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SECONDARY HYPERTENSION

Fibromuscular Dysplasia in Clinical Practice: A Case-based Review

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ABSTRACT

Fibromuscular dysplasia (FMD) is an idiopathic, nonatherosclerotic, noninflammatory disease with segmental involvement of the blood vessels that cause abnormal growth within the wall of an artery in any region of body. Fibromuscular dysplasia has been found in nearly every arterial bed in the body. However, the most common arteries affected are the renal and carotid arteries. It is a heterogeneous group of vascular lesions characterized by an idiopathic, noninflammatory, and nonatherosclerotic angiopathy of small and medium-sized arteries. The prevalence of FMD is estimated between 4 and 6% in the renal arteries and between 0.3 and 3% in the cervicoencephalic arteries.

Imaging and radiologists play an important role in diagnosing the abnormality with knowledge of patient complaints with respect to fibromuscular disease. The most common imaging finding is dilatations, beaded appearance of vessels, and aneurysms. The less common findings are tortuous vessels, ectasia, kinking, loops, and dissection. The radiologist should be aware of these so that FMD can be diagnosed in young females with hypertension not responding well to treatment or familial hypertension.

Its signs and symptoms help the radiologist to diagnose early. The objective of this review is therefore to increase radiologists' and clinicians' awareness of FMD's epidemiology, pathophysiology, clinical presentation, classical and minor/rare radiological findings, and possible complications in other arteries in the abdomen.

Epidemiology: The prevalence is unknown. It is most common in young women with a female to male ratio of 3:1, and is typically diagnosed between the ages of 30 and 50 years. It is less than 2% of all hypertensions.

Keywords: Computed tomography angiography, Digital subtraction angiography, Fibromuscular dysplasia, Hypertension, Magnetic resonance angiography, Percutaneous transluminal angioplasty, Renal arteries, Renal artery stenosis.

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CASE REPORT

Mrs. KVR, a 37-year-old woman, was seen in the blood pressure clinic of Apollo Hospital, Hyderabad, because of new-onset uncontrolled hypertension. Her family physician noted that the patient's blood pressure level was consistently above 200/120 mm Hg despite four antihypertensive drugs on optimal doses. Her blood urea nitrogen/creatinine/sodium/potassium levels, chest X-ray, and electrocardiogram were all normal.

Based on her history of new-onset progressive hypertension, workup was done for secondary causes. Computed tomography angiography (CTA) of renal arteries revealed bilateral significant fibromuscular dysplasia (FMD; Figs 1 and 2). As the blood pressure levels remained above 200/120 on medical treatment, she underwent bilateral renal artery angioplasty (with stent placement on one side); following successful renal angioplasty, her blood pressure started decreasing and became normal requiring discontinuation of antihypertensive drug therapy. At 3- to 4-month follow-up, her blood pressure was 132/84 mm Hg on no antihypertensive drugs. The clinical and blood pressure course indicated that her hypertension was cured. This case is a classical illustration of secondary hypertension due to FMD of renal arteries and prompt resolution of hypertension after successful angioplasty.

