Coexistence of Fibromuscular Dysplasia and Cystic Medial Necrosis in a Patient With Marfan’s Syndrome and Bilateral Carotid Artery Dissections

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Background  A primary arteriopathy is suspected in most patients with spontaneous dissections of the carotid artery, although the nature of this arteriopathy usually remains elusive. Angiographic changes of fibromuscular dysplasia (FMD), however, are found in 10% to 20% of patients with carotid dissections.

Case Description  A 26-year-old woman with Marfan’s syndrome presented with bilateral amaurosis fugax after surgical repair of an aortic dissection. Angiography revealed a dissection extending from the ascending aorta into the right internal carotid artery and, separate from the aortic dissection, a dissection of the left internal carotid artery. After surgery, microscopic examination of the right carotid artery revealed a medial dissection but no evidence of an underlying arteriopathy, while the left internal carotid artery displayed the typical features of FMD. Eighteen months later the patient died after resection of a large thoracoabdominal aortic dissecting aneurysm. Microscopic examination of the aorta revealed moderately extensive cystic medial necrosis.

Conclusions  Carotid dissections associated with Marfan’s syndrome may be the result of an extension of an aortic dissection or occur isolated from the aorta, even in the same patient. The occurrence of FMD in a patient with Marfan’s syndrome in conjunction with previous reports of FMD in a variety of connective tissue disorders suggests that FMD, like cystic medial necrosis, may be a nonspecific disease entity.

Key Words  • aneurysm • carotid arteries • dissection • fibromuscular dysplasia • Marfan’s syndrome

Several primary arteriopathies have been related to the development of cervical artery dissections, including those associated with such heritable connective tissue disorders as Ehlers-Danlos syndrome, Marfan’s syndrome, pseudoxanthoma elasticum, polycystic kidney disease, and α1-antitrypsin deficiency. In other cases, pathological examination of the vessel affected by dissection has disclosed the presence of localized cystic medial necrosis. Angiographic changes of fibromuscular dysplasia (FMD) have been reported in 10% to 20% of patients with cervical artery dissections. The pathological substrate of these angiographic changes, however, usually remains unknown. In the present report we describe a patient with Marfan’s syndrome and bilateral carotid artery dissections, in whom both cystic medial necrosis and FMD were found at surgery. The occurrence of FMD in a patient with Marfan’s syndrome in conjunction with previous reports of FMD in a variety of connective tissue disorders suggests that FMD, like cystic medial necrosis, may be a nonspecific disease entity.

Case Report

A 26-year-old woman with Marfan’s syndrome was referred to our institution because of multiple episodes of bilateral amaurosis fugax. Three months previously she had developed severe chest pain while playing volleyball and was found to have a type I aortic dissection. She underwent emergency repair of her aortic valve and replacement of the proximal aorta with a synthetic graft. Two weeks after surgery she developed multiple episodes of spontaneous pneumothorax at 20 years of age. Her father had a Marfanoid habitus and pectus excavatum but no history of cardiovascular disease.

On examination, the patient was 172 cm tall with a weight of 43 kg. A high-arched palate, retrognathism, mild thoracic scoliosis, arachnodactyly, and mild generalized joint laxity were noted. Her surgical incisions had healed well. Neurological examination revealed bilateral carotid bruits. Initially, fundoscopy was normal, but the patient had transient loss of vision in her left eye during examination, and sluggish retinal flow lasting approximately 5 minutes was noted. A computed tomographic (CT) scan of the head was normal. Echocardiography showed the expected postoperative changes as well as mitral valve prolapse. Angiographic studies revealed a dissection beginning just distal to the prosthesis in the ascending aorta extending into the innominate, right common carotid, and internal carotid arteries, with distal extension into the abdominal aorta (Fig 1). Separate from the aortic dissection, an isolated
dissection of the left internal carotid artery was noted (Fig 2). Both vertebral arteries displayed marked tortuosity (Fig 3). A CT scan of the abdomen showed lumbosacral dural ectasia.

The patient underwent a right subclavian to right internal carotid artery bypass with a saphenous vein graft and reimplantation of the right external carotid artery in the vein graft. She recovered well from the surgery, but left-sided amaurosis fugax persisted. Two months later, the left internal carotid artery segment involved with dissection was resected, and an interposition saphenous vein graft was placed. The internal carotid artery was found to be markedly elongated, and multiple small aneurysms were noted on inspection of the artery.

