Fibromuscular dysplasia

Fibromuscular dysplasia (FMD) is an arterial disease of unknown etiology and is comprised in a group of nonatherosclerotic and noninflammatory arterial diseases.

General information

A vasculopathy (angiopathy) affects primarily branches of the aorta, with renal artery involvement in 85% of cases (the most common site) and commonly associated with hypertension. The disease has an incidence of ≈ 1% and results in multifocal arterial constrictions and intervening regions of aneurysmal dilatation.

The second most commonly involved site is the cervical internal carotid artery (primarily near C1–2), with fibromuscular dysplasia (FMD) appearing on 1% of carotid angiograms, making FMD the second most common cause of extracranial carotid stenosis. [1] Bilateral cervical ICA involvement occurs in ≈ 80% of cases. 50% of patients with carotid FMD have renal FMD. Patients with FMD have an increased risk of intracranial aneurysms and neoplasms and are probably at a higher risk of carotid dissection. Aneurysms and fibromuscular dysplasia: The reported incidence of aneurysms with FMD [2] ranges from 20–50%.

Epidemiology

Cerebrovascular FMD occurs more frequently in women, and the mean age at which it is diagnosed is 50 years.

Etiology

The actual etiology remains unknown, although congenital defects of the tunica media (muscular layer) and the tunica intima of the artery have been identified, which may predispose the arteries to injury from otherwise well-tolerated trauma. A high familial rate of strokes, HTN, and migraine have supported the suggestion that FMD is an autosomal dominant trait with reduced penetrance in males [3].

Clinical features

Up to 50% of patients present with episodes of transient ischaemic attack or infarction. However, FMD may also be an incidental finding and some cases have been followed for 5 years without recurrence of ischemic symptoms, suggesting that FMD may be a relatively benign condition.

Headache

Headaches are commonly unilateral and may be mistaken for typical migraine. Syncope may be caused by involvement of the carotid sinus.

Horner syndrome

Horner syndrome occurs in ≈ 8% of cases. T-wave changes on EKG may be seen in up to one–third of cases, and may be due to involvement of the coronary arteries.

Headache, ECG-abnormalities, hypertension, mental distress, tinnitus, vertigo, arrhythmia, TIA, and syncope are frequent components. Hemicrania, sometimes combined with ipsilateral Horner's Syndrome, was found in patients with advanced lesions in the carotid artery of the same side. An associated occurrence of stroke in pedigrees, especially among young and middle-aged females, indicates that FMD in the majority of cases is inherited as an autosomal dominant trait with reduced penetrance in males. [4].

Intracranial artery involvement

Most often it affects the renal and internal carotid artery (ICA), although any artery can be involved.

Internal carotid arteries are affected in 25-30% of patients. When carotid arteries are involved, cervical segments C1-C2 are most often affected.

Intracranial aneurysms often occur in patients with fibromuscular dysplasia of the cephalic arterial system, their frequency being as high as 51%.

FMD has been associated with intracranial aneurysms in 7-50% cases, but FMD associated with a giant (> 2.5 cm) intracranial aneurysm is rare. Extracranial internal carotid aneurysms are uncommon, with only 3% caused by FMD [5].

Diagnosis

The most common angiographic pattern of cerebrovascular FMD is the “string-of-beads” deformity at the extracranial internal carotid artery.

The “gold-standard” for the diagnosis of FMD is the angiogram. The three angiographic types of FMD [6].

Angiographic classification of FMD

1 most common (80–100% of reported cases). Multiple, irregularly spaced, concentric narrowings with normal or dilated intervening segments giving rise to the so-called “string of pearls” appearance.

Corresponds with arterial medial fibroplasia

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2 focal tubular stenosis, seen in ≈ 7% of cases. Less characteristic for FMD than Type 1, and may also be seen in Takayasu's arteritis and other conditions

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3 "atypical FMD." Rare. May take on various appearances, most commonly consisting of diverticular outpouchings of one wall of the artery

Complications

Fibromuscular dysplasia (FMD) affecting the internal carotid artery (ICA) is considered a benign condition; however, retinal and cerebral ischemic events may occur.

Treatment

Medical therapy, including antiplatelet medication (e.g. aspirin), has been recommended. Direct surgical treatment is problem-ridden due to the difficult location (high carotid artery, near the base of the skull) and to the friable nature of the vessels, which makes anastamosis or arteriotomy closure difficult. Transluminal angioplasty has achieved some degree of success. Carotid-cavernous fistulas and arterial rupture have been reported as complications.

