Fibromuscular dysplasia — imaging and intervention

Ian C Duncan

FFRad(D)SA

*Unitas Interventional Unit
PO Box 14031
Lyttelton
0140*

Abstract

Fibromuscular dysplasia (FMD) is a non-atheromatous, non-inflammatory disorder of medium-sized arteries, usually affecting the carotid and renal arteries. Many cases remain undiagnosed or are discovered co-incidently, with relatively few producing significant clinical problems. FMD produces both typical and nonspecific angiographic patterns that can be mimicked by other arterial diseases. The pathology and radiological findings of FMD are reviewed here together with an overview of the available treatment options.

Introduction

Fibromuscular dysplasia (FMD) is a primary segmental non-atheromatous and non-inflammatory arteriopathy of unknown aetiology affecting intermediate-sized arteries in the body. It primarily affects the renal and carotid arteries but can also affect the vertebral, iliac, subclavian and visceral arteries.

Pathology

Its pathogenesis is unknown although various humoral, mechanical and genetic factors may play a role.[1] The first histological classification of renal arterial FMD was provided by McCormack *et al.* in 1967,[2] and was based upon the primary site of involvement within the arterial wall, being categorised as: (*i*) intimal fibroplasia; (*ii*) medial fibroplasia (with aneurysms); (*iii*) subadventitial fibroplasia; and (*iv*) fibromuscular hyperplasia.

In this report the term 'chain-of-beads' was first used to describe the angiographic appearance of medial fibroplasia. Two further subtypes of medial fibroplasia were described, namely the peripheral form limited to the outer media, and the diffuse form with a greater degree of medial disruption. Areas of marked medial fibrosis alternate with areas of medial thinning or absence, with the latter resulting in the aneurysmal dilatations seen (i.e. the 'beads'). A revised histological classification was provided by Harrison and McCormack in 1971.[3] FMD is now commonly classified into three types based on the predominant site of the dysplasia within the arterial wall being within the tunica intima, tunica media or tunica adventitia.

1. Medial FMD occurs in 80 - 95% of cases and is characterised by rings of fibrous proliferation and smooth muscle hyperplasia resulting in thickening of the media together with destruction of the internal and external elastic lamina.

2. Intimal FMD is found in 5 - 10% of cases and involves destruction of the internal elastic lamina and thickening of the intimal layer.

3. Adventitial FMD accounts for between 1% and 5% of cases and affects only the adventitial and periadventitial layers.

FMD occurs most frequently in women in the fourth to sixth decades of life. It can also be seen in children in whom the intimal subtype is commonest. FMD runs a relatively benign clinical course and is often discovered incidentally at angiography, being present in 0.25 - 1% of all cerebral angiograms .[4-6]

Angiographic patterns

Three radiographic patterns of FMD have been described. [7,8] The commonest and most classic pattern (type I) seen in 70 - 90% of cases is the 'string-of-beads' appearence with focal areas of dilatation alternating with focal areas of constriction simulating beads threaded onto a string.[9] This pattern is seen only with the medial and intimal types (Fig. 1). The second pattern (type II), seen in 10 - 20% of cases, is of a segmental, tubular stenotic appearance and may occur with any histologic type (Fig. 2). The third pattern (type III), seen in less than 5% of cases, is the formation of
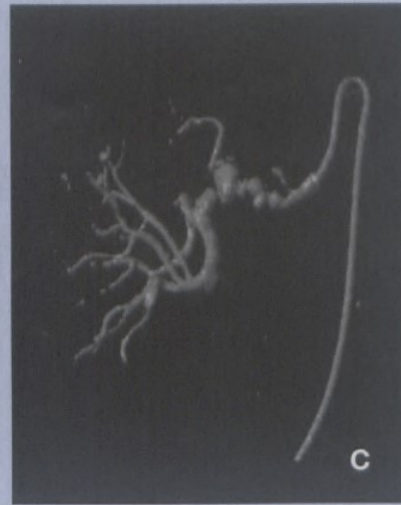
Fig. 1. A selective right renal arteriogram (Fig. 1a) shows the characteristic 'string-of-beads' or type I angiographic appearance. Also shown are volume rendered (Fig. 1b) and surface shaded display (Fig. 1c) reconstructions of the same vessel following three-dimensional rotational DSA.
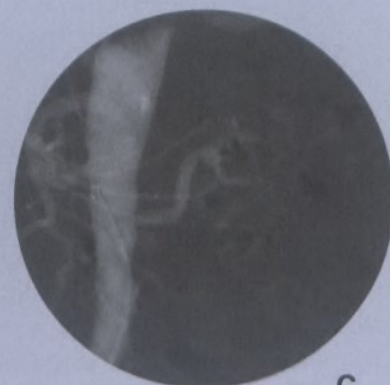