Her amaurosis fugax resolved, but subsequent radiographic studies showed enlargement of the false channel of the thoracic aortic dissection. One year later she underwent resection and replacement of the thoracoabdominal dissecting aneurysm. Six months later she developed increasing lower back pain, and she underwent resection and graft replacement of a false aneurysm at the distal anastomosis of the previous thoracoabdominal aortic graft replacement. She initially did well, but 2 weeks later she developed acute left groin pain and had a respiratory arrest. Emergency abdominal exploration revealed an intra-abdominal hematoma, but the patient died during surgery. An autopsy was not performed.

**Pathological Examinations**

Microscopic examination of the right internal carotid artery revealed dissection involving the outer layers of the arterial media (Fig 4). The false lumen was lined by
flat endothelium internal to a layer of cellular and partly muscularized fibrous tissue (Fig 4). No fibromuscular disarray or degenerative changes were identified in the nondissected portions of the media. The specimen from the left internal carotid artery showed FMD of the medial type with disorganized fibromuscular proliferation involving the arterial media accompanied by loss of elastic fibers (Fig 5). A medial dissection was noted in the distal aspect of the left internal carotid artery. The specimen from the aorta showed changes fulfilling the histopathologic criteria for cystic medial necrosis, i.e., a localized increase in pale ground substance in the media accompanied by loss of smooth muscle (Fig 6). In addition, fragmentation of elastic fibers was prominent (Fig 6).

Discussion

Marfan's Syndrome and Cystic Medial Necrosis

Carotid artery dissection associated with Marfan's syndrome is usually due to extension of an aortic dissection. Uncommonly, isolated dissections of the extracranial carotid and vertebral arteries or even the basilar artery have been reported in patients with Marfan's syndrome. In our patient, the right carotid artery dissection was an extension of the aortic dissection, while on the left the dissection only involved the internal carotid artery. The paucity of reports of isolated extra-aortic dissections in patients with Marfan's syndrome may be related to the arterial distribution of cystic medial necrosis. In patients with Marfan's sy-
drome, cystic medial necrosis is predominantly found in the aortic annulus and proximal aorta, but it is less frequent and less extensive in the more peripheral vasculature. Cystic medial necrosis is the most characteristic arterial lesion of Marfan's syndrome.14 It has also been described in patients with cervical artery dissections who had a family history of Marfan's syndrome or similar arterial lesions and who were believed to have incomplete expression of the syndrome.15,16 However, cystic medial necrosis is not a specific disease; it is found at autopsy in approximately 2% of the general population.17 Moreover, cystic medial necrosis has been associated with Ehlers-Danlos syndrome,18,19 Turner's syndrome,20-22 aortic coarctation,23 and autosomal dominant polycystic kidney disease,24 disorders which predispose to arterial dissection.

Fibromuscular Dysplasia

FMD is a heterogeneous vasculopathy that affects mainly medium-sized muscular arteries.9 The most common site is the renal artery, followed by the internal carotid, iliac, subclavian, and vertebral arteries.9 At autopsy, renal-artery FMD is found in about 1% of the population, but it is less common in the carotid artery.25 The etiology of FMD is unclear, and humoral factors, mechanical trauma, a genetic predisposition, ischemia of the arterial wall, and immunologic factors have all been implicated.9 However, FMD, similar to cystic medial necrosis, may be a nonspecific disease. Angiographic changes of FMD have been reported in patients with Ehlers-Danlos syndrome26,27 and Turner's syndrome,28 whereas histological evidence of FMD has been found in patients with mutations in the collagen type III gene,29 aortic coarctation,30 Turner's syndrome,31 and α1-antitrypsin deficiency.32 In addition, FMD has been described in patients with mesenchymal dysplasias of uncertain type.33-35 Thus, several connective tissue disorders predisposing the artery to dissection have been associated with cystic medial necrosis and/or FMD, although the coexistence of both arterial disorders in the same patient has, to our knowledge, not been reported previously. The presence of FMD in our patient with Marfan syndrome lends support to the notion that FMD is a nonspecific disease entity that may be associated with a variety of generalized connective tissue disorders.

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