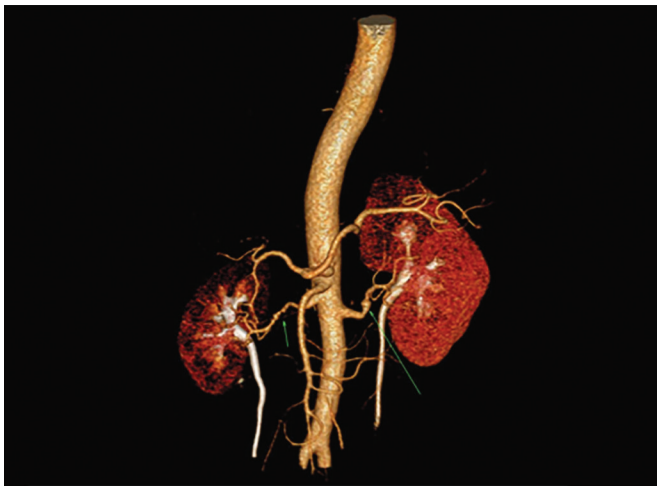

Fig. 1: Reconstructed CTA view bilateral FMD

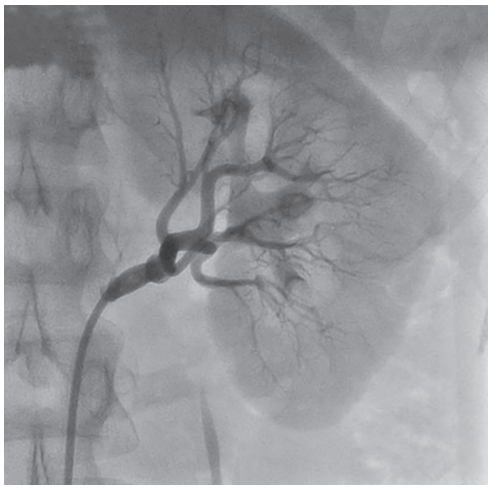

Fig. 2: Left renal artery after successful angioplasty of FMD lesions

INTRODUCTION

Fibromuscular dysplasia is a systemic vascular disease which predominantly affects small- and medium-sized arteries. Although this arterial anomaly can affect any artery, its hemodynamic and clinical relevance is limited to renal arteries. The FMD affecting the renal arteries is an important cause of "secondary" hypertension. There is ample evidence to suggest that mechanical correction of renal FMD improves or cures hypertension. The FMD is a nonatherosclerotic entity that occurs predominantly in females and in the younger individuals. Perhaps, renal artery involvement by FMD is more common than other vascular beds (visceral, craniocervical, or in the limbs). The exact prevalence of FMD is probably not known since every patient with hypertension is not subjected to workup and since arterial biopsies are rarely obtained. The most frequent manifestation of FMD is systemic hypertension due to renal artery involvement. The FMD is more common in women between the ages of 30 and 50 years. Women are 10 times more likely to have FMD than men.

Pathological Lesions in FMD

Typical FMD is idiopathic in nature, segmental, noninflammatory, and nonatherosclerotic, resulting in stenosis (of small- and medium-sized arteries). Three varieties of FMD have been described based on which layer of the artery is the culprit—intimal, medial, and perimedial. By far, the most common pathological type is medial FMD. Angiographically, medial FMD has the "string-of-beads" appearance. It has a classic image on angiography. Alternating regions of "thinned" media and "thickened" fibromuscular collagen are responsible for the "string-of-beads" appearance of medial FMD, usually involving the distal two-thirds of the main renal artery. While FMD is a nonatherosclerotic disease, it can coexist with atherosclerosis.

Intimal FMD occurs in less than 10% of all the lesions. Eccentric deposition of collagen and other fibrinous materials on the intima is based on the anatomy of the disease. At times, the angiographic features may mimic those of endarteritis. Intimal FMD may be highly focal and concentric, which may be mistaken for an atherosclerotic lesion.

Perimedial fibrodysplasia occurs in about 15% of the individuals afflicted with FMD. This pathological entity may cause severe stenosis.

Adventitical fibrodysplasia is very rare (less than 1%). Dense collagen deposition occurs in the adventia. The other layers of the artery are intact.

Pathogenesis

The precise etiology of FMD is unknown. Genetics may play a role due to high incidence of FMD in certain families. Although the exact genetic mutation or transmission is unknown, genetics may play a role in the inheritance of FMD. Hormonal factors are likely important as FMD occurs overwhelmingly among women. There may be a genetic susceptibility to FMD. Since FMD is not a common entity, large cohort studies are not available. The phenotypes in FMD are variable and may be confined to some subsets but not proven. Family-based studies with complementary genetic approaches are needed to identify genetic pathways for FMD. There are reports that cigarette smoking may be a risk factor for FMD.

Renal FMD and Hypertension

Atherosclerotic lesions of the renal artery are more common than FMD. However, correction of FMD improves or cures hypertension unlike atherosclerotic renal artery stenosis (RAS). Therefore, in the workup for secondary forms of hypertension, FMD should be considered especially in the young and in females. Any degree of hypertension in young women warrants consideration of FMD of renal arteries. It is a potentially reversible disorder and hence, should not be missed in the clinical setting. Usually, FMD (especially, the medial fibrodysplasia) is a stable condition and does not cause ischemic nephropathy. However, it can cause severe, progressive, and resistant hypertension. Thus, FMD of renal arteries should not be overlooked in suspected patients. The FMD typifies classical "renovascular" hypertension, which is mediated by the activation of renin–angiotensin system. Ischemia to the kidney caused by significant RAS stimulates renin release culminating in the generation of angiotensin-II, a powerful vasoconstrictor.