Fig. 2. A coronal gadolinium-enhanced MR angiogram (Fig. 2a) and digital subtraction flush abdominal aortogram (Fig. 2b) show a tubular focal stenosis in the proximal part of the left renal artery (type II angiographic pattern). The flush aortogram also shows mild beading in the superior mesenteric artery. This patient presented with hypertension which was difficult to manage medically. The lesion was treated by stent placement (Fig. 2c) after an inadequate response to initial balloon angioplasty, with an excellent clinical response.

saccular diverticula and septa. Occasionally unifocal webs or septa may be seen near the carotid bifurcation as the sole angiographic finding of FMD. Typically there is also associated tortuosity of the affected vessels.

The angiographic appearance may be difficult to distinguish from other pathological processes. Both intimal and medial types may sometimes be confused with atheromatous disease. The tubular stenotic pattern may appear similar to that seen in vasculitis or fibrotic strictures due to other causes or vessel dissection. The diverticular form may be indistinguishable from aneurysm formation secondary to trauma or atheroma. 'Standing waves' are concentric spastic contractions that can mimic the 'string-of-beads' appearance. However, these standing waves can be readily distinguished from FMD by virtue of the more even spacing of the narrowed bands and by the normal vessel calibre between the bands, whereas the dilatations of FMD are of greater calibre and the vessel tends to be more tortuous. Catheter tip induced spasm, particularly of the renal arteries following selective catheterisation, may occasionally be mistaken for vessel stenosis. MR angiography can be used

to identify FMD but is limited by turbulent and complex flow patterns that accompany the stenotic, irregular and tortuous vessels resulting in signal inhomogeneity and flow voids.[10]

Cephalocervical FMD

FMD is far more likely to affect the extracranial vessels than the intradural ones. 90 - 95% of cases involve the extracranial internal carotid arteries (ICA). In 12 - 43% of patients there is vertebral artery involvement but most of these cases have carotid artery involvement as well (Fig. 3). The changes of FMD typically affect the mid-portion of the extracranial ICA at the C1 and C2 levels sometimes extending up into the petrous segment. There is usually sparing of the carotid bifurcation and proximal ICA. The vertebral arteries are also usually affected at the C1 and C2 (or V3) levels.[11] 60 - 85% of cases have bilateral vessel involvement. Intracranial disease may be found in both anterior and posterior circulations, most commonly affecting the middle cerebral artery.[4,8]

Although most cases of cephalocervical FMD remain asymptomatic, ischaemic complications such as transient ischaemic attacks (TIAs) and cerebral infarctions may occur. Other symptoms related to cephalocervical FMD include pulsatile tinnitus, bruit, syncope, facial pain, Horner's syndrome or Raeder's syndrome.[12] Cerebral ischaemia may be due either to emboli or hypoperfusion related to tight stenotic lesions.[13]

An important complication of cephalocervical FMD is spontaneous mural dissection. The incidence of FMD-related dissections is unknown but as many as 15 - 20% of dissections of the carotid arteries are seen in patients with FMD.[12] The angiographic appearance of a dissection is highly variable ranging from subtle focal calibre changes through a tight long segmental stenosis (the 'string-sign') to complete occlusion. Sometimes a dissection cannot be distinguished from the disease itself and here MR imaging may be of assistance. In cases of dissection, intramural thrombus may be identified on T1-weighed images as a crescentic high signal intensity adja-

cent to a flow void.[14] Transmural dissections can result in arteriovenous fistulas of the carotid and vertebral arteries. Dissections can occasionally be bilateral.[15]

