruits produced by an accelerated blood circulation in renal arteries. Prevalence of abdominal bruits in patients with angiographically proven renal stenosis varies between 78%⁴ and 87%.⁵ The sensitivity and specificity of systolic and diastolic abdominal bruits is 39% and 99%, respectively.⁶ Epigastric or flank bruits have a sensitivity of 63% and a specificity of 90%.⁷ Some healthy patients and patients without renovascular disease may have abdominal bruits—these bruits being non-threatening or caused by unrelated pathological causes (e.g. hepatic carcinoma, arterio-venous fistula, celiac trunk stenosis, aortic aneurysm, etc.). In cases of young, asymptomatic, and normotensive patients with an abdominal bruit, no further studies are warranted. Given the low sensitivity of abdominal bruits in patients with renovascular disease, the sheer absence of a bruit does not rule out the chance of having renovascular hypertension.

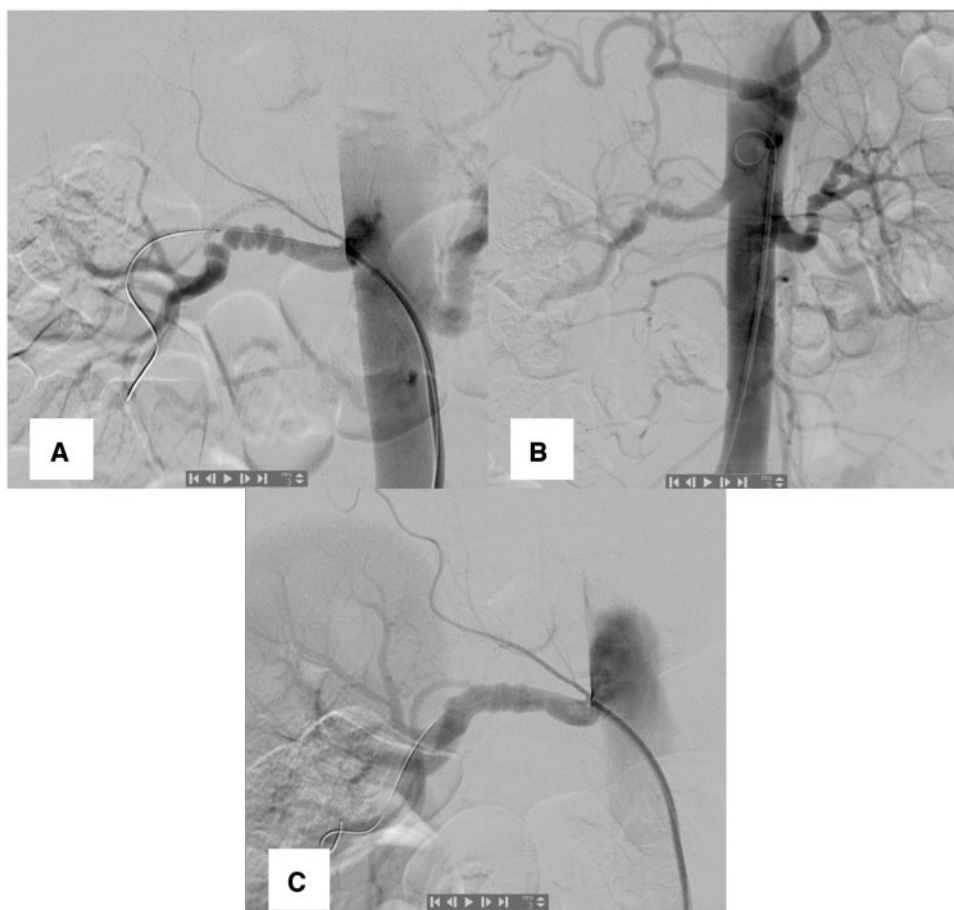


Figure 5 Arteriography showing fibromuscular dysplasia changes in right (A) and left (B) renal arteries. (C) Right renal artery after balloon angioplasty.

Duplex ultrasonography (DUS) is an inexpensive, non-invasive tool for the diagnosis of renal artery stenosis. This diagnostic method has no adverse effects. Duplex ultrasonography is usually the first imaging method to be employed when approaching a patient with suspicion of renal FMD. The main criteria evaluated are: peak systolic velocity (PSV), renal aortic ratio (RAR), resistance index (RI), and acceleration time (AT).⁸ Peak systolic velocity greater than 180 cm/s is the most accurate US parameter for diagnosing renal artery stenosis.

Haemodynamic effects of lumen occlusion, such as changes in either translesional pressure or flow, are usually difficult to detect until lumen occlusion reaches a critical level (i.e. in the vicinity of 70–80% lumen occlusion).⁹

Duplex ultrasonography may be negative in up to 10–20% of cases because of the operator's inexperience, obesity, or gas interposition. Duplex ultrasonography has a sensitivity of 82.9–85% and a specificity of 70–92%.^{10,11}

Computed tomography angiography has a sensitivity of 94% and a specificity of 93%. It is a relatively expensive method (compared to DUS) and carries the nephrotoxic and allergic risks associated with IV contrast exposure and ionizing radiation exposure.¹²

Magnetic resonance angiography has a sensitivity and specificity of 90% and 94%, respectively. It is also a relatively expensive technique

(compared to DUS). Some implanted devices, furthermore, are not compatible with the resonator (pacemakers) and patients with chronic kidney disease may develop nephrogenic systemic sclerosis if exposed to gadolinium.¹²

The first approach when managing patients with symptomatic FMD is treating blood pressure. Diet, exercise, antihypertensive drugs, control of smoking/alcohol intake must be prescribed. Antiplatelet therapy and statins may be useful.¹³ Renal artery revascularization may cure hypertension or improve blood pressure control. Hypertension cure is achieved in 36% of cases after angioplasty and in 54% after surgery. The probability of being cured varies inversely with age. Periprocedural complications occur in 12% of cases with angioplasty and in 17% of cases after surgery. Major complications occur in 6% of cases with angioplasty and in 15% of cases after surgery.¹⁴

When comparing surgical revascularization in patients with renal FMD vs renal atherosclerotic stenosis, long-term blood pressure control (up to 17 years) was observed in 93% and in 71% of patients, respectively. Improvement or stabilization of renal function was observed in 92% of renal FMD and in 68% in those with atherosclerosis.¹⁵

The limitations of the presented case were the difficulties while reaching the correct diagnosis. The first renal artery DUS did not

show abnormalities when the patient probably did have the FMD changes and renal artery stenosis by that time. Fortunately the clinical suspicion by her treating physician assured finding a diagnosis despite the normal results of DUS. Once a diagnosis was reached the pharmacological treatment was increased and then a renal artery angioplasty was performed as suggested in the guidelines. Further investigation is warranted to understand additional examples of this condition. Guidelines based on meta-analysis and systematic reviews are needed to improve the approach to these patients.

Supplementary material

Supplementary material is available at *European Heart Journal - Case Reports* online.

Slide sets: A fully edited slide set detailing this case and suitable for local presentation is available online as [Supplementary data](#).

Consent: The author/s confirm that written consent for submission and publication of this case report including image(s) and associated text has been obtained from the patient in line with COPE guidance.

Conflict of interest: none declared.

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