Ruptured femoropopliteal artery aneurysms in von Recklinghausen neurofibromatosis

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A 38-year-old woman with neurofibromatosis type 1 was referred for massive swelling of the left thigh, pain, and anemia. Angiography demonstrated three saccular aneurysms of the femoropopliteal artery. The largest measured 3 cm in diameter. Resection of the aneurysms and femoropopliteal interposition grafting using reversed saphenous vein was performed through a medial surgical approach. Arterial involvement in neurofibromatosis is a well known but infrequent occurrence. Stenotic lesions predominate. Aneurysmal defects are less common, and rupture of peripheral arteries is exceptional. Neurofibromatous invasion and dysplasia of the tunica media of the femoropopliteal vessel were confirmed by means of pathologic study. We think this is the second reported case of a femoropopliteal artery aneurysm and rupture associated with neurofibromatosis. (J Vasc Surg 2007;46:808-11.)

Von Recklinghausen neurofibromatosis, a phacomatosis inherited as an autosomal dominant trait of variable expressivity, occurs with an incidence of 1 per 3000.[1] The most common member of the group is neurofibromatosis type I, which varies in severity but which can affect all physiologic systems. Arterial involvement in von Recklinghausen neurofibromatosis is a well-known but infrequent occurrence. Stenotic lesions predominate, with the renal arteries being the site of predilection. Aneurysmal defects are less common.[2] We present an unusual case of multiple aneurysms of the left femoral and proximal popliteal artery, with rupture caused by neurofibromatosis.

CASE REPORT

A 38-year-old woman with a positive family and personal history of neurofibromatosis type I came to the emergency department with a 2-day history of pain and swelling of her left thigh. She denied any history of previous trauma, fractures, intravenous drug abuse, or recent infections of the area. Her medical history was significant for neurofibromatosis type I and for scoliosis. She had no history of diabetes mellitus, hypertension, or tobacco use. She was not taking any medications.

Physical examination revealed an alert individual with a normal blood pressure of 110/60 mm Hg and heart rate of 80 beats/min. There was massive swelling of the left thigh, and multiple café au lait skin macules and subcutaneous neurofibromata were present. There were no ulcers or signs of embolism. The patient's femoral, popliteal, dorsalis pedis, and posterior tibial pulses were all equally palpable and symmetric.

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Competition of interest: none.

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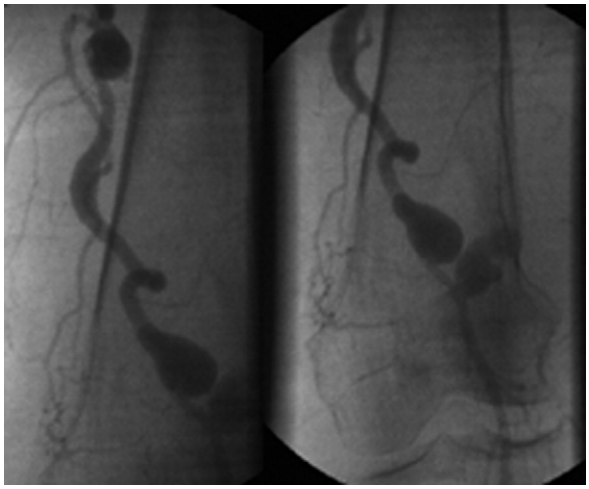

Fig 1. Angiography shows three femoropopliteal saccular aneurysms in a patient with von Recklinghausen neurofibromatosis.

Laboratory tests showed a white blood cell count of 12,800/mL, and the hemoglobin level was decreased to 6.7 g/dL. Angiography demonstrated three saccular aneurysms of the left femoral and proximal popliteal artery. The largest measured 3 cm in diameter (Fig 1). During the angiogram, her blood pressure dropped to 80/40 mm Hg, and her heart rate increased to 130 beats/min. She was resuscitated with intravenous fluids and taken immediately to the operating room.

We encountered a very large hematoma, brittle vessels, hypertrophied surrounding tissue, and excessive bleeding caused by neurofibromatosis invasion. The three aneurysms were resected, and there was no back-bleeding from the distal popliteal artery (Fig 2, A).

Femoropopliteal interposition grafting using reversed autogenous great contralateral saphenous vein was performed through an extended medial surgical approach. The vessel wall was friable, necessitating the use of fine sutures (8-0 polypropylene). Meticulous technique and gentle manipulation of the tissues resulted in an intraoperative blood loss of 2000 mL.