Intracranial complications include the development of sacular aneurysms in 20 - 50% of patients with cephalocervical FMD (Fig. 4).[4,8] These aneurysms can rupture resulting in subarachnoid haemorrhage (SAH) but non-aneurysmal SAH can also result from spontaneous intracranial arterial dissection. Transmural dissection of the cavernous ICA can result in a caroticocavernous fistula.[16]

Renovascular FMD

FMD is the second most common cause of renal arterial stenosis after atherosclerosis. Its exact prevalence in the general population is unknown as many cases are undoubtedly undiagnosed and often only become apparent during the investigation of hypertension.

FMD accounts for up to 25% of all cases of renovascular hypertension.[17]
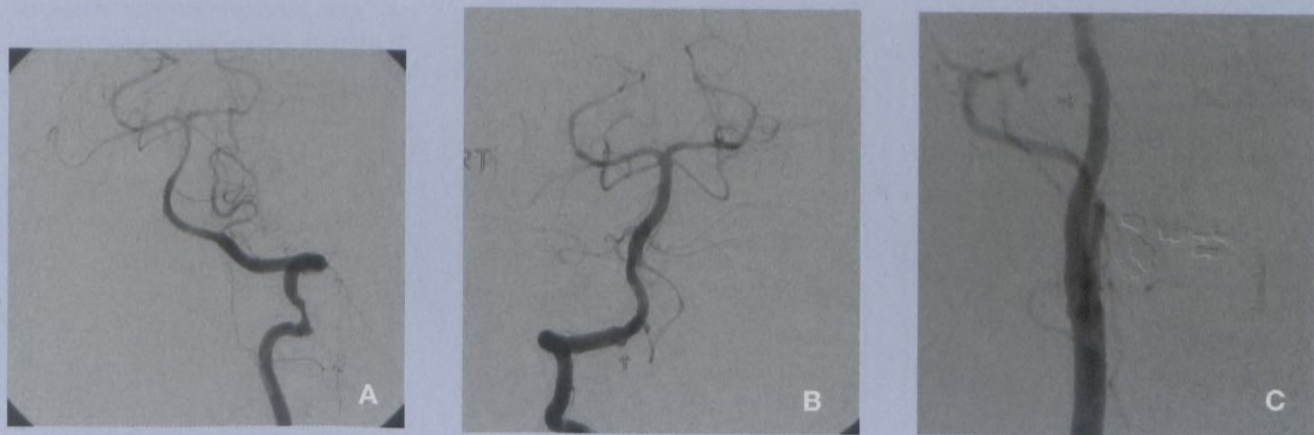