Clinical Suspicion

In young patients (especially, female) with any degree or duration of confirmed hypertension, workup for FMD-RAS is indicated.

- Age < 35 years, especially women
- Confirmed hypertension
- Accidental discovery of unilateral small kidney
- Abdominal bruit
- Known FMD in any vascular bed

Diagnostic Evaluation of FMD

Standard (conventional) renal arteriogram is the most definitive test (gold standard) to diagnose RAS due to FMD. However, certain less precise noninvasive tests may offer clues to the presence of RAS.

Duplex Ultrasound

Duplex ultrasound is much less sensitive than CTA or magnetic resonance angiography (MRA) for detecting RAS. However, it is less expensive and readily available for the initial screening purpose. The procedure, however, is highly operator dependent and requires the cooperation of the patient to hold their breath during the procedure. Duplex ultrasound may reveal RAS and also provide information about the kidney size. It is a reasonable first-line screening test but not conclusive and should be followed by CTA or MRA. Duplex ultrasound may show arterial stenosis, increase in peak systolic velocity, and a delayed systolic upstroke distal to the lesion. Blood vessel tortuosity and turbulence can be identified on color Doppler. While the duplex ultrasound may only serve as a screening test for RAS, it is a reliable technique to follow up the patients after angioplasty.

Computed Tomography Angiography and Magnetic Resonance Angiography

Both CTA and MRA provide acceptable sensitivity and specificity in detecting RAS from any cause including FMD. The CTA probably is slightly superior to MRA in providing the anatomy of renal arteries and the kidneys. The CTA offers superior spatial resolution compared with MRA. Also, distal renal artery is better visible with CTA compared with MRA. Calcifications can also be visualized with CTA. But irradiation and contrast-mediated renal injury are disadvantages of CTA.

The MRA may at times overestimate the degree of RAS. And spatial resolution is not optimal compared with CTA. The MRA is preferable for patients who may otherwise be at risk for contrast nephrotoxicity. The choice between CTA and MRA depends on the expertise available at the facility and experiment.

Renal scintigraphy and digital subtraction angiography have no convincing role in the diagnosis of RAS given the usefulness of CTA and MRA.

MANAGEMENT OF FMD

Once the diagnosis of RAS due to FMD is confirmed based on clinical assessment and a definitive procedure (CTA or MRA), appropriate management strategy should be planned to correct the lesion and to improve or cure hypertension. There are no randomized controlled studies comparing surgical revascularization of RAS (from FMD) with percutaneous transluminal angioplasty (PTA). However, the most preferred therapeutic choice to correct FMD is clearly PTA. At present, the need for surgical correction of FMD is not recommended given the success of PTA in treating this condition. Currently, PTA without stenting is the treatment of choice for patients with renovascular hypertension with FMD as the etiology. Primary PTA of the FMD lesions (unilateral or bilateral) should suffice; stenting is only indicated if there is significant periprocedural dissection or if angioplasty does not produce optimal relief of the stenosis.

In patients with RAS due to FMD, PTA of the lesions (unilateral or bilateral) results in a remarkable improvement (or cure) of hypertension provided the procedure is a technical success. In nearly 90% of patients, PTA results in a dramatic fall in blood pressure. Nearly a third of patients with FMD have involvement of branch renal artery that may pose technical challenges for performing PTA but can be attempted. For patients who are unable or unwilling to undergo PTA, hypertension should be treated medically. The treatment regimen should include blockers of the renin–angiotensin–aldosterone system. The goal is to control hypertension effectively.

There are no specific guidelines on how to follow up the patients with FMD who have undergone PTA. Perhaps, the first follow-up visit should be within the first month after PTA and 6 to 12 months thereafter based on the clinical assessment and blood pressure levels.

CONCLUSION

The RAS due to FMD is potentially a curable form of secondary hypertension. Clinical suspicion should lead to diagnostic workup followed by management strategy (usually PTA). Future research should identify genetic and environmental factors in the pathogenesis of FMD. It is also important to identify in the clinic those hypertensive patients who may have underlying FMD as the etiology. Certainly, FMD represents a truly correctible cause of hypertension in the community. Therefore, it is an important clinical entity because safe therapeutic options are available with superb clinical outcomes.

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