Systemic vascular diseases such as fibromuscular dysplasia, Ehlers-Danlos syndrome, Marfan syndrome, and Behçet's disease are known to cause spontaneous dissecting aneurysms of the cervical internal carotid artery. These diseases are generally associated with vascular fragility; therefore, invasive treatments are avoided in many cases of dissecting aneurysms, and a conservative approach is used for the primary disease. Surgical or intravascular treatment may be chosen when aneurysms are progressive or are associated with a high risk of hemorrhage; however, there is no consensus on which treatment is better.

Case series

The angiographic, clinical, and genetic characteristics of fibromuscular dysplasia (FMD) are reviewed in 37 patients (mean age 48 years) selected from a pool of 4000 angiograms of carotid or vertebral arteries. FMD was a neglected pathogenic factor in 28 patients with hemorrhagic or ischemic cerebral lesions. The aneurysms found in 19 patients had conventional appearance and were mainly located in the internal carotid or middle cerebral arteries and on the same side as the most affected cervical artery, which suggests that aneurysms and FMD are pathogenically related. A clinical syndrome is presented where headache, ECG-abnormalities, hypertension, mental distress, tinnitus, vertigo, arrhythmia, TIA, and syncope are frequent components. Hemicrania, sometimes combined with ipsilateral Horner's Syndrome, was found in patients with advanced lesions in the carotid artery of the

same side. An associated occurrence of stroke in pedigrees, especially among young and middle aged females, indicates that FMD in the majority of cases in inherited as an autosomal dominant trait with reduced penetrance in males [7)]

Case reports

Iampreechakul P, Siriwimonmas S. Spontaneous obliteration of spontaneous vertebral arteriovenous fistula associated with fibromuscular dysplasia after partial surgery: A case report. Interv Neuroradiol. 2016 Dec;22(6):717-727. doi: 10.1177/1591019916659263. Epub 2016 Aug 1. PMID: 27481913; PMCID: PMC5564354.

2014

Cohen et al. present a patient with carotid FMD presenting with a major ischemic stroke due to major embolic occlusion of the ICA in conjunction with a hemodynamic component caused by narrowing and beading of the lumen associated with FMD. The patient was successfully treated with intracranial stent-assisted thrombectomy followed by cervical ICA stenting that aimed to reconstruct and angioplasty the FMD-affected arterial segment. Recently, stent-based thrombectomy has emerged as the most effective endovascular option for the rapid revascularization of major intracranial occlusions; however, its use in a rare case of FMD-associated major stroke has not yet been reported [8)].

2011

A 52-year-old woman who presented with a sudden severe headache and went into a deep coma. She had been complaining of headaches for 2 weeks, but no specific imaging findings were obtained. A computed tomography scan obtained on admission showed a diffuse subarachnoid hemorrhage (SAH) from the cerebellomedullary cistern to the basal cistern with evidence of clot in the fourth and third ventricles.

A digital subtraction angiography made the diagnosis of cerebrovascular FMD. Right carotid angiography and left vertebral angiography showed the classic “string-of-beads” pattern with multiple constrictions of the lumen. Left carotid angiography showed a long segment of tubular stenosis. Right vertebral angiography also revealed the “string-of-beads” pattern and a ruptured aneurysm at the intracranial segment, which presented as a diverticulum-like outpouching. The patient was treated with conservative measures but passed away on the 23rd day of hospitalization. An autopsy was not performed. During the last three decades, there are only four previous reports which showed intracerebral ruptured aneurysms of the vertebral artery or its branch in adults with cerebrovascular FMD [9)].

2010

A cervicocephalic FMD patient with a history of right oculomotor nerve palsy in 2000. Angiography revealed bilateral internal carotid artery aneurysms and a fusiform aneurysm in the right vertebral artery. Typical “string-of-beads” phenomenon was observed in V2 segment of left vertebral artery. The right ICA giant aneurysm was treated by right ICA occlusion and superficial temporal artery to

middle cerebral artery bypass at that time. Five years later, the patient presented with paroxysmal weakness in right limbs. The subsequent angiography showed the enlargement of left ICA aneurysm. It was treated satisfactorily with left external carotid artery-saphenous vein-MCA bypass and left ICA ligation. During the long-term follow-up, the patient kept no neurological deficit and the angiography showed good patency of bilateral grafts and the lesions in bilateral vertebral arteries remained unchanged [10].