Fig. 3. Selective left (Fig. 3a) and right (Fig. 3b) vertebral arteriograms in a patient with transient vertebrobasilar ischaemic symptoms show the presence of fibromuscular dysplasia at the typical C1 and C2 levels. A selective right common carotid injection in a frontal projection also shows a slight focal irregularity along the lateral wall of the internal carotid artery just distal to the bulb, indicating just how subtle the angiographic findings can be in some vessels (Fig. 3c).
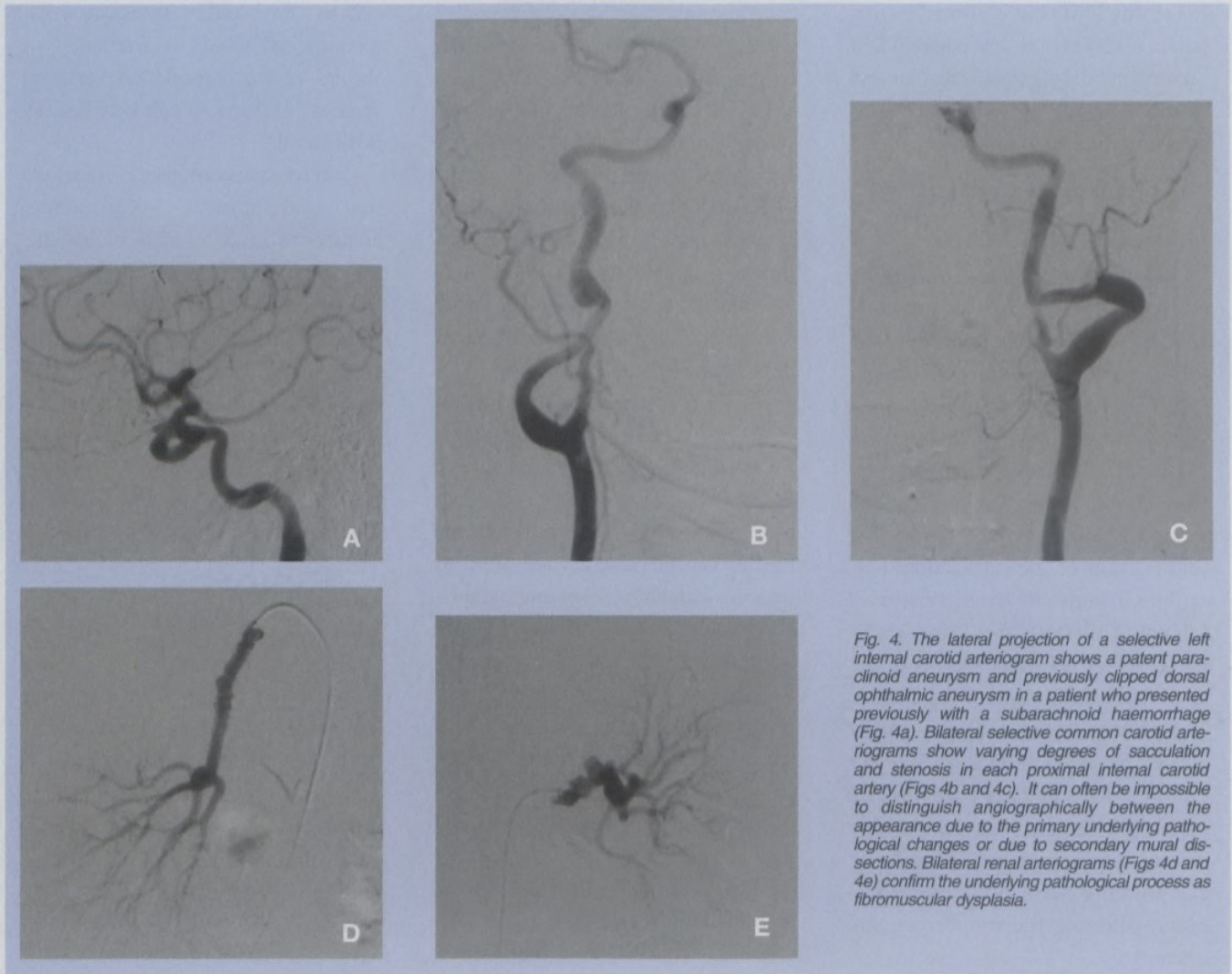
Fig. 4. The lateral projection of a selective left internal carotid arteriogram shows a patent paraclinoid aneurysm and previously clipped dorsal ophthalmic aneurysm in a patient who presented previously with a subarachnoid haemorrhage (Fig. 4a). Bilateral selective common carotid arteriograms show varying degrees of sacculation and stenosis in each proximal internal carotid artery (Figs 4b and 4c). It can often be impossible to distinguish angiographically between the appearance due to the primary underlying pathological changes or due to secondary mural dissections. Bilateral renal arteriograms (Figs 4d and 4e) confirm the underlying pathological process as fibromuscular dysplasia.

Renovascular hypertension due to FMD is said to occur in less than 0.5% of the general population.[18]

FMD is the commonest cause of renovascular hypertension in children.[19,20] Renal arterial FMD is reported to be progressive in 12 - 66% of patients with disease of the main renal artery,[21] but progression to clinical renal failure is very uncommon.[22] Complete occlusion of a renal artery resulting in total renal infarction has been reported.[23,24]

