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Review Article

Role of interventions in renal artery fibromuscular dysplasia: Where we are

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ABSTRACT

Fibromuscular dysplasia is a rare noninflammatory vascular disease predominantly affecting the renal arteries. It is a rare cause of hypertension accounting for 10% of cases of renovascular hypertension. The classical angiographic appearance of 'string of beads' seen in medial fibroplasia type which is most common. There are various imaging modalities for diagnosis but conventional angiography is still considered as gold standard. The various treatment option includes medical therapy, interventional revascularization of renal arteries and rarely surgical. Percutaneous angioplasty is the treatment of choice in patients of renal artery fibromuscular dysplasia with hypertension. Various studies concludes 40–50% cure rate of hypertension by percutaneous angioplasty. Early diagnosis and treatment is important to achieve good long-term results.

1. Introduction

Fibromuscular dysplasia is an idiopathic, noninflammatory, and nonatherosclerotic arterial disease that mainly affects renal and carotid system but can affect any vessel.[1] Renal vessel involvement is seen in 75% of patients with FMD. Females in their young age (20–40 years) affected by this disease. Incidence in male is very low.[2]

The exact prevalence of disease is unknown due to late presentation and nonspecific symptomatology.[3] Cragg and associates identified FMD in 3.8% (out of 1862) prospective renal donors who underwent for renal angiography.[4] In a recent study done on renal donors by CT angiography showed prevalence of 2.6% (68/2640) with mean age and sex of 52 ± 10 and 86.8%, respectively.[5]

Renal FMD is bilateral in more than 35% of patients and clinically presented as renovascular hypertension. Hypertension is attributed to activation of rennin-angiotensin system. In 5–10% of patients with renal FMD, aneurysm can also be seen.[6,7] Early diagnosis and treatment of this entity is must for good long-term results. Percutaneous angioplasty (PTA) is the treatment of choice with or without medical therapy for very good control of hypertension.

2. Pathophysiology, classification and clinical manifestation

Pathophysiology of FMD remains unclear, however proposed etiologic mechanisms include hormonal factors, mechanical trauma, metabolic and immunologic factors, intrinsic deficiency of elastic fibers. Some investigators have put forward a theory that links estrogen with a predisposition to the development of FMD.[8] However, neither oral contraceptives nor pregnancy appears to increase the risk for developing FMD.[9] Familial cases also have been reported along with association with HLA-DRw6 antigen.[10] Pathologically it is classified as three types on the basis of which layer of arterial wall is involved: intima, media and adventetia.[11]

3. Medial FMD

It is most common type contributing about 65–70% of the cases. Classically present as "string of beads" appearance on conventional angiography due to the repeating stenosis and post-stenotic dilatations of the renal artery due to differential collagen deposition and preserved elastic lamina. The lesions affect mainly the distal 2/3 of renal artery but can extend into the proximal part in advance stage.

4. Intimal FMD

This is the second most common type of FMD. Angiographically concentric stenosis or long tubular lesions, which are result of focal

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fibrotic band like constrictions due to increase collagen deposition within the intima often complicated by a fragmented or duplicated elastic lamina.

5. Adventitial FMD

This is the least common variant of FMD. It is due to hypertrophy of connective tissue at the junction of media and adventitia of the arterial wall and leads to unifocal stenosis can be at ostium, trunk or at bifurcation.

6. Angiographic classification

Pathological samples are rarely available in era of endovascular treatment so keeping this in mind one classification proposed by Kincaid et al.[10] on the basis of angiography is more commonly used to differentiate FMD into four types: multifocal, unifocal with a solitary stenosis (<1 cm), tubular type with a long concentric stenosis (>1 cm) and the mixed type. Savard et al.,[12] classified FMD into unifocal and multifocal types on angiography which is more simple and clinically relevant. Angiographic classification can be applied to all FMD patients, unlike earlier ones only for operated patients.[12]

7. Clinical manifestation

Renovascular hypertension is the most common clinical presentation of FMD as it is second leading cause after atherosclerosis. Renal artery stenosis caused by FMD usually presents with stage 2 or 3 hypertension or abrupt onset of medically resistant hypertension. Patients of FMD are hypertensive but renal insufficiency or raised creatinine is not so common as in atherosclerosis induced RAS.[5] In young patient's hypertension refractory to medical treatment should be sought for renal artery FMD.