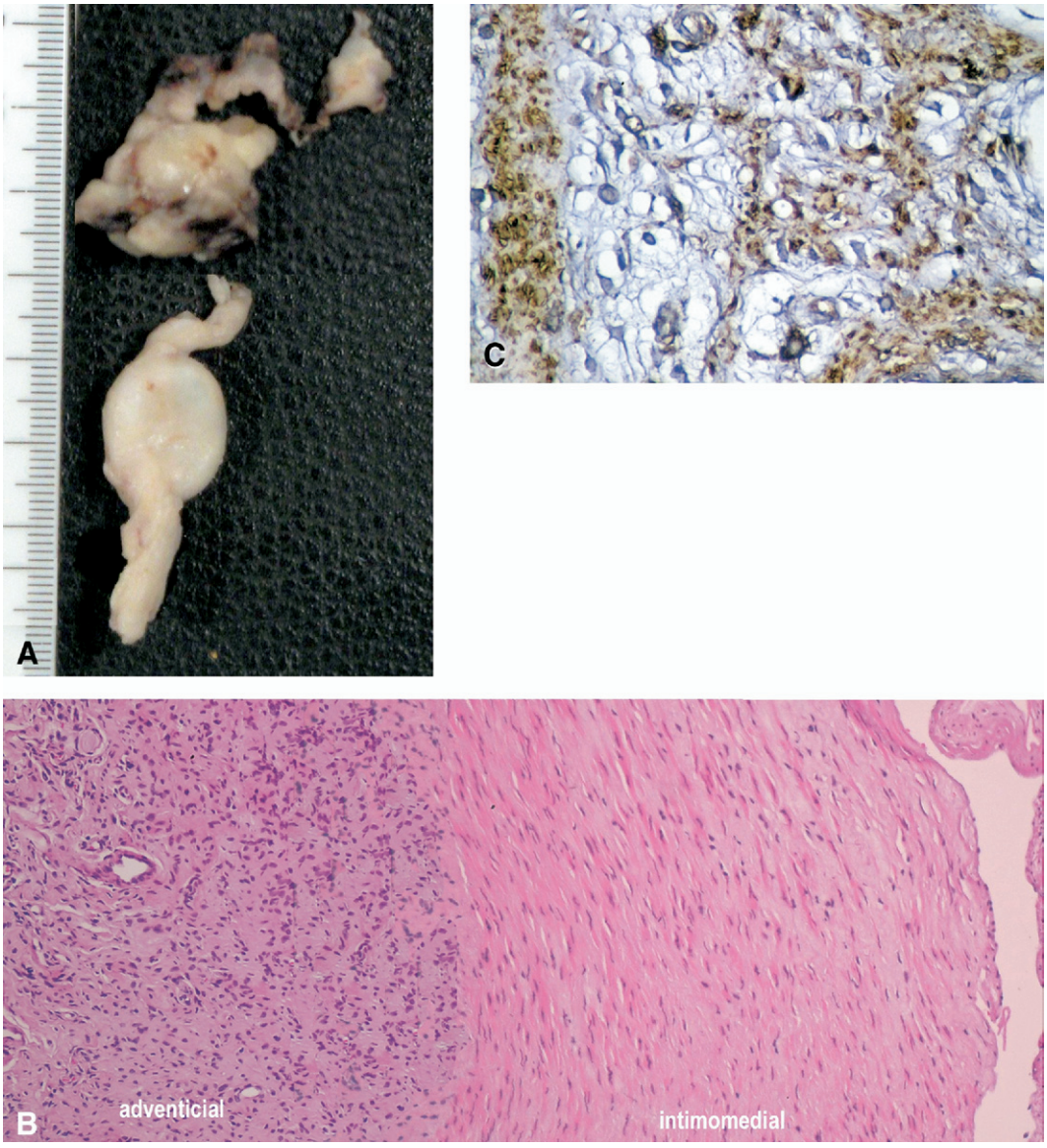

Fig 2. A, Popliteal aneurysm and invasion neurofibromatosis tissue. **B,** Cross-section of popliteal aneurysm wall (hematoxylin-eosin, original magnification ×100). Zonal vascular smooth muscle cell proliferation, mesodermal dysplasia *(intimomedial)*, proliferating, wavy spindle cells are invading adventitia, by invasion neurofibromatosis tissue *(adventitial)*. **C,** With S100 immunoperoxidase *(reddish brown)* staining of the aneurysm wall (original magnification ×100), proliferating cells stain positive for S100 protein, indicating a neural origin.

The patient made a full recovery, with no major adverse events, and was discharged 10 days postoperatively. At a 3-month review with ultrasound imaging of flow characteristics, the graft remained patent and there was no evidence of stenosis.

DISCUSSION

Neurofibromatosis was first described by von Recklinghausen in 1882.[3] Neurofibromatosis type I is an autosomal dominantly; the gene is located in the pericentric region of chromosome 17.[4] Heterogeneity is the clinical hallmark of neurofibromatosis, and at least seven varieties of the disease have been described, of which type 1 is the most common.[5]

The disease affects tissues of neural crest and mesodermal origin; therefore, the clinical features are diverse.[1] Most patients manifest the cutaneous stigmata of café-au-lait spots, pedunculated skin lesions (fibroma molluscum), and neurofibromata, which are clues to the diagnosis. Other features include Lisch nodules (hamartoma of the iris), kyphoscoliosis, dysplasia of the sphenoid, bowing and pseudarthrosis of the tibia, and an increased incidence of neoplasia, including pheochromocytoma, acoustic neuroma, meningioma, neurofibrosarcoma, astrocytoma, glioblastoma, and malignant schwannoma.[6] Our patient presented cutaneous stigmata classic, fibroma mollus-

cum, kyphoscoliosis, and long family history of neurofibromatosis.