2008

A rare case of FMD presenting with subarachnoid hemorrhage due to the rupture of 1 of 10 aneurysms located in the extra- and intracranial vertebral and posterior inferior cerebellar arteries. The FMD was treated successfully using flow reversal therapy, consisting of proximal occlusion of the VA with Guglielmi detachable coils, and was diagnosed histopathologically using a biopsy specimen of the distal superficial temporal artery. Originally FMD may be caused by a fragile arterial wall that may progress to the formation of an aneurysm due to hemodynamic stress. For this reason, FMD may be treatable by reducing this hemodynamic stress [11].

2004

Hans et al. report on a patient with fibromuscular dysplasia who presented with a right-sided giant calcified cavernous internal carotid artery (ICA) aneurysm and two additional supraophthalmic ICA aneurysms. Endovascular closure of the right ICA using detachable balloons was performed with collateralisation of the right hemisphere via the right-sided posterior communicating and the anterior communicating arteries. Repeat angiography after 6 months demonstrated spontaneous complete regression of the two supraophthalmic aneurysms, although the parent vessel was still perfused. In comparison to the former angiography, the flow within the parent vessel was reversed due to the proximal ICA balloon occlusion. MRI demonstrated that the aneurysms were not obliterated by thrombosis alone, but showed a real regression in size. This case report demonstrates that changes in cerebral hemodynamics potentially lead to plastic changes in the vessel architecture in adults and that aneurysms can be flow-related, even if not associated with high flow fistulas or arteriovenous malformations, especially in cases with an arterial wall disease [12].

A 53-year-old woman was admitted with severe subarachnoid hemorrhage due to rupture of an aneurysm associated with atypical intracranial fibromuscular dysplasia (FMD). Angiography demonstrated the aneurysm and very irregular form of the left internal carotid artery (ICA), the right ICA, and right proximal middle cerebral artery (MCA). Other arteries showed signs of atherosclerosis. The aneurysm was treated by embolization, but she subsequently died of shock of unknown cause. Detailed examination of serial angiograms detected enlargement of the aneurysm and progression of the irregular appearance of the ICA. FMD is a non-inflammatory and non-atheromatous arteriopathy that commonly affects the cervical ICA and sometimes the intracranial ICA. The association with saccular aneurysm is widely known and the prevalence of incidental aneurysms is higher than that in the general population. The common “string of beads” finding is easily distinguished from other vascular diseases, but non-specific findings such as “tubular stenosis” and “diverticular-like outpouching” are harder to differentiate. FMD is associated with various complications and appropriate periodic follow-up examination is required. Detailed analysis of serial angiograms may facilitate diagnosis of this condition [13].

1983

A 56-year-old woman was admitted with a history of five months of progressive horizontal diplopia, without headache or visual loss. She had no previous history of head injury or hypertension. Examination revealed only a left III and VI cranial nerve paresis; pupil reactions to light were normal, but there was a slight anisocoria (pupil diameter was 3 mm on the left and 2 mm on the right). Blood pressure was 120/ 70 mm Hg. Four-vessel angiography showed a typical “string of beads” appearance of both internal carotid arteries and a giant aneurysm (26 x 23 mm) of the left intracavcrnous carotid artery. CT scan before operation showed a circular area of increased density without calcification in the left cavernous region which rapidly and markedly enhanced as a dense and homogeneous mass with the same diameters as those obtained by angiography. Routine analysis, EEG, ECG and conventional radiographs were normal. Carotid artery ligation in the neck area was performed without complications. On follow-up examination four months later, there was an improvement in the diplopia and eye movements and the pupils were normal. On a repeat pre-contrast scan the aneurism was slightly hyperdense and, following infusion of contrast, there was a degree of non-homogeneous enhancement.

Intracranial aneurysms associated with fibromuscular dysplasia have the macroscopic appearance of “berry aneurysms”.“ In fact, an association between giant intracranial aneurysm and fibromuscular dysplasia, as observed in this patient, has only been previously reported in one case. This was an 11-year-old girl who died suddenly as the result of a subarachnoid haemorrhage. Postmortem examination showed a ruptured giant fusiform aneurysm of the basilar artery and fibromuscular dysplasia in the muscular arteries of all major organs; however, angiographic studies were not carried out and the histological examination of the craniocervical arteries is not mentioned. Although the aetiology of a giant intra-cranial aneurysm is no different from that of other aneurysms, fibrornuscular dysplasia is not mentioned as a cause. We are therefore of the opinion that when dealing with a giant intracranial aneurysm the possibility of fibromuscular dysplasia of the craniocervical arteries should be considered. [14].

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