Other clinical manifestation of renal artery FMD may be severe flank pain, hematuria, and rapidly progressive hypertension due to renal artery dissection and kidney infarction.[13] Other symptoms like headache, tinnitus and dizziness can occur as due to associated carotid or vertebral involvement, that's why it's always prudent to image intracranial and neck vessels in a case of renal artery FMD. Many case of FMD remains asymptomatic and discovered incidentally when imaging is done for other cause.[7]

8. Diagnosis

Diagnosis of FMD is very difficult after clinical examination as there are many differentials with similar picture. Due to empirical use of antihypertensive after onset of symptoms there is average delay of 3.6 ± 7.4 for making the diagnosis of FMD.[14] Functional imaging is also not very helpful as it does not differentiate between stenosis of FMD and atherosclerosis. Imaging modalities commonly used for evaluation of FMD consist of ultrasound (US) and color Doppler examination; CT or MR angiography however catheter based angiography remains the gold standard imaging modality.[15]

Conventional angiography is used to determine the accurate location and extent of lesion. An aortogram with selective renal angiography up to small intra-renal vessels and multiple views are required for correct diagnosis. Focal stenosis, the "string of beads" appearance and aneurysm formation are classical appearance on angiography (Fig. 1A, B). In most of the cases the classical appearance is mixed with other findings, especially in older age group where seen with atherosclerosis. Advantage of conventional angiography are: High spatial resolution, it can visualize the main renal arteries as well as the smaller branch vessels, Aneurysm formation and dissections in the small branches can be evaluated accurately, pressure wire and IVUS imaging can be done simultaneously. Translesional systolic pressure gradient difference >20 mmHg is diagnostic. Disadvantage of conventional angiography are radiation hazards, invasive procedure, iodine and risk of complication and no functional significance of lesion.[15]

The color Doppler ultrasound is least invasive and easily available tool to diagnose, but it has many drawback as it is operator dependent, quality of equipment, patient body habitus, complex vessels or accessory renal artery which lowers sensitivity, needs bowel preparation and no strict criteria to diagnose significant renal artery stenosis.

Discrepancy in renal size more than 1.5 cm is usually consider as significant finding in renovascular hypertension. Although many Doppler indices are helpful but for FMD per se only resistive index of use because its mainly involve renal artery distal from origin, so PSV and RAR (peak systolic velocity and renal artery to aorta PSV ratio) are not of so much importance. RI more than 0.8 suggest some structure abnormality in vessels. Also it is used in follow-up after revascularization to predict restenosis.

CT or MR angiography has almost equal sensitivity and specificity to diagnose the condition with some advantage and disadvantage over each other. Both have less accuracy for segmental branch disease and does not provide functional information. CT Angiography has high spatial resolution, minimal invasive, and short acquisition time but expose the patient to radiation and iodinated nephrotoxic contrast although later is not of big concern due to availability of more renal friendly contrast now a day. Contrast enhanced MRI is free of ionising radiation and uses gadolinium based agents which are very less nephrotoxic but has certain limitations like claustrophobia, difficulty in breath holding and incompatible prosthetics etc. Intravascular ultrasound accurately predicts severity of stenosis and assess accurate size of balloons. It is also used for follow-up and re-evaluation of restenosis.[16]

9. Differential diagnosis

9.1. Atherosclerosis

FMD induced renal artery stenosis patients are of younger age group and lack of atherosclerotic risk factor. Atherosclerosis induced stenosis involve proximal part of renal artery, while FMD involves middle or distal portion. Atherosclerosis is very frequently associated with renal functional impairment whereas FMD almost never.

9.2. Vasculitis

Being noninflammatory process, acute phase reaction marker like ESR and C-reactive protein are usually within normal range. Vasculitis can mimic as FMD on angiography and presents in same way but most common form of FMD has distinct classical 'string of beads' appearance.

9.3. Segmental arterial mediolysis

Segmental arterial mediolysis is also difficult to differentiate from FMD as it has features of spontaneous dissection, occlusion and aneurysm formation. Pathologically there is separation of outer media from adventitia that leads to more chances of dissection. It may have similar angiographic appearance of FMD due to cyclic repair and destruction of intimal layer. Unlike vasculitis, there is no inflammation or fibrinoid necrosis.

Patients with SAM usually have digestive tract involvement most commonly with celiac trunk branches. Men and women are equally affected with mean age of 40–80 years.