Arterial vasculopathy in a patient with von Recklinghausen disease was first described in 1945 by Reubi. He described three forms of vascular lesions, depending on the size of the vessel: pure intimal, intimal-aneurysmal, and adventitial-nodular.[7] He noted intimal proliferation with breakdown of muscle and elastic layers and adventitial nodular thickening. Feyrter[8] subsequently described an epithelioid form, with involvement of the entire vessel wall by neural cells.

In 1974, Greene et al[9] suggested that there were two primary types of vascular lesions associated with neurofibromatosis. The first type affected large vessels with perivascular neurofibromas or ganglioneuromas associated with degenerative changes in the adjacent vessel wall. The second type was present in small vessels and consisted of nodular aggregates of smooth muscle cells that they believed represented mesodermal dysplasia.[9]

The prognosis for neurofibromatosis, which is unpredictable for a given subject, depends essentially on the existence of cerebral tumors, which are responsible for death in 72% of cases.[1]

Vasculopathy in neurofibromatosis type I is well described in the literature but is rarely encountered clinically. The true incidence of this entity is unknown because many lesions may be asymptomatic. Although the renal artery is most frequently involved, any vessel may be affected. The lesions may be occlusive or cause aneurysmal degeneration of the blood vessel; hence, the clinical presentation can be indolent (hypertension) or dramatic (arterial rupture).[6]

Vasculopathies of neurofibromatosis type I resemble most closely those of the type IV Ehlers-Danlos syndrome. This syndrome is commonly present as multiple arterial aneurysms complicated by dissection or perforation.[10] The differentiation between these two syndromes requires a comparative evaluation of clinical, angiographic, histologic, and biochemical (for genetic markers) findings.[11]

Two distinct pathogenetic mechanisms have been identified: smooth muscle (mesodermal) dysplasia and direct vascular invasion by neurofibromatous tissue. Lesions manifest as stenosis, dissection, aneurysm formation, or rupture of the affected vessel.[6] Fibrodysplastic changes in the media with segmental fragmentation of the vessel wall caused by atrophy of the muscularis and formation of saccular aneurysms have been described.[2]

Although these two patterns of lesions were described affecting arteries of diverse diameter, we verify that mesodermal dysplasia and neurofibromatous invasion can coexist in the same artery, as confirmed in the histology of this patient (Fig 2, *B* and *C*). Mesodermal dysplasia causes a structural weakness of the tunica media that forces the use of fine polypropylene (8-0) for arterial reconstruction, the infiltration of neurofibromatous tissue with perivascular neurofibromas or ganglioneuromas and brittle vessels makes vascular dissection is extremely difficult and causes bleeding.

Cases of multiple aneurysms in the same patient have been reported.[2,12] Perhaps the silent nature of most lesions and the inaccessibility of involved vessels to clinical examination have resulted in an under-appreciation of its occurrence. An autopsy series of neurofibromatosis type I patients who died from other causes found vascular abnormalities in eight (44%) of 18 cases.[13] Screening of all patients with neurofibromatosis type I for arterial disease should be performed. Noninvasive imaging modalities such as duplex ultrasound scanning, magnetic resonance angiography, and computed tomography scanning are useful means of visualizing vessels.[6]

Reports of involvement of almost every major artery can be found in the literature, and no vessels are spared, including veins.[14] Aneurysms have been reported on the supraaortic trunks,[15,16] the descending thoracic aorta,[16] the renal arteries or their branches,[17,18] and the intracranial arteries.[19] Aneurysms of the visceral arteries are exceptional; the major concern is the ruptured splenic artery aneurysm.[17] The first patient who underwent surgical repair because of ruptured popliteal aneurysm resulting from neurofibromatosis was described by Bueno in 2005.[20]

Operative strategies may also differ in patients with neurofibromatosis. Options include ligation, ligation and resection, or ligation and resection with a bypass graft.[12] Other options could include endovascular stent graft exclusion, endovascular coil embolization, and bypass around the aneurysms (superficial femoral artery to below knee popliteal), or just ligation and bypass.

In a report of a ruptured brachial artery aneurysm, diffuse infiltration of the vessel wall by neurofibromatous tissue precluded a bypass grafting procedure. The authors concluded that such aneurysms should be ligated or resected without a bypass graft.[21] However, some arterial territories, such as at the popliteal level, seem not to tolerate the ligation.

CONCLUSION

Arterial manifestations of neurofibromatosis type I are unusual. Aneurysmal arterial degeneration is more unusual. Rupture of aneurysms in patients involved with neurofibromatosis is rare. Our experience with this case confirms the poor quality of the vessel wall, necessitating the use of fine sutures and meticulous technique for vascular reconstruction.

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