The angiographic appearance of renal arterial FMD may be mimicked by other diseases of the renal arteries including neurofibromatosis, Ehlers-Danlos disease, arteritis (including Takayasu's arteritis) and atherosclerosis. FMD can be either unilateral or bilateral in the renal arteries. Where unilateral the right side tends to be affected more often. The distal two-thirds of the renal artery are most often affected, with the disease often extending into the major segmental branches. FMD in a renal artery usually manifests as the typical 'string-of beads' appearance at angiography,[9] but it can manifest as a single focal stenosis. As in the brain, saccular renal arterial aneurysms may be found in association with FMD.[25]

Renovascular hypertension due to FMD tends to present at a younger mean age than that associated with atherosclerosis, usually in the third to fourth decades.[19,20,26] It is very important to diagnose the presence of FMD in young hypertensive patients as the disease is highly amenable to corrective treatment with a definite improvement in the long-term outcome of this subgroup of hypertensive patients.

Visceral and other sites

FMD can be found less commonly in other sites including the subclavian, brachial, external iliac and visceral arteries.[27] In the latter, severe stenosis can lead to mesenteric ischaemia.

Management: medical, surgical and interventional

FMD generally follows a benign clinical course. Most patients with craniocervical FMD do not experience clinical progression of the disease or a significantly increased risk of stroke. For patients who present with neurological symptoms, causes other than FMD for which the symptoms may be attributable should be excluded, e.g. atherosclerotic disease, intracranial aneurysms, etc. Patients with non-focal neurological symptoms or those who are asymptomatic or with isolated bruits may be treated on antiplatelet therapy alone.[28] For patients with focal ischaemic symptoms (TIAs or stroke) or haemodynamically significant stenoses more direct therapy should be considered.

The preferred surgical treatment to date has been graduated internal dilation of the stenosed vessels.[29,30] Either isolated septa or the entire length of the affected vessel may be excised with graft interposition. Extracranial aneurysms may be excised with reanostenosis and grafting as required.[31,32] Percutaneous transluminal angioplasty (PTA) and stenting have been described in the management of cervical FMD.[33-38] Intra-operative balloon angioplasty

carries the additional advantage of allowing back bleeding after the dilatations to wash out any debris resulting from the dilatations.[39,40] However the use of protective filter devices during carotid angioplasty that trap small clots and other material during balloon dilatation may make percutaneous cervical balloon angioplasty safer in the future.

The surgical management of renal arterial FMD includes aortorenal bypass, surgical reconstruction of the renal artery or renal autotransplantation .

Percutaneous transluminal renal angioplasty (PTRA) is, however, the current preferred method of treatment for renal arterial FMD,[41,42] with results at least as good as surgery.[43-45] Technical success rates for PTRA in cases of FMD-related renovascular hypertension run as high as 94% with 44 - 49% of patients considered cured and 43 - 45% classed as improved, yielding an 89 - 92% positive procedural benefit rate.[46,47] The long-term patency rates of PTRA in renovascular FMD are excellent, with 5 - 10-year patency rates of 87% - 89%.[48,49] Restenosis rates of 8 - 11.5% have been reported.[46,48] However, repeat dilatation of restenotic lesions is reported to be easier than the original PTRA as the recurrence is usually not as extensive as the original lesion.[41,48] FMD is more difficult to treat with PTRA in children possibly due to greater prevalence of intimal and advential subtypes.[50]

Stenoses in visceral, iliac and brachial arteries can be managed by either surgical reconstruction or by PTA. Selected cerebral, renal and visceral aneurysms can be managed by either coil embolisation or stent-graft insertion.[25,51]

Conclusion

FMD is a benign dysplastic arteriopathy which in many cases remains clinically occult, often found incidentally during vascular investigations for other reasons. Nevertheless it does produce vascular stenoses which can lead to ischaemia-related complications (embolic or homodynamic) such as transient ischaemic attacks, cerebral infarction, renovascular hypertension or mesenteric ischaemia. Other associated complications include arterial dissection, arteriovenous fistula formation, and cerebral and renal aneurysm formation. Clinically important vascular lesions can be treated surgically or by interventional methods. The results of PTRA are at least as good as surgery for renal arterial FMD, and PTRA is now the preferred treatment for renal lesions. PTA and stenting are viable alternatives to surgery in cervical disease although the potential for periprocedural cerebral embolism exists with unprotected angioplasty.

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